Electronic Supplementary Information

The Origin of Supramolecular Chirality in 1-Ferrocenyl Amino Acids

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Experimental section

Materials

All amino acid methyl ester hydrochlorides were purchased from HEOWNS Biochemical Technology Co., LTD, China. Ferrocenecarboxylic acid was purchased from Bide Pharmatech Ltd., (R)-2-Aminohexane was purchased from Alfa Aesar (China） chemical Co. Ltd. All reagents were used without further purification in this work. All water used in this work is deionized (DI) water. Ferrocenyl amino acids were synthesized according to the previous reports. [S1, S2]

Computational details

For all of different angles of Val (0-330^{o}) were constructed by gaussian view 06 according to the initial structure of single crystal. Gly, Ala, PGly, Pro and Val structures were determined by the single crystal structures. Especially, there was no hydrogen atom in the single crystal structure of Pro, so hydrogen atoms were added using Materials Studio 7.0. Initial Trp geometry structure was given by single crystal structures of the corresponding methyl ester compound (CCDC 652545). Leu, Ile, Tyr and HA were constructed by gaussian view 06. All the calculations were based on gaussian 16 program.

The optimization of Trp, Leu, Ile, Pro, Tyr and HA were carried out with ωB97XD/6-311g(d) basic set. The thermodynamic data of Val including electronic Energy (EE) + Thermal Free Energy Correction was calculated with ωB97XD/6-311g(d) basic set. Base on the optimized geometry, The electron circular dichroism (ECD) of Ala were calculated with b3lyp/6-311g(d) basic set.

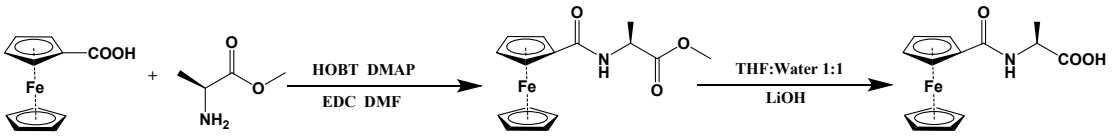
Characterizations

CD and Temperature-variable CD were measured with an Applied Photophysics ChirascanV100 model. ^{1}HNMR spectra and ^{13}C NMR spectra of synthesized products were obtained by BRUKER AVANCE III HD 400. High-Resolution Mass Spectra

(HR-MS) were performed on an Agilent Q-TOF 6510.

Synthesis methods

Synthesis of ferrocene amino acids



Ala was synthesized according to previous reports. To a 25 mL DMF at room temperature was added L-Alanine methyl ester hydrochloride(600mg), Ferrocenecarboxylic acid(300mg), HOBt(50mg), DMAP(50mg) and EDC (500mg). Then 500 μL TEA was added. After the addition was completed, the resulting pale brown mixture was stirred overnight to give a black solution. When the reaction was finished, the reaction mixture was extracted by DCM/water. And then the crude product was purified by silica gel column (DCM : MeOH = 200:1). The pure product obtained above was added into a mixture of tetrahydrofuran and water (1:1) with LiOH (800mg), followed by stirring at room temperature for 30 min. The mixture was neutralized with hydrochloric acid, and then washed by water for several times to obtain the final product. The following NMR and Mass spectra indicate the successful synthesis of target products.

Ile (82 %)：^{1}H NMR (400 MHz, DMSO-d_6) δ 12.19 (s, 1H), 4.63 – 4.49 (m, 2H), 4.01 – 3.88 (m, 3H), 3.80 (s, 5H), 1.59 – 1.50 (m, 1H), 1.13 (m, 1H), 0.95 – 0.84 (m, 1H), 0.58 – 0.46 (m, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.53, 169.25, 75.85, 70.05, 69.99, 69.26, 68.50, 68.35, 56.47, 35.43, 24.99, 15.65, 10.84. HRMS (TOF) m/z $[M+H]^+$, calcd for $C_{17}H_{21}FeNO_3$, 344.0949; found, 344.0906. FT-IR bands: 3431 cm^{-1}, 2962 cm^{-1}, 2361 cm^{-1}, 1723 cm^{-1}, 1613 cm^{-1}, 1530 cm^{-1}, 1415 cm^{-1}, 1103 cm^{-1}, 1021 cm^{-1}, 901 cm^{-1}, 809 cm^{-1}, 744 cm^{-1}.

HA (84 %)：^{1}H NMR (400 MHz, Methanol-d_4) δ 4.84 (q, 2H), 4.37 (t, 2H), 4.18 (s, 5H), 4.08 (m, 1H), 1.62 – 1.49 (m, 2H), 1.39 (m, 4H), 1.19 (d, 3H), 0.94 (td, 3H). ^{13}C NMR (101 MHz, Methanol-d_4) δ 172.69, 172.61, 77.08, 77.04, 71.64, 71.62, 70.74, 69.59, 69.13, 46.51, 46.41, 37.19, 37.16, 29.85, 23.63, 21.44, 21.41, 14.48. HRMS (TOF) m/z $[M+H]^+$, calcd for $C_{17}H_{23}FeNO$, 314.1207; found, 314.1225. FT-IR bands: 3444 cm^{-1}, 3311 cm^{-1}, 3082 cm^{-1}, 2976 cm^{-1}, 2935 cm^{-1}, 2852 cm^{-1}, 2388 cm^{-1}, 2292 cm^{-1}, 1621 cm^{-1}, 1539 cm^{-1}, 1456 cm^{-1}, 1378 cm^{-1}, 1305 cm^{-1}, 1112 cm^{-1}, 1011 cm^{-1}, 818 cm^{-1}, 681 cm^{-1}.

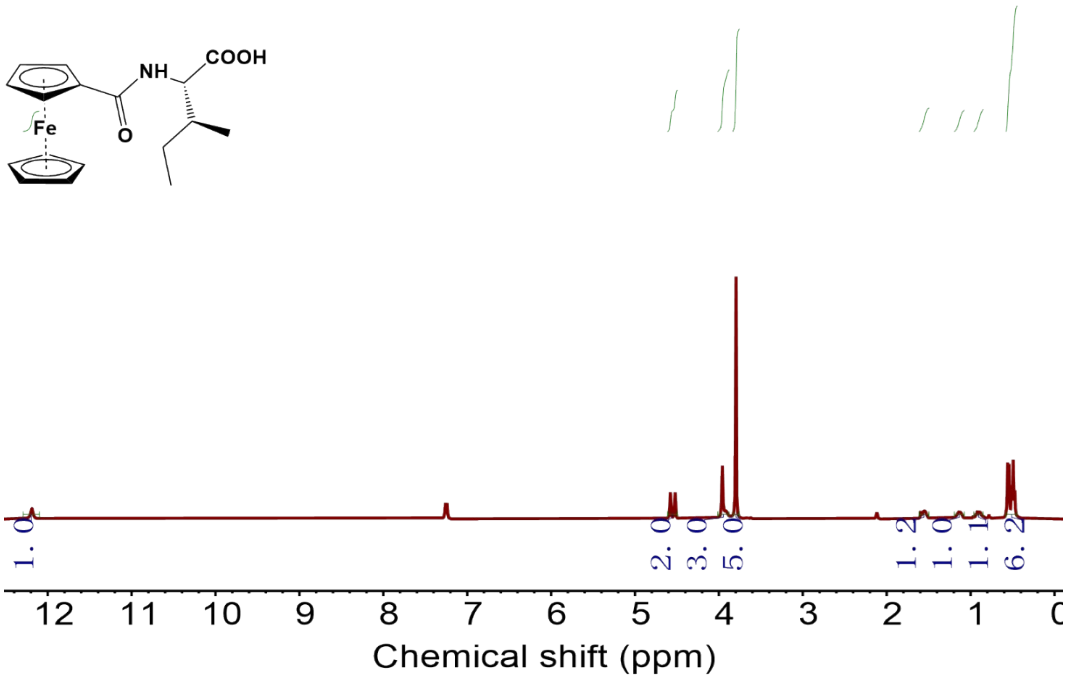


Figure S1. ^{1}H NMR spectrum of Ile.

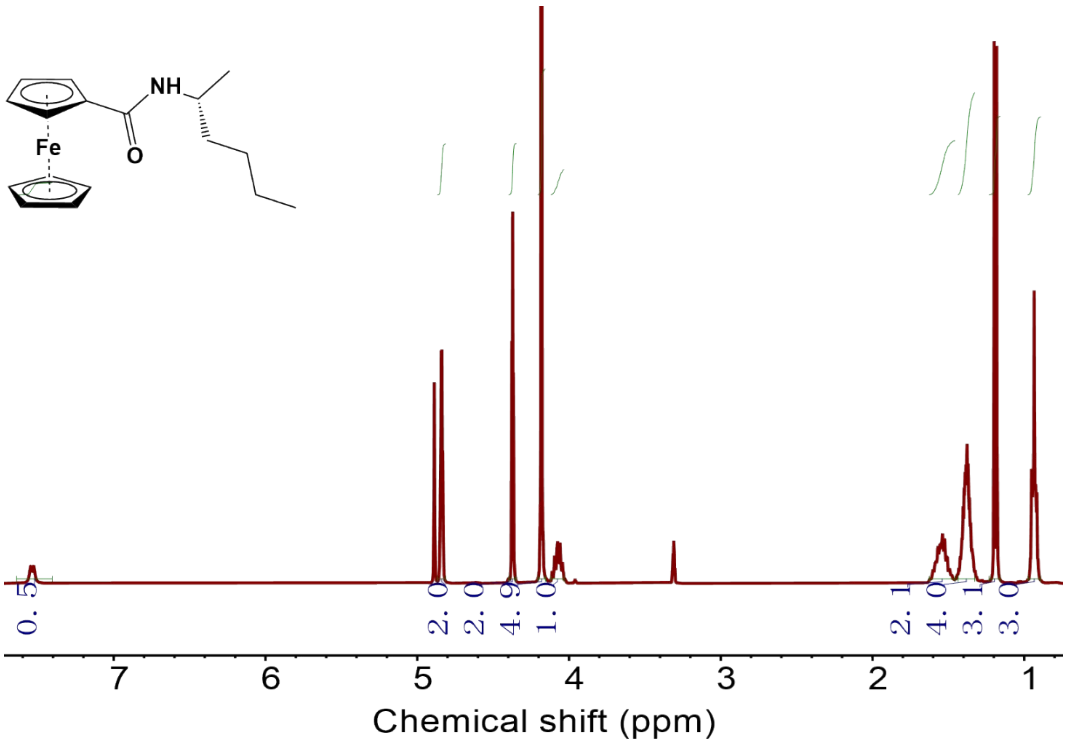


Figure S2. ^{1}H NMR spectrum of HA.

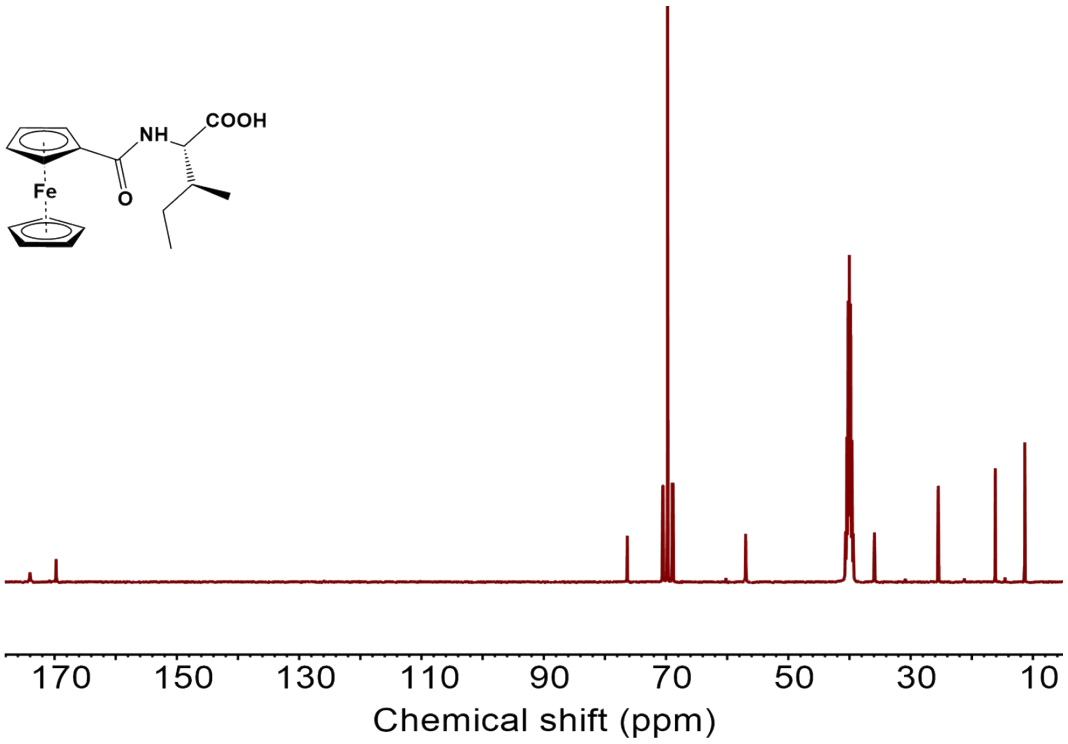


Figure S3. ^{13}C NMR spectrum of Ile.

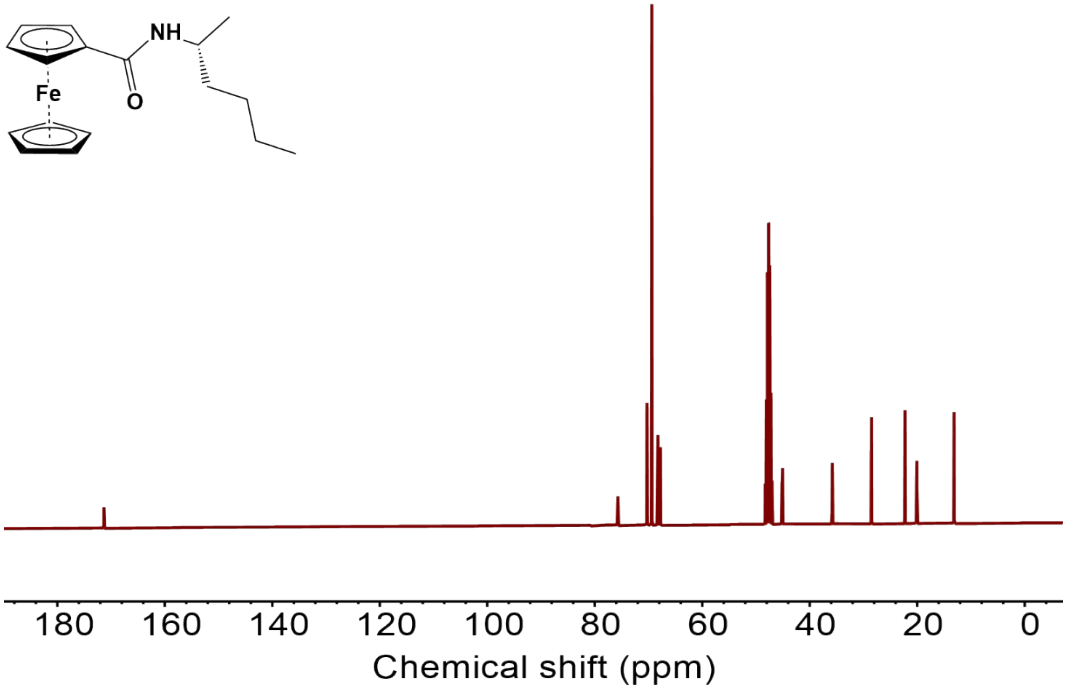


Figure S4. ^{13}C NMR spectrum of HA.

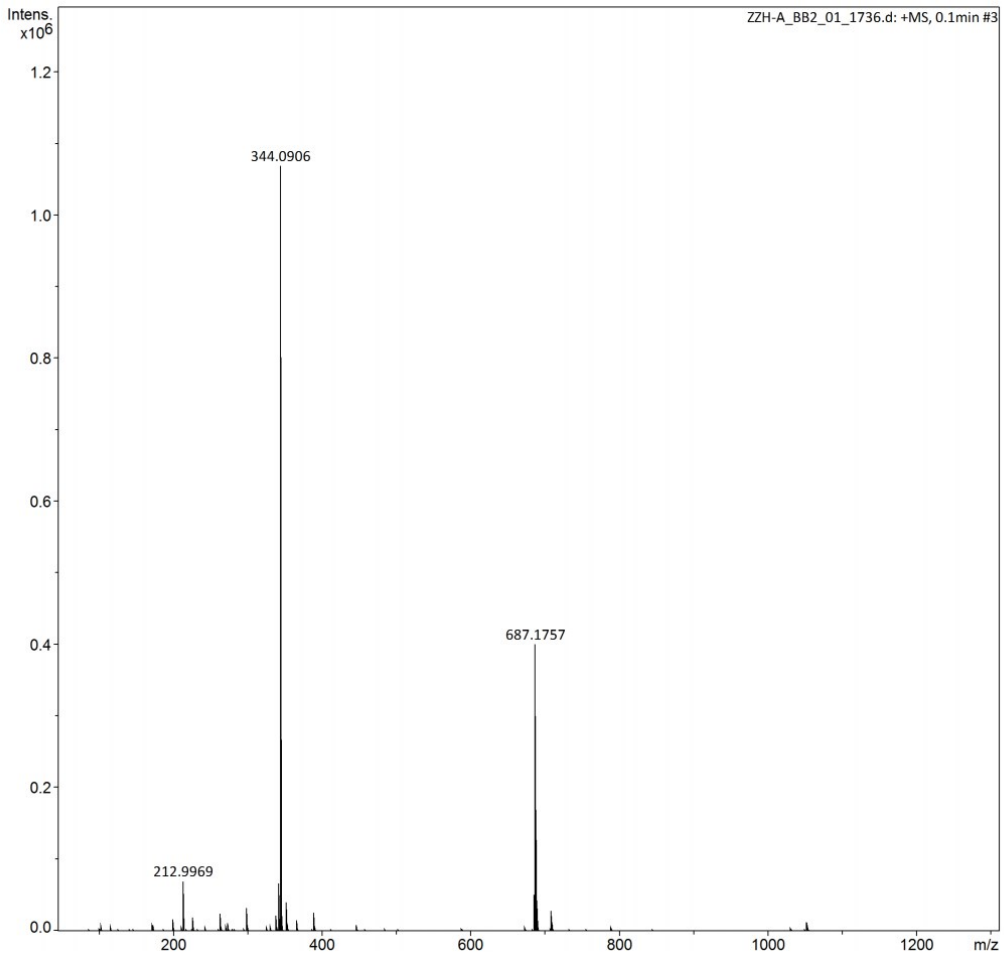


Figure S5. HRMS spectrum of Ile.

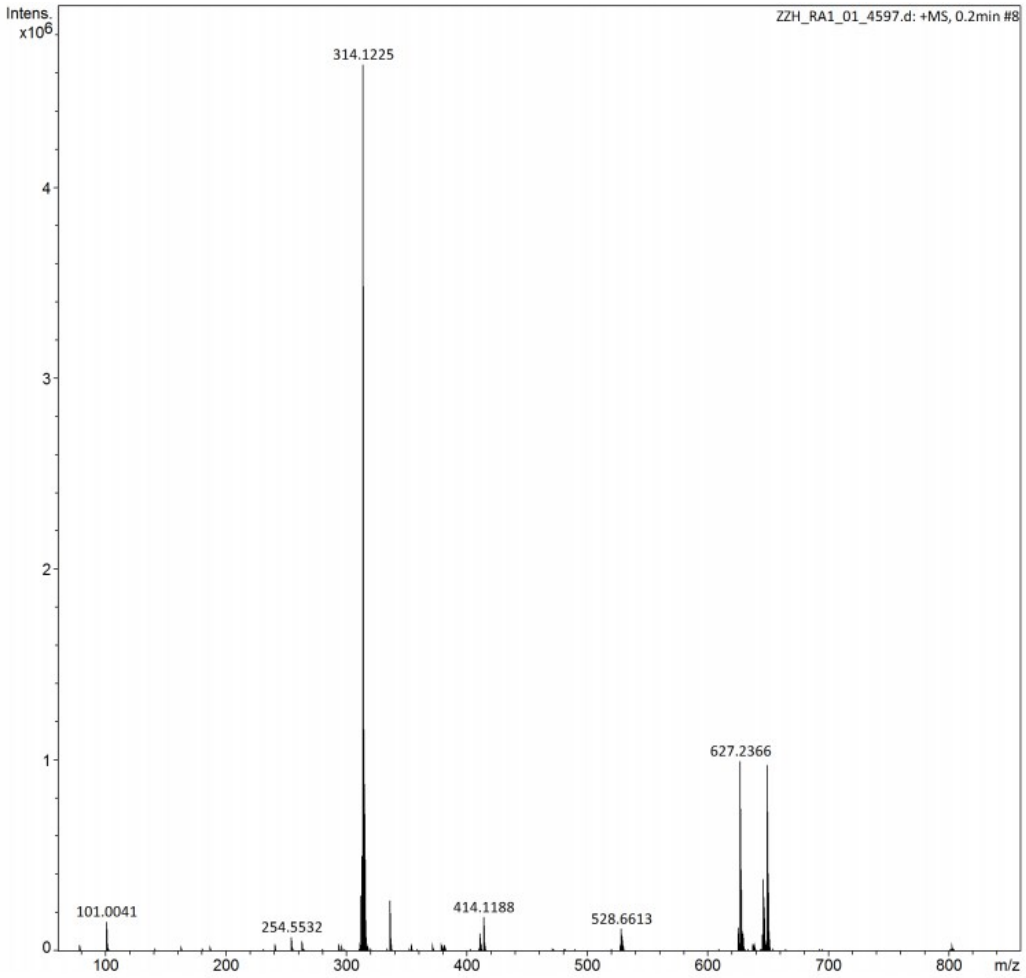


Figure S6. HRMS spectrum of HA.

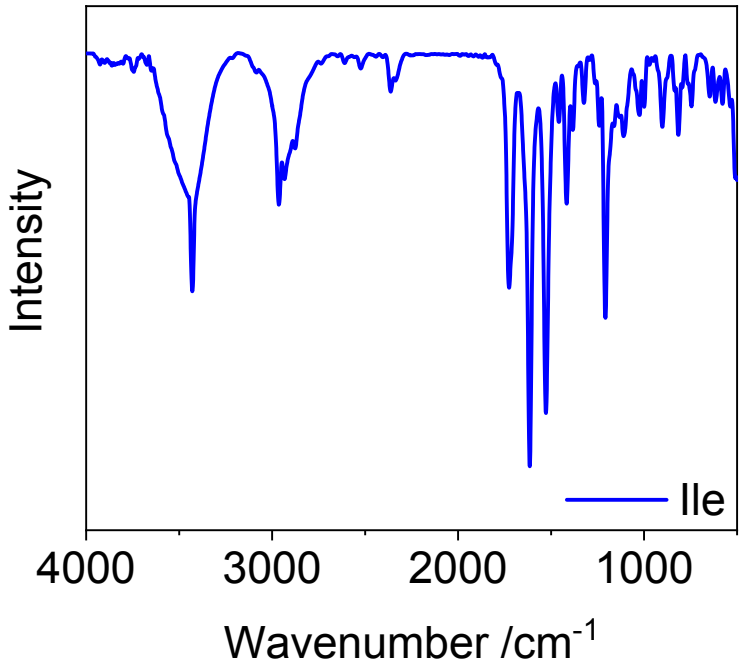


Figure S7. IR spectrum of Ile.

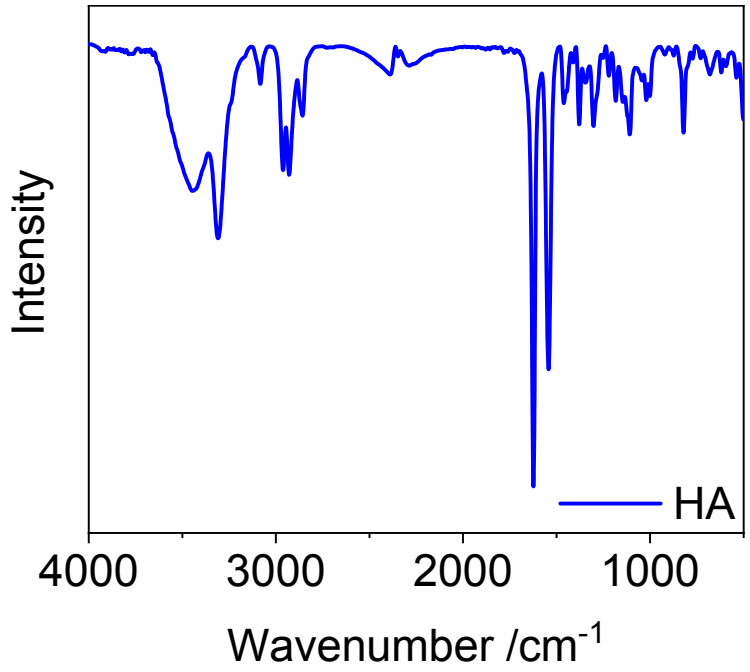


Figure S8. IR spectrum of HA.

Table S1 Crystal data of Val.

Deposition Number	2081843
Formula	C16 H19 Fe N O3
Temperature(K)	173
Wavelength	1.54184Å
Crystal system	monoclinic
Space group	P 2_1
a,b,c/Å	a 7.1314(3) b 10.4452(4) c 10.0130(5)
V, Å3	718.77(6)
Cell angles	α 90 β 105.488(5) γ 90
Z, Z'	Z: 2 Z': 0
R-factor (%)	3.58

Table S2 Crystal data of Ala.

Deposition Number	2081842
Formula	C14 H15 Fe N O3
Temperature(K)	173
Wavelength	1.54184Å
Crystal system	monoclinic
Space group	I2
a,b,c/Å	a 9.9913(2) b 9.9535(2) c 29.2374(6)
V, Å3	2884.05(10)
Cell angles	α 90 β 97.299(2) γ 90
Z, Z'	Z: 4 Z': 0
R-factor (%)	4.13

Table S3 Crystal data of PGly.

Deposition Number	2081841
Formula	C19 H17 Fe N O3
Temperature(K)	173
Wavelength	1.54184Å
Crystal system	monoclinic
Space group	P 2_1
a,b,c/Å	a 7.6376(7) b 10.6097(15) c 10.4208(14)
V, Å3	795.49(18)
Cell angles	α 90 β 109.602(13) γ 90
Z, Z'	Z: 2 Z': 0
R-factor (%)	4.55

References:

[S1] Z. Zong, P. Li, A. Hao and P. Xing, *J. Phys. Chem. Lett.* 2020, **11**, 4147.

[S2] D. Hür, S. F. E. Dal, G. A. Varol and E. Hür, *J. Organomet. Chem.*, 2011, **696**, 2543-2548.