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

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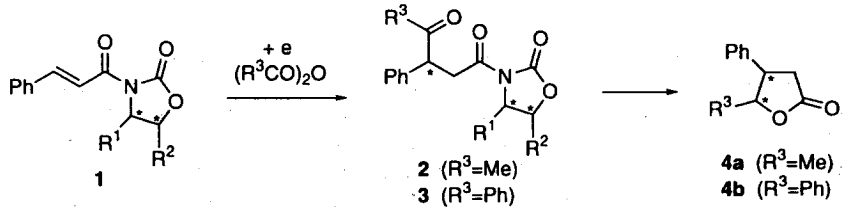
Abstract

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.

Keywords: acylation; coupling reaction; electrochemistry; lactones; oxazolidinones; reduction.

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 products[4] 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 Et_4NOTs (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 cm^2) and a platinum anode (2×2 cm^2). 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 $NaHCO_3$ aq. (50 mL), stirred for 1 h, and then extracted with CH_2Cl_2. 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

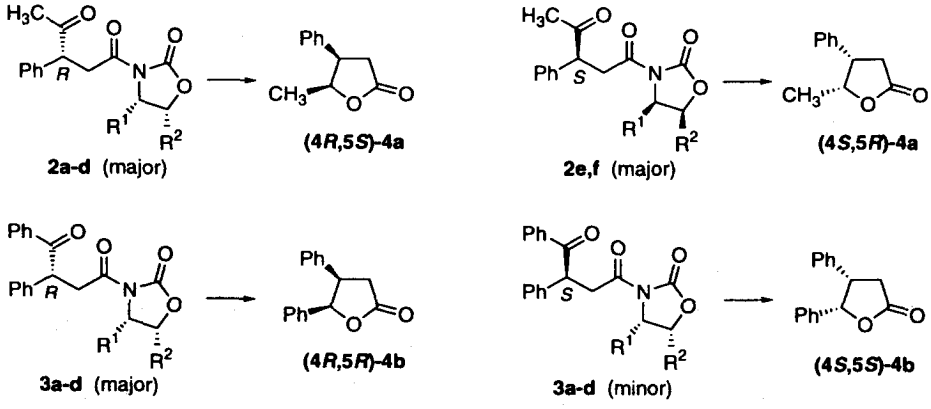
Table 1
Electroreductive coupling of chiral 3-*trans*-cinnamoyl-2-oxazolidinones with acid anhydrides

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

[a]Isolated Yields.
[b]Determined by ^{1}H-NMR spectra for **2a-f** and by separation of diastereomers for **3a-e**. Melting points and specific rotations ($[\alpha]^{25}_D$ in $CHCl_3$) 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).
[c]Electroreduction was carried out in THF containing Bu_4NClO_4.

(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 hydrodimers[2] 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 Bu_4NBH_4 in CH_2Cl_2 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.

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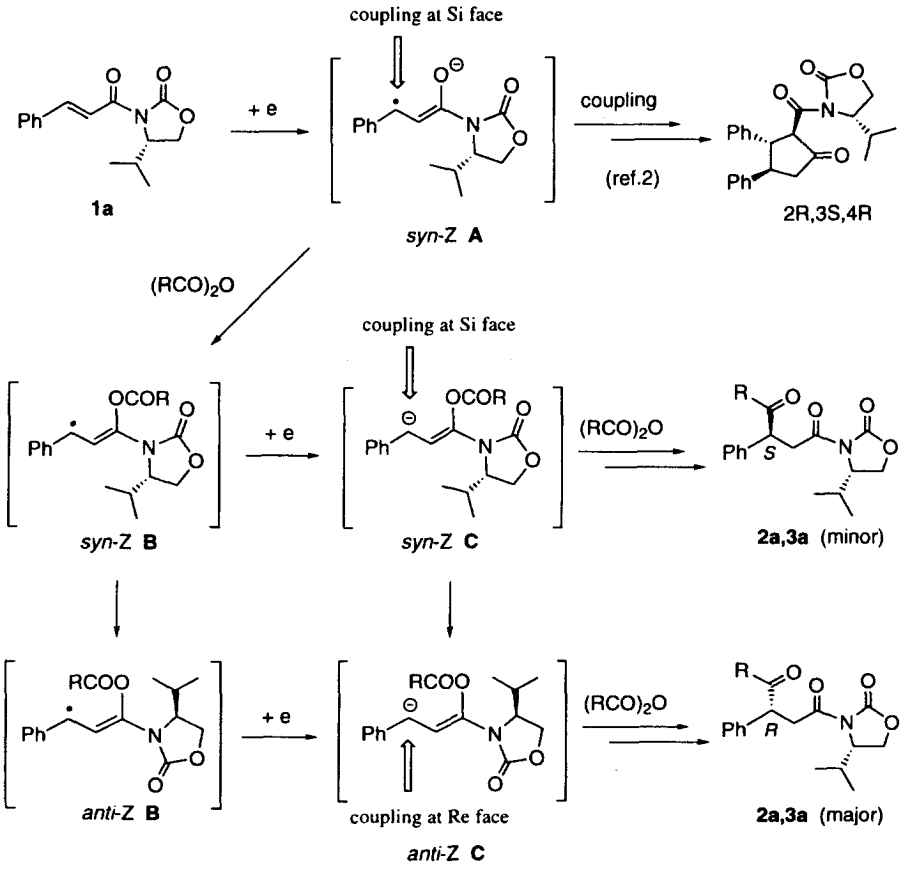
† The β-acetylation of **1c** afforded **2c** in a better yield and a similar diastereomeric excess (run 4), compared with the result obtained by the electroreduction with Mg electrodes.[3]

‡ (4*R*,5*S*)-**4a**: $[\alpha]_D^{25}$ +142 (*c*=0.90, $CHCl_3$). (4*S*5*R*)-**4a**: $[\alpha]_D^{25}$ −141 (*c*=0.80, $CHCl_3$). (4*R*,5*R*)-**4b**: mp 91–92°C, lit.[6b] 90–92°C; $[\alpha]_D^{25}$+58 (*c*=1.0, $CHCl_3$), lit.[6b] $[\alpha]_D^{25}$ +48 (*c*=1, $CHCl_3$). (4*S*,5*S*)-**4b**: mp 90–91°C; $[\alpha]_D^{25}$ −56 (*c*=0.60, $CHCl_3$).



Scheme 3. Proposed mechanism for the electroreductive coupling

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