

Stereoselective coupling of optically active 3-*trans*-cinnamoyl-2-oxazolidinones with acid anhydrides by electroreduction

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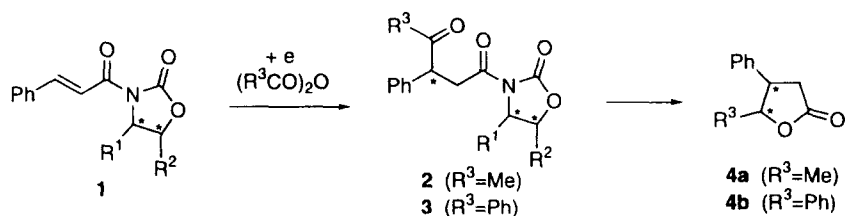
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Abstract

The electroreduction of chiral 3-*trans*-cinnamoyl-2-oxazolidinones with acid anhydrides gave β -acylated products stereoselectively. The products were transformed to optically active *cis*- β , γ -disubstituted- γ -lactones. © 1999 Elsevier Science Ltd. All rights reserved.

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The electroreductive β -acylation of α,β -unsaturated esters with acid anhydrides is a useful method for the synthesis of γ -ketoesters.¹ This fact prompted us to investigate the enantioselective β -acylation of α,β -unsaturated acid derivatives for the asymmetric synthesis of γ -ketoacid derivatives employing a chiral auxiliary method. On the other hand, we have recently reported that the stereoselective hydrocoupling of optically active 3-*trans*-cinnamoyl-2-oxazolidinones **1** was conveniently achieved by constant current electrolysis using an undivided cell.² Herein, we report that the stereoselective coupling of **1** with acid anhydrides is effected by the electroreduction under the similar conditions (Scheme 1).³ We also disclose that the β -acylated products **2** and **3** can easily be transformed into the corresponding β,γ -disubstituted- γ -lactones **4**. Chiral β,γ -disubstituted- γ -lactones are found in many natural products⁴ and, in addition, have been utilized as chiral building blocks for the synthesis of complex natural compounds.⁵ The present method provides a new route for the preparation of chiral β,γ -disubstituted- γ -lactones.⁶



Scheme 1.

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General procedure for the electroreduction is as follows. A solution of **1** (1 mmol), acetic anhydride (0.95 ml, 10 mmol), and Et₄NOTs (1.5 g, 5 mmol) in dry acetonitrile (16.5 mL) was put into a 40 mL beaker (3 cm diameter, 6 cm height) equipped with a lead cathode (5×5 cm²) and a platinum anode (2×2 cm²). Electricity was passed at a constant current of 0.1 A at room temperature until almost all of **1** was consumed (300–400 C). The mixture was poured into saturated NaHCO₃ aq. (50 mL), stirred for 1 h, and then extracted with CH₂Cl₂. The β-acetylated products **2a–f** were isolated as diastereomeric mixtures by column chromatography on silica gel. Major diastereomers of **2a–f** could be separated by recrystallization from hexane–ethyl acetate. Similarly, the β-benzoylated products **3a–e** were obtained using benzoic anhydride (1.13 g, 5 mmol) in place of acetic anhydride. Each isomer of **3a–e** could be separated by column chromatography on silica gel.

Table 1 summarizes the results of the electroreductive coupling of several optically active 3-*trans*-cinnamoyl-2-oxazolidinones **1a–f** with acetic anhydride or benzoic anhydride. This method afforded β-acetylated products **2a–f** (runs 1–7) and β-benzoylated products **3a–e** (runs 8–13) in moderate yields

Table 1
Electroreductive coupling of chiral 3-*trans*-cinnamoyl-2-oxazolidinones with acid anhydrides

Run	1	R ¹	R ²	R ³	Product	Yield (%) ^a	R:S ^b
1	1a	<i>i</i> -Pr (<i>S</i>)	H	Me	2a	60	80:20
2 ^c	1a	<i>i</i> -Pr (<i>S</i>)	H	Me	2a	55	83:17
3	1b	<i>i</i> -Bu (<i>S</i>)	H	Me	2b	58	75:25
4	1c	Bn (<i>S</i>)	H	Me	2c	62	78:22
5	1d	Me (<i>S</i>)	Ph (<i>R</i>)	Me	2d	67	75:25
6	1e	Ph (<i>R</i>)	H	Me	2e	66	27:73
7	1f	(<i>R</i>) Bornyl	(<i>S</i>)	Me	2f	54	25:75
8	1a	<i>i</i> -Pr (<i>S</i>)	H	Ph	3a	57	70:30
9 ^c	1a	<i>i</i> -Pr (<i>S</i>)	H	Ph	3a	52	73:37
10	1b	<i>i</i> -Bu (<i>S</i>)	H	Ph	3b	55	67:33
11	1c	Bn (<i>S</i>)	H	Ph	3c	60	70:30
12	1d	Me (<i>S</i>)	Ph (<i>R</i>)	Ph	3d	62	67:33
13	1e	Ph (<i>R</i>)	H	Ph	3e	60	33:67

^aIsolated Yields.

^bDetermined by ¹H-NMR spectra for **2a–f** and by separation of diastereomers for **3a–e**.

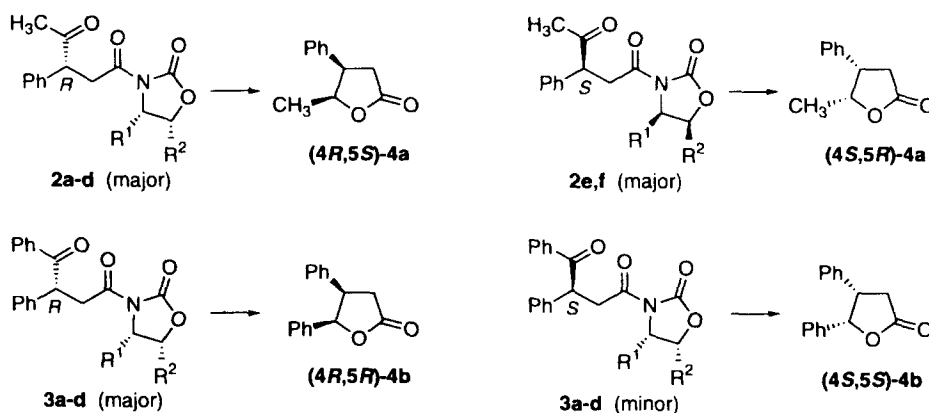
Melting points and specific rotations ([α]_D²⁵ in CHCl₃) of the products **2** were as follows.

R-2a: 105–107 °C; +343 (*c* = 1.09). **R-2b**: 123–125 °C; +316 (*c* = 1.00). **R-2c**: 205–207 °C; +296 (*c* = 1.01). **R-2d**: 144–146 °C; +213 (*c* = 0.53). **S-2e**: 136–138 °C; -341 (*c* = 1.04). **S-2f**: 194–196 °C; -263 (*c* = 1.01). **R-3a**: paste; +221 (*c* = 0.91). **S-3a**: 125–127 °C; -125 (*c* = 1.08). **R-3b**: 132–134 °C; +246 (*c* = 1.00). **S-3b**: 165–167 °C; -161 (*c* = 0.55). **R-3c**: 193–195 °C; +229 (*c* = 1.03). **S-3c**: 216–218 °C; -155 (*c* = 0.46). **R-3d**: 175–177 °C; +188 (*c* = 1.13). **S-3d**: 210–211 °C; -212 (*c* = 0.54). **R-3e**: 174–175 °C; +67 (*c* = 0.31). **S-3e**: 161–162 °C; -275 (*c* = 1.00).

^cElectroreduction was carried out in THF containing Bu₄NClO₄.

(54–67%) and diastereoselectivities (34–60% de) using acetonitrile as a solvent.[†] The major by-products were simply reduced 3-(3-phenylpropanoyl)-2-oxazolidinones (20–30% yields) and the hydrodimers² were obtained in trace amounts. The selectivities were slightly increased using THF as a solvent (runs 2 and 9), though it was difficult to separate the products from the by-products which were mainly mono- and di-*O*-acylated 1,4-butanediols derived from THF.

The obtained **2** were transformed to the corresponding *cis*- β,γ -disubstituted- γ -lactones **4**[‡] in 85–90% *cis*-selectivities and 50–60% yields by the treatment with Bu₄NBH₄ in CH₂Cl₂ at room temperature for 24–48 h (Scheme 2). The major isomers of the β -benzoylated products **3a–d** and the minor isomer of **3e** were converted to the known *cis*-(4*R*,5*R*)-4,5-diphenyl- γ -butyrolactone ((4*R*,5*R*)-**4b**).^{6b} Therefore, the absolute configurations were determined to be *R* for the major (minor) isomers of **3a–d** (**3e**) and to be *S* for the minor (major) isomers of **3a–d** (**3e**). It is likely that the major isomers of **2a–d** are also *R*-forms and those of **2e** and **2f** are *S*-forms.



Scheme 2.

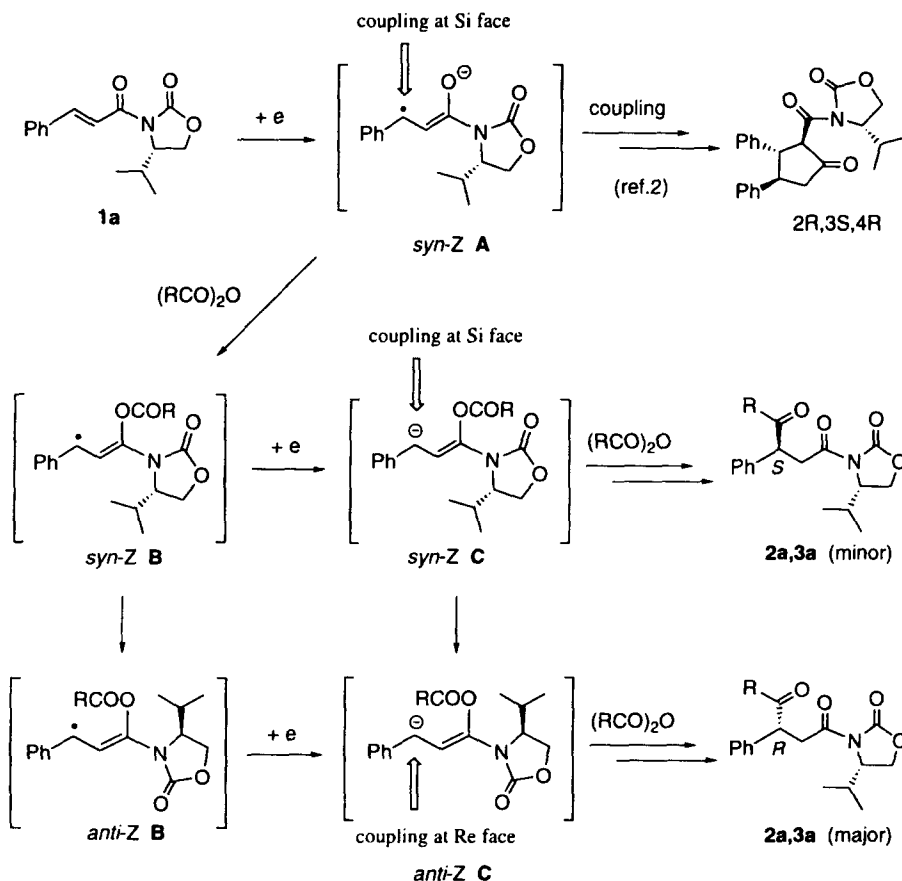
We have proposed the hypothesis of the reaction mechanism for the electroreductive hydrocoupling of **1**.² Namely, *syn*-*Z* type anion radical generated from **1a** by a single electron transfer couples each other at the less hindered *Si* face to give the cyclized hydrodimer stereoselectively. On the contrary, the results described above suggest that the reductive β -acylation of **1a** takes place at the *Re* face favorably. In order to explain the reversal of the preferential reaction face, the reaction mechanism as shown in Scheme 3 can be speculated. In the presence of excess amounts of an acid anhydride, *O*-acylation of the anion radical **A** generated from **1a** is much faster than the homo-coupling of **A**. The resultant *O*-acylated radical **B** is subsequently reduced to the anion **C**. In the stage of **B** or **C**, the *syn*-*Z* form is isomerized to the *anti*-*Z* form. Consequently, *C*-acylation of the *anti*-*Z* type anion **C** occurs at the less hindered *Re* face to give the *R*-isomer of **2a** (**3a**) selectively.

Acknowledgements

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[†] The β -acetylation of **1c** afforded **2c** in a better yield and a similar diastereomeric excess (run 4), compared with the result obtained by the electroreduction with Mg electrodes.³

[‡] (4*R*,5*S*)-**4a**: [α]_D²⁵ +142 (*c*=0.90, CHCl₃). (4*S*,5*R*)-**4a**: [α]_D²⁵ -141 (*c*=0.80, CHCl₃). (4*R*,5*R*)-**4b**: mp 91–92°C, lit.^{6b} 90–92°C; [α]_D²⁵ +58 (*c*=1.0, CHCl₃), lit.^{6b} [α]_D²⁵ +48 (*c*=1, CHCl₃). (4*S*,5*S*)-**4b**: mp 90–91°C; [α]_D²⁵ -56 (*c*=0.60, CHCl₃).



Scheme 3. Proposed mechanism for the electroreductive coupling

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