# Electrochemical Reduction of a Racemic Allyl β-Keto Ester Catalyzed by Nickel Complexes: Asymmetric Induction

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The nickel-catalyzed electroreductive cleavage of the allyl group of allyl 2-methyl-1-tetralone-2-carboxylate and allyl transfer to the carbonyl group has been examined. The control of the reaction conditions allowed us to orientate the selectivity. The use of chiral ligands led to modest asymmetric induction in the formation of 2-methyl-1-tetralone.

## Introduction

The deprotection of allyl esters and carbonates to form the parent alcohols and acids by a Pd-catalyzed C−O bond cleavage in the presence of a reducing agent is a process of great synthetic utility;[1] it is also used in the field of peptide and nucleoside chemistry.[2] From racemic allyl-β-keto esters and prochiral allyl enol carbonates, this Pd-catalyzed allyl cleavage carried out in the presence of an excess of homochiral amino alcohols led to the corresponding optically active ketones through a one-pot deallylation/decarboxylation/asymmetric protonation.[3] For example, the reaction of allyl 2-methyl-1-tetralone-2-carboxylate (**1**) in the presence of (−)-ephedrine afforded mainly (*R*)-2-methyl-1-tetralone (**2**).

On the other hand, the electrochemistry associated with the use of Ni$^{II}$ [4] or Pd$^{II}$ [5] catalysts has been reported as an efficient and mild method for the deprotection of allyl ethers and esters. Interestingly, the intramolecular transfer of the allyl unit to an aldehyde group leading to a homoallylic alcohol has been achieved using *o*-substituted allyl aryl ethers.[6]

We describe here the electrochemical reactivity of the allyl β-keto ester **1** in the presence of catalytic amounts of Ni$^{II}$ complexes bearing ligands which are achiral such as 2,2′-bipyridine (bipy), or homochiral such as (−)-ephedrine (Eph) and (+)-oxazoline (pyO)[7] [Equation (1) and Figure 1].

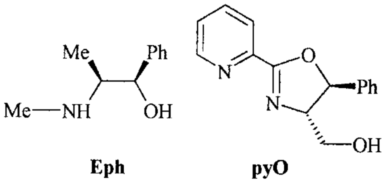

Figure 1. Chiral ligand structures

## Results and Discussion

### Electrochemical Reduction of 1 in the Presence of Ni-bipy Systems

The electrochemical reduction of **1** was examined with two different Ni$^{II}$ complexes: $[Ni(bipy)_3]\cdot 2BF_4$ and $[NiBr_2(bipy)]$. Both the cationic and molecular complex were added in a 10 mol % ratio with respect to **1**. Electrolyses were carried out at room temperature in DMF, under constant current-density conditions, in a single-compartment cell fitted with sacrificial Zn or Mg rod anodes and a stainless steel cathode. After electrolysis, the reaction mixture was initially treated with methyl iodide and potassium carbonate. The results are summarized in Equation (1) and Table 1. No reaction occurred in the absence of current and the reaction was inefficient in the absence of the Ni complex. Without Ni catalysis, the electrolysis with a Zn anode induced a low conversion of **1** leading to oligomerization products and small amounts of **2**. In contrast, we have been able to induce full consumption of **1** under both Ni catalysis and electrolysis, the main products being **2**, **3** and **4**.

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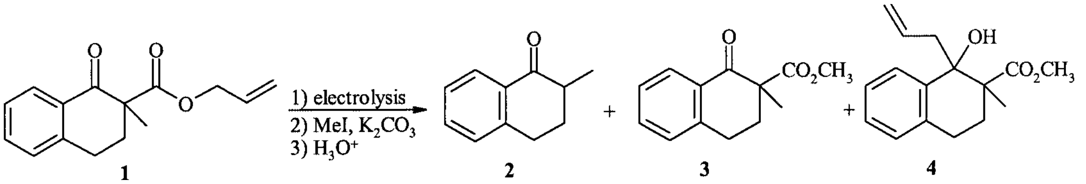

(1)

Table 1. Electroreduction of **1** in the presence of Ni-bipy catalytic systems

| Run | Catalyst | Anode | F/mol | Yield (%) **2** + **3** + **4** | **2**:**3**:**4** |
|---|---|---|---|---|---|
| 1 | $[NiBr_2(bipy)]$ | Mg | 2.4 | 98 | 63:6:31 |
| 2 | $[Ni(bipy)_3]\cdot 2BF_4$ | Mg | 2.1 | 81 | 96:0:4 |
| 3 | $[Ni(Br_2bipy)]$ | Zn | 2.4 | 98 | 27:18:55 |
| 4 | $[Ni(bipy)_3]\cdot 2BF_4$ | Zn | 2.1 | 83 | 35:7:58 |

The consumption of **1** was followed by GC; complete cleavage of the allyl ester group was observed after the passage of 2.1 to 2.4 F/mol. The subsequent loss of $CO_2$ was not complete, ranging from 63 to 96% with a Mg anode and from 27 to 35% with a Zn anode. The reaction selectivity was very dependent on the reaction conditions. In the presence of a Mg anode, the formation of ketone **2** occurred selectively with both $Ni^{II}$ complexes (runs 1 and 2, Table 1). With $[Ni(bipy)_3]\cdot 2BF_4$, the selectivity towards **2** reached 96%. In the case of $[NiBr_2(bipy)]$ as the catalyst, both deallylation/decarboxylation, leading to **2**, and allyl transfer, leading to **4**, occurred (**2**:**4** = 63:31). On going from a Mg to a Zn anode (presence of $Mg^{2+}$ or $Zn^{2+}$ ions in solution) we observed a lower tendency to decarboxylation and an increase in the allyl transfer process.

The selectivity for the carbonyl allylation was enhanced to between 55 and 58% in the presence of a Zn anode (entries 3, 4); such an increase of the efficiency of the allyl transfer using a Zn rather than a Mg anode has already been noted in the case of allyl transfer from allyl ethers to ketones.[6] Except in run 2, **4** was obtained as a single diastereomer; NMR studies have not yet allowed us to determine the relative configurations of the quaternary carbons.

### Preparation of Chiral $Ni^{II}$ Complexes

As **2** has a stereogenic center of known configuration,[8] we studied the enantioselectivity in the electrochemical reaction of racemic **1** using chiral catalysts. Cationic chiral $Ni^{II}$ complexes were prepared from nickel tetrafluoroborate and Eph or pyO in absolute ethanol following the procedure reported for the preparation of $[Ni(bipy)_3]\cdot 2BF_4$.[9] $[Ni(pyO)_3]\cdot 2BF_4$ was isolated and characterized by elemental analysis;[10] as well as for the analogous $Ni(bipy)_3^{2+}$ structure, an octahedral arrangement of the ligands is assumed on the basis of its magnetic susceptibility: the experimental value of 3.25 BM is close to the expected value for an octahedral geometry ($\mu$ = 3 BM).[11] The cationic complex obtained when using Eph as ligand is a poorly stable paramagnetic grey powder; the stoichiometry of the reaction led us to propose $[Ni(Eph)_3]\cdot 2BF_4$ as its formula. The molecular complexes $[NiBr_2(Eph)_n]$ and $[NiBr_2(pyO)_n]$ were prepared in situ by the addition of three equiv. of Eph or pyO to $[NiBr_2(dme)]$ in DMF (dme = dimethoxyethane).

### Chiral Induction in the Electrosynthesis of 2

Asymmetric induction by chiral metal complexes in electrochemical reactions has been scarcely studied.[12] In the field of electroreduction, no efficient asymmetric reactions have, to the best of our knowledge, been reported. The reaction of **1** with chiral $Ni^{II}$ complexes led to a mixture of compounds **2**−**4**, together with some decarboxylated **4**. Ketone **2** was the major compound. The results of the electroreduction of **1** to **2** in the presence of 10 mol % of the chiral $Ni^{II}$ complexes are presented in Table 2. Here again, **2** was obtained in higher yields with a Mg anode (runs 5−8: 50−66%) than with a Zn one (runs 9, 10: 31−44%). The best *ee* (17%) was reached using $[NiBr_2(pyO)_n]$ and a Mg anode (run 8), while no chiral induction was found using the corresponding cationic complex (runs 7 and 10). With Eph as the ligand, 13% *ee* was attained with the molecular complex and the Mg anode (run 6). With a Zn anode and $[Ni(Eph)_3]\cdot 2BF_4$, the *ee* of **2** was reduced to 8% (run 9). In all cases, the major enantiomer had the (*R*)-configuration as already observed under Pd-catalysis in the presence of Eph. These asymmetric inductions, although very moderate, constitute an interesting feature in the field of electrosynthesis catalyzed by chiral organometallic species.

Table 2. Electrosynthesis of **2** with chiral $Ni^{II}$ complexes

| Run | Catalyst | Anode | F/mol | Yield (%) | *ee* (%) |
|---|---|---|---|---|---|
| 5 | $[Ni(Eph)_3]\cdot 2BF_4$ | Mg | 2.5 | 50 | 2 |
| 6 | $[NiBr_2(Eph)_n]$ | Mg | 6.2 | 66 | 13 |
| 7 | $[Ni(pyO)_3]\cdot 2BF_4$ | Mg | 2.4 | 62 | 0 |
| 8 | $[NiBr_2(pyO)_n]$ | Mg | 2.8 | 56 | 17 |
| 9 | $[Ni(Eph)_3]\cdot 2BF_4$ | Zn | 4.4 | 31 | 8 |
| 10 | $[Ni(pyO)_3]\cdot 2BF_4$ | Zn | 3.7 | 44 | 0 |

From a mechanistic point of view, the reaction proceeds through the electrochemical generation of a $Ni^0$ complex, which adds oxidatively to the C−O bond of the allyl ester group of **1** to form a π-allyl $Ni^{II}$ complex, as in Pd chemistry.[13] The formation of π-allyl $Ni^{II}$ complexes from $Ni^0$ and allyl derivatives has been reported in chemical,[14] as well as in electrochemical reactions.[15,16] The formation of **2** and **3** can be explained by deallylation with or without decarboxylation, and **4** is formed from an intramolecular allyl transfer reaction to the carbonyl group, as in recently described reactions.[16]

In the overall process, the anode (Mg or Zn) provides $Mg^{2+}$ or $Zn^{2+}$ ions in solution.[17] At the cathode, the $Ni^{II}$ species, used in catalytic amounts, are reduced and can be recycled. The $Mg^{2+}$ or $Zn^{2+}$ ions formed during the reaction are responsible for the trapping and stabilisation of the intermediate carboxylates. This electrochemical reaction constitutes an example of paired electrosynthesis, in which both the anodic and cathodic processes are useful for the chemical reaction.

In conclusion, the electroreduction of allyl-β-keto esters such as **1** can be efficiently carried out under mild conditions using a Mg or Zn anode and catalytic quantities of $Ni^{II}$ complexes. The selectivity can be oriented by the control of the reaction conditions. Some modest asymmetric induction in the deallylation/decarboxylation/protonation process could be observed when using readily available homochiral $Ni^{II}$ complexes.

## Experimental Section

**General Electrolysis Procedure:** The electrochemical single-compartment cell is a cylindrical glass vessel (capacity 20 mL) equipped with a magnesium or zinc rod anode (immersed to 3 cm) and a stainless steel grid cathode. The intentiostatic electrolyses were carried out by using a stabilized constant current supply, Sodilec EDL 36.07. In the cell were introduced freshly distilled DMF (20 mL), $n$Bu$_4$NBF$_4$ (0.2 mmol), the Ni catalyst (0.1 mmol) and **1** (1 mmol). The solution was stirred and electrolyzed at a constant current of 60 mA (current density of 0.2 A/dm$^2$ and 5−15 V between electrodes), until total consumption of the starting material (checked by GLC analysis of aliquots), unless electrode passivation occurred. The crude mixture was then esterified with potassium carbonate (1.2 equiv.) and methyl iodide (2 equiv.). The solution was hydrolyzed with 0.1 M HCl saturated with NaCl, up to pH 1−2, and extracted with $Et_2O$. The organic layers, dried over $MgSO_4$, were filtered off and the solvents evaporated. The products were purified by $SiO_2$ column chromatography eluting with pentane/diethyl ether (90:10). The enantiomeric excess was determined by HPLC with a Chiracel OD-type column as already reported.[18]

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[10] Tri[(4*S*,5*S*)-(+)-pyridinooxazoline]nickel(II) tetrafluoroborate. Prepared according to ref.[9] Yield: 84%. $C_{45}H_{42}B_2F_8N_6NiO_6$ (995.2): calcd. C 54.31, H 4.25, N 8.44; found C 53.18, H 4.28, N 8.46. Magnetic susceptibility [$\mu_{eff.} = 2.828\ (\chi T)^{1/2}$]: experimental: $\chi T = 1.32$ and $\mu_{eff.} = 3.25$ MB.

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