Synthesis of [3]Ferrocenophanes via Samarium Diiodide Promoted Reductive Cyclizations of 1,1′-Dicinnamoylferrocenes

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ABSTRACT

A series of 1,1′-dicinnamoylferrocenes were converted to the corresponding [3]ferrocenophane diols (4a−e) in a stereoselective manner by using samarium diiodide to effect the intramolecular coupling reaction, aldol reaction, and reduction in one-pot operation. The major reaction pathway might be derived from a samarium chelated transition state (IA) having the moieties of s-cis enone and (Z)-enolate. A solid-state structure of such [3]ferrocenophane diol product showed that the cyclopentadienyl groups were in an eclipsed orientation and slightly tilted.

Much attention has been paid to the study of carbon-bridged ferrocenophanes due to their attractive features of chemical reactivities and potential use as building blocks for new materials. There are only a few reports on the conversion of 1,1′-dialkanoylferrocenes to [5]ferrocenophanes. For example, 1,1′-dicinnamoylferrocene (1a) has been treated with NaOH to give 1,5-dioxo-3-phenyl-[5]ferrocenophanes, presumably via a three-step sequence: (i) base-catalyzed hydration of a cinnamoyl moiety to afford an intermediate of β-hydroxy ketone, (ii) retro-aldol reaction to give an enolate intermediate, and (iii) intramolecular Michael addition on the β-carbon of the other cinnamoyl moiety to furnish the cyclization product. 1,1′-Diacylferrocene and 1,1′-dicrotonylylferrocene also undergo the similar reactions in HCl or EtONa solution to give 1,5-dioxo-2-ethylidene-[5]ferrocenophanes.

We herein demonstrate that use of SmI2 can convert a series of 1,1′-dicinnamoylferrocenes (1a−f) to the corresponding [3]ferrocenophanes (3a−f and 4a−f) with annulation of cyclopentyl rings. SmI2 is a widely utilized one-electron-transfer reducing agent, which also shows good reactivity toward acylferrocenes. Reduction, deoxygenation, and reductive coupling products have been obtained depending on the reaction conditions.

The following experimental procedure is typical. A deep blue SmI2 solution (0.1 M, 1.8 mmol) was prepared by treatment of Sm (331 mg, 2.2 mmol) with 1,2-diiodoethane (507 mg, 1.8 mmol) in anhydrous THF (18 mL) for 1.5 h at room temperature. The SmI2 solution was cooled in an ice
bath, and a THF (100 mL) solution of 1,1'-dicinnamolyferrocene (178 mg, 0.4 mmol) was added dropwise via a syringe pump over a period of 3 h. The mixture was stirred at 0 °C for an additional 3.5 h, and then filtered through a pad of silica gel by elution with EtOAc/hexane (1:1). The filtrate was concentrated and chromatographed on a silica gel column by elution with EtOAc/hexane (0–25%) to give two isomers of [3]ferrocenophane diols, 4a-minor (58 mg, 32%, less retained on silica gel) and 4a-major (88 mg, 49%).

Table 1 lists the results of the SmI2 promoted reductive cyclizations of other 1,1'-cinnamolyferrocenes. All reactions occurred readily at 0 °C in THF solutions without using dipolar additives such as hexamethylphosphoramide or N,N-dimethylacetamide. It was found that the minor stereomers were less retained on silica gel column than the corresponding major isomers. When a THF solution of 1a (0.5 mmol) was added dropwise to the freshly prepared SmI2 solution (1.8 mmol) over a period of 1 h, followed by stirring at 0 °C for a brief period (10 min), dione 2a and aldol 3a were obtained in 23% and 44% yields (entry 2). The 1H NMR analyses indicated that both products existed as single isomers. The starting material was entirely recovered when 0.8 mmol of 1a was treated with 0.45 mmol of SmI2 at 0 °C for 2 h (entry 3). The [3]ferrocenophane diols 4c (R = m-MeOC6H4) were obtained in an excellent yield (97%) by treatment of 1c (0.4 mmol) with an excess of SmI2 (1.8 mmol). When a less amount of SmI2 (0.9 mmol) was used, with respect to 0.4 mmol of ferrocene 1c, the intermediate aldol products 3c were isolated in 70% yield (entry 6). Because of the low solubility of 1f (R = p-C6H4F) in THF, it only reacted sluggishly with SmI2 to give the aldol products 3f in 15% yield along with a recovery of the starting material.

A sample of 4a-major diol was obtained by recrystallization from CHCl3/hexane, and the (1S*,3S*,4S*,5S*,6R*) configuration was rigorously determined by an X-ray diffraction analysis (Figure 1). The solid-state 4a-major contained two cyclopentadienyl groups in an eclipsed orientation (ring twist angle = 2.7° ± 0.2). The Cp rings were just slightly displaced (ring tilt angle = 9.63° ± 0.12) despite 4a-major having an additional annulation of five-membered ring.

A reaction pathway (Scheme 1) is proposed to explain the stereochemical outcome. The samarium-chelated transition state Σ1, having the moieties of s-cis enone and (Z)-enolate, could undergo a coupling reaction to link the β,β'-carbons to give the meso-type intermediate Σ*. The subsequent aldol

![Figure 1. ORTEP drawing of compound 4a-major.](image-url)
reaction of \( \text{II} \) could be mediated by samarium ion to give \( \text{III} \) with the carbonyl and hydroxyl groups on the same face. Further reduction of the carbonyl group with \( \text{SmI}_2 \), followed by abstraction of hydrogen atom from the less hindered exo face, would afford \( 4a \)-major in a stereoselective fashion. All the transition states \( \text{I} - \text{IV} \) showed their dispositions similar to the single-crystal structure of \( 4a \)-major.

Attempts to crystallize \( 2a, 3a, 3c, 3f \), or the minor isomers of \( 4a-e \) failed. The stereochemistry of minor products \( 3c \) and \( 4a \) were inferred from their NOESY spectra (500 MHz). The NOE correlations of H-3 (at \( \delta \) 3.55, m), H-4 (at \( \delta \) 3.89, dd, \( J = 12.4, 9.7 \) Hz), and H-5 (at \( \delta \) 4.63, d, \( J = 12.4 \) Hz) in \( 3c \)-minor aldol indicated that these protons were on the same face. A D\(_2\)O-exchangeable signal at \( \delta \) 2.86 (s) was attributed to the hydroxyl group, which likely formed intramolecular hydrogen bonding with the carbonyl group.

In addition to the NOE correlations of H-3 (at \( \delta \) 3.64, m), H-4 (at \( \delta \) 4.00, br d, \( J = 12.6 \) Hz), and H-5 (at \( \delta \) 2.69, br d, \( J = 12.6 \) Hz), the \( 4a \)-minor diol also showed the NOE correlation of H-6 (at \( \delta \) 4.31, br d, \( J = 5.0 \) Hz) with H-4.

On the basis of mechanistic consideration (Scheme 1), the \( 3 \)-major and \( 4 \)-major products were thus assigned to have the \((1S^*,3S^*,4S^*,5R^*)\) and \((1S^*,3S^*,4S^*,5S^*,6R^*)\) configurations, whereas the corresponding \( 3 \)-minor and \( 4 \)-minor isomers were assigned to have the \((1R^*,3S^*,4S^*,5R^*)\) and \((1R^*,3S^*,4S^*,5R^*,6S^*)\) configurations. After a prolonged reaction time, the transition state \( \text{II}' \) might undergo conformational interchange to the transition state \( \text{III}' \). Both \( \text{II}' \) and \( \text{III}' \) would afford dione \( 2 \) upon protonation. The aldol reaction of \( \text{II}' \) would give \( 3 \)-minor products via a chelated transition state \( \text{III}' \). Further reduction of \( \text{III}' \) would also occur in a stereoselective manner to give \( 4 \)-minor diols.

Other reaction pathways via the transition states \( \text{I}_B, \text{I}_C, \) and \( \text{I}_D \) were disfavored due to the steric effects. Transition state \( \text{I}_B \) with the moieties of \( s\)-trans enone and \((E)\)-enolate might exert certain repulsion between Cp rings and the \( \beta \)-hydrogen atoms. The transition states \( \text{I}_C \) and \( \text{I}_D \) with \( s\)-cis/E enone or \( s\)-trans/Z enone arrangements would cause severe strains in the intramolecular coupling reactions. Formation of the \( dl\)-type isomer \( \text{I}_C \) or \( \text{I}_D \) would be less likely, in accordance with no finding of the \( 2a \) isomer in our present study.

In summary, our present \( \text{SmI}_2 \) promoted method is the first report on the efficient reductive cyclization of 1,1'-dicinnamoylferrocenes in a stereoselective manner. Application of this method to synthesize strained \([m]\)ferrocenophanes is currently under investigation.

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**Supporting Information Available:** Additional experimental procedures and spectral data of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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