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 (I_A) 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 ferrocenophanes¹ 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.² For example, 1,1'-dicinnamoylferrocene (**1a**) has been treated with NaOH to give 1,5-dioxo-3-phenyl-[5]ferrocenophanes,^{2a} 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'-Diacrylferrocene and 1,1'-

dicrotonylferrocene also undergo the similar reactions in HCl or EtONa solution to give 1,5-dioxo-2-ethylidene-[5]ferro-cenophanes.^{2c,d}

We herein demonstrate that use of SmI_2 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.³ SmI₂ is a widely utilized oneelectron-transfer reducing agent, which also shows good reactivity toward acylferrocenes.⁴ Reduction, deoxygenation, and reductive coupling products have been obtained depending on the reaction conditions.

The following experimental procedure is typical. A deep blue SmI_2 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 SmI_2 solution was cooled in an ice

⁽¹⁾ For a recent review of ferrocenophanes with all carbon bridges, see: Heo, R. W.; Lee, T. R. J. Organomet. Chem. **1999**, 578, 31.

^{(2) (}a) Winstead, J. A. J. Org. Chem. **1972**, *37*, 1271. (b) Barr, T. H.; Watts, W. E. Tetrahedron **1968**, *24*, 3219. (c). Barr, T. H.; Watts, W. E. Tetrahedron **1969**, *25*, 861.

⁽³⁾ The reductive cyclizations of 1,3-diphenyl-2-propen-1-one by using SmI₂ or SmCl₃/Zn give 1,3,4-triphenyl-2-benzoylcyclopentanol. See: (a) Cabrera, A.; Lagadec, R. L.; Sharma, P.; Arias, J. L.; Toscano, R. A.; Velasco, L.; Gavino, R.; Alvarez, C.; Salmon, M. J. Chem. Soc., Perkin Trans. 1 1998, 3609. (b) Zhou, L.-h.; Shi, D.-q.; Gao, Y.; Shen, W.-b.; Dai, G.-y.; Chen, W.-x. Tetrahedron Lett. 1997, 38, 2729.

^{(4) (}a) Neo, A. G.; Gref, A.; Riant, O. *Chem. Commun.* **1998**, 2353. (b) Christensen, T. B.; Riber, D.; Daasbjerg, K.; Skrydstrup, T. *Chem. Commun.* **1999**, 2051. (c) Jong, S.-J.; Chen, C.-T.; Fang, J.-M. *J. Organomet. Chem.***1999**, 590, 42. For the reaction of ferrocenyl ketone with Zn/Me₃-SiCl, see: (d) Denifl, P.; Hradsky, A.; Bildstein, B.; Wurst, K. *J. Organomet. Chem.* **1996**, 523, 79.



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 gradients of 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'-cinnamoylferrocenes.⁵ All reactions occurred readily at 0 °C in THF solutions without using dipolar additives such as hexamethylphosphoramide or *N*,*N*-dimethylacetamide.⁶ 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

Table 1. SmI₂-Mediated Intramolecular Coupling Reactions of 1,1'-Dicinnamoylferrocenes 1a-f (THF, 0 °C)^{*a*}

entry	substrate	R	SmI_2	products (yields; ratio of isomers)
1	1a	C ₆ H ₅	4.5^{b}	4a (81%; 60:40)
2^c	1a		3.6^{b}	2a (23%; 100:0)
				3a (44%; 100:0)
3	1a		0.6^{b}	no reaction
4	1b	p-CH ₃ C ₆ H ₄	4.5^{b}	4b (72%; 62:38)
5	1c	m-MeOC ₆ H ₄	4.5^{b}	4c (97%; 86:14)
6^d	1c		2.3^{b}	3c (70%; 69:31)
7	1d	m-CF ₃ C ₆ H ₄	4.5^{b}	4d (61%; 52:48)
8	1e	p-FC ₆ H ₄	4.5^{b}	4e (47%; 100:0)
9 ^e	1f	p-ClC ₆ H ₄	4.5^{b}	3f (15%; 100:0)

^{*a*} According to the typical experimental procedure (see text) by addition of a THF solution of substrate (0.4 mmol) to a SmI₂ solution (1.8 mmol) over a period of 3 h and stirring for 3.5 h at 0 °C. ^{*b*} The molar proportion of SmI₂ to substrate. ^{*c*} The substrate was added to a SmI₂ solution over 1 h and stirred for 10 min at 0 °C. ^{*d*} The substrate (0.4 mmol) was added to a SmI₂ solution (0.9 mmol) over 1.5 h and stirred for 1 h at 0 °C. ^{*e*} Because of low solubility of **1f** in THF, the SmI₂ solution was added to the THF solution of substrate at 0 °C. 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** ($\mathbf{R} = m$ -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** ($\mathbf{R} = p$ -ClC₆H₄) 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).⁷ The solid-state **4a**-major



Figure 1. ORTEP drawing of compound 4a-major.

contained two cyclopentadienyl groups in an eclipsed orientation (ring twist angle = $2.7^{\circ} \pm 0.2$). The Cp rings were just slightly displaced (ring tilt angle = $9.63^{\circ} \pm 0.12$) despite **4a**-major having an additional annulation of five-membered ring.⁸

A reaction pathway (Scheme 1) is proposed to explain the stereochemical outcome. The samarium-chelated transition state I_A , 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 II_A . The subsequent aldol

⁽⁵⁾ All new compounds are characterized by spectral methods (IR, MS, HRMS, 1 H and 13 C NMR).

⁽⁶⁾ Additives HMPA and DMA can promote the reduction of enones to the corresponding ketones. See: Fujita, Y.; Fukuzumi, S.; Otera, J. *Tetrahedron Lett.* **1997**, *38*, 2121.

⁽⁷⁾ Crystal data for **4a**-major: monoclinic, a = 11.9621 (2), b = 7.6080 (2), c = 23.7632 (5) Å, V = 2129.94 (8) Å³, crystal size $0.25 \times 0.2 \times 0.15$ mm, T = 296 (2) K, space group $P2_1/c$, Z = 4, absorption coefficient = 0.731 mm⁻¹, reflections collected 12124, independent reflections 3741 ($R_{int} = 0.0239$). Final *R* indices [$I > 2\sigma(I)$] R1 = 0.0300, wR2 = 0.0777, *R* indices (all data) R1 = 0.0388, wR2 = 0.0816. Refinement method: full-

<sup>matrix least-squares on F².
(8) The Cp rings in the crystal structure of [3]ferrocenophane-1-one are slightly staggered with a ring twist angle of 11.8° and a ring tilt angle of 8.8°. See: Jones, N. D.; Marsh, R. E.; Richards, J. H.</sup> *Acta Crystallogr.* 1965, *19*, 330.



reaction of II_A could be mediated by samarium ion to give III_A with the carbonyl and hydroxyl groups on the same face. Further reduction of the carbonyl group with SmI₂, followed by abstraction of hydrogen atom from the less hindered *exo* face, would afford **4a**-major in a stereoselective fashion. All the transition states $I_A - IV_A$ 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 δ 3.55, m), H-4 (at δ 3.89, dd, J = 12.4, 9.7 Hz), and H-5 (at δ 4.63, d, J = 12.4 Hz) in **3c**-minor aldol indicated that these protons were on the same face. A D₂O-exchangeable signal at δ 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 δ 3.64, m), H-4 (at δ 4.00, br d, J = 12.6 Hz), and H-5 (at δ 2.69, br d, J = 12.6 Hz), the **4a**-minor diol also showed the NOE correlation of H-6 (at δ 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 $(1S^*, 3S^*, 4S^*, 5S^*)$ 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 $(1R^*, 3S^*, 4S^*, 5R^*)$ and $(1R^*, 3S^*, 4S^*, 5R^*, 6S^*)$ configurations. After a prolonged reaction time, the transition state II_A might undergo confomational interchange to the transition state II_A' . Both II_A and II_A' would afford dione 2 upon protonation. The aldol reaction of II_A' would give 3-minor products via a chelated transition state III_A' . Further reduction of III_A' would also occur in a stereoselective manner to give 4-minor diols.



Other reaction pathways via the transition states I_B , I_C , and I_D were disfavored due to the steric effects. Transition state I_B with the moieties of *s*-trans enone and (*E*)-enolate might exert certain repulsion between Cp rings and the β -hydrogen atoms. The transition states I_C and 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 I_C or I_D would be less likely, in accordance with no finding of the **2a** isomer in our present study.

In summary, our present 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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