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Preparation of α-Alkyl-β-Amino Acids via β-Alanine Ni(II) Complex

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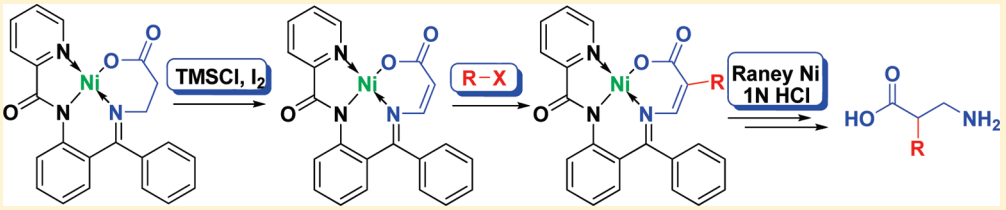
Supporting Information

ABSTRACT:



A new β-amino acrylic acid Ni(II) complex has been developed and used for the synthesis of α-alkyl-β-amino acids via alkylation with alkyl halides under operationally convenient conditions. The pivotal α-alkylated intermediate can be converted into the corresponding α-alkyl-β-amino acids via two steps with a wide range of substituents.

INTRODUCTION

α-Substituted β-amino acids (β^2-amino acids) are useful building blocks of natural products[1] and potent pharmaceutical drugs.[2] The β^2-amino acids have been widely used for the synthesis of enzyme inhibitors,[3] antivirus drugs,[4] and antibacterial drugs,[5] as well as in the treatment of inflammatory disease and pain;[6] furthermore, they have gained considerable attention in the biochemical studies.[7] It is these pharmaceutical and biochemical applications that have provided the motivation to devise an efficient synthetic methodology. The synthesis of racemic β^2-amino acids is operationally convenient and industrially attractive. Nowadays, chiral resolution has been commonly used in companies and academies. Thus, the racemic β^2-amino acids can be optically resolved to both enantiopure isomers with resoluting agents. In this view, the synthesis of racemic β^2-amino acids is important.[8] Until date, alkylation,[9] Knoevenagel condensation,[10] Mannich reaction,[11] Baylis-Hillman reaction,[12] Michael reaction,[13] and other methods[14] have been used in the synthesis of racemic β^2-amino acids. For instance, Avila-Ortiz et al. report the alkylation of 3-amino propanoate derivates with benzyl iodide at low temperature;[9a] however, this method requires a strong base and harsh reaction condition. Lee et al. describe a Knoevenagel condensation of cyanoacetate and aldehyde with subsequent hydrogenation,[10] but this approach requires a reduction step to convert the cyano moiety to an amino group using expensive catalyst. Moumne et al. describe a Mannich reaction that leads to β^2-amino acids,[11a] and Hofling et al. report an approach that generates the β^2-amino acids via Baylis-Hillman reaction and Michael reaction.[12a] However, these methods rely on the use of a relatively rare reactant that might limit their broad applications. There are few approaches for the preparation of β^2-amino acids in substituted variants, due to the usage of expensive, dangerous or toxic reagents, or elaborate reaction conditions. Therefore, there is an urgent requirement for developing a synthetic approach of β^2-amino acids that is operationally convenient, environmentally benign, and industrially available.

Recently, Ni(II) complexes of the Schiff base of glycine and β-alanine have been used to synthesize α- and β-amino acids.[15] In particular, the 2-[*N*-(α-picolyl)amino]benzophenone (PABP) ligand has been developed and successfully utilized for the synthesis of nonpeptide amino acids.[16] This method, rivaling the aforementioned synthetic methodologies of β^2-amino acids, possesses many merits, such as operationally convenient reaction procedures, low cost materials, and easy recovery of the ligands. Previously, we reported the preparation of α-aryl-β-amino acids[16f] and α,α-disubstituted β-amino acids via Ni(II) complex.[16g] However, the α-monosaturated alkyl-β-amino acids were not obtained under these conditions. To overcome the shortcoming, we developed a new type of β-amino acrylic acid Ni(II) complex **2**. Baylis-Hillman-type[17] alkylation of **2** with alkyl halides resulted in the formation of Ni(II) complex **4**, which afforded the corresponding β^2-amino acid upon hydrogenation and subsequent decomposition. Unexpectedly, direct decomposition of **4** led to the formation of the 3-arylpropanal (Scheme 1). We report herein a short, straightforward, synthetic method of β^2-amino acids **6** from β-amino acrylic acid Ni(II) complex **2** via alkylation, hydrogenation, and hydrolization.

RESULTS AND DISCUSSION

We initiated our studies by the synthesis of the β-amino acrylic acid Ni(II) complex **2** and various reaction conditions were

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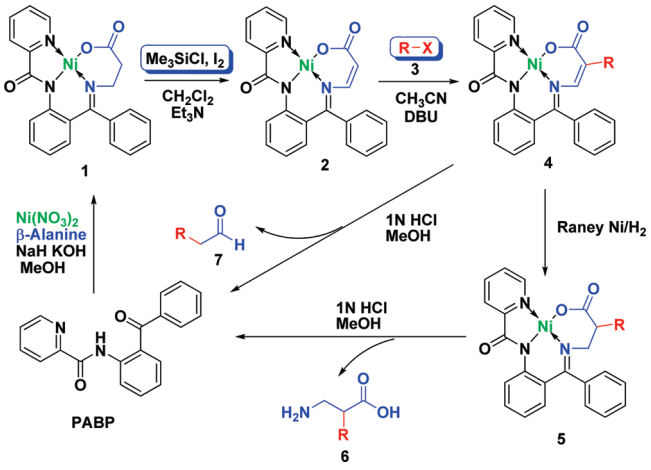
Scheme 1. Preparation of α-Alkyl-β-Amino Acids and 3-Aryl-Propanal via Ni(II) Complex



Scheme 2. Mechanism of the Synthesis of the β-Amino Acrylic Acid Ni(II) Complex 2

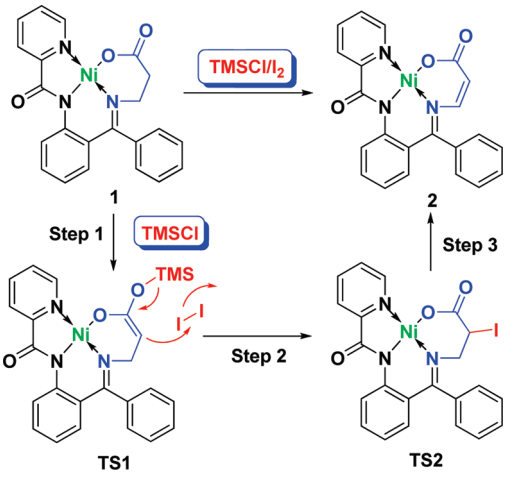
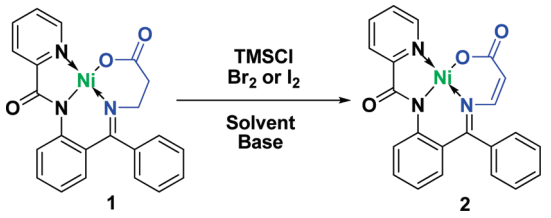


Table 1. Optimization of the Reaction Conditions[a]



entry	solvent	equiv of TMSCl	base	halogen	temp (°C)	yield (%)
1	DMF	0	*t*-BuOK	Br_2	r.t.	trace
2	DMF	0	NaOH	Br_2	r.t.	0
3	DMF	0	TEA	Br_2	r.t.	0
4	DMF	10	TEA	Br_2	r.t.	11
5	DMF	10	TEA	I_2	r.t.	52
6	THF	10	TEA	I_2	r.t.	21
7	toluene	10	TEA	I_2	r.t.	trace
8	CH_3OH	10	TEA	I_2	r.t.	0
9	CH_2Cl_2	10	TEA	I_2	r.t.	72
10	CH_2Cl_2	3	TEA	I_2	r.t.	34
11	CH_2Cl_2	5	TEA	I_2	r.t.	78
12	CH_2Cl_2	5	TEA	I_2	−20	13
13	CH_2Cl_2	5	TEA	I_2	0	40
14	CH_2Cl_2	5	TEA	I_2	40	81
15	CH_2Cl_2	5	TEA	I_2	60	80

[a] Reactions were run with 0.234 mmol of 1, 0.468 mmol of halogen, in 4 mL of solvent and 1 mL of TEA with TMSCl for 2 h.

examined. By using bromine combined with the potassium *tert*-butoxide (*t*-BuOK) in DMF, only trace of the target product was detected (Table 1, entry 1). Then various bases, such as triethylamine (TEA), sodium hydrate (NaOH), were examined. Unfortunately, the reaction could not be conducted and only the starting material **1** was recovered (entries 2−3). Surprisingly, we obtained the product **2** in a low yield (11%), when TEA was selected as base and 10 equiv of chlorotrimethylsilane (TMSCl) and bromine were applied in DMF at room temperature (entry 4). Considering too many byproducts were generated by using bromine in this reaction condition, we replaced bromine with iodine and then found that the yield of the product increased to 52% (entry 5). Subsequently different solvents were screened, and the results showed that dichloromethane was the optimal solvent (entries 6−9). Furthermore, we tried to reduce the amounts of TMSCl, and the investigations revealed that the product **2** was afforded in 78% yield when 5 equiv of TMSCl was used (entries 9−11). Finally, the reaction temperature was found to be an important factor in this transformation. The yield of the product decreased rapidly when the reaction temperature was lowered, while raising the temperature facilitated the good yield (entries 11−15). To explain this result, we assumed that the mechanism of the synthesis of the β-amino acrylic acid Ni(II) complex **2** comprised three steps (Scheme 2). For step one, β-alanine Ni(II) complex **1** was converted to silyl enol ether **TS1** by TMSCl, which resulted in the activation of the α-position of the carboxyl. Then, iodine was attacked by the activated α-carbon to afford the intermediate **TS2**. Finally, the intermediate **TS2** was converted to product **2** via the elimination of iodine.

Considering the operationally convenient reaction procedures, we used 1.0 equiv of β-alanine Ni(II) PABP **1**, 5.0 equiv of TMSCl, and 2.0 equiv of iodine in a dichloromethane/TEA (V/V = 4/1) mixture to obtain the key intermediate **2** at room temperature. We proceeded to carry out the alkylation of this key intermediate **2** in the present study. As a model reaction, we carried out alkylation of the β-amino acrylic acid Ni(II) complex **2** with benzyl chloride **3a**. However, the application of *t*-BuOK as base in DMF did not provide the desirable product **4a** (Table 2, entry 1). Then we screened other bases and solvents. Quite unexpectedly, when DMF and 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) were employed, the yield of the target product **4a** increased with a corresponding increase in the concentration of **2** in DMF. Having noticed that the concentration of **2** played a significant role in this reaction, we therefore proceeded to investigate the solvent effect in detail. As expected, an increase of the concentration of **2** led to an increase in the yield of the target product. After the concentration (1 mol/L of **2**) was fixed, we rescreened the solvents and bases and found that acetonitrile was the optimal solvent (entries 2−5). Unfortunately, there was no improvement in the yield when other bases, such as sodium

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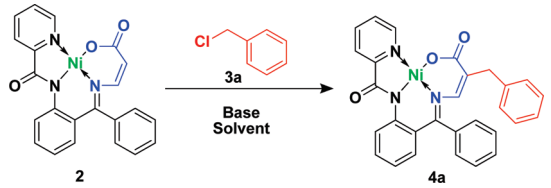
Table 2. Optimization of the Alkylation Conditions[a]



entry	base	solvent	temp (°C)	yield (%)
1	*t*-BuOK	DMF	r.t.	0
2	DBU	DMF	r.t.	60
3	DBU	CH_2Cl_2	r.t.	trace
4	DBU	toluene	r.t.	0
5	DBU	CH_3CN	r.t.	87
6	NaH	CH_3CN	r.t.	10
7	TEA	CH_3CN	r.t.	30
8	DABCO	CH_3CN	r.t.	46
9[b]	DBU	neat	r.t.	91
10	DBU	CH_3CN	−20	40
11	DBU	CH_3CN	0	73
12	DBU	CH_3CN	40	85
13	DBU	CH_3CN	60	86

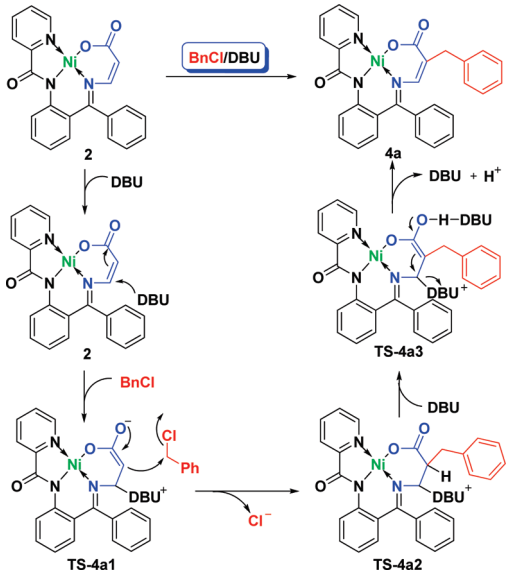
[a] Reactions were run with 0.234 mmol of **2**, 0.352 mmol of **3a**, 0.352 mmol of DBU in 0.23 mL of solvent for 1 h. [b] Reaction was run with 0.234 mmol of **2**, 0.352 mmol of DBU in 0.936 mmol of **3a**.

hydride (NaH), TEA, and 1,4-diazabicyclo[2.2.2]octane (DABCO), were employed (entries 5−8). Although the solvent-free reaction could provide the target Ni(II) complex **4a** in 91% yield, up to 4.0 equiv of benzyl chloride was necessary to solve **2** (entry 9). Finally, we focused on the effect of reaction temperature (entries 10−13). A decrease in the reaction temperature resulted in a decrease of the reaction rate and conversion, whereas an increase in the temperature did not bring about any apparent improvement in the conversion. From the viewpoint of practical applications, we chose DBU as the base and acetonitrile as the solvent and carried out the reaction at ambient temperature (this solvent-base system and temperature were the optimized conditions), with the aim of demonstrating the generality of the alkylation (entry 5).

The intriguing result of this alkylation motivated us to study its mechanism. A probable mechanism of the alkylation, which was analogic to the Baylis−Hillman reaction,[17] is illustrated in Scheme 3. The nucleophilic addition of the nitrogen of DBU onto the carbon−carbon double bond of β-amino acrylic acid Ni(II) complex **2** gave a charged zwitterionic intermediate **TS-4a1**, which would add to the electrophilic benzyl chloride producing the intermediate **TS-4a2**. Then the nitrogen of excess DBU connected with the oxygen of **TS-4a2** by hydrogen bonding to promote the enolization of **TS-4a2** and formed enol ether **TS-4a3**. Finally, the elimination of the DBU gave the alkylated product **4a**.

Then we investigated the scope of this reaction in detail; the results are summarized in Table 3. A wide variety of halides **3** was used in the reaction and the corresponding products were isolated in moderate to good yields. Benzyl chlorides bearing an electron-donating group or halogen groups were well tolerated in this reaction (entries 2 and 4−6), while those with an electron-withdrawing group typically gave a low yield (entry 3). Steric effects were also observed: alkylation of

Scheme 3. Probable Mechanism of the Alkylation of Ni(II) Complex 2



mono- and multisubstituted benzyl chlorides proceeded with ease to afford the product in reasonable yields (entries 7−12), while the sterically hindered benzhydryl chloride was less reactive (entry 13). Additionally, we probed the substrate scope of the reaction, that is, the feasibility of extending this reaction to chloromethyl heterocycles. The product yield in the reaction of 2-(chloromethyl)quinoline was lower than that in the reaction of 1-(chloromethyl)naphthalene, presumably because of the electron-withdrawing effect of quinoline (entry 14). Alkyl chlorides did not afford the desired product at all, while alkyl bromides and alkyl iodides gave the corresponding products in low and reasonable yields, respectively, which was a trend typically observed in alkylation reactions (entries 15−17). The primary iodoalkanes afforded the target product in reasonable yield (entries 17−21), while the secondary iodoalkane could hardly react with the Ni(II) complex **2** due to the steric effect (entry 22).

Two steps were required to obtain α-alkyl β-alanine **6** from compound **4**. Initially, Raney Ni was used as the catalyst for hydrogenation of the carbon−carbon double bond in **4**, so that **5** could be obtained in good yield. Then, asymmetric hydrogenation was attemped under several conditions. Unfortunately, these attempts were all failed. By using chiral catalysts (e.g., RuCl [(*R*,*R*)-Tsdpen](*p*-cymene)), the reactions could not be conducted and only **4** was recovered. While using Raney Ni with chiral ligends, such as (*R*)-BINAL, (*R*)-BINAP, and cinchonine, only racemic product was obtained. Then, we tried the decomposition of **5**. The Ni(II) complex **5** were stirred in a methanol/HCl (1 N) mixture at room temperature to afford the target amino acid **6**; PABP was quantitatively recovered in this step (Scheme 4).

Meanwhile, attempts were made to hydrolyze **4a** directly in the methanol/HCl (1 N) mixture. Under this condition, unexpectablely, PABP was recovered and **7a** was isolated in 61% yield (Scheme 5). A possible mechanism of the generation of **7a** was proposed in Scheme 6. For step one, the Ni(II) complex **4a** was hydrolyzed to 3-amino acrylic acid **TS-7a1** by 1N HCl and released the ligand PABP. Then, 2-benzyl-3-iminopropanoic acid **TS-7a2** was transformed via the imine-enamine tautomerism of **TS-7a1**. In the third step, hydrolization of **TS-7a2** afforded the α-

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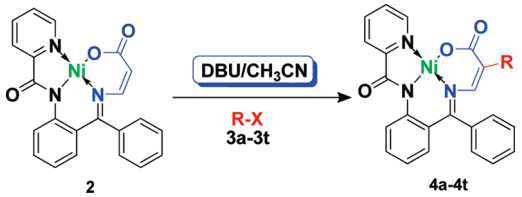
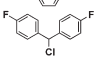
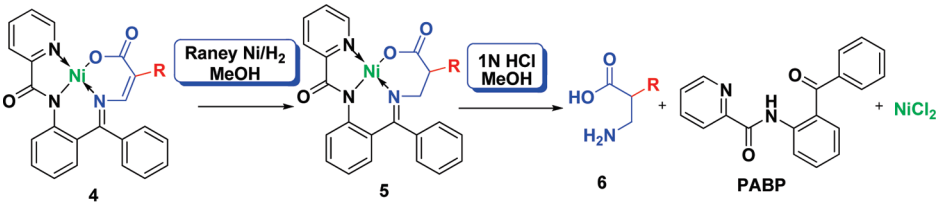
Table 3. Alkylation of Ni(II) Complex 2 with Alkyl Halides 3[a]



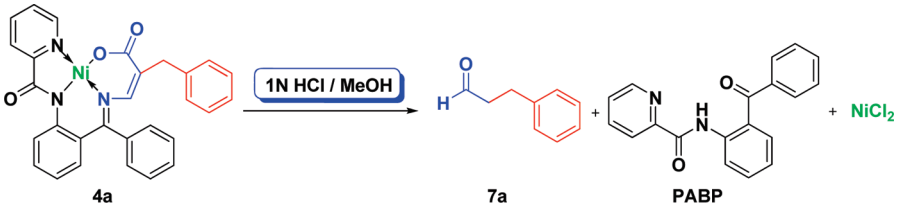
entry	alkyl halide **3**	products	yield (%)	entry	alkyl halide **3**	products	yield (%)
1		**4a**	85	12		**4l**	64
2		**4b**	83	13		**4m**	44
3		**4c**	54	14		**4n**	48
4		**4d**	78	15		**4o**	0
5		**4e**	68	16		**4o**	27
6		**4f**	70	17		**4o**	63
7		**4g**	82	18		**4p**	69
8		**4h**	80	19		**4q**	60
9		**4i**	83	20		**4r**	54
10		**4j**	79	21		**4s**	62
11		**4k**	74	22		**4t**	trace

[a] Reactions were run with 0.234 mmol of **2**, 0.353 mmol of **3a**-**3t** in 0.23 mL CH_3CN under the 0.353 mmol DBU for 1 h.

Scheme 4. Decomposition of Ni(II) Complexes 4 to Release Amino Acids 6



Scheme 5. Decomposition of Ni(II) Complex 4a to Release Propanal 7a



benzyl malonaldehydic acid **TS-7a3**. Finally, **TS-7a3** converted to 3-phenylpropanal **7a** via decarboxylation.

In summary, we have successfully developed a new β-amino acrylic acid Ni(II) complex **2** and applied it for alkylation with alkyl halides under operationally convenient conditions, without recourse to inert atmosphere, dry solvents, and low temperatures. Thus, the key advantages such as experimental simplicity and attractive cost structure could be realized. A broad range of benzyl substrates could be employed in the reaction. The results of this study demonstrate that our method can be used for the synthesis of a variety of β^2-amino acids.

EXPERIMENTAL SECTION

Procedure for the Synthesis of 2. A solution of chlorotrimethylsilane (11.5 mmol) in dichloromethane (10 mL) was added dropwise to a stirred solution of β-alanine Ni(II) complex **1** (2.3 mmol) in dichloromethane (20 mL) and triethylamine (10 mL) at 0 °C. After

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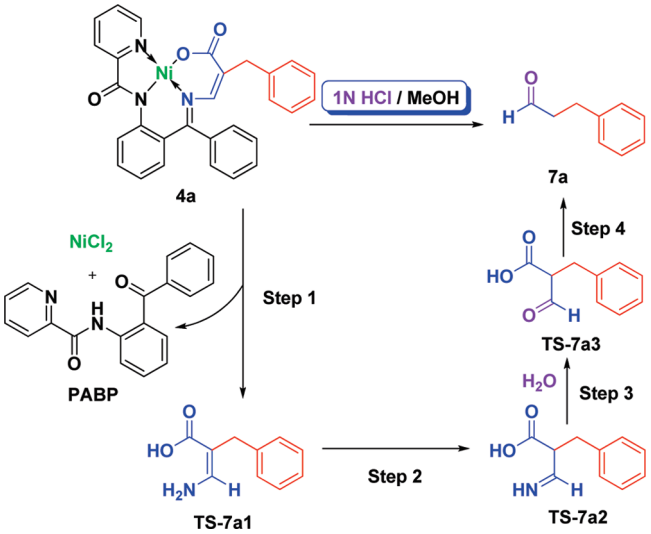
Scheme 6. Possible Mechanism of the Synthesis of 7a



0.5 h, a solution of iodine (4.6 mmol) in dichloromethane (10 mL) was slowly added to the mixture within 2 h. The resulting mixture was then stirred at ambient temperature for 2 h. The reaction was quenched by pouring the crude reaction mixture over 50 mL of aq. sat. NH_4Cl. The suspension was extracted with dichloromethane (3 times). The combined organic layers were dried with $MgSO_4$, concentrated, and purified by column chromatography on silica gel (dichloromethane/methanol = 50/1) to give **2** as a black-red solid (78% yield).

Ni(II)-PABP/3-Amino-acrylic Acid Schiff Base Complex 2. Dark-red solid. Mp 114−116 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.52 (d, J = 8.1 Hz, 1H), 8.30 (d, J = 5.7 Hz, 1H), 8.00 (t, J = 7.2 Hz, 1H), 7.91 (d, J = 7.2 Hz, 1H), 7.58−7.48 (m, 4H), 7.41−7.34 (m, 1H), 7.13 (d, J = 6.6 Hz, 2H), 6.81−6.77 (m, 2H), 6.42 (d, J = 8.7 Hz, 1H), 5.56 (d, J = 8.7 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 119.7, 121.4, 123.4, 124.0, 126.8, 128.1, 129.0, 129.2, 131.0, 134.8, 135.5, 135.8, 140.5, 142.2, 143.6, 145.4, 152.3, 169.3, 174.9 ppm. MS (EI, m/z): 427 $[M]^+$; HRMS (EI): calcd for $C_{22}H_{15}N_3NiO_3$ $[M]^+$ 427.0467; found 427.0475.

Procedure for the Synthesis of 4a. Benzyl chloride **3a** (1.76 mmol) and DBU (1.76 mmol) were added to a stirred solution of compound **2** (1.17 mmol) in acetonitrile (1.15 mL). The heterogeneous solution was stirred at ambient temperature for 1 h. The reaction was quenched by pouring the crude reaction mixture over 20 mL aq sat. NaCl. The suspension was extracted with dichloromethane (3 times). The combined organic layers were dried with $MgSO_4$, concentrated, and purified by column chromatography on silica gel (dichloromethane/methanol = 100/1) to give **4a** as a dark-red solid.

Ni(II)-PABP/3-Amino-2-benzylacrylic Acid Schiff Base Complex 4a. Dark-red solid. Mp 234−236 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.52 (d, J = 8.7 Hz, 1H), 8.28 (d, J = 5.1 Hz, 1H), 7.99−7.96 (m, 1H), 7.89 (d, J = 7.5 Hz, 1H), 7.50−7.45 (m, 2H), 7.41−7.30 (m, 3H), 7.10−7.08 (m, 2H), 6.99−6.92 (m, 4H), 6.77−6.71 (m, 2H), 5.95 (s, 1H), 3.50 (s, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 37.1, 121.3, 123.2, 123.9, 126.1, 126.8, 128.0, 128.4, 128.9, 129.1, 130.5, 131.9, 134.2, 135.2, 135.9, 140.5, 143.2, 145.5, 152.5, 167.0, 169.3, 173.1 ppm. MS (EI, m/z): 517 $[M]^+$. HRMS (EI): calcd for $C_{29}H_{21}N_3NiO_3$ $[M]^+$ 517.0936; found 517.0939.

Ni(II)-PABP/3-Amino-2-(4-methoxybenzyl)acrylic Acid Schiff Base Complex 4b. Dark-red solid. Mp 76−78 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.51 (d, J = 8.7 Hz, 1H), 8.28 (d, J = 4.5 Hz, 1H), 7.98 (t, J = 7.5 Hz, 1H), 7.89 (d, J = 7.5 Hz, 1H), 7.51−7.44 (m, 2H), 7.41−7.31 (m, 3H), 6.95−6.87 (m, 4H), 6.80−6.71 (m, 2H), 6.63 (d, J = 8.4 Hz, 2H), 6.02 (s, 1H), 3.75 (s, 3H), 3.47 (s, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 36.3, 55.2, 113.8, 121.3, 123.2, 123.9, 126.7, 128.0, 128.9, 130.1, 130.2, 130.3, 134.2, 135.1, 136.0, 140.4, 143.2, 145.5, 152.4, 157.9, 169.3, 173.0 ppm. MS (EI, m/z): 547 $[M]^+$. HRMS (EI): calcd for $C_{30}H_{23}N_3NiO_4$ $[M]^+$ 547.1042; found 547.1032.

Ni(II)-PABP/3-Amino-2-(4-(trifluoromethyl)benzyl)acrylic Acid Schiff Base Complex 4c. Dark-red solid. Mp 87−90 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.51 (d, J = 8.4 Hz, 1H), 8.27 (d, J = 4.8 Hz, 1H), 8.12−7.99 (m, 1H), 7.91 (d, J = 7.8 Hz, 1H), 7.51−7.44 (m, 3H), 7.37−7.32 (m, 4H), 7.10 (d, J = 8.1 Hz, 2H), 6.90 (d, J = 6.9 Hz, 2H), 6.75−6.71 (m, 2H), 5.89 (s, 1H), 3.56 (s, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 36.8, 121.4, 123.3, 124.0, 125.4, 126.8, 127.4, 127.8, 128.2, 128.7, 128.9, 129.4, 130.0, 130.6, 131.0, 132.4, 132.8, 134.5, 135.3, 135.9, 140.6, 140.7, 142.6, 143.3, 145.5, 152.4, 166.6, 169.4, 173.6 ppm. MS (EI, m/z): 585 $[M]^+$. HRMS (EI): calcd for $C_{30}H_{20}F_3N_3NiO_3$ $[M]^+$ 585.0810; found 585.0811.

Ni(II)-PABP/3-Amino-2-(4-fluorobenzyl)acrylic Acid Schiff Base Complex 4d. Dark-red solid. Mp 229−232 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.51 (d, J = 8.7 Hz, 1H), 8.27 (d, J = 5.4 Hz, 1H), 7.99 (t, J = 7.8 Hz, 1H), 7.89 (d, J = 7.5 Hz, 1H), 7.50−7.46 (m, 2H), 7.42−7.26 (m, 3H), 7.02−6.92 (m, 4H), 6.81−6.72 (m, 4H), 5.93 (s, 1H), 3.47 (s, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 36.3, 114.9, 115,1, 115.3, 121.3, 123.2, 123.9, 126.8, 127.9, 128.8, 128.9, 130.3, 130.5, 131.7, 134.0, 134.3, 135.2, 136.0, 140.5, 143.3, 145.5, 152.4, 166.8, 169.3, 173.3 ppm. MS (EI, m/z): 535 $[M]^+$. HRMS (EI): calcd for $C_{29}H_{20}FN_3NiO_3$ $[M]^+$ 535.0842; found 535.0841.

Ni(II)-PABP/3-Amino-2-(4-chlorobenzyl)acrylic Acid Schiff Base Complex 4e. Dark-red solid. Mp 162−164 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.51 (d, J = 8.7 Hz, 1H), 8.27 (d, J = 5.1 Hz, 1H), 7.99−7.96 (m, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.52−7.45 (m, 2H), 7.41−7.31 (m, 3H), 7.07 (d, J = 8.1 Hz, 2H), 6.91 (d, J = 8.1 Hz, 4H), 6.77−6.72 (m, 2H), 5.94 (s, 1H), 3.47 (s, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 36.4, 121.4, 123.3, 123.9, 126.8, 127.9, 128.2, 128.5, 128.7, 129.0, 130.0, 130.5, 131.4, 132.0, 134.4, 135.2, 135.9, 140.5, 140.6, 143.3, 145.5, 152.4, 166.7, 169.4, 173.4 ppm. MS (EI, m/z): 551 $[M]^+$. HRMS (EI): calcd for $C_{29}H_{20}ClN_3NiO_3$ $[M]^+$ 551.0547; found 551.0546.

Ni(II)-PABP/3-Amino-2-(4-bromobenzyl)acrylic Acid Schiff Base Complex 4f. Dark-red solid. Mp 240−243 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.51 (d, J = 8.4 Hz, 1H), 8.27 (d, J = 6.3 Hz, 1H), 8.02−7.96 (m, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.53−7.45 (m, 2H), 7.42−7.34 (m, 3H), 7.23−7.20 (m, 2H), 6.91 (d, J = 6.9 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 6.77−6.72 (m, 2H), 5.92 (s, 1H), 3.45 (s, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 36.5, 120.1, 121.3, 123.3, 123.9, 126.7, 127.9, 128.2, 128.7, 129.0, 130.0, 130.5, 130.9, 131.4, 131.5, 134.4, 135.2, 135.9, 137.4, 140.5, 140.6, 143.3, 145.5, 152.4, 166.6, 169.4, 173.4 ppm. MS (EI, m/z): 595 $[M]^+$. HRMS (EI): calcd for $C_{29}H_{20}BrN_3NiO_3$ $[M]^+$ 595.0042; found 595.0028.

Ni(II)-PABP/3-Amino-2-(2-methylbenzyl)acrylic Acid Schiff Base Complex 4g. Dark-red solid. Mp 184−187 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.51 (d, J = 8.7 Hz, 1H), 8.32 (d, J = 5.4 Hz, 1H), 8.00−7.96 (m, 1H), 7.90 (d, J = 7.5 Hz, 1H), 7.51−7.49 (m, 1H), 7.41−7.38 (m, 1H), 7.34−7.30 (m, 3H), 7.13−7.11 (m, 1H), 6.95−6.82 (m, 5H), 6.74−6.67 (m, 2H), 5.67 (s, 1H), 3.53 (s, 2H), 2.10 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.4, 34.5, 121.2, 123.2, 123.9, 126.0, 126.4, 126.7, 127.9, 128.4, 128.8, 129.8, 130.2, 131.1, 134.2, 135.1, 135.8, 136.1, 140.0, 140.5, 143.1, 145.5, 152.4, 167.1, 169.3, 173.1 ppm. MS (EI, m/z): 531 $[M]^+$. HRMS (EI): calcd for $C_{30}H_{23}N_3NiO_3$ $[M]^+$ 531.1093; found 531.1086.

Ni(II)-PABP/3-Amino-2-(3-methylbenzyl)acrylic Acid Schiff Base Complex 4h. Dark-red solid. Mp 107−109 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.51 (d, J = 8.7 Hz, 1H), 8.25 (d, J = 3.6 Hz, 1H), 8.01−7.95 (m, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.48−7.45 (m, 2H), 7.40−7.30 (m, 3H), 7.01−6.87 (m, 4H), 6.79−6.70 (m, 4H), 6.02 (s, 1H), 3.50 (s, 2H), 2.22 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.4, 37.0,

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121.3, 123.2, 123.9, 126.1, 126.7, 126.9, 128.0, 128.3, 128.7, 128.9, 129.9, 130.4, 132.2, 134.2, 135.1, 135.9, 137.7, 138.1, 140.4, 143.2, 145.5, 152.4, 167.1, 169.3, 173.0 ppm. MS (EI, *m*/*z*): 531 $[M]^+$. HRMS (EI): calcd for $C_{30}H_{23}N_3NiO_3$ $[M]^+$ 531.1093; found 531.1092.

Ni(II)-PABP/3-Amino-2-(4-methylbenzyl)acrylic Acid Schiff Base Complex 4i. Dark-red solid. Mp 69−71 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.51 (d, J = 6.0 Hz, 1H), 8.28 (d, J = 5.4 Hz, 1H), 7.98 (t, J = 7.2 Hz, 1H), 7.89 (d, J = 7.5 Hz, 1H), 7.50−7.44 (m, 2H), 7.40−7.30 (m, 3H), 6.94−6.83 (m, 6H), 6.77−6.71 (m, 2H), 5.95 (s, 1H), 3.46 (s, 2H), 2.25 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.0, 36.7, 121.3, 123.2, 123.9, 126.7, 128.0, 128.9, 129.0, 129.1, 130.3, 132.2, 134.2, 135.1, 135.5, 136.0, 140.4, 143.2, 145.6, 152.5, 167.0, 169.4, 173.1 ppm. MS (EI, *m*/*z*): 531 $[M]^+$. HRMS (EI): calcd for $C_{30}H_{23}N_3NiO_3$ $[M]^+$ 531.1093; found 531.1086.

Ni(II)-PABP/3-Amino-2-(2,5-dimethylbenzyl)acrylic Acid Schiff Base Complex 4j. Dark-red solid. Mp 89−90 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.50 (d, J = 8.7 Hz, 1H), 8.32 (d, J = 5.1 Hz, 1H), 8.00 (t, J = 7.5 Hz, 1H), 7.90 (d, J = 7.5 Hz, 1H), 7.51−7.47 (m, 1H), 7.41−7.38 (m, 1H), 7.35−7.27 (m, 3H), 6.85 (d, J = 7.2 Hz, 2H), 6.80−6.65 (m, 5H), 5.67 (s, 1H), 3.48 (s, 2H), 2.16 (s, 3H), 2.06 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.0, 20.9, 34.6, 121.2, 123.2, 123.9, 126.7, 127.1, 127.9, 128.4, 128.6, 130.1, 130.6, 131.3, 132.9, 134.1, 135.1, 135.8, 135.9, 140.5, 143.1, 145.5, 152.4, 167.0, 169.3, 173.0 ppm. MS (EI, *m*/*z*): 545 $[M]^+$. HRMS (EI): calcd for $C_{31}H_{25}N_3NiO_3$ $[M]^+$ 545.1249; found 545.1250.

Ni(II)-PABP/3-Amino-2-(2,4,6-trimethylbenzyl)acrylic Acid Schiff Base Complex 4k. Dark-red solid. Mp 123−125 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.49 (d, J = 8.7 Hz, 1H), 8.36 (d, J = 5.4 Hz, 1H), 8.02−7.98 (m, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.53−7.48 (m, 1H), 7.38−7.23 (m, 4H), 6.79−6.65 (m, 4H), 6.55 (s, 2H), 5.52 (s, 1H), 3.51 (s, 2H), 2.16 (s, 3H), 2.05 (s, 6H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.0, 20.7, 30.4, 121.2, 123.2, 123.9, 126.7, 127.8, 128.0, 128.7, 129.7, 130.1, 131.4, 134.1, 135.1, 135.2, 135.9, 136.0, 138.6, 140.5, 143.0, 145.5, 152.4, 167.1, 169.4, 173.0 ppm. MS (EI, *m*/*z*): 559 $[M]^+$. HRMS (EI): calcd for $C_{32}H_{27}N_3NiO_3$ $[M]^+$ 559.1406; found 559.1415.

Ni(II)-PABP/3-Amino-2-(naphthalen-1-ylmethyl)acrylic Acid Schiff Base Complex 4l. Dark-red solid. Mp 130−132 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.46 (d, J = 8.4 Hz, 1H), 8.35 (d, J = 5.1 Hz, 1H), 8.00 (t, J = 7.5 Hz, 1H), 7.89 (d, J = 7.5 Hz, 1H), 7.80 (t, J = 9.0 Hz, 2H), 7.57−7.46 (m, 4H), 7.31−7.27 (m, 1H), 7.18−7.05 (m, 3H), 6.77 (t, J = 7.8 Hz, 2H), 6.69 (t, J = 7.5 Hz, 1H), 6.56 (d, J = 7.5 Hz, 1H), 6.46 (d, J = 7.5 Hz, 2H), 5.63 (s, 1H), 4.03 (s, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 34.0, 121.2, 123.1, 123.9, 124.4, 125.1, 125.6, 126.1, 126.7, 127.1, 127.6, 128.0, 128.5, 129.7, 131.6, 133.9, 134.0, 134.3, 135.1, 140.5, 140.6, 143.1, 145.5, 152.5, 166.8, 169.3, 173.1 ppm. MS (EI, *m*/*z*): 567 $[M]^+$. HRMS (EI): calcd for $C_{33}H_{23}N_3NiO_3$ $[M]^+$ 567.1093; found 567.1097.

Ni(II)-PABP/3-Amino-2-(bis(4-fluorophenyl)methyl)acrylic Acid Schiff Base Complex 4m. Dark-red solid. Mp 150−153 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.54 (d, J = 9.0 Hz, 1H), 8.21 (d, J = 5.7 Hz, 1H), 8.00−7.97 (m, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.48−7.32 (m, 4H), 7.29−7.23 (m, 1H), 7.02−6.97 (m, 4H), 6.86−6.68 (m, 8H), 5.86 (s, 1H), 5.48 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 49.9, 115,2, 115.4, 121.4, 123.3, 124.0, 126.9, 127.8, 128.5, 128.9, 130.0, 130.1, 130.3, 134.4, 134.5, 135.3, 135.8, 137.4, 140.6, 142.7, 143.4, 145.6, 152.4,160.2, 162.7, 166.1, 169.5, 174.2 ppm. MS (EI, *m*/*z*): 629 $[M]^+$. HRMS (EI): calcd for $C_{35}H_{23}F_2N_3NiO_3$ $[M]^+$ 629.1061; found 629.1069.

Ni(II)-PABP/3-Amino-2-(quinolin-2-ylmethyl)acrylic Acid Schiff Base Complex 4n. Dark-red solid. Mp 75−78 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.50 (d, J = 8.1 Hz, 1H), 8.26 (d, J = 5.4 Hz, 1H), 7.99−7.95 (m, 2H), 7.90−7.84 (m, 2H), 7.76 (d, J = 8.4 Hz, 1H), 7.69−7.63 (m, 1H), 7.53−7.44 (m, 2H), 7.37−7.29 (m, 2H), 7.14−7.04 (m, 3H), 6.84−6.66 (m, 4H), 6.27 (s, 1H), 3.88 (s, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 40.0, 121.2, 121.4, 122.1, 123.2, 123.9, 125.9, 126.7, 126.8, 127.4, 128.0, 128.5, 128.8, 128.9, 129.0, 129.2, 129.9, 130.3, 131.0, 134.3, 134.8, 135.2, 135.5, 135.6, 136.5, 140.5, 141.1, 143.3, 145.4, 152.4, 159.5, 166.7, 169.3, 173.3 ppm. MS (EI, *m*/*z*): 568 $[M]^+$. HRMS (EI): calcd for $C_{32}H_{22}N_4NiO_3$ $[M]^+$ 568.1045; found 568.1053.

Ni(II)-PABP/2-(Aminomethylene)butanoic Acid Schiff Base Complex 4o. Dark-red solid. Mp 182−184 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.53 (d, J = 8.4 Hz, 1H), 8.27 (d, J = 5.1 Hz, 1H), 8.01−7.96 (m, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.57−7.45 (m, 4H), 7.39−7.34 (m, 1H), 7.12 (d, J = 6.6 Hz, 2H), 6.80 (d, J = 4.5 Hz, 2H), 6.32 (s, 1H), 2.19 (q, J = 7.2 Hz, 2H), 0.88 (t, J = 7.2 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 12.7, 24.7, 121.3, 123.2, 123.9, 126.7, 128.2, 128.9, 129.3, 130.8, 134.1, 135.1, 136.1, 138.4, 140.4, 143.2, 145.6, 152.5, 172.6 ppm. MS (EI, *m*/*z*): 455 $[M]^+$. HRMS (EI): calcd for $C_{24}H_{19}N_3NiO_3$ $[M]^+$ 455.0780; found 455.0787.

Ni(II)-PABP/2-(Aminomethylene)-6,6,6-trifluorohexanoic Acid Schiff Base Complex 4p. Dark-red solid. Mp 215−217 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.54 (d, J = 8.4 Hz, 1H), 8.25 (d, J = 4.2 Hz, 1H), 8.00 (t, J = 7.5 Hz, 1H), 7.91 (d, J = 6.9 Hz, 1H), 7.56−7.47 (m, 5H), 7.40−7.34 (m, 1H), 7.12 (d, J = 6.6 Hz, 2H), 6.80 (d, J = 6.0 Hz, 2H), 6.35 (s, 1H), 2.19 (t, J = 7.5 Hz, 2H), 2.04−1.95 (m, 2H), 1.66−1.61 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.2, 30.5, 33.2, 121.4, 123.2, 124.0, 126.8, 128.0, 129.1, 131.0, 134.4, 135.3, 136.0, 139.5, 140.5, 143.4, 145.5, 152.4, 166.7, 169.4, 173.3 ppm. MS (EI, *m*/*z*): 537 $[M]^+$. HRMS (EI): calcd for $C_{26}H_{20}F_3N_3NiO_3$ $[M]^+$ 537.0810; found 537.0823.

Ni(II)-PABP/2-(Aminomethylene)hexanoic Acid Schiff Base Complex 4q. Dark-red solid. Mp 167−170 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.53 (d, J = 8.4 Hz, 1H), 8.28 (d, J = 4.2 Hz, 1H), 8.01−7.96 (m, 1H), 7.90 (d, J = 7.5 Hz, 1H), 7.57−7.48 (m, 4H), 7.38−7.35 (m, 1H), 7.11 (d, J = 6.6 Hz, 2H), 6.81−6.76 (m, 2H), 6.27 (s, 1H), 2.12 (t, J = 6.6 Hz, 2H), 1.67−1.63 (m, 2H), 0.95−0.86 (m, 2H), 0.81 (t, J = 6.9 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ 13.9, 22.5, 30.7, 31.4, 121.3, 123.2, 123.9, 126.7, 128.3, 129.0, 129.3, 130.8, 134.2, 135.2, 136.1, 138.6, 140.5, 143.2, 145.6, 152.6, 169.4, 172.5 ppm. MS (ESI, *m*/*z*): 484 $[M + H]^+$. HRMS (EI): calcd for $C_{26}H_{24}N_3NiO_3$ $[M + H]^+$ 484.1171; found 484.1147.

Ni(II)-PABP/2-(Aminomethylene)-4-methylpentanoic Acid Schiff Base Complex 4r. Dark-red solid. Mp 132−135 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.53 (d, J = 8.7 Hz, 1H), 8.27 (br, 1H), 8.02−7.96 (m, 1H), 7.90 (d, J = 7.5 Hz, 1H), 7.56−7.48 (m, 4H), 7.38−7.33 (m, 1H), 7.12 (d, J = 8.4 Hz, 2H), 6.80−6.75 (m, 2H), 6.26 (s, 1H), 1.96 (d, J = 6.6 Hz, 2H), 1.87−1.79 (m, 1H), 0.81 (d, J = 6.6 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ 22.6, 27.6, 41.0, 121.3, 123.2, 123.9, 126.8, 128.3, 129.0, 129.3, 130.7, 134.2, 135.2, 136.1, 139.3, 140.5, 143.2, 145.6, 152.5, 169.4, 172.6 ppm. MS (ESI, *m*/*z*): 484 $[M + H]^+$. HRMS (EI): calcd for $C_{26}H_{24}N_3NiO_3$ $[M + H]^+$ 484.1171; found 484.1160.

Ni(II)-PABP/2-(Aminomethylene)heptanoic Acid Schiff Base Complex 4s. Dark-red solid. Mp 82−84 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.53 (d, J = 8.4 Hz, 1H), 8.27 (d, J = 5.4 Hz, 1H), 8.02−7.96 (m, 1H), 7.90 (d, J = 7.5 Hz, 1H), 7.57−7.48 (m, 4H), 7.39−7.35 (m, 1H), 7.11 (d, J = 8.7 Hz, 2H), 6.80−6.76 (m, 2H), 6.27 (s, 1H), 2.11 (t, J = 6.9 Hz, 2H), 1.33−1.17 (m, 6H), 0.82 (t, J = 6.0 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.0, 22.4, 28.3, 31.5, 31.6, 121.3, 123.2, 123.9, 128.3, 129.0, 129.3, 130.7, 135.2, 136.2, 138.7, 140.5, 143.2, 145.6, 152.6, 169.4, 172.5 ppm. MS (ESI, *m*/*z*): 498 $[M + H]^+$. HRMS (EI): calcd for $C_{27}H_{26}N_3NiO_3$ $[M + H]^+$ 498.1328; found 498.1325.

Procedure for the Synthesis of 5a. In a hydrogenation flask was placed compound **4a** and 10 mL of methanol before the addition of Raney-Ni suspended in 10 mL of water. The resulting mixture was pressurized to hydrogen and mechanically stirred at room temperature for 1 h. The reaction mixture was filtered and the filtrate was concentrated in a rotary evaporator to afford the crude product. The crude residue was purified by column chromatography on silica gel (dichloromethane/methanol = 50/1) to give **5a** as a red solid in 78% yield.

Ni(II)-PABP/ α-Benzyl-β-alanine Schiff Base Complex 5a. Red solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.49 (d, J = 8.4 Hz, 1H), 8.36 (d, J = 5.4 Hz, 1H), 8.00−7.96 (m, 1H), 7.91 (d, J = 7.8 Hz, 1H), 7.50−7.45 (m, 1H), 7.35−7.29 (m, 3H), 7.16−7.07 (m, 4H), 6.99−6.96 (m, 2H), 6.82−6.78 (m, 1H), 6.73−6.70 (m, 2H), 6.62 (d, J = 8.1 Hz, 1H), 3.45−3.42 (m, 2H), 3.14 (d, J = 15.9 Hz, 1H), 2.86−2.78 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 36.1, 56.3, 121.3, 123.6, 123.8, 126.0, 126.3, 126.7, 127.9, 128.5, 128.9, 129.4, 133.1, 134.4, 135.3, 140.5, 146.0, 152.8, 173.8 ppm. MS (EI, m/z): 519 $[M]^+$. HRMS (EI): calcd for $C_{29}H_{23}N_3NiO_3$ $[M]^+$ 519.1093; found 519.1095.

Ni(II)-PABP/3-Amino-2-(2,5-dimethylbenzyl)propanoic Acid Schiff Base Complex 5j. Obtained as a red solid by column chromatography (dichloromethane/methanol = 50/1), yield 73%. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.49 (d, J = 8.4 Hz, 1H), 8.38 (d, J = 4.5 Hz, 1H), 7.99 (t, J = 7.5 Hz, 1H), 7.91 (d, J = 6.6 Hz, 1H), 7.50−7.46 (m, 1H), 7.38−7.25 (m, 3H), 7.02 (t, J = 7.8 Hz, 1H), 6.93 (d, J = 7.8 Hz, 1H), 6.87−6.82 (m, 2H), 6.74−6.69 (m, 1H), 6.63−6.58 (m, 3H), 3.50−3.42 (m, 2H), 3.13 (dd, J_1 = 13.2 Hz, J_2 = 2.4 Hz, 1H), 2.80−2.79 (m, 1H), 2.64 (t, J = 13.2 Hz, 1H), 2.14 (s, 6H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.8, 20.8, 33.1, 47.5, 56.2, 121.2, 123.5, 123.8, 125.7, 126.5, 126.6, 127.1, 127.7, 128.6, 128.8, 129.1, 130.3, 130.4, 132.8, 133.0, 134.3, 135.0, 135.2, 137.3, 140.4, 141.9, 145.9, 152.7, 169.3, 173.7, 177.6 ppm. MS (EI, m/z): 547 $[M]^+$. HRMS (EI): calcd for $C_{31}H_{27}N_3NiO_3$ $[M]^+$ 547.1406; found 547.1412.

Ni(II)-PABP/2-(Aminomethyl)-6,6,6-trifluorohexanoic Acid Schiff Base Complex 5p. Obtained as a red solid by column chromatography (dichloromethane/methanol = 50/1), yield 85%. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.51 (d, J = 8.4 Hz, 1H), 8.33 (d, J = 5.1 Hz, 1H), 8.00 (t, J = 7.2 Hz, 1H), 7.91 (d, J = 6.3 Hz, 1H), 7.54−7.45 (m, 3H), 7.35−7.27 (m, 1H), 7.15−7.13 (m, 1H), 7.06−7.04 (m, 1H), 6.78−6.72 (m, 2H), 3.62−3.53 (m, 1H), 3.22 (dd, J_1 = 13.2 Hz, J_2 = 2.4 Hz, 1H), 2.51−2.49 (m, 1H), 2.15−1.96 (m, 2H), 1.53−1.29 (m, 4H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.9, 28.7, 33.6 (q, J = 28.5 Hz), 46.4, 57.0, 121.4, 123.6, 123.8, 125.4, 126.4, 126.7, 127.0, 127.7, 128.2, 128.8, 129.1, 129.4, 129.9, 133.2, 134.4, 135.6, 140.5, 142.1, 145.8, 152.6, 169.3, 173.7, 177.3 ppm. MS (EI, m/z): 539 $[M]^+$. HRMS (EI): calcd for $C_{26}H_{22}F_3N_3NiO_3$ $[M]^+$ 539.0967; found 539.0989.

Procedure for the Synthesis of 6a. The complex **5a** was decomposed by a suspension in a mixture of aqueous 1 N HCl (1 mL) and MeOH (15 mL) for half an hour until the red color of the solution disappeared. The reaction was cooled to room temperature and then evaporated to dryness. Water (20 mL) was added to the residue to form a clear solution; then this solution was separated by column chromatography on C_{18}-reversed phase (230−400 mesh) silica gel. Pure water as eluent was employed to remove the green $NiCl_2$ and excess HCl, and then a methanol/water mixture (V/V = 4/1) was used to obtain the product **6a** as a white solid (89% yield). The ligand PABP decomposed from **4a** was recovered (96%) by MeOH eluent, and the column chromatography was washed with 100 mL of methanol for further use.

α-Benzyl-β Alanine 6a. White solid. ^{1}H NMR (D_2O, 400 MHz) δ 7.50−7.36 (m, 5H), 3.34−3.04 (m, 5H) ppm. ^{13}C NMR (D_2O, 100 MHz) δ 38.0, 42.2, 47.3, 129.6, 131.3, 131.5, 139.9, 179.1 ppm. MS (ESI, m/z): 178 $[M - H]^+$. HRMS (ESI): calcd for $C_{10}H_{12}NO_2$ $[M - H]^+$ 178.0868; found 178.0874.

3-Amino-2-(2,5-dimethylbenzyl)propanoic Acid 6j. Obtained as a white solid by column chromatography on C_{18}-reversed phase (230−400 mesh) silica gel (methanol/water = 1/1), yield 92%. ^{1}H NMR (D_2O, 400 MHz) δ 7.23 (s, 1H), 7.13 (s, 2H), 3.12−2.99 (m, 3H), 2.82−2.81
(m, 2H), 2.36 (s, 6H) ppm. ^{13}C NMR (D_2O, 100 MHz) δ 20.3, 22.3, 35.2, 42.2, 45.9, 130.3, 132.7, 133.0, 136.0, 138.0, 138.5, 178.6 ppm. MS (ESI, m/z): 230 $[M + Na]^+$. HRMS (ESI): calcd for $C_{12}H_{17}NO_2Na$ $[M + Na]^+$ 230.1157; found 230.1151.

2-(Aminomethyl)-6,6,6-trifluorohexanoic Acid 6p. Obtained as a white solid by column chromatography on C_{18}-reversed phase (230−400 mesh) silica gel (water), yield 83%. ^{1}H NMR (D_2O, 400 MHz) δ 3.34−3.12 (m, 2H), 2.80−2.75 (m, 1H), 2.26−2.17 (m, 2H), 1.79−1.60 (m, 4H) ppm. ^{13}C NMR (D_2O, 100 MHz) δ 19.1, 28.5, 32.8 (q, J = 28.0 Hz), 40.2, 42.6, 127.7 (q, J = 274.4 Hz), 176.9 ppm. MS (ESI, m/z): 222 $[M + Na]^+$. HRMS (ESI): calcd for $C_7H_{12}NO_2F_3Na$ $[M + Na]^+$ 222.0713; found 222.0718.

Procedure for the Synthesis of 7a. The complex **4a** was hydrolyzed by stirring a suspension in a mixture of aqueous 1 N HCl (1 mL) and methanol (15 mL) for 30 min at room temperature until the red color of the solution disappeared. The reaction was evaporated to dryness and purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to give **7a** as colorless liquid (61% yield) and the ligand PABP (92% yield).

3-Phenylpropanal 7a. Colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.77 (t, J = 1.2 Hz, 1H), 7.29−7.25 (m, 2H), 7.20−7.16 (m, 3H), 2.92 (d, J = 7.6 Hz, 2H), 2.73 (dt, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.9, 45.1, 126.1, 128.1, 128.4, 140.2, 201.4 ppm. MS (EI, m/z): 134 $[M]^+$. HRMS (EI): calcd for $C_9H_{10}O$ $[M]^+$ 134.0732; found 134.0728.

■ ASSOCIATED CONTENT

Supporting Information. Copies of ^{1}H NMR and ^{13}C NMR spectra for all products and crystallographic information files (CIF) of **4a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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