JOC The Journal of Organic Chemistry

Featured Article

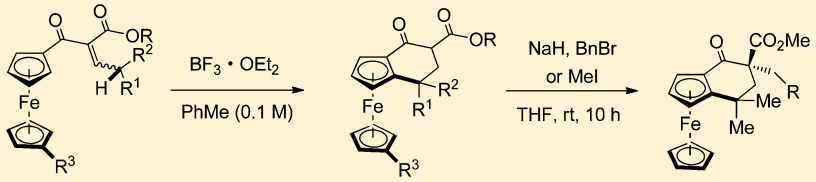
pubs.acs.org/joc

BF_3·OEt_2-Promoted Synthesis of 2,3-Metallocenocyclohexanones: A 1,2-Hydride Shift and Cationic Cyclization Strategy

Congfa He, Jie Wang, and Zhenhua Gu*

Department of Chemistry, University of Science and Technology of China, 96 Jinzhai Road, Hefei, Anhui 230026, P. R. China

Supporting Information



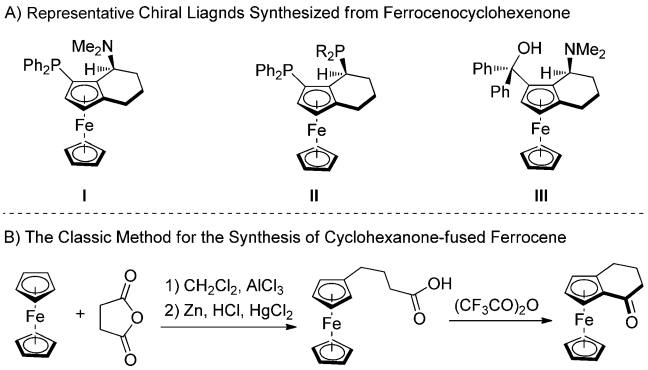
ABSTRACT: A BF_3·OEt_2-promoted cyclization of metallocenyl enones to form cyclohexanone-fused metallocenes is reported. 2,3-Metallocenocyclohexanones were formed exclusively, and no normal Nazarov-type cyclopentanone analogues were detected. The reaction possibly proceeded via an unusual cationic 1,2-hydride shift followed by Friedel–Crafts alkylative cyclization process. During the studies of the alkylation reaction of these keto esters, an unusual and rare facial selectivity was observed. The electrophiles would be attacked from the same face as the second Cp ring.

INTRODUCTION

The discovery of ferrocene and elucidation of its sandwich-like structure is an important event in organic chemistry, which is also regarded as the starting point of modern organometallic chemistry.[1,2] The discovery of ferrocene was serendipitous; however, it had a great impact on several related fields, including material science, catalysis, biochemistry, and electrochemical sensors, etc.[3,4] Because of its good stability and its unique sandwich-like structure, ferrocene as well as its planar chiral analogues were also proven to be one of the most successful scaffolds for chiral ligands or catalysts in organic synthesis. The wide applications in various areas required the synthesis of different functionalized ferrocenes for different purposes. Although great efforts were made, methods that could be applied to efficiently functionalize ferrocenes and other related metallocenes are still limited.

2,3-Ferrocenocyclohexanone was the first optically active planar chiral ferrocene compound,[5] and some useful ligands and catalysts, such as aminophosphine **I**,[6a] diphosphine **II**,[6a] and aminoalcohol **III**,[6b] were prepared from chiral 2,3-ferrocenocyclohexanone (Scheme 1A). However, there are very limited methods that could be applied to synthesize 2,3-ferrocenocyclohexanone derivatives, which currently were prepared from ferrocene via a classic multistep synthesis developed in the 1950s: Friedel–Crafts acylation, Clemmensen reduction, and Friedel–Craft acylation (Scheme 1B).[7] To our knowledge, currently this is the only reliable and practical method for the synthesis of this class of compounds, which still suffered from its low functional group tolerance and structural diversity. For example, it is hard to introduce other functionalities in the 2,3-ferrocenocyclohexanone skeleton via this protocol. Thus, the development of practical and convenient methods for the synthesis of cyclohexanone-fused metallocenes is urgent yet still challenging. Here, we report an alternative synthesis of this class of compounds via an unusual BF_3·OEt_2-promoted cationic 1,2-hydride shift followed by Friedel–Crafts alkylative cyclization.

Scheme 1. Synthesis of 2,3-Ferrocenocyclohexenone and Its Application



RESULTS AND DISCUSSION

Nazarov cyclization reaction is a powerful method for the construction of cyclopentenone analogues via a 4π-electrocyclic ring closure process, where the formation of pentadienyl cation intermediate is crucial.[8] As a result of contributions from the groups of West, Frontier, Flynn, Tius, and others, a variety of cyclopentenones with different functionalities have been synthesized, including the application of complex natural product synthesis.[9] By introducing cyclopropanyl functionality in place of the vinyl group into the molecules, cyclohexanone analogues could be obtained.[10] Originally, in order to access

Received: July 2, 2015
Published: July 29, 2015

DOI: 10.1021/acs.joc.5b01511
J. Org. Chem. 2015, 80, 7865–7875

some ring-fused ferrocenes, we hypothesized that ferrocenocyclopentanones might be synthesized via Brønsted or Lewis acid catalyzed Nazarov cyclization of metallocenylenones.

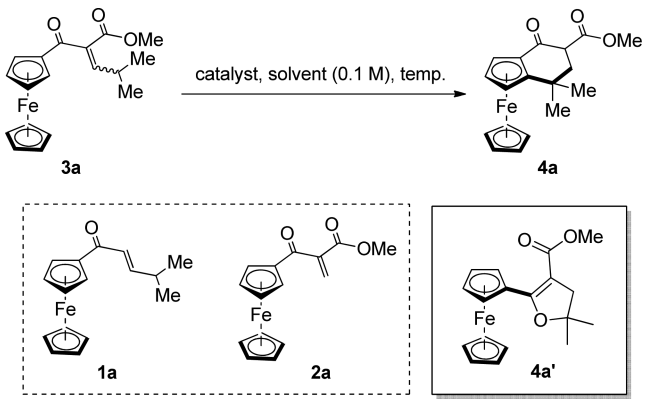
Initially, we chose enones **1a** and **2a** as the substrates; however, no cyclized product could be obtained, and most of **1a** was recovered, while **2a** completely decomposed. In the presence of stoichiometric $AlCl_3$, it was interesting to find that cyclohexanone analogue **4a** formed in 27% yield when enone **3a** was used, and no cyclopentanone product was detected (Table 1, entry 1). In a classic Nazarov reaction, cyclohexenones were usually prepared by introducing a cyclopropyl group via ring-opening processes.[10] Compound **4a** was possibly formed via 1,2-hydride shift followed by Friedel–Crafts type carbocation cyclization. This type of rearrangement/cyclization process was also observed by Frontier, Eisenberg, and coworkers in the Nazarov cyclization of 2-furyl and 2-benzofuryl enones.[11] It should be noted that in their studies only 2-furyl enone analogues underwent this type of rearrangement, which was significantly different from pyrrolyl, indolyl, and thienyl enones. This interesting observation promoted us to pursue further investigation. With the Frontier catalyst system [5 mol % of $Sc(OTf)_3$ and stoichiometric $LiClO_4$],[12] no product was found and only starting material was recovered either at ambient conditions or elevated reaction temperature (entry 2). Neither Ti(O-*i*-Pr)$_4$ nor (+)-CSA was effective catalyst for this transformation, and the starting material merely changed (entries 3 and 4). To our delight, the reaction gave 50% of cyclohexanone product **4a** when $BF_3{\cdot}OEt_2$ was used (entry 5). Further screening of different solvents indicated that DMF, MeCN, and THF were ineffective for this reaction, while toluene was superior over other solvents (entries 6–9). Increasing the loading of $BF_3{\cdot}OEt_2$ could significantly improve the isolated yield of **4a** to 88% even at only 40 °C, where 4% of byproduct **4a′** could be isolated (entry 10). The requirement of large amounts of $BF_3{\cdot}OEt_2$ was possibly due to the relatively higher Lewis basicity of the product **4a** over enone ester **3a**. By use of $BF_3{\cdot}CH_3CN$ as Lewis acid, relative lower yields were obtained along with isolation of an unidentified Ritter-type product (entries 11 and 12).

We tested the generality of this protocol by applying different substituted metallocenylenones to the optimized conditions (Table 2). The enone with a 3-pentyl side chain was also a compatible substrate, although a relatively lower yield was obtained (entry 1). The reaction of enone containing a 2-butyl or 1-(1-phenylpropyl) side chain gave a mixture of planar and center chiral diastereomers with dr of 3:1 and 1:1, respectively (entries 2 and 3). Currently, though it is still not very clear, it is thought that the diastereoselectivity is possibly controlled by steric differences of the substitutents. It should be noted that the cyclized compound from **3d** contains the mixture of enol and ketone, along with the diastereomers, whose spectroscopies are messy. However, this could be overcome by the decarboxylative reaction to form ketone **5d**. The reactions of enones with cyclopentyl, cyclohexyl, and cycloheptyl chains worked uneventfully to give spiro compounds in good to excellent yields (entries 4–6). With ethyl ester, the reaction also proceeded smoothly to give **4h** in excellent yield (entry 7), while the bulky menthyl ester **3i** was inert under our standard conditions probably due to the steric congestion (entry 8). The reaction of **3j**, an enone with 1-(2-methylpropyl) substituent, only resulted the decomposition of starting material (entry 9). The substituent on the second Cp ring could be either an electron-donating group or an electron-withdrawing group, where the strong electron-deficient substituent significantly decreased the reaction rate (entries 10–12). For example, when **3l**, bearing a benzoyl group at the second Cp ring, was used as the substrate, a total of 36 h was necessary for the reaction to reach full conversion even in the presence of 6.0 equiv of $BF_3{\cdot}OEt_2$ (entry 11). Notably, bis(cyclopentadienyl)ruthenium (ruthenocene) derivatives were suitable substrates, which showed superior reactivity over ferrocenylenones, and relatively higher yields could be achieved (entries 13–15).

The NMR spectra of the keto esters show a pair of mixtures due to the keto–enol equilibrium, and the spectra of **4** vary depending on the workup, solvent, and concentration for NMR, which was difficult to assign. However, the keto esters readily underwent decarboxylative reaction under aqueous basic conditions to deliver metallocenyl ketones, which provided clear and simplified spectroscopies in comparison with the keto esters (Scheme 2).

The alkylation of keto ester **4a** by the use of MeI and BnBr provided alkylated products **6a** and **6b** in moderate to good yields with excellent stereoselectivity, which also gave clear NMR spectroscopies via inhibition of the formation of enols. It is interesting to find that the alkylation took place at the same face as the second Cp ring, which was confirmed by NOE correlation studies and single-crystal X-ray analysis.[13] This unexpected facial selectivity was possibly caused by the block of the coordinated solvents to sodium atom. To avoid the steric congestion, the coordination molecules would stay at the outer

Table 1. Reaction Condition Optimization[a]

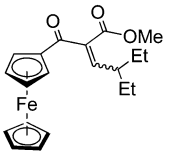
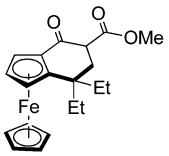
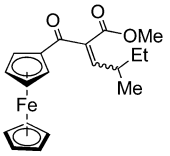
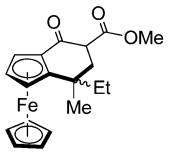
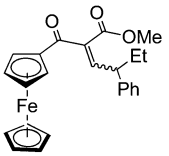
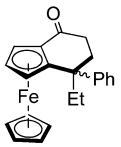
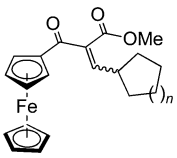
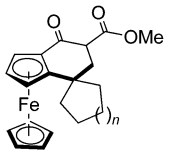
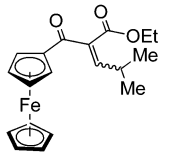
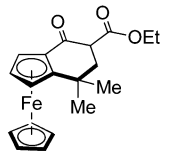
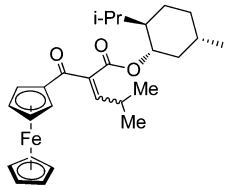
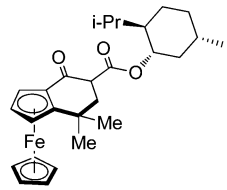
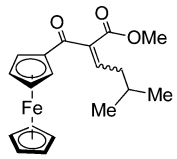
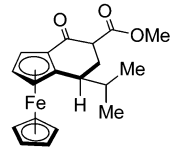
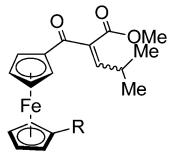
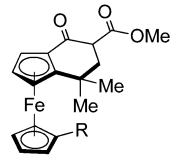
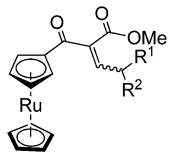
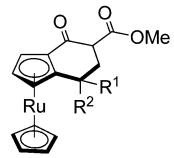


entry	cat. (equiv)	solvent	T (°C)	yield (%)
1	$AlCl_3$ (1.0)	DCE	80	27
2[b]	$Sc(OTf)_3$ + $LiClO_4$ (1.0)	DCE	rt to 80	–
3	Ti(O*i*Pr)$_4$ (1.0)	DCE	80	–[c]
4	(+)-CSA (1.0)	DCE	100	–
5	$BF_3{\cdot}OEt_2$ (1.0)	DCE	80	50
6	$BF_3{\cdot}OEt_2$ (1.0)	DMF	80	–
7	$BF_3{\cdot}OEt_2$ (1.0)	CH_3CN	80	–
8	$BF_3{\cdot}OEt_2$ (1.0)	THF	40	–
9	$BF_3{\cdot}OEt_2$ (1.0)	toluene	80	59
10	$BF_3{\cdot}OEt_2$ (3.0)	toluene	40	88[d]
11[e]	$BF_3{\cdot}MeCN$ (1.0)	toluene	80	33
12[e]	$BF_3{\cdot}MeCN$ (3.0)	toluene	80	38

[a]The reaction was conducted on **3a** (24 mg, 0.070 mmol) in the indicated solvent (0.10 M) at 40–80 °C. [b]5 mol % of $Sc(OTf)_3$. [c]The recovered SM was contaminated with 16% of isopropyl ester. [d]4% of **4a′** was isolated. [e]An unidentified product with HRMS $[M+H]^+$ 382.1108 was isolated.

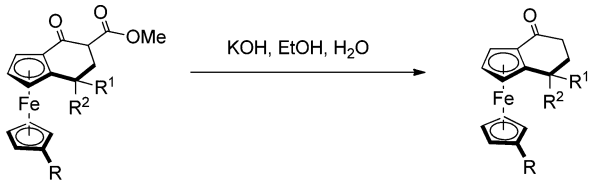
DOI: 10.1021/acs.joc.5b01511
J. Org. Chem. 2015, 80, 7865–7875

Table 2. Substrate Scope[a]

entry	substrate	product	time/h	yield/%
1	 **3b**	 **4b**	4	67
2	 **3c**	 **4c**	3	88 (dr 3:1)
3	 **3d**	 **5d**	8	50[b] (dr 1:1)
4	 **3e**, n = 1	 **4e**	3	71
5	**3f**, n = 2	**4f**	3	87
6	**3g**, n = 3	**4g**	4	78
7	 **3h**	 **4h**	2	94
8	 **3i**	 **4i**	10	No Rx.
9	 **3j**	 **4j**	5	decomp.
10	 **3k**, R = *t*-Bu	 **4k**	4	70
11[c]	**3l**, R = COPh	**4l**	36	60
12	**3m**, R = $CONMe_2$	**4m**	5	80
13	 **3n**, $R^1 = R^2$ = Me	 **4n**	4	99
14	**3o**, R^1, R^2 = -$(CH_2)_4$-	**4o**	4	86
15	**3p**, R^1, R^2 = -$(CH_2)_5$-	**4p**	6	97

[a]The reactions were conducted on 0.070 mmol of **3** in toluene (0.1 M) at 80 °C for the time indicated in the table. [b]The yield was for two steps: cyclization and decarboxylation. [c]6.0 equiv of BF_3·OEt_2 was used.

Scheme 2. Decarboxylation of 4



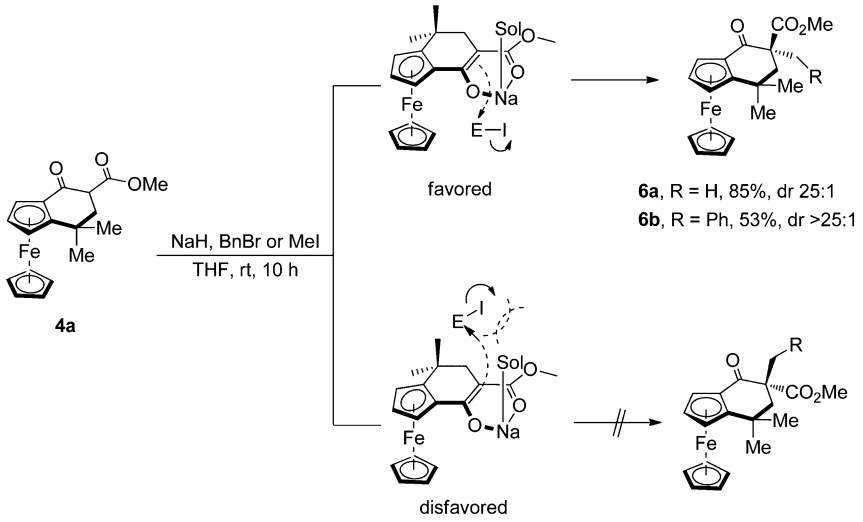
4a, R = H, $R^1 = R^2$ = Me — **5a**, 93%
4f, R = H, R^1, R^2 = -$(CH_2)_4$- — **5f**, 49%
4m, R = $CONMe_2$, $R^1 = R^2$ = Me — **5m**, 56%

sphere of ferrocene skeleton, which led to the complete block of the top face. Thus, the electrophiles would come from the same face as the second Cp ring (Scheme 3). Considering that the solvent could play an important role for this facial selectivity, additional investigations were conducted in different solvents. In DMF, the reaction gave the best diastereoselectivity and yield. However, to our surprise, good facial selectivity still could be achieved in "non-coordination" solvents such toluene and CH_2Cl_2, which indicated that more complicated intermediates could account for this facial selectivity.

The plausible pathways of this transformation are listed in Scheme 4A. The interaction of BF_3·OEt_2 with the malonate moiety of **3** would give **A**, whose resonnance structure is zwitterion **B**. The 1,2-hydride shift of **B** would afford tertiary cation **D**, while no normal Nazarov product **C** was formed from the cyclization of **B**. The reason that ferrocenocyclopetanone product **C** is not formed is that the ferrocene Cp ring would not undergo a ring-slippage reaction.[14] The intramolecular Friedel−Crafts alkylation of **D** followed by aqueous workup delivered the product **4**. According to the results of Frontier and Eisenberg's calculation,[11a] the furyl structure is crucial for the rearrangement and cyclization process.[15] It was found that furyl cation **D1** was 1.11 kcal/mol lower than **B1** while the corresponding pyrrolyl intermediate **D2** was 1.72 kcal/mol higher than **B2**, which gave normal Nazarov 4π-electrocyclization product. However, the formation of metallocenyl keto esters **4** was possibly not only controlled by the relative stability between **D** and **B** but also influenced by steric facts since the expected stable cation **G** failed to furnish the

DOI: 10.1021/acs.joc.5b01511
J. Org. Chem. 2015, 80, 7865−7875

Scheme 3. Alkylation of 4



Solvent Effects on the Alkylation of Compound **4a**

entry	solvent	yield/% (**6b**)	dr
1	DMF	86%	>25:1
2	toluene	49%	12.5:1
3	DCM	60%	15:1

pentanone compound **7q** (Scheme 4B). An alternative 6π-electrocyclization pathway was also plausible: deprotonation of **B** would give metallocenyldiene **F**, which would deliver the final product after 6π-electrocyclic ring closure and isomerization. However, on the basis of the formation of **4a′** as well as the failure of the cyclization of **3j**, the cationic alkylative cyclization pathway is preferred.

CONCLUSION

In conclusion, we reported a $BF_3{\cdot}OEt_2$-promoted cyclization of metallocenylenones via a rare 1,2-hydride shift of the allylic cation followed by a Friedel−Crafts alkylation process. This method provided an efficient way to access cyclohexanone-fused metallocenes, which would be good supplement for the synthesis of ring-fused metallocenes. An unusual facial selectivity was observed during the studies of alkylation of compounds **4**.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under a nitrogen atmosphere in flame-dried glassware unless the reaction procedure states otherwise. Tetrahydrofuran (THF) was distilled from sodium benzophenone in a continuous still under an atmosphere of N_2. Dioxane was distilled from sodium benzophenone under an atmosphere of nitrogen. Dichloromethane was distilled from calcium hydride in a still under an atmosphere of nitrogen. Room-temperature reactions were carried out between 20 and 25 °C. Flash column chromatography was performed using 40−63 μm silica gel as the stationary phase. ^{1}H and ^{13}C NMR spectra were referenced by using solvent residue as an internal reference (^{1}H NMR: 7.26 ppm for $CDCl_3$; ^{13}C NMR: 77.00 ppm for $CDCl_3$). Electron spray ionization (ESI) mass spectrometry data were acquired by using an LTQ analyzer.

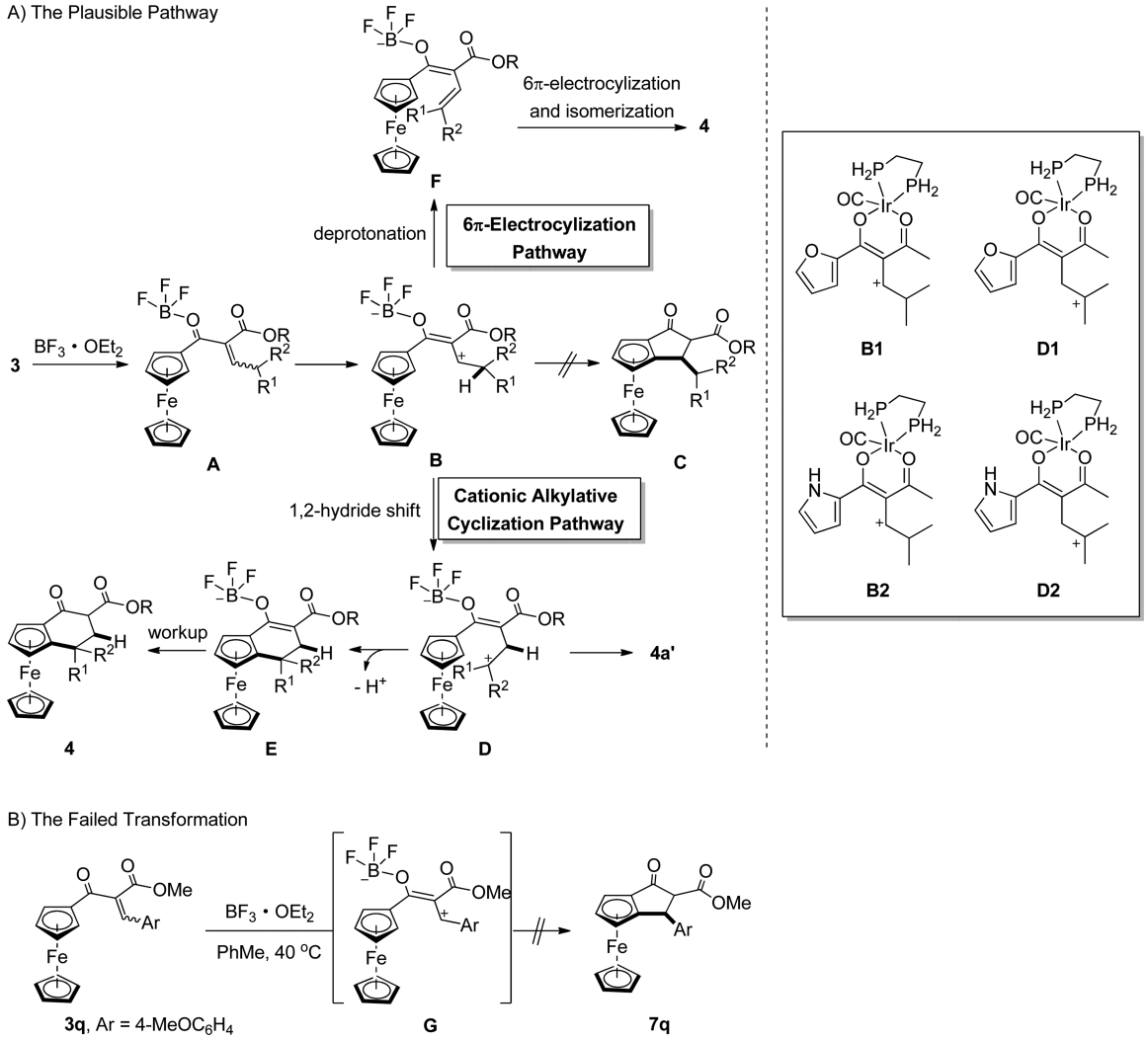
Preparation of Compound ***1a****.*[16] *n*-Butyllithium (2.4 M in hexane, 0.88 mL, 2.1 mmol, 1.05 equiv) was added to a solution of diisopropylamine (0.29 mL, 2.1 mmol, 1.05 equiv) in THF (2.0 mL) at −20 °C dropwise. After the addition, the mixture was stirred at −20 °C for 30 min and then chilled to −78 °C. Acetylferrocene (0.456 g, 2.0 mmol, 1.0 equiv) in THF (2.0 mL) was added to the mixture, and the resulting mixture was stirred for 30 min followed by the addition of isobutyraldehyde (0.2 mL, 2.2 mmol, 1.1 equiv). After the mixture was stirred at −78 °C for 30 min, it was quenched with saturated aqueous Na_2CO_3, and the mixture was extracted with ethyl acetate (20 mL × 3). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate = 20:1) to afford **1a** as a red solid (0.150 g, 26%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (dd, J = 15.6, 7.2 Hz, 1 H), 6.46 (dd, J = 15.6, 1.2 Hz, 1 H), 4.82 (t, J = 2.0 Hz, 2 H), 4.53 (t, J = 2.0 Hz, 2 H), 4.18 (s, 5 H), 2.58−2.50 (m, 1 H), 1.14 (d, J = 6.8 Hz, 6 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.5, 151.8, 123.7, 80.3, 72.4, 70.0, 69.7, 31.2, 21.6; HRMS (APCI) calcd for $C_{16}H_{18}O^{56}FeNa$ $[M + Na]^+$ 305.0605, found 305.0617.

Preparation of Compound ***2a****.*[17] The mixture of sodium hydride (60% in mineral oil, 0.224 g, 5.6 mmol, 2.8 equiv), dimethyl carbonate (0.360 g, 4.0 mmol, 2.0 equiv), and toluene (2.0 mL) was heated to reflux. Acetylferrocene (0.456 g, 2.0 mmol, 1.0 equiv) in toluene was added dropwise to the mixture within 10 min. After additional reflux for 2 h, the solution was cooled to room temperature and quenched with acetic acid (1.0 mL), followed by the addition of water. The mixture was extracted with ethyl acetate (50 mL × 3), and the combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate = 5:1) to afford methyl 3-oxo-3-ferrocenylpropanoate as a red solid (0.484 g, 85%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.79 (t, J = 2.0 Hz, 2 H), 4.57 (t, J = 2.0 Hz, 2 H), 4.26 (s, 5 H), 3.78 (s, 3 H), 3.76 (s, 2 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.7, 167.9, 78.2, 72.9, 70.0, 69.6, 52.2, 46.6; HRMS (ESI) calcd for $C_{14}H_{14}O_3{}^{56}FeNa$ $[M + Na]^+$ 309.0190, found 309.0182.

The mixture of 3-oxo-3-ferrocenylpropanoate (0.286 g, 1.0 mmol, 1.0 equiv), HCHO (37% aq, 80 μL, 1.0 mmol, 1.0 equiv), and $Cu(OAc)_2$ (18.2 mg, 0.1 mmol, 0.1 equiv) in AcOH (4.0 mL) was stirred at 90 °C for 4 h. After the mixture was cooled to the room temperature, the solvent was removed. The residue was purified by

DOI: 10.1021/acs.joc.5b01511
J. Org. Chem. 2015, 80, 7865−7875

Scheme 4. Plausible Pathways



column chromatography on silica gel (hexanes/ethyl acetate = 20:1) to afford **2a** as a red solid (63.2 mg, 21%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.58 (d, J = 0.8 Hz, 1 H), 6.10 (d, J = 0.8 Hz, 1 H), 4.77 (t, J = 2.0 Hz, 2 H), 4.59 (t, J = 2.0 Hz, 2 H), 4.25 (s, 5 H), 3.84 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 196.2, 164.9, 141.5, 129.2, 77.7, 73.1, 70.6, 70.3, 52.4; HRMS (EI) calcd for $C_{15}H_{14}O_3{}^{56}Fe$ $[M]^+$ 298.0292, found 298.0297.

*Preparation of Compound **3a** (Typical Procedure A).* Titanium(IV) chloride (1.8 mmol in 0.2 mL CH_2Cl_2, 2.6 equiv) was added dropwise to dry THF (3.0 mL) at 0 °C. A mixture of the methyl 3-oxo-3-ferrocenylpropanoate (0.200 g, 0.70 mmol, 1.0 equiv) and isobutyraldehyde (0.061 g, 0.84 mmol, 1.2 equiv) in dry THF (3.0 mL) was added to the above solution dropwise and stirred at 0 °C for an additional 0.5 h. The mixture was then added by pyridine (0.4 mL) and warmed to room temperature. After being stirred for 24 h, the reaction was quenched by addition of water and extracted with ethyl acetate three times. The combined organic phase was washed with a saturated solution of sodium bicarbonate followed by brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate = 10:1) to afford **3a** as a red solid (0.195 g, 82%, E/Z = 7.4:2.6): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (d, J = 11.2 Hz, 0.74 H), 6.48 (d, J = 10.4 Hz, 0.26 H), 4.75 (t, J = 2.0 Hz, 0.52 H), 4.74 (t, J = 2.0 Hz, 1.48 H), 4.55 (t, J = 2.0 Hz, 2.00 H), 4.25 (s, 3.70 H), 4.22 (s, 1.30 H), 3.81 (s, 2.22 H), 3.80 (s, 0.78 H), 3.22−3.12 (m, 0.26 H), 2.62−2.52 (m, 0.74 H), 1.14 (d, J = 6.8 Hz, 1.56 H), 1.02 (d, J = 6.4 Hz, 4.44 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 198.0, 195.8, 166.0, 165.4, 153.9, 153.5, 132.9, 132.0, 79.9, 78.2, 72.6, 72.5, 70.6, 70.4, 70.2, 70.1, 52.0, 51.9, 29.1, 28.8, 22.2, 21.9; HRMS (ESI) calcd for $C_{18}H_{20}O_3{}^{56}FeNa$ $[M + Na]^+$ 363.0660, found 363.0660.

*Preparation of Compound **3b**.* The reaction of methyl 3-oxo-3-ferrocenylpropanoate (0.200 g, 0.70 mmol, 1.0 equiv) and 2-ethylbutanal (84 mg, 0.84 mmol, 1.2 equiv) by following typical procedure A afforded **3b** (0.165 g, 64%, E/Z = 6.0:4.0): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (d, J = 11.6 Hz, 0.6 H), 6.43 (d, J = 10.8 Hz, 0.4 H), 4.76 (t, J = 1.6 Hz, 0.8 H), 4.74 (t, J = 1.6 Hz, 1.2 H), 4.55 (t, J = 1.6 Hz, 0.8 H), 4.53 (t, J = 2.0 Hz, 1.2 H), 4.24 (s, 3.0 H), 4.22 (s, 2.0 H), 3.82 (s, 1.8 H), 3.79 (s, 1.2 H), 2.83−2.73 (m, 0.4 H), 2.18−2.09 (m, 0.6 H), 1.65−1.54 (m, 1.0 H), 1.50−1.25 (m, 3 H), 0.95 (t, J = 7.6 Hz, 2.40 H), 0.80 (t, J = 7.6 Hz, 3.60 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 198.4, 195.5, 166.4, 165.3, 152.0, 151.8, 135.8, 134.2, 80.1, 78.2, 72.6, 72.2, 70.6, 70.3, 70.2, 52.1, 51.8, 42.6, 42.1, 27.6, 26.8, 11.9, 11.4; HRMS (ESI) calcd for $C_{20}H_{24}O_3{}^{56}FeNa$ $[M + Na]^+$ 391.0973, found 391.0974.

*Preparation of Compound **3c**.* The reaction of methyl 3-oxo-3-ferrocenylpropanoate (0.200 g, 0.70 mmol, 1.0 equiv) and 2-methylbutanal (90 mg, 1.05 mmol, 1.5 equiv) by following typical procedure A afforded **3c** (0.174 g, 70%, E/Z = 7.0:3.0): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (d, J = 11.2 Hz, 0.70 H), 6.46 (d, J = 10.4 Hz, 0.30 H), 4.78−4.75 (m, 1.30 H), 4.72−4.71 (m, 0.70 H), 4.56−4.53 (m, 2.00 H), 4.25 (s, 3.50 H), 4.22 (s, 1.50 H), 3.81 (s, 2.10 H), 3.80 (s, 0.90 H), 2.99−2.92 (m, 0.30 H), 2.37−2.29 (m, 0.70 H), 1.52−1.43 (m, 0.60 H), 1.40−1.33 (m, 1.40 H), 1.12 (d, J = 6.8 Hz, 0.90 H), 1.00 (d, J = 6.8 Hz, 2.10 H), 0.97 (t, J = 7.2 Hz, 0.90 H), 0.82 (t, J = 7.6 Hz,

DOI: 10.1021/acs.joc.5b01511
J. Org. Chem. 2015, 80, 7865−7875

2.10 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 198.0, 195.6, 166.1, 165.3, 152.8, 152.7, 134.1, 133.0, 80.0, 78.3, 72.60, 72.55, 72.4, 72.3, 70.7, 70.5, 70.3, 70.1, 70.0, 52.0, 51.8, 35.7, 35.5, 29.6, 29.3, 19.8, 19.4, 11.8, 11.5; HRMS (ESI) calcd for $C_{19}H_{22}O_3{}^{56}FeNa$ $[M + Na]^+$ 377.0816, found 377.0817.

Preparation of Compound ***3d***. The reaction of methyl 3-oxo-3-ferrocenylpropanoate (0.200 g, 0.70 mmol, 1.0 equiv) and 2-phenylbutanal (0.124 g, 0.84 mmol, 1.2 equiv) by following typical procedure A afforded **3d** (0.172 g, 59%, *E*/*Z* = 6.7:3.3): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.28 (m, 2.00 H), 7.27−7.19 (m, 2.00 H), 7.16 (d, *J* = 11.6 Hz, 0.67 H), 7.07−7.05 (m, 1.00 H), 6.73 (d, *J* = 10.8 Hz, 0.33 H), 4.89−4.88 (m, 0.67 H), 4.69−4.68 (m, 0.33 H), 4.68−4.66 (m, 0.33 H), 4.60−4.58 (m, 0.66 H), 4.52 (t, *J* = 2.0 Hz, 0.67 H), 4.47−4.44 (m, 1.34 H), 4.21 (s, 3.35 H), 4.20−4.17 (m, 0.33 H), 4.13 (s, 1.65 H), 3.82 (s, 2.00 H), 3.81 (s, 1.00 H), 3.37 (dt, *J* = 11.2, 7.2 Hz, 0.67 H), 1.90−1.86 (m, 0.67 H), 1.77−1.70 (m, 1.34 H), 0.96 (t, *J* = 7.2 Hz, 1.00 H), 0.75 (t, *J* = 7.2 Hz, 2.00 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 197.8, 195.6, 165.9, 165.1, 150.1, 149.3, 142.2, 141.3, 133.8, 133.0, 128.8, 128.6, 127.6, 127.5, 126.8, 126.7, 79.7, 78.2, 72.7, 72.6, 72.2, 71.2, 70.51, 70.47, 70.4, 70.3, 70.2, 69.6, 52.1, 51.9, 47.2, 46.3, 29.4, 28.5, 12.0, 11.6; HRMS (ESI) calcd for $C_{24}H_{24}O_3{}^{56}FeNa$ $[M + Na]^+$ 439.0973, found 439.0972.

Preparation of Compound ***3e***. The reaction of methyl 3-oxo-3-ferrocenylpropanoate (0.200 g, 0.70 mmol, 1.0 equiv) and cyclopentanecarbaldehyde (83 mg, 0.84 mmol, 1.2 equiv) by following typical procedure A afforded **3e** (0.199 g, 78%, *E*/*Z* = 8.0:2.0): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (d, *J* = 11.2 Hz, 0.80 H), 6.61 (d, *J* = 10.4 Hz, 0.20 H), 4.75 (t, *J* = 2.0 Hz, 0.40 H), 4.73 (t, *J* = 2.0 Hz, 1.60 H), 4.55 (t, *J* = 2.0 Hz, 1.60 H), 4.54 (t, *J* = 2.0 Hz, 0.40 H), 4.24 (s, 4.00 H), 4.21(s, 1.00 H) 3.81 (s, 2.40 H), 3.79 (s, 0.60 H), 3.31−3.21 (m, 0.20 H), 2.69−2.58 (m, 0.80 H), 2.03−1.97 (m, 0.40 H), 1.83−1.75 (m, 2.00 H), 1.71−1.63 (m, 2.00 H), 1.54−1.49 (m, 1.60 H), 1.43−1.33 (m, 2.00 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 198.0, 195.8, 166.1, 165.3, 152.9, 152.5, 133.5, 132.2, 79.9, 78.3, 72.6, 72.5, 70.6, 70.3, 70.2, 70.1, 52.0, 51.8, 40.3, 39.9, 33.5, 33.2, 25.6; HRMS (ESI) calcd for $C_{20}H_{22}O_3{}^{56}FeNa$ $[M + Na]^+$ 389.0816, found 389.0815.

Preparation of Compound ***3f***. The reaction of methyl 3-oxo-3-ferrocenylpropanoate (0.500 g, 1.75 mmol, 1.0 equiv) and cyclohexanecarbaldehyde (0.236 g, 2.10 mmol, 1.2 equiv) by following typical procedure A afforded **3f** (0.440 g, 66%, *E*/*Z* = 7.3:2.7): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (d, *J* = 10.8 Hz, 0.73 H), 6.52 (d, *J* = 10.4 Hz, 0.27 H), 4.74−4.73 (t, *J* = 2.0 Hz, 2.00 H), 4.55−4.53 (t, *J* = 2.0 Hz, 2.00 H), 4.24 (s, 3.65 H), 4.21 (s, 1.35 H), 3.80 (s, 0.81 H), 3.79 (s, 2.19 H), 2.95−2.85 (m, 0.27 H), 2.34−2.23 (m, 0.73 H), 1.89−1.82 (m, 0.54 H), 1.80−1.75 (m, 0.54 H), 1.71−1.60 (m, 4.19 H), 1.43−1.32 (m, 0.54 H), 1.27−1.15 (m, 4.19 H); $^{13}C\{^{1}H\}$ NMR (400 MHz, $CDCl_3$) δ 198.0, 195.9, 166.0, 165.5, 152.6, 152.1, 133.1, 132.4, 80.0, 78.3, 72.6, 72.4, 70.6, 70.3, 70.07, 70.04, 52.0, 51.8, 38.7, 38.3, 32.1, 31.8, 25.7, 25.5, 25.2, 24.9; HRMS (ESI) calcd for $C_{21}H_{24}O_3{}^{56}FeNa$ $[M + Na]^+$ 403.0973, found 403.0970.

Preparation of Compound ***3g***. The reaction of methyl 3-oxo-3-ferrocenylpropanoate (0.200 g, 0.70 mmol, 1.0 equiv) and cycloheptanecarbaldehyde (0.132 g, 1.05 mmol, 1.5 equiv) by following typical procedure A afforded **3g** (0.131 g, 47%, *E*/*Z* = 7.3:2.7): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 (d, *J* = 11.2 Hz, 0.73 H), 6.59 (d, *J* = 10.4 Hz, 0.27 H), 4.74 (t, *J* = 2.0 Hz, 0.54 H), 4.72 (t, *J* = 2.0 Hz, 1.46 H), 4.54−4.53 (t, *J* = 2.0 Hz, 2.00 H), 4.24 (s, 3.65 H), 4.21 (s, 1.35 H), 3.788 (s, 0.81 H), 3.785 (s, 2.19 H), 3.08−2.98 (m, 0.27 H), 2.52−2.39 (m, 1.00 H), 1.89−1.83 (m, 0.54 H), 1.77−1.32 (m, 11.19 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 198.1, 196.0, 166.0, 165.6, 153.2, 152.6, 131.8, 130.9, 80.0, 78.3, 72.6, 72.4, 70.6, 70.3, 70.10, 70.06, 52.0, 51.8, 39.7, 39.5, 34.0, 33.5, 28.41, 28.37, 26.4, 26.0; HRMS (ESI) calcd for $C_{22}H_{26}O_3{}^{56}FeNa$ $[M + Na]^+$ 417.1129, found 417.1134.

Preparation of Compound ***3h***. The mixture of sodium hydride (60% in mineral oil, 0.224 g, 5.6 mmol, 2.8 equiv), diethyl carbonate (0.473 g, 4.0 mmol, 2.0 equiv), and toluene (2.0 mL) was heated to reflux. Acetylferrocene (0.456 g, 2.0 mmol, 1.0 equiv) in toluene was added dropwise to the mixture within 10 min. After additional reflux for 2 h, the solution was cooled to room temperature and quenched with acetic acid (1.0 mL), followed by addition of water. The mixture was extracted with ethyl acetate (30 mL × 3), and the combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate = 10:1) to afford ethyl 3-oxo-3-ferrocenylpropanoate as a red solid (0.368 g, 61%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.80 (t, *J* = 2.0 Hz, 2 H), 4.56 (t, *J* = 2.0 Hz, 2 H), 4.26 (s, 5 H), 4.24 (q, *J* = 7.2 Hz, 2 H), 3.74 (s, 2 H), 1.30 (t, *J* = 7.2 Hz, 3 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 195.9, 167.5, 78.2, 72.9, 70.0, 69.6, 61.2, 46.8, 14.1; HRMS (ESI) calcd for $C_{15}H_{16}O_3{}^{56}FeNa$ $[M + Na]^+$ 323.0347, found 323.0340.

The reaction of ethyl 3-oxo-3-ferrocenylpropanoate (0.210 g, 0.70 mmol, 1.0 equiv) and isobutyraldehyde (76 mg, 1.05 mmol, 1.5 equiv) by following typical procedure A afforded **3h** (0.100 g, 40%, *E*/*Z* = 7.4:2.6): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79 (d, *J* = 10.8 Hz, 0.74 H), 6.46 (d, *J* = 10.0 Hz, 0.26 H), 4.75 (t, *J* = 2.0 Hz, 0.52 H), 4.73 (d, *J* = 2.0 Hz, 1.48 H), 4.54 (t, *J* = 2.0 Hz, 2.00 H), 4.27 (q, *J* = 7.2 Hz, 2.00 H), 4.25 (s, 3.70 H), 4.22 (s, 1.30 H), 3.20−3.10 (m, 0.26 H), 2.67−2.54 (m, 0.74 H), 1.290 (t, *J* = 6.8 Hz, 0.78 H), 1.286 (t, *J* = 7.2 Hz, 2.22 H), 1.14 (d, *J* = 6.4 Hz, 1.56 H), 1.03 (d, *J* = 6.4 Hz, 4.44 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 198.1, 165.0, 153.5, 153.4, 133.4, 132.3, 80.0, 78.2, 72.6, 72.4, 70.6, 70.4, 70.10, 70.06, 61.2, 61.0, 29.1, 28.8, 22.2, 22.0, 14.2, 14.1; HRMS (ESI) calcd for $C_{19}H_{22}O_3{}^{56}FeNa$ $[M + Na]^+$ 377.0816, found 377.0811.

Preparation the Compound ***3i***. A mixture of *l*-menthol (0.328 g, 0.21 mmol, 3.0 equiv) and methyl 3-oxo-3-ferrocenylpropanoate (0.200 g, 0.70 mmol, 1.0 equiv) was refluxed in toluene under N_2 atmosphere until the total consumption of methyl 3-oxo-3-ferrocenylpropanoate by TLC. The product menthyl 3-oxo-3-ferrocenylpropanoate was obtained by chromatography (hexane/ethyl acetate = 10:1) as a red solid (0.278 g, 97%), the excess *l*-menthol was removed by sublimation at 90 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.80−4.78 (m, 2 H), 4.75 (dd, *J* = 10.8, 4.4 Hz, 1 H), 4.55 (t, *J* = 1.6 Hz, 2 H), 4.27 (s, 5 H), 3.76 (d, *J* = 15.2 Hz, 1 H), 3.71 (d, *J* = 14.8 Hz, 1 H), 2.10−2.07 (m, 1 H), 1.94−1.86 (m, 1 H), 1.69−1.64 (m, 2 H), 1.53−1.45 (m, 1 H), 1.41−1.36 (m, 1 H), 1.10−1.04 (m, 1 H), 1.00 (t, *J* = 11.2 Hz, 1 H), 0.91 (d, *J* = 6.4 Hz, 3 H), 0.87 (d, *J* = 6.8 Hz, 3 H), 0.86−0.83 (m, 1 H), 0.77 (d, *J* = 7.2 Hz, 3 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 196.0, 167.2, 78.2, 75.3, 72.82, 72.80, 70.0, 69.6, 69.5, 47.1, 46.9, 40.7, 34.1, 31.3, 26.0, 23.2, 21.9, 20.7, 16.1; HRMS (ESI) calcd for $C_{23}H_{30}O_3{}^{56}FeNa$ $[M + Na]^+$ 433.1442, found 433.1450.

Typical Procedure B.[11a] The mixture of menthyl 3-oxo-3-ferrocenylpropanoate (0.228 g, 0.56 mmol, 1.0 equiv), isobutyraldehyde (62 mg, 0.85 mmol, 1.5 equiv), piperidine (53 μL, 0.56 mmol, 1.0 equiv), AcOH (5.4 μL, 0.29 mmol, 0.5 equiv), and 4 Å MS (0.6 g) in benzene (6 mL) was refluxed for 48 h under N_2. The mixture was allowed to reach room temperature, ethyl acetate was added, and the mixture was filtered through Celite. The solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate = 10:1) to afford **3i** as a red solid (0.148 g, 57%, *E*/*Z* = 7.0:3.0): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.74 (d, *J* = 10.8 Hz, 0.70 H), 6.43 (d, *J* = 10.0 Hz, 0.30 H), 4.84−4.80 (m, 0.30 H), 4.81−4.80 (m, 0.70 H), 4.79−4.78 (m, 0.30 H), 4.76−4.75 (m, 0.30 H), 4.72 (td, *J* = 10.8, 4.4 Hz, 0.70 H), 4.63−4.62 (m, 0.70 H), 4.54−4.52 (m, 1.30 H), 4.50−4.49 (m, 0.70 H), 4.25 (m, 3.50 H), 4.21 (m, 1.50 H), 3.16−3.07 (m, 0.30 H), 2.73−2.64 (m, 0.70 H), 2.12−2.07 (m, 0.30 H), 2.06−2.00 (m, 0.70 H), 1.90−1.84 (m, 0.30 H), 1.82 (dd, *J* = 8.0, 1.2 Hz, 0.30 H), 1.71−1.60 (m, 3.50 H), 1.52−1.44 (m, 1.00 H), 1.36−1.28 (m, 1.00 H), 1.14 (d, *J* = 6.4 Hz, 1.80 H), 1.08 (d, *J* = 2.8 Hz, 2.10 H), 1.06 (d, *J* = 2.8 Hz, 2.10 H), 1.03−0.93 (m, 1.90 H), 0.90 (d, *J* = 6.8 Hz, 0.90 H), 0.88 (d, *J* = 6.4 Hz, 2.10 H), 0.83 (d, *J* = 6.8 Hz, 0.90 H), 0.80 (d, *J* = 7.2 Hz, 2.10 H), 0.75 (d, *J* = 6.8 Hz, 0.90 H), 0.70 (d, *J* = 6.8 Hz, 2.10 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 198.1, 195.8, 165.3, 164.6, 152.7, 152.6, 134.1, 132.9, 80.2, 78.2, 75.2, 72.39, 72.36, 72.1, 71.8, 70.69, 70.67, 70.3, 70.0, 69.93, 69.89, 46.83, 46.78, 40.65, 40.63, 34.1, 31.4, 31.3, 29.1, 28.7, 25.7, 25.6, 23.1, 23.0, 22.21, 22.16, 22.1, 22.0, 21.9, 20.7, 16.1, 15.9; HRMS (ESI) calcd for $C_{27}H_{36}O_3{}^{56}FeNa$ $[M + Na]^+$ 487.1912, found 487.1905.

DOI: 10.1021/acs.joc.5b01511
J. Org. Chem. 2015, 80, 7865−7875

Preparation the Compound ***3j.*** The reaction of methyl 3-oxo-3-ferrocenylpropanoate (0.100 g, 0.35 mmol, 1.0 equiv) and 3-methylbutanal (36 mg, 0.42 mmol, 1.2 equiv) by following typical procedure A afforded **3j** (0.074 g, 60%, *E*/*Z* = 7.7:2.3): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (t, *J* = 7.6 Hz, 0.23 H), 6.72 (t, *J* = 7.6 Hz, 0.77 H), 4.76 (t, *J* = 2.0 Hz, 1.54 H), 4.72 (t, *J* = 2.0 Hz, 0.46 H), 4.56−4.53 (m, 2.00 H), 4.24 (s, 1.15 H), 4.22 (s, 3.85 H), 3.81 (s, 0.69 H), 3.79 (s, 2.31 H), 2.45 (t, *J* = 7.2 Hz, 1.54 H), 2.06 (t, *J* = 7.2 Hz, 0.46 H), 1.91−1.82 (m, 0.77 H), 1.80−1.70 (m, 0.23 H), 1.01 (d, *J* = 6.8 Hz, 4.62 H), 0.89 (d, *J* = 6.4 Hz, 1.38 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 198.0, 195.7, 166.0, 165.2, 146.9, 146.8, 135.9, 134.7, 79.8, 78.2, 72.6, 72.5, 70.5, 70.3, 70.2, 70.0, 52.0, 51.8, 38.6, 38.2, 28.5, 28.3, 22.5, 22.4; HRMS (ESI) calcd for $C_{19}H_{22}O_3{}^{56}FeNa$ [M + Na]$^+$ 377.0816, found 377.0816.

Preparation of Compound ***3k.*** A solution of 2-methylpropan-2-ol (92 μL, 1.0 mmol, 1.0 equiv) in dichloromethane (3 mL) was added to the mixture of acetylferrocene (0.228 g, 1.0 mmol, 1.0 equiv) and $AlCl_3$ (0.267 g, 2.0 mmol, 2.0 equiv) in dichloromethane (5 mL) at 0 °C within 30 min. After being stirred for 12 h, the reaction was quenched by addition of crushed ice and extracted with dichloromethane (30 mL × 3). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate = 40:1) to afford the 1-acetyl-1′-*tert*-butylferrocene as a red solid (60 mg, 21%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.75 (t, *J* = 2.0 Hz, 2 H), 4.50 (t, *J* = 2.0 Hz, 2 H), 4.12 (t, *J* = 2.0 Hz, 2 H), 4.05 (t, *J* = 2.0 Hz, 2 H), 2.38 (s, 3 H), 1.20 (s, 9 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 202.0, 103.9, 79.1, 72.7, 69.7, 69.1, 66.6, 31.3, 30.2, 27.4; HRMS (ESI) calcd for $C_{16}H_{21}O^{56}Fe$ [M + H]$^+$ 285.0942, found 285.0934.

The mixture of sodium hydride (60% in mineral oil, 24.0 mg, 0.59 mmol, 2.8 equiv), dimethyl carbonate (38.0 mg, 0.42 mmol, 2.0 equiv), and toluene (0.4 mL) was heated to reflux. 1-Acetyl-1′-*tert*-butylferrocene (60 mg, 0.21 mmol, 1.0 equiv) in toluene was added dropwise to the mixture within 10 min. After additional reflux for 2 h, the solution was cooled to room temperature and quenched with acetic acid (0.1 mL), followed by the addition of water. The mixture was extracted with ethyl acetate (5 mL × 3), and the combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate = 5:1) to afford methyl 3-oxo-3-(1′-*tert*-butyl)ferrocenylpropanoate as a red solid (48.0 mg, 67%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.77 (t, *J* = 2.0 Hz, 2 H), 4.56 (t, *J* = 1.6 Hz, 2 H), 4.19 (t, *J* = 2.0 Hz, 2 H), 4.10 (t, *J* = 2.0 Hz, 2 H), 3.78 (s, 3 H), 3.74 (s, 2 H), 1.20 (s, 9 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 196.5, 195.7, 168.01, 167.97, 107.3, 104.4, 78.0, 73.4, 70.3, 70.2, 69.8, 69.3, 68.8, 66.8, 66.5, 52.3, 46.6, 46.5, 31.3, 31.2, 30.7, 30.3; HRMS (ESI) calcd for $C_{18}H_{22}O_3{}^{56}FeNa$ [M + Na]$^+$ 365.0816, found 365.0816.

The reaction of methyl 3-oxo-3-(1′-*tert*-butyl)ferrocenylpropanoate (0.176 g, 0.52 mmol, 1.0 equiv) and isobutyraldehyde (56 mg, 0.77 mmol, 1.5 equiv) by following typical procedure A afforded **3k** (0.110 g, 53%, *E*/*Z* = 7.0:3.0): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (d, *J* = 10.8 Hz, 0.70 H), 6.47 (d, *J* = 10.4 Hz, 0.30 H), 4.72 (t, *J* = 2.0 Hz, 0.60 H), 4.71 (t, *J* = 2.0 Hz, 1.40 H), 4.55−4.53 (m, 2.00 H), 4.20 (t, *J* = 2.0 Hz, 1.40 H), 4.15 (t, *J* = 2.0 Hz, 0.60 H), 4.08 (t, *J* = 2.0 Hz, 1.40 H), 4.04 (t, *J* = 2.0 Hz, 0.60 H), 3.81 (s, 2.10 H), 3.79 (s, 0.90 H), 3.21−3.12 (m, 0.30 H), 2.61−2.52 (m, 0.70 H), 1.194 (s, 6.30 H), 1.189 (s, 2.70 H), 1.13 (d, *J* = 6.4 Hz, 1.80 H), 1.01 (d, *J* = 6.8 Hz, 4.20 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.8, 195.6, 165.4, 153.9, 153.6, 133.0, 132.0, 104.2, 104.1, 79.7, 73.1, 73.0, 70.8, 70.2, 69.9, 69.6, 67.1, 66.9, 52.0, 51.8, 31.3, 30.3, 29.1, 28.8, 22.2, 22.0; HRMS (ESI) calcd for $C_{22}H_{28}O_3{}^{56}FeNa$ [M + Na]$^+$ 419.1286, found 419.1284.

Preparation of Compound ***3l.*** A solution of benzoyl chloride (0.553 g, 3.95 mmol, 1.5 equiv) in CH_2Cl_2 (5 mL) was added to a mixture of acetylferrocene (0.600 g, 2.63 mmol, 1.0 equiv) and $AlCl_3$ (0.701 g, 5.26 mmol, 2.0 equiv) in CH_2Cl_2 (20 mL) at 0 °C. After being stirred for additional 3 h at room temperature, the reaction was quenched by the addition of crushed ice and extracted with CH_2Cl_2 (30 mL × 3). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The resulting mixture was purified by column chromatography on silica gel (hexanes/ethyl acetate = 10:1) to afford 1-acetyl-1′-benzoylferrocene as red solid (0.366 g, 42%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.2 Hz, 2 H), 7.58 (t, *J* = 7.2 Hz, 1 H), 7.49 (t, *J* = 7.6 Hz, 2 H), 4.92 (t, *J* = 1.6 Hz, 2 H), 4.75 (t, *J* = 1.6 Hz, 2 H), 4.58 (t, *J* = 1.6 Hz, 2 H), 4.50 (t, *J* = 1.6 Hz, 2 H), 2.29 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 201.4, 197.9, 139.1, 132.0, 128.4, 128.1, 80.6, 79.5, 74.1, 73.9, 72.9, 71.3, 27.5; HRMS (ESI) calcd for $C_{19}H_{16}O_2{}^{56}FeNa$ [M + Na]$^+$ 355.0397, found 355.0390.

The mixture of sodium hydride (60% in mineral oil, 0.112 g, 2.8 mmol, 2.8 equiv), dimethyl carbonate (0.178 g, 1.98 mmol, 2.0 equiv), and toluene (1.0 mL) was heated to reflux. 1-Acetyl-1′-benzoylferrocene (0.328 g, 0.99 mmol, 1.0 equiv) in toluene was added dropwise to the mixture within 10 min. After additional reflux for 2 h, the solution was cooled to room temperature and quenched with acetic acid (0.5 mL) followed by the addition of water. The mixture was extracted with ethyl acetate (30 mL × 3), and the combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate = 10:1) to afford methyl 3-oxo-3-(1′-benzoyl)-ferrocenylpropanoate as a red solid (0.159 g, 41%): ^{1}H NMR (400 MHz, $CDCl_3$) selected peaks for keto: δ 7.84 (d, *J* = 7.2 Hz, 2 H), 7.58 (t, *J* = 7.2 Hz, 1 H), 7.48 (t, *J* = 7.2 Hz, 2 H), 4.96 (t, *J* = 1.6 Hz, 2 H), 4.75 (t, *J* = 2.0 Hz, 2 H), 4.64 (t, *J* = 1.6 Hz, 2 H), 4.55 (t, *J* = 1.6 Hz, 2 H), 3.74 (s, 3 H), 3.67 (s, 2 H); ^{13}C{^{1}H} NMR (100 MHz, CDCl3) δ 197.8, 195.3, 167.6, 138.9, 132.1, 128.4, 128.1, 79.7, 79.5, 74.6, 74.5, 74.0, 73.0, 72.9, 72.7, 71.3, 69.0, 52.3, 46.4; HRMS (ESI) calcd for $C_{21}H_{18}O_4{}^{56}FeNa$ [M + Na]$^+$ 413.0452, found 413.0451.

The reaction of methyl 3-oxo-3-(1′-benzoyl)ferrocenylpropanoate (50 mg, 0.128 mmol, 1.0 equiv), isobutyraldehyde (14 mg, 0.190 mmol, 1.5 equiv), piperidine (13.3 μL, 0.145 mmol, 1.1 equiv), AcOH (1.2 μL, 0.067 mmol, 0.5 equiv), and 4 Å MS (0.2 g) by following typical procedure B afforded **3l** (42.9 mg, 76%, *E*/*Z* = 3.0:1.0): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87−7.84 (m, 2.00 H), 7.60−7.56 (m, 1.00 H), 7.51−7.47 (m, 2.00 H), 6.81 (d, *J* = 11.2 Hz, 0.75 H), 6.42 (d, *J* = 10.0 Hz, 0.25 H), 4.96 (t, *J* = 2.0 Hz, 1.50 H), 4.95 (t, *J* = 2.0 Hz, 0.50 H), 4.76−4.74 (m, 2.00 H), 4.68−4.67 (m, 1.50 H), 4.61 (t, *J* = 2.0 Hz, 0.50 H), 4.54 (t, *J* = 2.0 Hz, 2.00 H), 3.79 (s, 2.25 H), 3.77 (s, 0.75 H), 3.16−3.10 (m, 0.25 H), 2.50−2.44 (m, 0.75 H), 1.11 (d, *J* = 6.4 Hz, 1.50 H), 0.99 (d, *J* = 6.4 Hz, 4.50 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 198.1, 197.1, 165.7, 165.0, 154.8, 154.0, 139.1, 132.6, 132.0, 131.9, 131.6, 128.4, 128.3, 128.2, 128.1, 80.9, 79.4, 74.9, 74.8, 73.0, 72.9, 72.1, 71.5, 52.1, 51.9, 29.2, 28.8, 22.1, 21.9; HRMS (ESI) calcd for $C_{25}H_{24}O_4{}^{56}FeNa$ [M + Na]$^+$ 467.0922, found 467.0926.

Preparation of Compound ***3m.*** A solution of acetyl chloride (0.204 g, 2.60 mmol, 1.5 equiv) in CH_2Cl_2 (10 mL) was added to a solution of *N*,*N*-dimethylferrocenecarboxamide (0.455 g, 1.73 mmol, 1.0 equiv) and $AlCl_3$ (0.691 g, 5.20 mmol, 3.0 equiv) in CH_2Cl_2 (20 mL) at 0 °C. After additional stirring for 1 h at room temperature, the reaction was quenched by the addition of crushed ice and extracted with CH_2Cl_2 (30 mL × 3). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The resulting mixture was purified by column chromatography on silica gel (hexanes/ethyl acetate = 1:1) to afford 1′-acetyl-*N*,*N*-dimethylferrocenecarboxamide (0.466 g, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.81 (t, *J* = 2.0 Hz, 2 H), 4.62 (t, *J* = 2.0 Hz, 2 H), 4.57 (t, *J* = 2.0 Hz, 2 H), 4.32 (t, *J* = 2.0 Hz, 2 H), 3.06 (bs, 6 H), 2.42 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 202.1, 169.2, 80.7, 80.1, 73.9, 71.9, 71.3, 70.6, 38.9, 36.2, 27.6; HRMS (EI) calcd for $C_{15}H_{17}NO_2{}^{56}Fe$ [M]$^+$ 299.0609, found 299.0585.

The mixture of sodium hydride (60% in mineral oil, 0.112 g, 2.8 mmol, 2.8 equiv), dimethyl carbonate (0.180 g, 2.0 mmol, 2.0 equiv), and toluene (1.0 mL) was heated to reflux. 1′-Acetyl-*N*,*N*-dimethylferrocenecarboxamide (0.300 g, 1.0 mmol, 1.0 equiv) in toluene was added dropwise to the mixture within 10 min. After additional reflux for 2 h, the solution was cooled to room temperature and quenched with acetic acid (0.5 mL), followed by the addition of water. The mixture was extracted with ethyl acetate (30 mL × 3). The

DOI: 10.1021/acs.joc.5b01511
J. Org. Chem. 2015, 80, 7865−7875

combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate = 1:1) to afford methyl 3-oxo-3-(1′-*N*,*N*-dimethycarboxyl)ferrocenylpropanoate as a red solid (0.283 g, 80%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.80 (t, J = 2.0 Hz, 2 H), 4.64 (t, J = 2.0 Hz, 2 H), 4.61 (t, J = 2.0 Hz, 2 H), 4.35 (t, J = 2.0 Hz, 2 H), 3.89 (s, 2 H), 3.75 (s, 3 H), 3.03 (bs, 6 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 196.3, 169.2, 168.2, 81.6, 79.2, 74.4, 72.1, 71.7, 70.6, 52.2, 46.6, 39.0, 36.2; HRMS (EI) calcd for $C_{17}H_{19}NO_4{}^{56}Fe$ [M]$^+$ 357.0664, found 357.0653.

The reaction of 3-oxo-3-(1′-*N*,*N*-dimethycarboxyl)-ferrocenylpropanoate (0.350 g, 0.98 mmol, 1.0 equiv) and isobutyraldehyde (0.106 g, 1.47 mmol, 1.5 equiv), piperidine (98 μL, 1.08 mmol, 1.1 equiv), AcOH (9.1 μL, 0.49 mmol, 0.5 equiv), and 4 Å MS (1.0 g) by following typical procedure B afforded **3m** (0.220 g, 55%, E/Z = 7.7:2.3): ^{1}H NMR (400 MHz, $CDCl_3$) selected peaks for the major isomer δ 6.82 (d, J = 11.2 Hz, 0.77 H), 6.48 (d, J = 10.4 Hz, 0.23 H), 4.79−4.78 (m, 2.00 H), 4.67−4.64 (m, 4.00 H), 4.41 (t, J = 2.0 Hz, 1.54 H), 4.35 (t, J = 2.0 Hz, 0.46 H), 3.81 (s, 3.00 H), 3.06 (m, 0.23 H), 3.06 (bs, 6.00 H), 2.55−2.46 (m, 0.77 H), 1.13 (d, J = 6.8 Hz, 1.38 H), 1.09 (d, J = 6.8 Hz, 4.62 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.7, 195.3, 169.2, 166.0, 165.1, 154.1, 153.5, 132.8, 131.8, 81.1, 80.4, 75.2, 75.1, 72.1, 72.03, 71.93, 71.7, 71.5, 71.4, 52.0, 51.9, 38.9, 36.2, 29.1, 28.9, 22.1, 21.8; HRMS (ESI) calcd for $C_{21}H_{25}NO_4{}^{56}FeNa$ [M + Na]$^+$ 434.1031, found 434.1037.

Preparation of Compound ***3n***. The mixture of sodium hydride (60% in mineral oil, 0.112 g, 2.8 mmol, 2.8 equiv), dimethyl carbonate (0.180 g, 2.0 mmol, 2.0 equiv), and toluene (1.0 mL) was heated to reflux. Acetylruthenocene (0.280 g, 1.0 mmol, 1.0 equiv) in toluene was added dropwise to the mixture within 10 min. After additional reflux for 2 h, the solution was cooled to room temperature and quenched with acetic acid (0.5 mL), followed by the addition of water. The mixture was extracted with ethyl acetate (30 mL × 3). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate = 5:1) to afford methyl 3-oxo-3-ruthenocenylpropanoate (0.308 g, 93%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.10 (t, J = 2.0 Hz, 2 H), 4.82 (t, J = 2.0 Hz, 2 H), 4.63 (s, 5 H), 3.76 (s, 3 H), 3.64 (s, 2 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.5, 167.9, 83.1, 74.1, 72.3, 70.9, 52.3, 45.8; HRMS (ESI) calcd for $C_{14}H_{14}O_3{}^{102}RuNa$ [M + Na]$^+$ 354.9884, found 354.9886.

The reaction of methyl 3-oxo-3-ruthenocenylpropanoate (0.232 g, 0.70 mmol, 1.0 equiv) and isobutyraldehyde (76 mg, 0.84 mmol, 1.5 equiv) by following typical procedure A afforded **3n** (0.206 g, 76%, E/Z = 7.9:2.1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.76 (d, J = 10.8 Hz, 0.79 H), 6.55 (d, J = 10.4 Hz, 0.21 H), 5.03 (t, J = 2.0 Hz, 2.00 H), 4.81 (t, J = 1.6 Hz, 0.42 H), 4.79 (t, J = 1.6 Hz, 1.58 H), 4.60 (s, 3.95 H), 4.58 (s, 1.05 H), 3.78 (s, 0.63 H), 3.76 (s, 2.37 H), 3.19−3.10 (m, 0.21 H), 2.70−2.58 (m, 0.79 H), 1.11 (d, J = 6.4 Hz, 1.26 H), 1.06 (d, J = 6.4 Hz, 4.74 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.5, 194.4, 165.7, 165.3, 154.1, 153.1, 132.2, 131.7, 84.6, 82.8, 73.9, 73.6, 72.5, 72.3, 72.1, 71.4, 52.0, 51.8, 29.4, 28.6, 22.2, 22.1; HRMS (ESI) calcd for $C_{18}H_{20}O_3{}^{102}RuNa$ [M + Na]$^+$ 409.0354, found 409.0355.

Preparation of Compound ***3o***. The reaction of methyl 3-oxo-3-ruthenocenylpropanoate (0.232 g, 0.70 mmol, 1.0 equiv) and cyclopentanecarbaldehyde (82 mg, 0.84 mmol, 1.2 equiv) by following typical procedure A afforded **3o** (0.176 g, 61%, E/Z = 8.2:1.8): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (d, J = 11.2 Hz, 0.82 H), 6.68 (d, J = 10.0 Hz, 0.18 H), 5.04−5.02 (m, 2.00 H), 4.81−4.79 (m, 2.00 H), 4.59 (s, 4.10 H), 4.58 (s, 0.90 H), 3.773 (s, 0.54 H), 3.769 (s, 2.46 H), 3.29−3.18 (m, 0.18 H), 2.74−2.63 (m, 0.82 H), 2.01−1.95 (m, 0.54 H), 1.87−1.80 (m, 1.84 H), 1.76−1.53 (m, 3.16 H), 1.45−1.31 (m, 2.46 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.5, 194.3, 165.8, 165.3, 153.0, 152.0, 132.8, 132.0, 84.6, 82.8, 73.9, 73.6, 72.5, 72.3, 72.1, 71.4, 52.0, 51.8, 40.5, 39.8, 33.5, 33.4, 25.6; HRMS (ESI) calcd for $C_{20}H_{22}O_3{}^{102}RuNa$ [M + Na]$^+$ 435.0510, found 435.0518.

Preparation of Compound ***3p***. The reaction of methyl 3-oxo-3-ruthenocenylpropanoate (0.186 g, 0.56 mmol, 1.0 equiv) and cyclohexanecarbaldehyde (94 mg, 0.84 mmol, 1.5 equiv) by following typical procedure A afforded **3p** (0.166 g, 70%, E/Z = 5.6:4.4): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78 (d, J = 11.2 Hz, 0.56 H), 6.58 (d, J = 10.4 Hz, 0.44 H), 5.02 (t, J = 2.0 Hz, 2.00 H), 4.80 (t, J = 2.0 Hz, 0.88 H), 4.79 (t, J = 2.0 Hz, 1.12 H), 4.59 (s, 2.80 H), 4.58 (s, 2.20 H), 3.77 (s, 1.32 H), 3.75 (s, 1.68 H), 2.92−2.82 (m, 0.44 H), 2.36−2.26 (m, 0.56 H), 1.83−1.63 (m, 5.00 H), 1.40−1.31 (m, 1.00 H), 1.26−1.10 (m, 4.00 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.4, 194.5, 165.6, 165.4, 152.8, 151.8, 132.3, 132.0, 84.6, 82.7, 73.8, 73.5, 72.5, 72.2, 72.0, 71.3, 51.9, 51.7, 38.7, 38.1, 32.1, 31.8, 25.6, 25.5, 25.2, 25.0; HRMS (ESI) calcd for $C_{21}H_{24}O_3{}^{102}RuNa$ [M + Na]$^+$ 449.0667, found 449.0677.

Preparation of Compound ***3q***. The reaction of methyl 3-oxo-3-ferrocenylpropanoate (0.200 g, 0.70 mmol, 1.0 equiv) and 4-methoxybenzaldehyde (0.114 g, 0.84 mmol, 1.5 equiv) by following typical procedure A afforded **3q** (0.240 g, 85%, E/Z = 10.0:1.0): ^{1}H NMR (400 MHz, $CDCl_3$) major isomer: δ 7.85 (s, 1 H), 7.36 (d, J = 8.8 Hz, 2 H), 6.75 (d, J = 8.8 Hz, 2 H), 4.64 (t, J = 2.0 Hz, 2 H), 4.44 (t, J = 2.0 Hz, 2 H), 4.15 (s, 5 H), 3.88 (s, 3 H), 3.75 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 199.4, 165.8, 161.2, 142.2, 140.1, 132.4, 131.5, 129.7, 125.9, 114.2, 114.0, 79.5, 72.9, 72.5, 70.8, 70.5, 70.2, 70.1, 69.7, 55.4, 55.2, 52.3, 52.2; HRMS (APCI) calcd for $C_{22}H_{20}O_4{}^{56}FeNa$ [M + Na]$^+$ 427.0609, found 427.0616.

BF_3·OEt_2-Promoted Cyclization of Metallocenyl Enones. *Preparation of Compound* ***4a***. BF_3·OEt_2 (26.0 μL, 0.21 mmol, 3.0 equiv) was added to the solution of **3a** (24.1 mg, 0.071 mmol, 1.0 equiv) in toluene (0.7 mL), and then the reaction was warmed to 80 °C. After being stirred for 4 h, the reaction was quenched with aqueous sodium bicarbonate and extracted with ethyl acetate (10 mL × 3). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate = 10:1) to afford **4a** as a red solid (21.1 mg, 88%). Compound **4a′** (7.5 mg, 4%) could be isolated by column chromatography on silica gel when the reaction was conducted at the scale of 0.204 g (0.60 mmol) of **3a**. **4a**: ^{1}H NMR (400 MHz, $CDCl_3$) selected peaks for keto: δ 4.89 (dd, J = 2.8, 1.6 Hz, 1 H), 4.56 (t, J = 2.4 Hz, 1 H), 4.41 (dd, J = 2.4, 1.2 Hz, 1 H), 4.31 (s, 5 H), 3.84 (s, 3 H), 3.42 (dd, J = 13.2, 5.2 Hz, 1 H), 2.73 (t, J = 13.2 Hz, 1 H), 1.97 (dd, J = 13.2, 5.2 Hz, 1 H), 1.48 (s, 3 H), 1.14 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 198.5, 171.9, 103.3, 72.6, 71.1, 70.5, 69.9, 68.1, 65.8, 52.8, 52.3, 41.9, 30.2, 29.4, 28.8; HRMS (ESI) calcd for $C_{18}H_{20}O_3{}^{56}FeNa$ [M + Na]$^+$ 363.0660, found 363.0660. **4a′**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.09 (t, J = 2.0 Hz, 2 H), 4.34 (t, J = 2.0 Hz, 2 H), 4.16 (s, 5 H), 3.71 (s, 3 H), 2.78 (s, 2 H), 1.46 (s, 6 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.2., 166.0, 98.8, 84.4, 72.6, 70.5, 70.0, 69.7, 50.7, 44.4, 28.3; HRMS (ESI) calcd for $C_{18}H_{20}O_3{}^{56}FeNa$ [M + Na]$^+$ 363.0660, found 363.0659.

Preparation of Compound ***5a***. The mixture of **4a** (18.1 mg, 0.053 mmol, 1.0 equiv) and KOH (12.3 mg in 0.20 mL H_2O, 0.22 mmol, 4.0 equiv) in EtOH (1.0 mL) were refluxed under N_2 for 4 h. After being cooled to room temperature, the mixture was quenched by the addition of HCl (1.0 M) and extracted with ethyl acetate (10 mL × 3). The combined organic layer was washed with brine and dried over Na_2SO_4. After filtration, the solvent was removed. The residue was purified by chromatography on silica gel (hexane/ethyl acetate = 10:1) to obtain **5a** as a red solid (14.0 mg, 93%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.86 (dd, J = 2.4, 1.2 Hz, 1 H), 4.50 (t, J = 2.4 Hz, 1 H), 4.38 (dd, J = 2.4, 1.2 Hz, 1 H), 4.21 (s, 5 H), 2.60−2.50 (m, 1 H), 2.44−2.30 (m, 2 H), 1.83−1.74 (m, 1 H), 1.46 (s, 3 H), 1.12 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 204.6, 103.8, 73.6, 70.5, 70.1, 67.7, 65.3, 38.2, 36.1, 30.2, 29.1, 28.9; HRMS (ESI) calcd for $C_{16}H_{19}O{}^{56}Fe$ [M + H]$^+$ 283.0785, found 283.0776.

Preparation of Compound ***4b***. The reaction of **3b** (25.8 mg, 0.07 mmol, 1.0 equiv) and BF_3·OEt_2 (26.0 μL, 0.21 mmol, 3.0 equiv) afforded **4b** (17.3 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) (keto) δ 4.89 (dd, J = 2.4, 1.2 Hz, 1 H), 4.58 (t, J = 2.4 Hz, 1 H), 4.44 (dd, J = 2.4, 1.2 Hz, 1 H), 4.31 (s, 5 H), 3.84 (s, 3 H), 3.41 (dd, J = 13.2, 5.2 Hz, 1 H), 2.57 (t, J = 13.2 Hz, 1 H), 2.18 (dd, J = 12.8, 5.2 Hz, 1 H), 1.84−1.74 (m, 2 H), 1.32−1.25 (m, 2 H), 0.99 (t, J = 7.6 Hz, 3 H), 0.66 (t, J = 7.2 Hz, 3 H), (enol) 12.4 (brs, 0.58 H), 4.68 (dd, J = 2.4, 1.2 Hz, 0.58 H), 4.35 (t, J = 2.4 Hz, 0.58 H), 4.19 (dd, J = 2.4, 1.2 Hz,

DOI: 10.1021/acs.joc.5b01511
J. Org. Chem. 2015, 80, 7865−7875

0.58 H), 4.17 (s, 2.90 H), 3.79 (s, 1.74 H), 2.65 (d, J = 15.2 Hz, 0.58 H), 2.36 (d, J = 15.2 Hz, 0.58 H), 2.00−1.92 (m, 1.16 H), 1.64−1.55 (m, 1.16 H), 1.02 (t, J = 7.6 Hz, 1.74 H), 0.53 (t, J = 7.6 Hz, 1.74 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.4, 172.3, 102.1, 72.7, 71.4, 70.9, 70.6, 70.0, 69.9, 65.7, 52.3, 51.9, 38.8, 35.5, 28.8, 28.6, 8.1, 7.6; HRMS (ESI) calcd for $C_{20}H_{24}O_3{}^{56}FeNa$ $[M + Na]^+$ 391.0973, found 391.0974.

Preparation of Compound ***4c***. The reaction of **3c** (24.8 mg, 0.07 mmol, 1.0 equiv) and $BF_3{\cdot}OEt_2$ (26.0 μL, 0.21 mmol, 3.0 equiv) afforded **4c** (21.8 mg, 88%, dr = 3:1). The following data refer to the keto-isomers: ^1H NMR (400 MHz, $CDCl_3$) δ (major isomer) 4.90 (dd, J = 2.4, 1.2 Hz, 1 H), 4.55 (t, J = 2.4 Hz, 1 H), 4.41−4.40 (m, 1 H), 4.30 (s, 5 H), 3.84 (s, 3 H), 3.37 (dd, J = 13.2, 5.2 Hz, 1 H), 2.52 (t, J = 13.2 Hz, 1 H), 2.11 (dd, J = 13.2, 5.6 Hz, 1 H), 2.04−1.95 (m, 1 H), 1.90−1.81 (m, 1 H), 1.08 (s, 3 H), 1.05 (t, J = 7.6 Hz, 3 H), (minor isomer) 4.88 (dd, J = 2.8, 1.2 Hz, 0.35 H), 4.56 (t, J = 2.8 Hz, 0.35 H), 4.41−4.40 (m, 0.35 H), 4.32 (s, 1.75 H), 3.83 (s, 1.05 H), 3.39 (dd, J = 13.2, 5.2 Hz, 0.35 H), 2.69 (t, J = 13.2 Hz, 0.35 H), 2.06 (dd, J = 13.6, 5.6 Hz, 0.35 H), 1.46−1.33 (m, 0.70 H), 1.39 (s, 1.05 H), 0.80 (t, J = 7.2 Hz, 1.05 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.6, 198.4, 172.1, 172.0, 104.4, 102.6, 72.5, 71.2, 71.0, 70.5, 69.9, 69.3, 68.0, 65.72, 65.69, 52.5, 52.3, 52.2, 40.0, 38.3, 33.8, 33.6, 33.2, 32.5, 25.5, 24.6, 9.1, 8.1; HRMS (ESI) calcd for $C_{19}H_{22}O_3{}^{56}FeNa$ $[M + Na]^+$ 377.0816, found 377.0808.

Preparation of Compound ***5d***. $BF_3{\cdot}OEt_2$ (26.0 μL, 0.21 mmol, 3.0 equiv) was added to the solution of **3d** (29.1 mg, 0.070 mmol, 1.0 equiv) in toluene (0.7 mL), and then the reaction was warmed up to 80 °C. After being stirred for 8 h, the reaction was quenched with a solution of sodium bicarbonate followed extraction with ethyl acetate (10 mL × 3). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated.

The above residue was dissolved in ethanol (1.0 mL) followed by the addition of a mixture of aqueous KOH (15.7 mg in 0.3 mL H_2O, 0.28 mmol, 4.0 equiv) and refluxed for 5 h.[18] The mixture was allowed to reach room temperature, water was added, and the resulting mixture was extracted with ethyl acetate three times. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate = 10:1) to afford **5d** as a red solid (12.6 mg, 50%, dr =1:1): ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, J = 8.8, 1.2 Hz, 2 H), 7.46 (t, J = 7.2 Hz, 2 H), 7.33 (tt, J = 7.2, 1.2 Hz, 1 H), 7.19 (tt, J = 7.6, 1.2 Hz, 2 H), 7.12 (tt, J = 7.2, 1.2 Hz, 1 H), 7.03−7.01 (m, 2 H), 4.95 (dd, J = 2.8, 1.2 Hz, 1 H), 4.87 (dd, J = 2.4, 1.2 Hz, 1 H), 4.71 (dd, J = 2.4, 1.2 Hz, 1 H), 4.66 (t, J = 2.4 Hz, 1 H), 4.50 (t, J = 2.8 Hz, 1 H), 4.37 (dd, J = 2.4, 1.2 Hz, 1 H), 4.29 (s, 5 H), 3.94 (s, 5 H), 2.96 (td, J = 12.4, 4.0 Hz, 1 H), 2.76 (dt, J = 17.6, 4.0 Hz, 1 H), 2.60 (dd, J = 9.6, 3.2 Hz, 2 H), 2.52−2.43 (m, 2 H), 2.31−2.26 (m, 1 H), 2.27−2.2.16 (m, 2 H), 2.05−1.95 (m, 2 H), 1.85−1.76 (m, 1 H), 0.87 (t, J = 7.6 Hz, 3 H), 0.61 (t, J = 7.6 Hz, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 204.3, 204.2, 144.3, 143.1, 128.1, 127.9, 127.5, 126.9, 126.4, 126.0, 102.4, 102.3, 75.0, 73.8, 70.9, 70.6, 70.5, 70.4, 70.30, 70.28, 65.5, 65.4, 42.2, 41.4, 36.2, 35.6, 35.5, 35.3, 34.0, 31.2, 9.7, 9.4; HRMS (ESI) calcd for $C_{22}H_{22}O^{56}FeNa$ $[M + Na]^+$ 381.0918, found 381.0923.

Preparation of Compound ***4e***. The reaction of **3e** (25.6 mg, 0.07 mmol, 1.0 equiv) and $BF_3{\cdot}OEt_2$ (26.0 μL, 0.21 mmol, 3.0 equiv) afforded **4e** (18.2 mg, 71%): ^1H NMR (400 MHz, $CDCl_3$) (keto) δ 4.87 (dd, J = 2.4, 1.2 Hz, 1 H), 4.54 (t, J = 2.4 Hz, 1 H), 4.40 (dd, J = 2.4, 1.2 Hz, 1 H), 4.30 (s, 5 H), 3.83 (s, 3 H), 3.37 (dd, J = 13.6, 5.2 Hz, 1 H), 2.83 (t, J = 12.8 Hz, 1 H), 2.28−2.14 (m, 1 H), 2.06 (dd, J = 13.2, 5.2 Hz, 1 H), 1.85−1.64 (m, 6 H), 1.45−1.40 (m, 1 H), (enol) δ 12.39 (brs, 0.38 H), 4.66 (dd, J = 2.4, 1.2 Hz, 0.38 H), 4.33 (t, J = 2.4 Hz, 0.38 H), 4.17 (s, 1.90 H), 4.16 (dd, J = 2.4, 1.2 Hz, 0.38 H), 3.79 (s, 1.14 H), 2.65 (d, J = 14.8 Hz, 0.38 H), 2.50 (d, J = 14.8 Hz, 0.38 H), 2.28−2.14 (m, 0.38 H), 1.85−0.80 (m, 2.66 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 199.0, 171.8, 102.2, 73.0, 71.3, 70.4, 69.9, 68.7, 65.9, 53.9, 52.2, 41.7, 40.8, 39.6, 39.3, 25.5, 24.9; HRMS (ESI) calcd for $C_{20}H_{22}O_3{}^{56}FeNa$ $[M + Na]^+$ 389.0816, found 389.0812.

Preparation of Compound ***4f***. The reaction of **3f** (38.0 mg, 0.10 mmol, 1.0 equiv) and $BF_3{\cdot}OEt_2$ (40.0 μL, 0.30 mmol, 3.0 equiv) afforded **4f** (33.1 mg, 87%): ^1H NMR (400 MHz, $CDCl_3$) selected peaks for keto: δ 4.90 (dd, J = 2.4, 1.2 Hz, 1 H), 4.54 (t, J = 2.4 Hz, 1 H), 4.47 (dd, J = 2.0, 1.2 Hz, 1 H), 4.31 (s, 5 H), 3.84 (s, 3 H), 3.32 (dd, J = 12.0, 6.8 Hz, 1 H), 2.49 (dd, J = 13.6, 6.4 Hz, 1 H), 2.45 (t, J = 13.2 Hz, 1 H), 1.94−1.81 (m, 2 H), 1.75−1.38 (m, 5 H), 1.33−1.17 (m, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.8, 172.1, 103.8, 72.8, 71.1, 70.9, 70.8, 70.5, 70.4, 69.8, 68.2, 65.8, 52.3, 51.8, 37.4, 36.9, 35.3, 32.8, 26.0, 22.5, 21.8; HRMS (ESI) calcd for $C_{21}H_{25}O_3{}^{56}Fe$ $[M + H]^+$ 381.1153, found 381.1150.

Preparation of Compound ***5f***. A solution of **4f** (26.0 mg, 0.068 mmol, 1.0 equiv) and DABCO (76.3 mg, 0.68 mmol, 10 equiv) in toluene (1.0 mL) was refluxed under N_2. Until the total consumption of **4f**, the reaction was cooled to room temperature. The mixture was purified by chromatography on silica gel (hexane/ethyl acetate = 10:1) to obtain **5f** as a red solid (10.8 mg, 49%): ^1H NMR (400 MHz, $CDCl_3$) δ 4.87 (dd, J = 2.4, 1.2 Hz, 1 H), 4.49 (t, J = 2.4 Hz, 1 H), 4.43 (dd, J = 2.4, 1.2 Hz, 1 H), 4.21 (s, 5 H), 2.54−2.48 (m, 1 H), 2.33−2.24 (m, 2 H), 2.10−2.00 (m, 1 H), 1.90−1.80 (m, 2 H), 1.75−1.62 (m, 3 H), 1.54−1.45 (m, 1 H), 1.44−1.36 (m, 1 H), 1.34−1.27 (m, 2 H), 1.17 (td, J = 12.8, 4.4 Hz, 1 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 204.9, 104.4, 73.9, 70.5, 70.0, 67.9, 65.4, 37.2, 36.8, 35.2, 32.9, 31.3, 26.1, 22.6, 21.9; HRMS (ESI) calcd for $C_{19}H_{22}O^{56}FeNa$ $[M + Na]^+$ 345.0918, found 345.0922.

Preparation of Compound ***4g***. The reaction of **3g** (27.6 mg, 0.07 mmol, 1.0 equiv) and $BF_3{\cdot}OEt_2$ (26.0 μL, 0.21 mmol, 3.0 equiv) afforded **4g** (21.4 mg, 78%): ^1H NMR (400 MHz, $CDCl_3$) selected peaks for keto: δ 4.88 (dd, J = 2.4, 1.2 Hz, 1 H), 4.57 (t, J = 2.4 Hz, 1 H), 4.48 (dd, J = 2.4, 1.2 Hz, 1 H), 4.31 (s, 5 H), 3.84 (s, 3 H), 3.38 (dd, J = 13.2, 5.2 Hz, 1 H), 2.59 (t, J = 12.8 Hz, 1 H), 2.24 (dd, J = 12.8, 5.2 H, 1 H), 2.16−2.10 (m, 1 H), 1.94−1.88 (m, 1 H), 1.74−1.36 (m, 10 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.7, 172.1, 104.6, 72.4, 71.2, 71.1, 70.7, 70.5, 70.0, 68.7, 65.8, 52.25, 52.20, 40.5, 40.4, 39.9, 36.1, 31.1, 30.6, 23.44, 23.36; HRMS (ESI) calcd for $C_{22}H_{26}O_3{}^{56}FeNa$ $[M + Na]^+$ 417.1129, found 417.1125.

Preparation of Compound ***4h***. The reaction of **3h** (24.8 mg, 0.07 mmol, 1.0 equiv) and $BF_3{\cdot}OEt_2$ (26.0 μL, 0.21 mmol, 3.0 equiv) afforded **4h** (23.3 mg, 94%): ^1H NMR (400 MHz, $CDCl_3$) selected peaks for keto: δ 4.89 (dd, J = 2.8, 1.2 Hz, 1 H), 4.55 (t, J = 2.4 Hz, 1 H), 4.41 (dd, J = 2.4, 1.2 Hz, 1 H), 4.32 (s, 5 H), 4.31 (q, J = 7.2 Hz, 2 H), 3.39 (dd, J = 13.2, 5.2 Hz, 1 H), 2.73 (t, J = 13.2 Hz, 1 H), 1.98 (dd, J = 12.8, 5.2 Hz, 1 H), 1.48 (s, 3 H), 1.36 (t, J = 7.2 Hz, 3 H), 1.15 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.6, 171.4, 103.3, 72.6, 71.1, 70.6, 70.4, 69.8, 68.0, 65.7, 61.2, 53.0, 41.9, 30.2, 29.4, 28.8, 14.3; HRMS (ESI) calcd for $C_{19}H_{23}O_3{}^{56}Fe$ $[M + H]^+$ 355.0997, found 355.0991.

Preparation of Compound ***4k***. The reaction of **3k** (27.7 mg, 0.07 mmol, 1.0 equiv) and $BF_3{\cdot}OEt_2$ (26.0 μL, 0.21 mmol, 3.0 equiv) afforded **4k** (19.3 mg, 70%): ^1H NMR (400 MHz, $CDCl_3$) (keto) δ 4.86 (dd, J = 2.4, 1.2 Hz, 1 H), 4.56 (t, J = 2.4 Hz, 1 H), 4.41−4.40 (m, 1 H), 4.37−4.35 (m, 1 H), 4.34−4.32 (m, 1 H), 4.26−4.23 (m, 1 H), 4.08−4.07 (m, 1 H), 3.84 (s, 3 H), 3.43 (dd, J = 13.2, 5.2 Hz, 1 H), 2.69 (t, J = 12.8 Hz, 1 H), 1.96 (dd, J = 13.2, 5.6 Hz, 1 H), 1.48 (s, 3 H), 1.18 (s, 9 H), 1.14 (s, 3 H), (enol) δ 4.88 (dd, J = 2.4, 1.2 Hz, 0.66 H), 4.60 (t, J = 2.4 Hz, 0.66 H), 4.42−4.41 (m, 0.66 H), 4.26−4.23 (m, 0.66 H), 4.18−4.16 (m, 0.66 H), 4.11−4.10 (m, 0.66 H), 4.07−4.06 (m, 0.66 H), 4.05 (s, 1.98 H), 2.50 (d, J = 14.8 Hz, 0.66 H), 2.44 (d, J = 14.8 Hz, 0.66 H), 1.48 (s, 1.98 H), 1.19 (s, 5.94 H), 0.95 (s, 1.98 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.3, 172.0, 104.1, 103.7, 102.8, 102.3, 72.4, 72.1, 71.9, 70.5, 70.3, 69.9, 69.8, 68.5, 68.3, 68.2, 67.8, 66.6, 66.4, 66.2, 55.3, 52.7, 52.2, 41.8, 35.4, 31.3, 30.7, 30.4, 30.34, 30.31, 29.71, 29.65, 28.8, 27.8; HRMS (ESI) calcd for $C_{22}H_{28}O_3{}^{56}FeNa$ $[M + Na]^+$ 419.1286, found 419.1277.

Preparation of Compound ***4l***. The reaction of **3l** (36.6 mg, 0.082 mmol, 1.0 equiv) and $BF_3{\cdot}OEt_2$ (60.0 μL, 0.49 mmol, 6.0 equiv) afforded **4l** (22.1 mg, 60%): ^1H NMR (400 MHz, $CDCl_3$) (keto) δ 7.81 (d, J = 7.6 Hz, 2 H), 7.58−7.52 (m, 1 H), 7.49−7.42 (m, 2 H), 5.06 (dd, J = 2.4, 1.2 Hz, 1 H), 4.98 (dd, J = 2.4, 1.2 Hz, 1 H), 4.91 (dd, J = 2.8, 1.2 Hz, 1 H), 4.82 (dd, J = 2.4, 1.2 Hz, 1 H), 4.75 (dd, J = 2.4, 1.2 Hz, 1 H), 4.52 (dd, J = 2.4, 1.2 Hz, 1 H), 4.37 (dd, J = 2.4, 1.2 Hz, 1 H), 3.82 (s, 3 H), 3.40 (dd, J = 13.2, 5.2 Hz, 1 H), 2.66 (t, J =

DOI: 10.1021/acs.joc.5b01511
J. Org. Chem. 2015, 80, 7865−7875

13.2 Hz, 1 H), 1.97 (dd, J = 13.2, 5.2 Hz, 1 H), 1.36 (s, 3 H), 1.11 (s, 3 H), (enol) δ 12.2 (s, 0.50 H), 7.81 (d, J = 7.6 Hz, 1.0 H), 7.58−7.52 (m, 0.5 H), 7.49−7.42 (m, 1.0 H), 5.02 (dd, J = 2.8, 1.6 Hz, 0.50 H), 4.94 (dd, J = 2.4, 1.2 Hz, 0.50 H), 4.70 (dd, J = 2.4, 1.2 Hz, 0.50 H), 4.58−4.56 (m, 0.50 H), 4.52 (t, J = 2.4 Hz, 0.50 H), 4.34 (t, J = 2.4 Hz, 0.50 H), 4.14 (dd, J = 2.4, 0.8 Hz, 0.50 H), 3.79 (s, 1.50 H), 2.46 (d, J = 15.2 Hz, 0.50 H), 2.36 (d, J = 15.2 Hz, 0.50 H), 1.35 (s, 1.50 H), 0.90 (s, 1.50 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.0, 197.9, 172.1, 171.6, 139.4, 139.1, 132.0, 131.7, 128.4, 128.18, 128.16, 128.1, 104.9, 79.2, 75.6, 74.7, 74.5, 74.3, 73.9, 73.34, 73.31, 73.1, 72.7, 72.3, 70.9, 67.6, 67.3, 65.8, 52.7, 52.4, 51.4, 41.8, 37.3, 30.5, 30.1, 29.4, 28.7, 28.4, 27.7; HRMS (ESI) calcd for $C_{25}H_{24}O_4{}^{56}FeNa$ $[M + Na]^+$ 467.0922, found 467.0922.

Preparation of Compound ***4m***. The reaction of **3m** (28.8 mg, 0.07 mmol, 1.0 equiv) and $BF_3{\cdot}OEt_2$ (26.0 μL, 0.21 mmol, 3.0 equiv) afforded **4m** (23.1 mg, 80%): ^1H NMR (400 MHz, $CDCl_3$) selected peaks for keto δ 4.92 (dd, J = 2.8, 1.2 Hz, 1 H), 4.78−4.77 (m, 1 H), 4.69 (dd, J = 2.8, 1.2 Hz, 1 H), 4.66 (t, J = 2.4 Hz, 1 H), 4.54−4.50 (m, 2 H), 4.49 (dd, J = 2.8, 1.2 Hz, 1 H), 3.83 (s, 3 H), 3.42 (dd, J = 13.2, 5.6 Hz, 1 H), 3.04 (brs, 6 H), 2.71 (t, J = 13.2 Hz, 1 H), 1.99 (dd, J = 13.2, 5.6 Hz, 1 H), 1.50 (s, 3 H), 1.13 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.2, 171.8, 169.1, 104.0, 101.2, 93.6, 80.6, 74.5, 73.0, 72.6, 72.4, 72.2, 72.0, 71.7, 71.6, 71.53, 71.48, 71.0, 67.8, 67.4, 65.6, 52.7, 52.2, 51.3, 42.0, 38.9, 37.4, 36.4, 30.6, 30.1, 29.4, 28.7, 28.6, 27.8; HRMS (ESI) calcd for $C_{21}H_{25}NO_4{}^{56}FeNa$ $[M + Na]^+$ 434.1031, found 434.1027.

Preparation of Compound ***5m***. The mixture of **4m** (40.5 mg, 0.099 mmol, 1.0 equiv) and KOH (22.1 mg in 0.4 mL H_2O, 0.394 mmol, 4.0 equiv) was refluxed under N_2 in EtOH (2.0 mL) for 4 h. The mixture was quenched by the addition of HCl (1.0 M) and extracted with EtOAc three times. The combined organic layer was then washed with brine and dried over Na_2SO_4. After filtration, the solvent was removed, and the residue was purified by chromatography on silica gel (hexane/ethyl acetate = 10:1) to afford **5m** as a red solid (19.7 mg, 56%): ^1H NMR (400 MHz, $CDCl_3$) δ 4.89 (dd, J = 2.8, 1.2 Hz, 1 H), 4.71 (dd, J = 2.4, 1.6 Hz, 1 H), 4.69 (dd, J = 2.4, 1.2 Hz, 1 H), 4.56 (t, J = 2.4 Hz, 1 H), 4.44 (dd, J = 2.4, 1.2 Hz, 1 H), 4.34−4.31 (m, 2 H), 3.08 (bs, 3 H), 3.05 (bs, 3 H), 2.55−2.45 (m, 1 H), 2.42−2.31 (m, 2 H), 1.82−1.73 (m, 1 H), 1.48 (s, 3 H), 1.11 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 204.1, 169.0, 104.7, 80.0, 74.2, 73.2, 72.2, 72.1, 71.51, 71.47, 70.0, 66.8, 38.9, 38.0, 36.5, 36.2, 30.2, 29.0, 28.9; HRMS (ESI) calcd for $C_{19}H_{23}NO_2{}^{56}FeNa$ $[M + Na]^+$ 376.0976, found 376.0979.

Preparation of Compound ***4n***. The reaction of **3n** (27.0 mg, 0.07 mmol, 1.0 equiv) and $BF_3{\cdot}OEt_2$ (26.0 μL, 0.21 mmol, 3.0 equiv) afforded **4n** (27.0 mg, 99%): ^1H NMR (400 MHz, $CDCl_3$) selected peaks for keto: δ 5.14 (dd, J = 2.0, 1.6 Hz, 1 H), 4.76−4.75 (m, 2 H), 4.68 (s, 5 H), 3.79 (s, 3 H), 3.37 (dd, J = 13.2, 5.2 Hz, 1 H), 2.30 (t, J = 12.8 Hz, 1 H), 1.87 (dd, J = 12.8, 5.2 Hz, 1 H), 1.27 (s, 3 H), 1.24 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.1, 171.7, 106.0, 78.2, 72.9, 72.7, 72.3, 71.8, 70.5, 67.3, 52.5, 52.2, 42.7, 29.9, 29.6, 28.2; HRMS (ESI) calcd for $C_{18}H_{21}O_3{}^{102}Ru$ $[M + H]^+$ 387.0534, found 387.0536.

Preparation of Compound ***4o***. The reaction of **3o** (28.8 mg, 0.07 mmol, 1.0 equiv) and $BF_3{\cdot}OEt_2$ (26.0 μL, 0.21 mmol, 3.0 equiv) afforded **4o** (24.7 mg, 86%): ^1H NMR (400 MHz, $CDCl_3$) selected peaks for keto: δ 5.13 (dd, J = 2.4, 0.8 Hz, 1 H), 4.76 (t, J = 2.4 Hz, 1 H), 4.73 (dd, J = 2.4, 0.8 Hz, 1 H), 4.67 (s, 5 H), 3.79 (s, 3 H), 3.31 (dd, J = 13.2, 4.8 Hz, 1 H), 2.42 (t, J = 12.8 Hz, 1 H), 1.96 (dd, J = 12.8, 4.8 Hz, 1 H), 1.91−1.50 (m, 8 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.6, 171.6, 104.5, 78.6, 72.8, 72.7, 72.5, 71.8, 71.1, 67.4, 53.6, 52.2, 41.55, 41.50, 40.0, 38.3, 25.6, 24.6; HRMS (ESI) calcd for $C_{20}H_{22}O_3{}^{102}RuNa$ $[M + Na]^+$ 435.0510, found 435.0505.

Preparation of Compound ***4p***. The reaction of **3p** (29.8 mg, 0.07 mmol, 1.0 equiv) and $BF_3{\cdot}OEt_2$ (26.0 μL, 0.21 mmol, 3.0 equiv) afforded **4p** (28.8 mg, 97%): ^1H NMR (400 MHz, $CDCl_3$) selected peaks for keto: δ 5.14 (dd, J = 2.4, 1.2 Hz, 1 H), 4.82 (dd, J = 2.4, 1.2 Hz, 1 H), 4.75 (t, J = 2.4 Hz, 1 H), 4.68 (s, 5 H), 3.79 (s, 3 H), 3.26 (dd, J = 13.2, 5.2 Hz, 1 H), 2.38 (dd, J = 13.2, 4.8 Hz, 1 H), 2.00 (t, J = 13.2 Hz, 1 H), 1.75−1.25 (m, 10 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.4, 171.8, 106.4, 78.4, 72.8, 72.7, 72.2, 71.7, 70.7, 67.3, 52.2, 51.5, 37.7, 36.6, 36.1, 32.5, 25.9, 22.8, 21.8. HRMS (ESI) calcd for $C_{21}H_{24}O_3{}^{102}RuNa$ $[M + Na]^+$ 449.0667, found 449.0657.

Procedures for Alkylation of Keto Ester.[19] *Preparation of Compound* ***6a***. To a 10 mL round-bottomed flask containing a suspension of NaH (60% in mineral oil, 2.2 mg, 0.054 mmol, 1.32 equiv) in THF (0.5 mL) was added **4a** (14.0 mg, 0.041 mmol, 1.0 equiv) in THF (0.5 mL) dropwise at 0 °C. The mixture was stirred at rt for 1 h. The resulting nearly homogeneous mixture was cooled with an ice bath, and CH_3I (9.3 mg, 0.066 mmol, 1.6 equiv) was added. The resulting mixture was stirred at room temperature overnight. Water was added, the organic solvent was removed by evaporation under reduced pressure, and the residue was extracted with ethyl acetate. The organic phase was dried over Na_2SO_4, filtrated, and concentrated, and the residue was purified by chromatography on silica gel (hexane/ethyl acetate = 10:1) to give **6a** as a red solid (12.3 mg, 85%, dr = 25:1): ^1H NMR (400 MHz, CDCl3) δ 4.99 (dd, J = 2.4, 1.2 Hz, 1 H), 4.55 (t, J = 2.4 Hz, 1 H), 4.37 (dd, J = 2.4, 1.2 Hz, 1 H), 4.19 (s, 5 H), 3.61 (s, 3 H), 2.44 (d, J = 14.0 Hz, 1 H), 2.34 (d, J = 13.6 Hz, 1 H), 1.57 (s, 3 H), 1.43 (s, 3 H), 1.03 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 201.9, 175.2, 102.8, 73.1, 71.2, 70.2, 67.6, 66.5, 53.0, 52.5, 51.0, 30.7, 30.2, 29.5, 24.3; HRMS (ESI) calcd for $C_{19}H_{22}O_3{}^{56}FeNa$ $[M + Na]^+$ 377.0816, found 377.0813.

Preparation of Compound ***6b***. The reaction of **4a** (35.0 mg, 0.103 mmol, 1.0 equiv), benzyl bromide (52.8 mg, 0.309 mmol, 3.3 equiv), and NaH (60% in mineral oil, 15.0 mg, 0.371 mmol, 3.6 equiv) afforded **6b** (23.4 mg, 53%, dr >25:1): ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 8.8 Hz, 2 H), 7.33 (t, J = 7.6 Hz, 2 H), 7.24 (t, J = 7.2 Hz, 1 H), 4.88 (dd, J = 2.8, 1.2 Hz, 1 H), 4.45 (t, J = 2.4 Hz, 1 H), 4.27 (dd, J = 2.4, 1.2 Hz, 1 H), 3.78 (d, J = 13.2 Hz, 1 H), 3.68 (s, 5 H), 3.64 (s, 3H), 2.92 (d, J = 13.2 Hz, 1 H), 2.50 (d, J = 13.6 Hz, 1 H), 2.31 (d, J = 13.6 Hz, 1 H), 1.38 (s, 3 H), 1.03 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 199.8, 174.6, 136.6, 132.3, 128.0, 127.2, 101.9, 74.4, 71.0, 69.7, 67.2, 66.3, 58.7, 52.6, 45.5, 40.9, 31.1, 30.5, 29.73; HRMS (ESI) calcd for $C_{25}H_{26}O_3{}^{56}FeNa$ $[M + Na]^+$ 453.1129, found 453.1133.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01511.

^1H and $^{13}C\{^1H\}$ NMR spectra for all new compounds (PDF)

CIF file for compound **6b** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: zhgu@ustc.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the "973" project from the MOST of China (2015CB856600), NSFC (21272221, 21472179), the Recruitment Program of Global Experts, and the Fundamental Research Funds for the Central Universities (WK 2060190028, 2060190026 and 3430000001).

■ REFERENCES

(1) For the discovery of ferrocene, see: (a) Kealy, T. J.; Pauson, P. L. *Nature* **1951**, *168*, 1039. (b) Miller, S. A.; Tebboth, J. A.; Tremaine, J. F. *J. Chem. Soc.* **1952**, 632.

(2) (a) Wilkinson, G.; Rosenblum, M.; Whiting, M. C.; Woodward, R. B. *J. Am. Chem. Soc.* **1952**, *74*, 2125. (b) Fischer, E. O.; Pfab, W. *Z. Naturforsch., B: J. Chem. Sci.* **1952**, *7*, 377.

DOI: 10.1021/acs.joc.5b01511
J. Org. Chem. 2015, 80, 7865−7875

(3) (a) *Ferrocenes*; Hayashi, T., Togni, A., Eds.; VCH: Weinheim, 1995. (b) *Metallocenes*; Togni, A., Haltermann, R. L., Eds.; VCH: Weinheim, 1998. (c) *Ferrocenes*; Štěpnicka, P., Ed.; Wiley: Chichester, 2008. (d) *Chiral Ferrocenesin Asymmetric Catalysis*, Dai, L.-X., Hou, X.-L., Eds.; Wiley-VCH: Weinheim, 2010.
(4) (a) Hayashi, T.; Kumada, M. *Acc. Chem. Res.* **1982**, *15*, 395. (b) Halterman, R. L. *Chem. Rev.* **1992**, *92*, 965. (c) Togni, A. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1475. (d) Barlow, S.; O'Hare, D. *Chem. Rev.* **1997**, *97*, 637. (e) Richards, C. J.; Locke, A. J. *Tetrahedron: Asymmetry* **1998**, *9*, 2377. (f) Fu, G. C. *Acc. Chem. Res.* **2000**, *33*, 412. (g) Dai, L.-X.; Tu, T.; You, S.-L.; Deng, W.-P.; Hou, X.-L. *Acc. Chem. Res.* **2003**, *36*, 659. (h) Colacot, T. J. *Chem. Rev.* **2003**, *103*, 3101. (i) Fu, G. C. *Acc. Chem. Res.* **2004**, *37*, 542. (j) Gómez Arrayás, R.; Adrio, J.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2006**, *45*, 7674. (k) Fu, G. C. *Acc. Chem. Res.* **2006**, *39*, 853. (l) Arae, S.; Ogasawara, M. J. *Yuki Gosei Kagaku Kyokaishi* **2012**, *70*, 593. (m) Barlow, S.; O'Hare, D. *Chem. Rev.* **1997**, *97*, 637.
(5) Thomson, J. B. *Tetrahedron Lett.* **1959**, *1*, 26.
(6) (a) Sturm, T.; Weissensteiner, W.; Spindler, F.; Mereiter, K.; López-Agenjo, A. M.; Manzano, B. R.; Jalón, F. A. *Organometallics* **2002**, *21*, 1766. (b) Wally, H.; Widhalm, M.; Weissensteiner, W.; Schlögl, K. *Tetrahedron: Asymmetry* **1993**, *4*, 285.
(7) (a) Rinehart, K. L., Jr.; Curby, R. J., Jr.; Sokol, P. E. *J. Am. Chem. Soc.* **1957**, *79*, 3290. (b) Brunner, H.; Muschiol, M.; Nuber, B. *Z. Naturforsch., B: J. Chem. Sci.* **1994**, *49b*, 991.
(8) (a) Santelli-Rouvier, C.; Santelli, M. *Synthesis* **1983**, *1983*, 429. (b) Denmark, S. E.; Habermas, K. L.; Jones, T. K. *Org. React.* **1994**, *45*, 1. (c) Pellissier, H. *Tetrahedron* **2005**, *61*, 6479. (d) Tius, M. A. *Eur. J. Org. Chem.* **2005**, *2005*, 2193.
(9) (a) Denmark, S. E.; Jones, T. K. *J. Am. Chem. Soc.* **1982**, *104*, 2642. (b) Harrington, P. E.; Tius, M. A. *Org. Lett.* **1999**, *1*, 649. (c) Tius, M. A.; Chu, C. C.; Nieves-Colberg, R. *Tetrahedron Lett.* **2001**, *42*, 2419. (d) Aggarwal, V. K.; Belfield, A. J. *Org. Lett.* **2003**, *5*, 5075. (e) Liang, G.; Gradl, S. N.; Trauner, D. *Org. Lett.* **2003**, *5*, 4931. (f) Grant, T. N.; West, F. G. *J. Am. Chem. Soc.* **2006**, *128*, 9348. (g) Grant, T. N.; Rieder, C. J.; West, F. G. *Chem. Commun.* **2009**, 5676. (h) Basak, A. K.; Shimada, N.; Bow, W. F.; Vicic, D. A.; Tius, M. A. *J. Am. Chem. Soc.* **2010**, *132*, 8266. (i) Brooks, J. L.; Caruana, P. A.; Frontier, A. J. *J. Am. Chem. Soc.* **2011**, *133*, 12454. (j) Kerr, D. J.; Miletic, M.; Chaplin, J. H.; White, J. M.; Flynn, B. L. *Org. Lett.* **2012**, *14*, 1732. (k) Wu, Y.-K.; West, F. G. *Org. Lett.* **2014**, *16*, 2534. (l) You, X.; Xie, X.; Sun, R.; Chen, H.; Li, S.; Liu, Y. *Org. Chem. Front.* **2014**, *1*, 940. (m) Dethe, D. H.; Boda, R.; Murhade, G. M. *Org. Chem. Front.* **2015**, *2*, 645.
(10) (a) De Simone, F.; Andres, J.; Torosantucci, R.; Waser, J. *Org. Lett.* **2009**, *11*, 1023. (b) Patil, D. V.; Phun, L. H.; France, S. *Org. Lett.* **2010**, *12*, 5684. (c) De Simone, F.; Gertsch, J.; Waser, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 5767. (d) Phun, L. H.; Patil, D. V.; Cavitt, M. A.; France, S. *Org. Lett.* **2011**, *13*, 1952. (e) De Simone, F.; Saget, T.; Benfatti, F.; Almeida, S.; Waser, J. *Chem. - Eur. J.* **2011**, *17*, 14527. (f) Aponte-Guzán, J.; Taylor, J. E., Jr.; Tillman, E.; France, S. *Org. Lett.* **2014**, *16*, 3788. (g) Shenje, R.; Williams, C. W.; Francois, K. M.; France, S. *Org. Lett.* **2014**, *16*, 6468. (h) Cavitt, M. A.; Phun, L. H.; France, S. *Chem. Soc. Rev.* **2014**, *43*, 804.
(11) (a) Vaidya, T.; Manbeck, G. F.; Chen, S.; Frontier, A. J.; Eisenberg, R. *J. Am. Chem. Soc.* **2011**, *133*, 3300. (b) Vaidya, T.; Cheng, R.; Carlsen, P. N.; Frontier, A. J.; Eisenberg, R. *Org. Lett.* **2014**, *16*, 800.
(12) Malona, J. A.; Colbourne, J. M.; Frontier, A. J. *Org. Lett.* **2006**, *8*, 5661.
(13) CCDC 1401059. For details, see the Supporting Information.
(14) O'Connor, J. M.; Casey, C. P. *Chem. Rev.* **1987**, *87*, 307.
(15) This type of 1,2-hydride shift and alkylation was also observed in 3-acylindole by Bergman and Venemalm; see: Bergman, J.; Venemalm, L. *Tetrahedron Lett.* **1987**, *28*, 3741.
(16) Chong, J. M.; Shen, L.; Taylor, N. J. *J. Am. Chem. Soc.* **2000**, *122*, 1822.
(17) (a) Jiang, Y.; Chen, X.; Zheng, Y.; Xue, Z.; Shu, C.; Yuan, W.; Zhang, X. *Angew. Chem., Int. Ed.* **2011**, *50*, 7304. (b) Shenje, R.; Martin, M. C.; France, S. *Angew. Chem., Int. Ed.* **2014**, *53*, 13907.
(18) Nicolaou, K. C.; Gray, D. L. F. *J. Am. Chem. Soc.* **2004**, *126*, 607.
(19) Ohkuma, T.; Sandoval, C. A.; Srinivasan, R.; Lin, Q.; Wei, Y.; Muniz, K.; Noyori, R. *J. Am. Chem. Soc.* **2005**, *127*, 8288.

DOI: 10.1021/acs.joc.5b01511
J. Org. Chem. 2015, 80, 7865−7875