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Construction of spiro-oxaquinolizidinone framework of Upenamide via organoiron complexes

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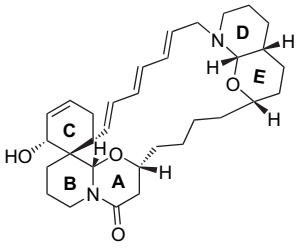
Abstract—An organoiron approach toward the synthesis of an elaborated tricyclic spiro-oxaquinolizidinone ring has been accomplished. The key intermediate was efficiently prepared through a nitrile addition to the appropriately functionalized cyclohexadienylium–$Fe(CO)_3$ perchlorate salt to install the requisite quaternary center in the spiro-oxaquinolizidinone ring.

1. Introduction

Upenamide (**1**) was isolated in 2000 from the branching sponge of *Echinochalina* sp. by Kelly and co-workers (Fig. 1).[1] Upenamide is a macrocyclic alkaloid possessing both a unique spiro-oxaquinolizidinone core (ABC tricyclic ring) and hemiaminal core (DE bicyclic ring) systems. Despite having an interesting framework, there has been no wide study on its biological activity because of its scarcity. To the best of our knowledge, no total synthesis has been reported so far. Synthetic studies toward both the heterocyclic ring systems of this architecturally complex natural product have been presented.[2] However, the presence of a unique spiro-oxaquinolizidinone core (ABC ring) has made it a challenge for synthetic chemists. To date, reported syntheses of the spiro-oxaquinolizidinone ring system[2b] lack the requisite functionalities at the C-ring for further elaboration of a 20-membered macrocycle present in Upenamide.

Our general strategies for the synthesis of the tricyclic spiro-oxaquinolizidinone core (ABC-ring system) of Upenamide are outlined in Scheme 1. The key element in this scheme consists of the nitrile addition to the appropriately functionalized cyclohexadienylium–$Fe(CO)_3$ salt to construct the requisite substrate having a quaternary carbon center for elaboration to the final spiro-oxaquinolizidinone ring. Recently our laboratory was involved in developing a methodology for the successful addition of nitrile to cyclohexadienylium–$Fe(CO)_3$ backbone via the perchlorate salt.[3,4] On the basis of this strategy we envisaged that compound **I** could be elaborated to the targeted ABC ring of Upenamide via two routes: (i) the initial construction of the oxazinanone ring A, followed by an intramolecular N-alkylation of the amide to form ring B (route A), and (ii) synthesis of an acetal β-hydroxy amide intermediate, followed by deacetalization and an intramolecular cyclization for the consecutive formation of both rings A and B (route B).



Upenamide (**1**)

Figure 1. Structure of Upenamide.

2. Results and discussion

We first undertook model studies concerning construction of the ABC ring of Upenamide that lacks the carbonyl group of the amide in A-ring using the less lengthy reaction sequences of route A. The 4-methoxycinnamic acid **2** was identified as a suitable starting material and this was first converted into 4-methoxyphenyl-propan-1-ol by $LiAlH_4$ reduction.[5] The tricarbonyl{1-4-η-[3-acetoxy-1-(4-methoxycyclohexa-1,3-dienylium)-propane]}iron perchlorate **5** was synthesized as previously reported according to Scheme 2[3,6,7] via (i) Birch reduction to give **3**, (ii) protection of the alcohol as the acetate, (iii) conjugation of the 1,4-diene to afford **4a** and **4b**, (iv) complex formation with $Fe(CO)_5$, and (v) hydride abstraction with triphenylmethanium perchlorate.

The addition reaction of TMS-CN to **5** furnished **6** in 71% yield.[3,4] The acetate group in **6** was removed under basic

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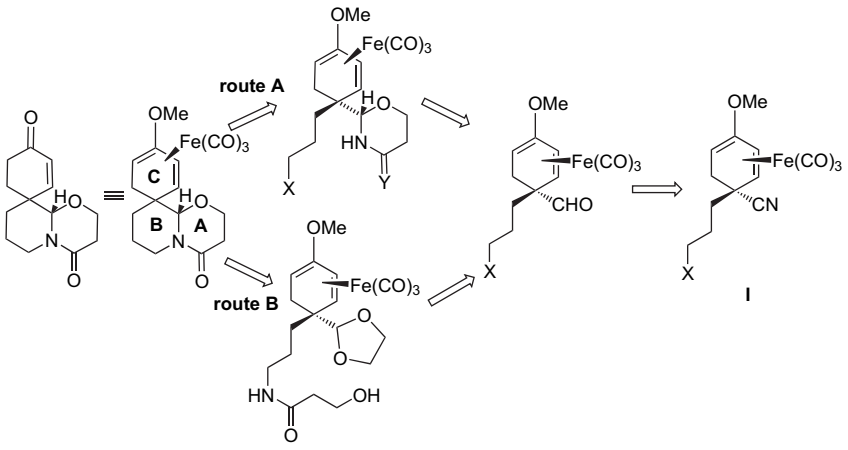
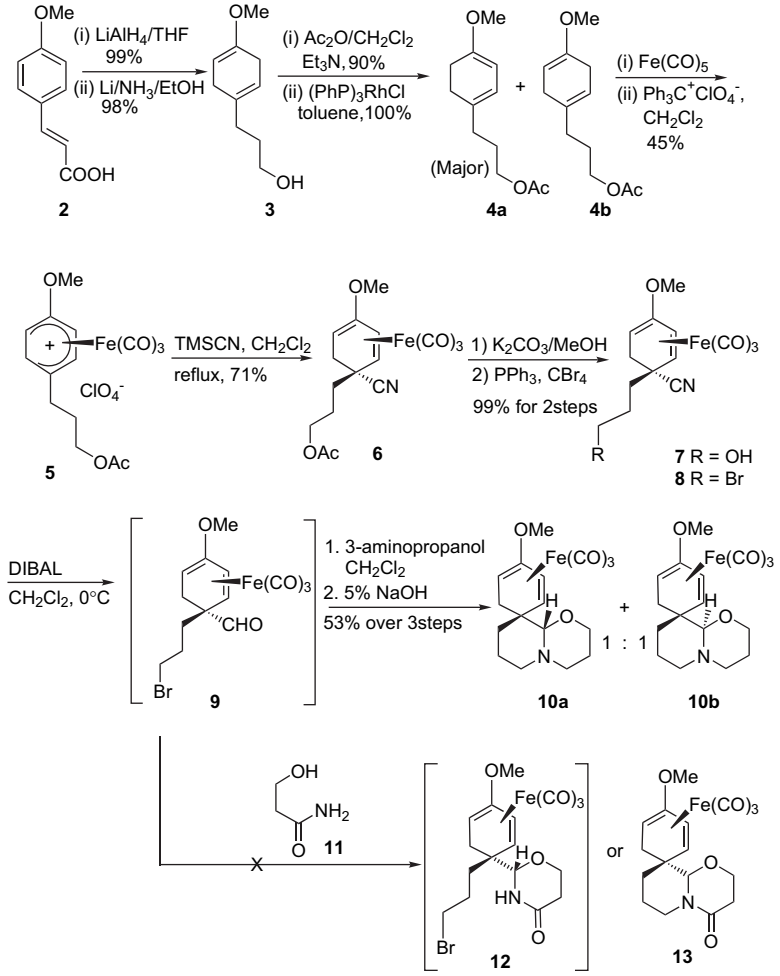


Scheme 1. Retrosynthetic analysis for tricyclic core (ABC-ring system) of Upenamide.

hydrolysis condition to afford the free alcohol **7**, which was subsequently converted to the corresponding bromide **8** in near quantitative yield. Treatment of **8** with DIBAL successfully resulted in the conversion of the nitrile into the corresponding aldehyde **9**. Reaction of aldehyde **9** with 3-aminopropanol under Hoye conditions[5] successfully furnished the spiro-octapyran[2,3-*b*]pyridine core **10** in 53% yield after three steps, and as a 1:1 mixture of diastereomers (Scheme 2).

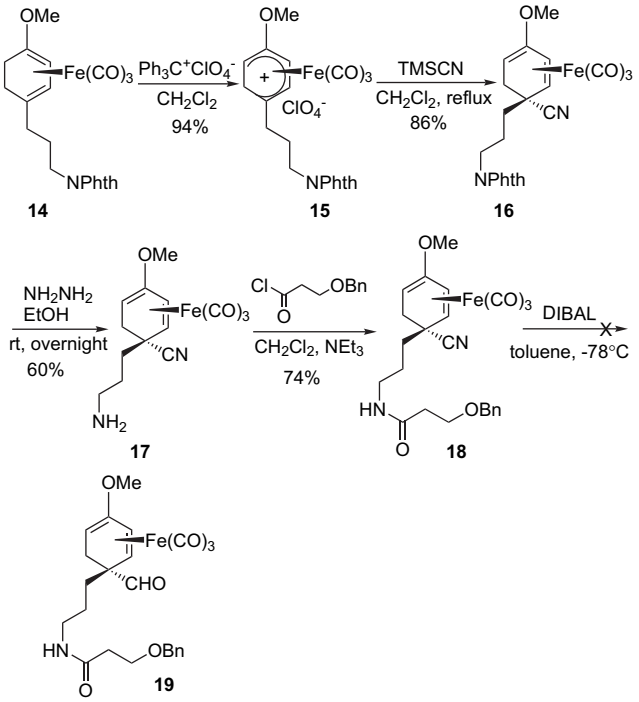
Having achieved the synthesis of **10**, we then tried the reaction of **9** with hydroxyamide **11** to synthesize the spiro-oxaquinolizidinone core of Upenamide. Unfortunately, no desired cyclization product **12** or **13** was formed using condensation conditions,[8] and only starting material was recovered even after a prolonged reaction time (Scheme 2). We believe that the failure might be attributed either to the poorer reactivity of the amide group, or the increased reversibility of the unstable cyclic acetal-amide under the reaction



Scheme 2.

conditions. In this study, we have shown that the reactivity of nitrogen atom is a key issue for this intermolecular cyclization via route A.

We next planned to introduce the A and B rings of the tricyclic spiro-oxaquinolizidinone core (ABC-ring system) of Upenamide via route B. Similarly, cyclohexadienylium–$Fe(CO)_3$ perchlorate salt **15** was synthesized from 4-methoxycinnamic acid **2** via (i) Birch reduction, (ii) esterification of the unstable acid, (iii) conjugation of the 1,4-diene, (iv) complex formation with $Fe(CO)_5$, (v) reduction of the ester to the alcohol, (vi) conversion of alcohol to phthalimide by Mitsunobu reaction to afford **14**, and (vii) hydride abstraction with triphenylmethanium perchlorate (Scheme 3).[4,6,7] TMS-CN addition to **15** furnished product **16** in 86% yield.

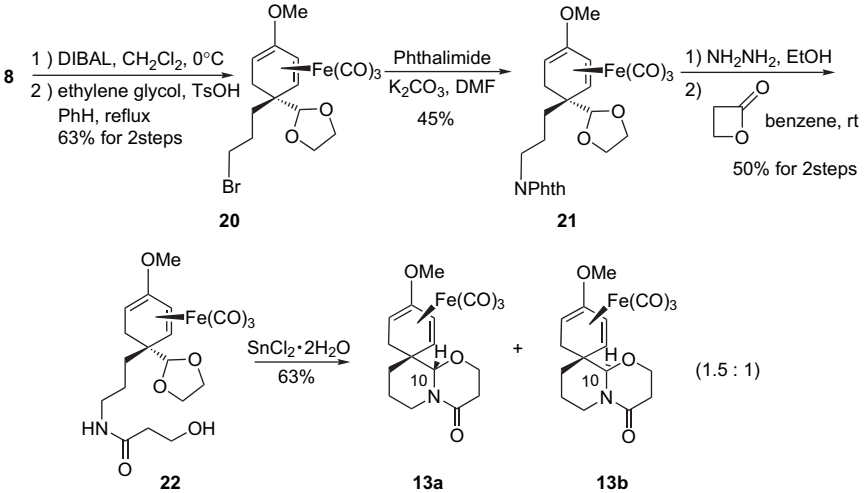


Scheme 3.

Treatment of the phthalimide compound **16** with hydrazine gave the requisite amino product **17** in 60% yield. It is interesting to note that no intramolecular cyclization of the amine to the nitrile was observed under this reaction condition. For the facile construction of the oxaquinolizidinone ring,[2b,9] we investigated the transformation of the amino group in **17** into the hydroxyamide derivative, followed by the reduction of the nitrile into the aldehyde for the intramolecular cyclization reaction. Reaction of **17** with 3-benzyloxypropionyl chloride (synthesized from the mono-benzylation of propane-1,3-diol followed by oxidation to the acid and conversion to the acid chloride)[10,11] gave the amide **18** in 74% yield. We were unable to convert the nitrile group in **18** into the aldehyde **19** after several experiments (Scheme 3).

We thought that the amide bond present in **18** might be an undesirable limitation to the above synthetic route. At this stage, we considered using the intermediate **9** whereby the nitrile functional group of **8** has been successfully converted to the aldehyde prior to the formation of the amide bond. The unstable aldehyde **9** was then subjected to protection using ethylene glycol to furnish the cyclic acetal **20**. It is interesting to note that the bromo-substituent in **9** survived these reaction conditions. The introduction of the amino group into **20** was carried out by the conversion of the bromo-functional group to the phthalimide **21**, followed by deprotection using hydrazine to furnish the amino-precursor.[4,7] With the cyclic acetal-amine precursor in hand, we examined methods for the elaboration to the requisite oxaquinolizidinone (AB) core.[2b,12] The β-hydroxy amide **22** was prepared through the nucleophilic ring opening of β-propiolactone in an unoptimized 50% yield (Scheme 4).

The unstable β-hydroxy amide **22** was used immediately for the next reaction without further purification. To our delight, treatment of **22** in dichloromethane with stannous chloride dihydrate afforded the spiro-oxaquinolizinone **13** in a moderate 63% yield, as a 1.5:1 mixture of diastereomers. The stereochemistry of the newly formed stereocenter at C-10 can be clearly seen in ^1H NMR spectrum. The ^1H NMR spectrum indicated the predominate compound to be the desired isomer **13a**, since this shows a lower field singlet at δ 4.40



Scheme 4.

characteristic of the C-10 proton pointing toward the olefinic group. The other diastereomer **13b** showed a singlet at δ 4.20 for the C-10 proton (Scheme 4).

In summary, we have explored the scope of utilizing organo-iron complex for the construction of the spiro-oxaquinolizinone (ABC ring) core of Upenamide. It would be worth noting that this methodology allows the synthesis of a functionalized C-ring, which is otherwise difficult to synthesize, for the ready access to the total synthesis of Upenamide.

3. Experimental section

3.1. General

Chemicals were purchased and used as received. All reactions were performed under an inert atmosphere of nitrogen. Diethyl ether and tetrahydrofuran (THF) were distilled from sodium benzophenone. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride. ^{1}H NMR spectra were recorded on a 200 MHz or 400 MHz NMR instrument using $CDCl_3$ as solvent. Chemical shifts were reported in parts per million (ppm) with reference to TMS. Elemental analysis was performed using an elemental analyzer. High resolution mass spectra were recorded using Bruker APEX II. All the melting points were recorded on a Fisher Johns Melting Apparatus and are uncorrected. Chromatography was performed using silica gel 60 and preparative thin layer chromatography (TLC) was performed on silica gel 60 PF_{254} plates (20×20 cm). Compound **5**, **6**, **15**, **16**, **17** were prepared according to reported procedures.[3,4,6,7]

3.1.1. Tricarbonyl[2-5-η-3-bromo-(1-cyano-4-methoxycyclohexa-2,4-dienyl)propane]iron (8). To a solution of the complex **6** (375 mg, 1.00 mmol) in MeOH (10 mL) was added K_2CO_3 (200 mg, 1.50 mmol). The mixture was stirred at 0 °C for 1 h. After the reaction was completed, 1 M aqueous HCl was added and the reaction mixture was evaporated in vacuo. To the mixture was added CH_2Cl_2 and then washed with saturated aqueous $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4 and evaporated to give alcohol complex **7** as an orange oil, suitable for use in the next reaction. To the solution of alcohol complex in CH_2Cl_2 (20 mL) was added PPh_3 (390 mg, 1.50 mmol) and the mixture was cooled to 0 °C. Then, carbon tetrabromide (0.5 g, 1.50 mmol) was added to the mixture. After stirring at room temperature overnight, the reaction mixture was evaporated to dryness and purified by chromatography (ether) to give **8** (400 mg, 99%) as a pale yellow oil. R_f: 0.58 (hexane/EtOAc=5:1); IR (CH_2Cl_2): 2308, 2056, 1985 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.17 (dd, J=6.4, 2.0 Hz, 1H), 3.69 (s, 3H), 3.47 (m, 1H), 3.47–3.37 (m, 2H), 2.59 (d, J=6.4 Hz, 1H), 2.35 (dd, J=15.2, 2.0 Hz, 1H), 2.12–2.03 (m, 1H), 1.98–1.92 (m, 1H), 1.77–1.64 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.6, 124.8, 63.9, 55.0, 53.5, 53.2, 40.7, 38.7, 36.9, 32.9, 28.4. Mass (FAB): m/z 397 (M^+: $C_{14}H_{14}{}^{81}BrNO_4Fe$), 395 ($M^+$: $C_{14}H_{14}{}^{79}BrNO_4Fe$), 371 ($M^+-CO$, M^+: $C_{14}H_{14}{}^{81}BrNO_4Fe$), 369 ($M^+-CO$, M^+: $C_{14}H_{14}{}^{79}BrNO_4Fe$), 339 ($M^+-2CO$); HRMS (FAB) calcd for $C_{14}H_{15}{}^{79}BrNO_4Fe$ (M^++1): 395.9535, found: 395.9528.

3.1.2. Tricarbonyl{2-5-η-1,1′-octahydropyrano[2,3-*b*]pyridine}iron (10). To a solution of the complex **8** (146 mg, 0.37 mmol) in CH_2Cl_2 (10 mL) was slowly added DIBAL (20% in toluene, 0.54 mL, 0.74 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. After the reaction was completed, 1 M aqueous HCl was added and the reaction mixture was filtered with Celite. To the mixture was added CH_2Cl_2 and then washed with saturated aqueous $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4 and evaporated to give aldehyde complex **9** as an orange oil, suitable for use in the next reaction.

To a solution of the complex **9** (100 mg, 2.53 mmol) in CH_2Cl_2 (5 mL) was added 3-amino-1-propanol (0.1 mL, 1.31 mmol). The mixture was stirred at room temperature overnight. After the reaction was completed, 5% aqueous NaOH (5 mL) was added and the reaction mixture was stirred for 20 min. To the mixture was added CH_2Cl_2 and then washed with saturated aqueous $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, evaporated to dryness, and purified by chromatography (CH_2Cl_2/MeOH=20:1) to give **10** (50 mg, 53%) as a pale yellow oil. Two diastereomers: 1:1; R_f: 0.64 (CH_2Cl_2/MeOH=20:1); IR (CH_2Cl_2): 2047, 1960 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): **10a**: δ 5.11 (dd, J=6.5, 2.5 Hz, 1H), 4.08 (dd, J=11.5, 5.0 Hz, 1H), 3.63 (s, 3H), 3.59 (t, J=11.5 Hz, 1H), 3.28 (m, 1H), 3.23 (s, 1H), 2.98–2.70 (m, 2H), 2.57 (d, J=6.5 Hz, 1H), 2.29–1.89 (m, 4H), 2.07 (dd, J=15.0, 2.5 Hz, 1H), 1.62–1.05 (m, 4H), 1.43 (dd, J=15.0, 2.5 Hz, 1H). **10b**: δ 5.09 (dd, J=6.8, 2.0 Hz, 1H), 3.99 (dd, J=11.5, 5.0 Hz, 1H), 3.63 (s, 3H), 3.41 (t, J=11.5 Hz, 1H), 3.26 (m, 1H), 2.96 (s, 1H), 2.98–2.70 (m, 3H,), 1.83 (dd, J=15.0, 2.5 Hz, 1H), 1.62–1.05 (m, 4H), 1.29 (dd, J=15.0, 2.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): **10a**: δ 211.9, 140.1, 98.1, 68.5, 66.5, 57.8, 54.3, 54.0, 53.4, 52.8, 42.1, 39.1, 35.0, 21.2, 20.9. **10b**: δ 211.5, 140.0, 98.0, 67.7, 64.7, 57.8, 54.2, 54.0, 53.4, 52.8, 41.1, 39.1, 35.0, 21.2, 20.9. Mass (FAB): m/z 376 (M^++1), 347 (M^+-CO), 291 (M^+-3CO); HRMS (FAB) calcd for $C_{17}H_{22}NO_5Fe$ (M^++1): 376.0848, found: 376.0842.

3.1.3. Tricarbonyl{2-5-η-[3-benzyloxy-*N*-3-(1-cyano-4-methoxycyclohexa-2,4-dienyl)propyl]propioamide}iron (18). To a solution of the complex **16** (423 mg, 0.90 mmol) in absolute EtOH (20 mL) was slowly added hydrazine (0.40 mL, 7.10 mmol). The mixture was stirred at room temperature overnight. The solvent and hydrazine were evaporated in vacuo and then CH_2Cl_2 was added to the mixture. The mixture was filtered and the filtrate was concentrated to afford amine complex **17** (0.25 g) in 60% yield. The amine complex **17** was used in the next step without further purification where it was dissloved in CH_2Cl_2 (15 mL), purged with argon, and cooled to 0 °C. Excess triethylamine was added to the reaction mixture. Then, a solution of 3-benzyloxypropionyl chloride[11,12] in CH_2Cl_2 (10 mL) was added dropwise. After 3 h of stirring at room temperature the reaction mixture was washed with 1 M aqueous HCl, saturated aqueous $NaHCO_3$, and brine. The organic phase was dried over Na_2SO_4 and evaporated to give **18** (440 mg, 99%) as an orange oil. R_f: 0.36 (CH_2Cl_2/EtOAc=10:1); IR (CH_2Cl_2): 3446, 3392, 2226, 2059, 1983, 1676 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.30 (m, 5H), 6.38 (br s, 1H), 5.13 (dd, J=6.4 and 2.8 Hz, 1H), 4.53 (s, 2H),

3.72 (t, J=5.6 Hz, 2H), 3.66 (s, 3H), 3.42 (m, 1H), 3.27–3.23 (m, 2H), 2.51 (d, J=6.4 Hz, 1H), 2.47 (t, J=5.6 Hz, 2H), 2.28 (dd, J=15.2 and 2.8 Hz, 1H), 1.65 (dd, J=15.2 and 2.8 Hz, 1H), 1.65–1.40 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 141.8, 137.9, 128.8, 128.2, 128.0, 125.0, 73.5, 66.5, 64.0, 55.0, 53.6, 53.1, 40.6, 39.0, 37.2, 37.1, 25.5. Mass (EI): m/z 495 (M^++1), 441 (M^++1−CO−CN), 439 (M^++1−2CO), 410 (M^+−3CO); HRMS (FAB) calcd for $C_{24}H_{27}N_2O_6Fe$ (M^++1): 495.1219, found: 495.1226.

3.1.4. Tricarbonyl{2-5-η-3-bromo-[1-(1,3)-dioxolane-4-methoxycyclohexa-2,4-dienyl]propane}iron (20). To a solution of the complex **8** (146 mg, 0.37 mmol) in CH_2Cl_2 (10 mL) was slowly added DIBAL (20% in toluene, 0.54 mL, 0.74 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. After the reaction was completed, 1 M aqueous HCl was added and the reaction mixture was filtered with Celite. To the mixture was added CH_2Cl_2 and then washed with saturated aqueous $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4 and evaporated to give aldehyde complex **9** as an orange oil, suitable for use in the next reaction. A mixture of ethylene glycol (1 mL) and catalytic amount of *p*-toluenesulfonic acid was added to a solution at aldehyde complex in benzene (30 mL) and heated under reflux overnight by the aid of a Dean–Stark apparatus. After cooling to room temperature, the reaction mixture was washed with saturated aqueous $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, evaporated the solvent, and purified by chromatography (hexane/EtOAc=5:1) to give dioxolane complex **20** as an orange oil (100 mg, 63%). R_f: 0.53 (hexane/EtOAc=5:1); IR (CH_2Cl_2): 2047, 1978 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.11 (dd, J=6.4, 2.5 Hz, 1H), 4.39 (s, 1H), 3.93 (m, 2H), 3.81 (m, 2H), 3.65 (s, 3H), 3.35 (t, J=6.8 Hz, 2H), 3.30 (m, 1H), 2.42 (d, J=6.4 Hz, 1H), 1.99–1.84 (m, 3H), 1.58–1.45 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 211.6, 140.8, 109.6, 65.6, 65.4, 65.2, 55.5, 54.7, 53.7, 43.7, 36.9, 36.7, 34.8, 28.1. Mass (FAB): m/z 443 (M^++1), 414 (M^+−CO), 386 (M^+−2CO), 358 (M^+−3CO); HRMS (FAB) calcd for $C_{16}H_{20}{}^{79}BrO_6Fe$ (M^++1): 442.9794, found: 442.9787.

3.1.5. Tricarbonyl{2-5-η-3-phthalimido-[1-(1,3)-dioxolane-4-methoxycyclohexa-2,4-dienyl]propane}iron (21). To a solution of the complex **20** (100 mg, 0.23 mmol) in DMF (5 mL) was added K_2CO_3 (38 mg, 0.27 mmol) and phthalimide (40 mg, 0.27 mmol). The reaction mixture was stirred at room temperature for 2 days. After the reaction was completed, water was added and the reaction mixture was extracted with ethyl acetate. The organic phase was washed with brine, dried over Na_2SO_4, and evaporated to give crude complex **21**. The crude mixture was purified by chromatography (Hexane/EtOAc=5:1) to give pure complex **21** as a pale yellow solid (50 mg, 45%). R_f: 0.11 (hexane/EtOAc=5:1); IR (CH_2Cl_2): 2058, 1987, 1779 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.81 (m, 2H), 7.67 (m, 2H), 5.05 (dd, J=6.0, 2.0 Hz, 1H), 4.34 (s, 2H), 3.85–3.72 (m, 6H), 3.61 (s, 3H), 3.22 (m, 1H), 2.38 (d, J=6.0 Hz, 1H), 1.78–1.22 (m, 6H). Mass (FAB): m/z 510 (M^++1), 481 (M^+−CO), 453 (M^+−2CO), 425 (M^+−3CO); HRMS (FAB) calcd for $C_{24}H_{24}NO_8Fe$ (M^++1): 510.0852, found: 510.0849.

3.1.6. Tricarbonyl[2-5-η-1,1′-(4-oxaquinolizidinone)]-iron (13). To a solution of the complex **21** (72 mg, 0.14 mmol) in absolute EtOH (10 mL) was slowly added hydrazine (0.05 mL, 1.00 mmol). The mixture was stirred at room temperature overnight. The solvent and hydrazine were evaporated in vacuo and then CH_2Cl_2 was added to the mixture. The mixture was filtered and the filtrate was concentrated to afford an amine complex, which was used in the next step without further purification. Then, to a solution of the amine complex in benzene (5 mL) was slowly added β-propiolactone (0.03 mL, 0.42 mmol). After stirring at room temperature overnight, the reaction mixture was concentrated in vacuo and purified by chromatography (EtOAc) to give hydoxyamide complex **22** as an orange oil (24 mg, 50%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.00 (br, 1H, –NH), 5.09 (dd, J=6.5, 2.0 Hz, 1H), 4.40 (s, 2H), 3.94–3.74 (m, 6H), 3.61 (s, 3H), 3.30–3.10 (m, 3H), 2.45–2.37 (m, 3H), 1.82 (dd, J=15.0, 2.0 Hz, 1H), 1.50–1.37 (m, 6H).

The complex **22** was used in the next step immediately due to its instability. Therefore, to a solution of hydoxyamide complex **22** in CH_2Cl_2 (5 mL) was added tin(II) chloride dihydrate (10 mg, 0.13 mmol). After stirring at room temperature for 1 day, the reaction mixture was filtered through Celite and the filtrate was concentrated. The residue was purified by chromatography (CH_2Cl_2) to give the desired complex **13** (**13a/13b**=1.5:1) as a pale yellow oil (13 mg, 63%). R_f: 0.25 (CH_2Cl_2); IR (CH_2Cl_2): 2047, 1966, 1653 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): **13a**: δ 5.18 (dd, J=6.8, 2.0 Hz, 1H), 4.70 (m, 1H), 4.40 (br s, 1H), 4.08 (m, 1H), 3.67 (s, 3H), 3.24 (m, 1H), 2.75–2.38 (m, 3H), 2.39 (d, J=6.8 Hz, 1H), 1.88 (dd, J=14.4, 2.0 Hz, 1H), 1.60–1.25 (m, 4H), 1.42 (dd, J=14.4, 2.0 Hz, 1H). **13b**: δ 5.15 (dd, J=6.4, 2.0 Hz, 1H), 4.62 (m, 1H), 4.20 (br s, 1H), 4.08 (m, 1H), 3.67 (s, 3H), 3.29 (m, 1H), 2.75–2.38 (m, 3H), 2.05 (d, J=6.4 Hz, 1H), 1.70–1.25 (m, 6H); ^{13}C NMR: δ 211.8, 90.7, 66.7, 62.6, 57.8, 54.6, 49.2, 40.7, 54.1, 40.2, 37.8, 33.7, 20.4. Mass (FAB): m/z 390 (M^++1), 362 (M^++1−CO), 333 (M^+−2CO), 305 (M^+−3CO); HRMS (ESI) calcd for $C_{17}H_{20}NO_6Fe$ (M^++1): 390.0640, found: 390.0638.

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References and notes

1. Jimenez, J. I.; Goetz, G.; Mau, C. M. S.; Yoshida, W. Y.; Scheuer, P. J.; Williamson, R. T.; Kelly, M. *J. Org. Chem.* **2000**, *65*, 8465–8469.
2. For earlier studies on the synthesis of Upenamide, see: (a) Maia, A. A.; Mons, S.; Gil, R. P. D.; Marazano, C. *Eur. J. Org. Chem.* **2004**, 1057–1062; (b) Reid, M.; Taylor, R. J. K. *Tetrahedron Lett.* **2004**, *45*, 4181–4183; (c) Kiewel, K.; Luo, Z.; Sulikowski, G. A. *Org. Lett.* **2005**, *7*, 5163–5165.
3. (a) Ong, C. W.; Chien, C. J. *Organometallics* **1993**, *12*, 241–243; (b) Ong, C. W.; Chao, Y. K.; Chang, Y. A. *Tetrahedron Lett.* **1994**, *35*, 6303–6304.
4. Ong, C. W.; Wang, H. M.; Chang, Y. A. *J. Org. Chem.* **1996**, *61*, 3996–3998.

5. (a) Hoye, T. R.; North, J. T.; Yao, L. J. *J. Am. Chem. Soc.* **1994**, *116*, 2617–2618; (b) Hoye, T. R.; North, J. T.; Yao, L. J. *J. Org. Chem.* **1994**, *59*, 6904–6910.
6. Pearson, A. J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1255–1260.
7. (a) Pearson, A. J.; Rees, D. C. *J. Am. Chem. Soc.* **1982**, *104*, 1118–1119; (b) Pearson, A. J.; Rees, D. C. *J. Chem. Soc., Perkin Trans. 1* **1982**, 2467–2478.
8. Ito, K.; Sekiya, M. *Chem. Pharm. Bull.* **1972**, *20*, 1762–1767.
9. Winterfeld, K.; Michael, H. *Arch. Pharm. Ber. Dtsch. Pharm. Ges.* **1961**, 65–76.
10. Gennari, C.; Cozzi, P. G. *J. Org. Chem.* **1988**, *53*, 4015–4021.
11. Davis, F. A.; Kasu, P. V. N.; Sundarababu, G.; Qi, H. *J. Org. Chem.* **1997**, *62*, 7546–7547.
12. Ford, K. L.; Roskamp, E. J. *Tetrahedron Lett.* **1992**, *33*, 1135–1138.