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Synthesis of trifluoromethyl substituted nucleophilic glycine equivalents and the investigation of their potential for the preparation of α-amino acids

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ABSTRACT

The synthetic preparation of several Ni(II) complexed Schiff Bases of glycine will be introduced, as well as investigations into their reactivity and utility. Key to these investigations is the incorporation of electron-withdrawing trifluoromethyl groups within the framework of the conjugated system that stabilizes the enolate derived from the glycine component. Reactivity was evaluated for each of the complexes under phase transfer catalyzed alkylations with hydroxide bases, as well as the DBU catalyzed Michael Additions of optically active 3′-substituted-2-oxazoladinone amides of unsaturated carboxylic acids. It was found that the trifluoromethyl containing nucleophilic glycine equivalents were more reactive than their non-trifluoromethyl analogues in both reaction types. Therefore, the application of these modified Ni(II) complexes of glycine Schiff Bases are useful for the preparation of α-amino acids through phase transfer catalyzed alkylation as well as the preparation of optically pure β-substituted pyroglutamic acid precursors.

1. Introduction

It would be difficult to overstate the biological importance of α-amino acids, the building blocks of life, and perhaps the most studied class of organic compounds [1]. Besides their primary function as structural units of peptides and proteins, α-amino acids also serve countless biological functions in most living things. Nature's exceptional utility of this unique family of compounds has inspired research into the development of novel synthetic variations of these structures for use in pharmaceutical, agricultural, and food industries [2–4]. In particular the role of nonproteinogenic amino acids has been central to the development of de novo designed peptides [5], due to their influence on the secondary and tertiary structure [6], biological activity [7], and degradative resistance of the system [8].

In order to keep pace with the accelerating application of these vital molecules, advances in the fundamental science of their synthesis remain necessary. While numerous methods have been developed for the preparation of specific nonproteinogenic amino acids, each has suffered from inherent limitations [9]. However, what is needed is a practical and relatively inexpensive general method or set of methodologies, which will in turn support and accelerate the potential for advances within the fields of medicine and human health.

Currently, one of the most widely applicable and efficient methods for the synthesis of nonproteinogenic α-amino acids is the alkylation of glycine derivatives. There are a number of nucleophilic glycine equivalents to choose from in the literature, each of which has their own advantages and disadvantages. However, among the options available, the Nickel (II) complexed imine of glycine has emerged as an attractive option [10]. Like many other nucleophilic glycine equivalents, this family also utilizes a Schiff Base to protect the amino moiety; however it is unique due to the predictable enolate geometry and the enhanced imine stability offered through the incorporation of the metal center.

This family of metal complexed nucleophilic glycine equivalents derives its versatility for the preparation of α-amino acids from its modular design [10]. (Fig. 1) This design allows the modification of the nucleophilic glycine equivalent for the specific synthetic

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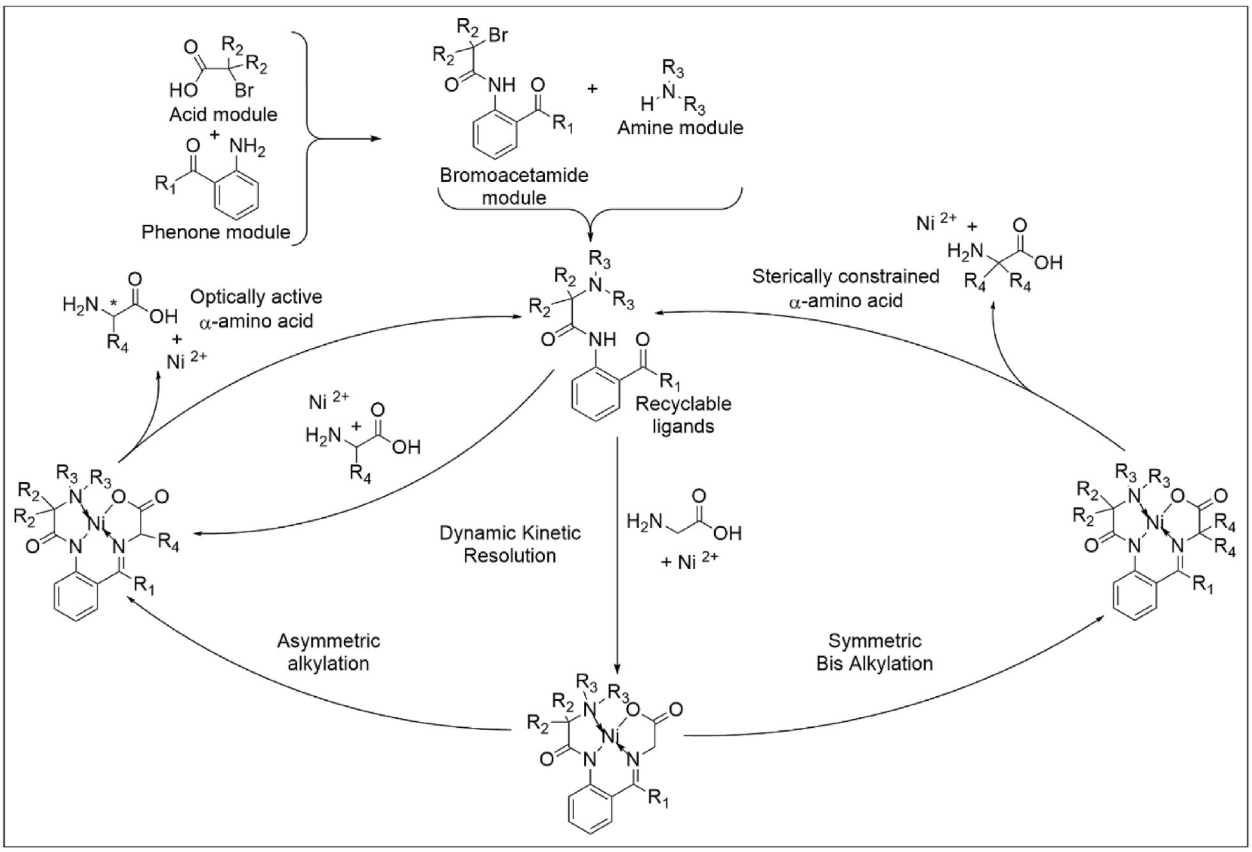


Fig. 1. Design and Application of Modular Ni(II) Complexes of α -Amino Acid Schiff Bases.

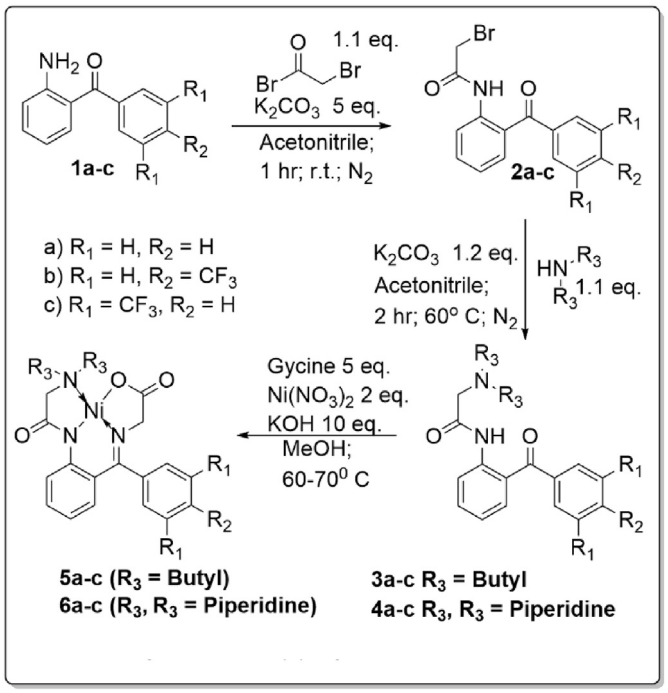
requirements for the preparation of their desired α-amino acid by simply utilizing the appropriate modules during the preparation of the complex. To this point, several modules have been investigated, such as the alteration of the amine module, which allows for solubility control in various organic solvents, as well as the introduction of a stereochemical center which allows for a mechanism to manipulate the three dimensional orientation of the substituent on the amino acid [11]. Additionally, the phenone module has been varied in order to increase the steric availability of the active site surrounding the glycine methylene unit. These investigations have yielded advances in the preparation of α,α-disubstituted α-amino acids, β-substituted pyroglutamic acids, as well as the dynamic kinetic resolution or stereochemical inversion of α-amino acids [12,13]. However despite these advances, there has been little focus on the reactivity of the complex based on the adjustment of the electronic nature of the conjugated system that stabilizes the glycine enolate.

It was hypothesized that the acidity of the protons of the nucleophilic glycine equivalent and therefore the reactivity of the complex could be enhanced through the incorporation of electron withdrawing groups within the benzophenone module. The benzophenone module was selected for the placement of these groups as they are involved in the extended conjugate system responsible for the stabilization of the enolate derived from the methylene unit of the glycine Schiff Base. Therefore a new series of Ni(II) complexed nucleophilic glycine equivalents bearing trifluoromethyl groups on the benzophenone module were prepared to evaluate this hypothesis.

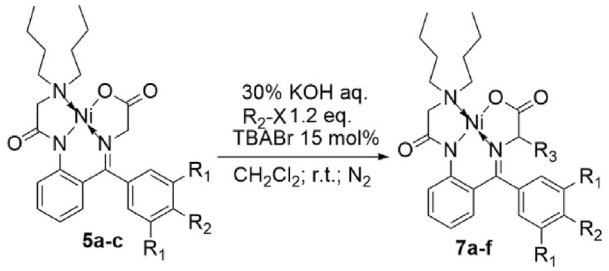
2. Results and discussion

The initial step of this process was to prepare the necessary trifluoromethylalated 2-aminobenzophenones. This was accomplished by the preparation of Grignard Reagents from 4-trifluoromethylbromobenzene, or 3,5-bis-trifluoromethylbromobenzene, followed by the addition of 2-aminobenzonitrile [14,15]. The final trifluoromethylalated 2-aminobenzo-phenones **1b-c** were realized after the hydrolysis of the imine to the corresponding ketone. Phenone modules **1b-c** as well as the commercially available **1a** were treated with a bromoacetyl bromide in acetonitrile with potassium carbonate as the base to produce the corresponding bromoacetamide modules **2a-c** in high chemical yield, >90%. Without purification, the modules **2a-c** were treated with secondary amines to afford the 2-aminoacetamide ligands **3a-c** in the case of dibutylamine, and **4a-c** with piperidine. These substitution reactions were conducted in acetonitrile with potassium carbonate as the sacrificial base, producing the appropriate products in high yield, >90%, and chemical purity. Ni(II) complexes of glycine Schiff Bases were prepared from each of the ligands synthesized. This was accomplished by subjecting the ligand to a methanolic solution of Ni(II) nitrate, glycine and potassium hydroxide while heating the solution to 60-70 °C. Each of the complexes were afforded in high chemical yield, >90%, by pouring the reaction mixture over water and filtering the precipitate. The complexes were purified by short flash silica columns with mixtures of acetone in dichloromethane as the eluant to afford the pure products in high chemical purity for the subsequent investigations (see Scheme 1).

Initial attempts to analyze the reactivity of each of these



Scheme 1. Synthesis of Ni(II) Glycine Schiffs Bases 5a-c, 6a-c.



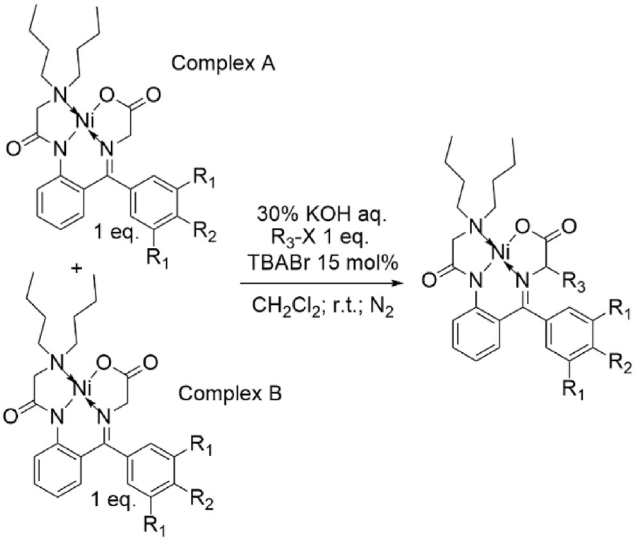
Scheme 2. Alkylation of Ni(II) Complexed Nucleophilic Glycine Equivalents 5a-c.

complexes centered on the alkylation of the methylene unit with alkyl halides under phase transfer conditions. The dibutyl series of complexes **5a-c** were selected for these investigations due to their solubility, and previous successful applications of complex **5a** for this type of reaction. However, before conducting the competitive reaction studies, references needed to be prepared for each of the potential reaction products. Benzylation of complexes were achieved by subjecting each glycine equivalent **5a-c** to benzyl bromide in dichloromethane with 30% aqueous potassium hydroxide as the base. Tetrabutylammonium bromide (TBABr), 0.15 eq., was added to the reaction to assist in the delivery of the base to the reactive complex. (Scheme 2). Benzylated complexes **7a-c** were each obtained in high chemical yield with virtually complete conversion of the starting nucleophilic glycine equivalents (Table 1, entries 1–3). Preparation of alanine containing complexes **7d-f**, entries 4–6, were realized by a similar process with the substitution of methyl iodide for the activated benzyl bromide. Again in each of these cases the expected products **7d-f**, were produced in high chemical yield with nearly complete conversion.

In order to compare the reactivity of each complex, a series of competitive reactions were conducted (Scheme 3). Initially a stock solution of each of the complexes **5a-c** were prepared in CD_2Cl_2. For the first investigation a mixture of the benzophenone derived

Table 1
Alkylation of Ni(II) Complexed Nucleophilic Glycine Equivalents **5a-c**.

Entry	R_1	R_2	X	Time	Product	Conv. %	Yield %
1	Ph	Bn	Br	1 h	**7a**	>99	94
2	4-CF_3-Ph	Bn	Br	1 h	**7b**	>99	96
3	3,5-Bis(CF_3)-Ph	Bn	Br	1 h	**7c**	>99	92
4	Ph	CH_3	I	1 h	**7d**	>99	97
5	4-CF_3-Ph	CH_3	I	1 h	**7e**	>99	99
6	3,5-Bis(CF_3)-Ph	CH_3	I	1 h	**7f**	>99	92



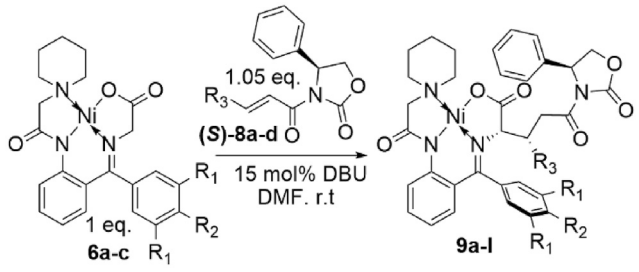
Scheme 3. Competitive Alkylation of 7a-c Under Phase Transfer Conditions.

complex **5a** and the mono-trifluoromethylated complex **5b** were prepared by the addition of aliquots of each solution until an equimolar mixture was reached, based on the integration of the glycine methylene protons in ^{1}H NMR. Approximately 0.9 equivalents of benzyl bromide, and 0.15 eq. of TBAB, and 30% potassium hydroxide were added to the mixture of complexes in dichloromethane. This reaction mixture was allowed to react, with vigorous stirring, for approximately 1 hour under a nitrogen atmosphere. Analysis of the crude reaction material by ^{1}H NMR was utilized to determine that the benzylated product of the complex bearing the trifluoromethyl group **7b** was produced exclusively (Table 2, entry 1). Repeating this procedure with the competitive reaction between complexes **5b** and **5c** yielded both potential products in a 63:28 ratio favoring product **7c**. (entry 2) Similar results were obtained when methyl iodide is substituted for the activated benzyl bromide. As the competitive reaction between the non-trifluoromethyl containing complex **6a** and the mono-trifluoromethyl containing complex **5b** exclusively yields product **7e** (entry 3). While the comparison between complexes **5b** and **5c** result in a virtually even distribution of products **7e** and **7f**. Analysis

Table 2
Competitive Alkylation of **7a-c** Under Phase Transfer Conditions.

Entry	Complex A			Complex B			R_3	X	Time	Product Mixture	
		R_1	R_2		R_1	R_2				Products	mol %[a]
1	**5a**	H	H	**5b**	CF_3	H	Bn	Br	1 h	**7a:7b**	<1:>99
2	**5b**	CF_3	H	**5c**	H	CF_3	Bn	Br	1 h	**7b:7c**	38:62
3	**5a**	H	H	**5b**	CF_3	H	CH_3	I	1 h	**7d:7e**	<1:>99
4	**5b**	CF_3	H	**5c**	H	CF_3	CH_3	I	1 h	**7e:7f**	41:59

[a] Determined by analysis of crude ^{1}H NMR.



Scheme 4. DBU catalyzed Michael Addition Reactions of Nucleophilic Glycine Equivalents 6a-c.

of these results indicate that the trifluormethylated complexes **5b-c** were much more reactive than the non-trifluoromethylated version **5a** (entry 4). However, it remained unclear which of the two triflulormethylated **5b-c** complexes were more reactive, and what role the acidity versus the steric availability of the reactive site may be playing during these reactions.

To investigate the reactivity of these complexes further, it was decided to apply them to diazabicycloundec-7-ene (DBU) catalyzed Michael Addition reactions of 3′-substituted-2-oxazoladinone amides of unsaturated carboxylic acids [16]. It was expected that the mild conditions associated with these reactions may serve to reveal more reactivity differences between these complexes. However, previous studies of this reaction type, have found that the piperidine derived nucleophilic glycine complexes such as **6a** are more reactive than the dibutyl derived complexes.[12a] Therefore, the piperidine derived complexes were the focus of these studies. However, as with the previous experiments, reference compounds for each product were needed, in order to aid in determining the outcome of the competition reaction series. Therefore, complexes **6a-c** were subjected to the DBU catalyzed reactions with various optically active Michael Acceptors **(*S*)-8a-d** (Scheme 4). The Michael Acceptors were selected in order to obtain a variation in steric availability of the reaction site as well as those which would be electronically more or less favorable to nucleophilic attack. The least sterically constrained of the series was the methyl substituted **(*S*)-8a**, which reacted with all three of the nucleophilic glycine equivalents in 5 min or less providing the corresponding products **9a-c** in very high yield and exceptional chemical and diastereomeric purity (Table 3, entries 1–3). Increasing the steric demand on the topographically controlled addition reaction by substituting a methyl group for an isopropyl group in the reaction between Ni(II) complexes **9a-c** and **(*S*)-8b** required slightly longer reaction times (25 min) to produce the products **9d-f** in the desired yields and chemical conversion (entries 4–6). The application of phenyl substituted α,β-unsaturated electrophiles allowed the opportunity to increase the steric effects and allow for more control of the electronic nature of the acceptor. Therefore, the *o*-trifluoromethylphenyl containing **(*S*)-8c** was applied for the successful preparation of pyroglutamic acid precursors **9g-l** (entries 7–9) without complication in approximately 1 h. Additionally, preparation of products **9e-g** through the application of electronically disadvantaged and sterically demanding acceptors **(*S*)-8c** was also accomplished with the selectivity and chemical purity of the previous examples in 2 h (entries 10–12).

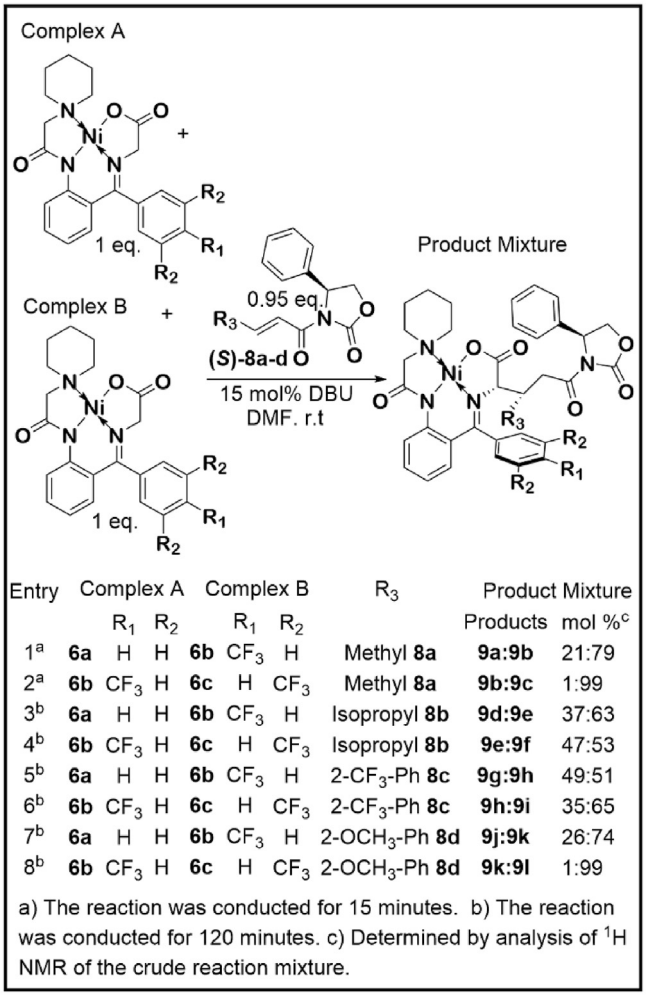
Having demonstrated the utility of the series for the preparation of optically pure β-substituted pyroglutamic acid precursors, attention was diverted to establishing a reactivity profile of the complexes for these DBU catalyzed reactions. As described previously for the phase transfer homologation study, the complexes **6a-c** were investigated through a series of experiments involving equimolar solutions of two complexes with limited electrophiles to establish the reaction

derived nucleophilic glycine equivalent **6a** and the 4′-trifluoromethylbenzophenone containing analogue **6b**, reinforced the observations noted for the phase transfer catalyzed reaction with the application of acceptors **(*S*)-8a-b,d** as the trifluoromethyl containing nucleophilic glycine outcome of each case (Scheme 5). The

Table 3
DBU Catalyzed Michael Addition Reactions of Nucleophilic Glycine Equivalents **6a-c**.

Entry	R_1	R_2	Time min	Product[a] **9**	% Yield
1	Ph	Methyl **8a**	5	**a**	86
2	4-CF_3-Ph	Methyl **8a**	5	**b**	91
3	3,5-bis–(CF_3)–Ph	Methyl **8a**	5	**c**	90
4	Ph	isopropyl **8b**	25	**d**	99
5	4-CF_3-Ph	Isopropyl **8b**	25	**e**	95
6	3,5-bis–(CF_3)–Ph	isopropyl **8b**	25	**f**	93
7	Ph	2-CF_3-Ph **8c**	60	**9**	98
8	4-CF_3-Ph	2-CF_3-Ph **8c**	60	**h**	98
9	3,5-bis–(CF_3)–Ph	2-CF_3-Ph **8c**	60	**i**	96
10	Ph	2-OCH_3-Ph **8d**	120	**j**	98
11	4-CF_3-Ph	2-OCH_3-Ph **8d**	120	**k**	89
12	3,5-bis–(CF_3)–Ph	2-OCH_3-Ph **8d**	120	**1**	91

[a] The products were obtained with de <98% by analysis of ^{1}H NMR.



Entry	Complex A			Complex B			R_3	Product Mixture	
		R_1	R_2		R_1	R_2		Products	mol %[c]
1[a]	**6a**	H	H	**6b**	CF_3	H	Methyl **8a**	**9a:9b**	21:79
2[a]	**6b**	CF_3	H	**6c**	H	CF_3	Methyl **8a**	**9b:9c**	1:99
3[b]	**6a**	H	H	**6b**	CF_3	H	Isopropyl **8b**	**9d:9e**	37:63
4[b]	**6b**	CF_3	H	**6c**	H	CF_3	Isopropyl **8b**	**9e:9f**	47:53
5[b]	**6a**	H	H	**6b**	CF_3	H	2-CF_3-Ph **8c**	**9g:9h**	49:51
6[b]	**6b**	CF_3	H	**6c**	H	CF_3	2-CF_3-Ph **8c**	**9h:9i**	35:65
7[b]	**6a**	H	H	**6b**	CF_3	H	2-OCH_3-Ph **8d**	**9j:9k**	26:74
8[b]	**6b**	CF_3	H	**6c**	H	CF_3	2-OCH_3-Ph **8d**	**9k:9l**	1:99

a) The reaction was conducted for 15 minutes. b) The reaction was conducted for 120 minutes. c) Determined by analysis of ^{1}H NMR of the crude reaction mixture.

Scheme 5. DBU Catalyzed Competition Studies for the Homologation of Nucleophilic Glycine Equivalents 6a-c.

Table 4
DBU Catalyzed Competition Studeis for the Alkylation of Nucleophilic Glycine Equivalents **6a-c**.

Entry	Complex A			Complex B			R_3	Product Mixture	
		R_1	R_2		R_1	R_2		Products	mol %[c]
1[a]	**6a**	H	H	**6b**	CF_3	H	Methyl **8a**	**9a:9b**	21:79
2[a]	**6b**	CF_3	H	**6c**	H	CF_3	Methyl **8a**	**9b:9c**	1:99
3[b]	**6a**	H	H	**6b**	CF_3	H	Isopropyl **8b**	**9d:9e**	37:63
4[b]	**6b**	CF_3	H	**6c**	H	CF_3	Isopropyl **8b**	**9e:9f**	47:53
5[b]	**6a**	H	H	**6b**	CF_3	H	2-CF_3-Ph **8c**	**9g:9h**	49:51
6[b]	**6b**	CF_3	H	**6c**	H	CF_3	2-CF_3-Ph **8c**	**9h:9i**	35:65
7[b]	**6a**	H	H	**6b**	CF_3	H	2-OCH_3-Ph **8d**	**9j:9k**	26:74
8[b]	**6b**	CF_3	H	**6c**	H	CF_3	2-OCH_3-Ph **8d**	**9k:9l**	1:99

[a] The reaction was conducted for 15 min.
[b] The reaction was conducted for 120 min.
[c] Determined by analysis of ^{1}H NMR of the crude reaction mixture.

competition experiments involving the benzophenone equivalent **6b** reacted to produce products **9b**, **9e** and **9k** selectively (Table 4, entries 1, 3, and 7). However, the application of sterically hindered but electronically favored Michael acceptor **(*S*)-8c** led to nearly equimolar amounts of each of the possible products **9g-h**. Direct comparison of the two trifluoromethyl containing glycine equivalents **6b-c** resulted in the formation of only the product derived from the bis-trifluoromethyl containing complex **6c**, with the application of the conjugated electrophiles **(*S*)-8a,d** (entries 2 and 8 respectively). While the application of the 2-trifluorophenyl acceptor **(*S*)-8c** produced the respective products in a 2:1 ratio favoring the product derived from the bis-trifluoromethylated glycine equivalent **6c** (entry 6). However, application of Michael Acceptor **(*S*)-8b** produced both possible products **9e-f** in a virtually equal amounts. These results indicate that complex **6c** is more reactive if the steric effects of the Michael Acceptor are low (entry 2), or if the Michael Acceptor is bulky and relatively unreactive due to electronic effects of its substituents (entry 8). However, if sterically challenged but activated electrophiles are employed, the differences in the reactivity of the complexes **6b** and **6c** are diminished. This is potentially be due to a balance between the increased reactivity of **6c** through stabilization of the enolate and the increased steric interference contributed by the bulky trifluoromethyl groups on its aromatic ring.

3. Conclusion

In conclusion, several new electronically enhanced nucleophilic glycine equivalents have been prepared and their utility and reactivity investigated. As expected, the trifluoromethyl substituted nucleophilic glycine equivalents were more reactive that those without the electron-withdrawing substituent. More specifically, it was been discovered that there is a significant difference in reactivity that exists between the benzophenone derived complex **5a** and the trifluoromethyl containing derivative **5b** under the conditions of phase transfer catalyzed alkylation reactions. Although to a notable but lesser extent, a difference between the application of analogues **6a**, and **6b** under the milder conditions of the DBU catalyzed Michael Addition reaction of optically active of 3′-substituted-2-oxazoladinone amides of unsaturated carboxylic acids was observed. Despite the increase steric strain introduced by the 3,5-bis-triflurometylphenyl moiety of complex **6c**, it was found to be the most reactive species for the preparation of β-substituted pyroglutamic acid precursors.

4. Experimental section

^{1}H, and ^{13}C NMR were performed on a Brüker Advance 300 spectrometer using TMS, and $CDCl_3$ as internal standards. High Resolution Mass Spectra (HRMS) were recorded on a Waters SynaptG2 high-mass-resolution Q-TOF mass spectrometer. Optical rotations were measured on Rudolph Autopol III polarimeter. Melting points (M.p.) are uncorrected and were obtained in open capillaries. All reagents and solvents, unless otherwise stated, are commercially available and were used as received. Chiral (*S*)−*N*-(*E*-enoyl)-4-phenyl-1,3-oxazoline-2-ones **8a-d** were prepared according to the general method given in ref. 13. Unless otherwise stated, yields refer to isolated yields of products of greater than 95% purity as estimated by ^{1}H, and ^{13}C NMR spectrometry. All new compounds were characterized by ^{1}H, ^{13}C NMR and HRMS.

Preparation of trifluoromethylated 2-aminobenzophenones 1b-c. General Procedure: To activated magnesium turnings (2.0 eq.) in dry THF was slowly added the trifluoromethylated bromobenzene (2.1 eq.). Following the complete addition of the bromobenzene, the reaction was catalyzed by heat until a brown color was observed and the reaction began to reflux on its own. After the exothermic reaction concluded and the magnesium metal was consumed, the reaction was allowed to cool to room temperature before the dropwise addition of 2-aminobenzonitrile (0.95 eq.) in THF. Following the complete addition, the reaction was allowed to reflux overnight with stirring. The reaction was cooled, slowly quenched with water followed by 3 *N* HCl, and refluxed for 12 h. The resulting solution was carefully neutralized with concentrated sodium bicarbonate. The crude product was obtained by extraction with the addition of methylene chloride. The final purified products **1b-c** were obtained by column chromatography with ethyl acetate and hexane as the mobile phase. The products were obtained in greater than 72% yield.

2-[4-(trifluoromethyl)benzoyl]aniline 1b: M.p. 101.3 °C. ^{1}H NMR δ 6.13 (2H, bs), 6.52 (1H, m), 6.67 (1H, d, J = 8.3 Hz), 7.23 (2H, m), 7.64 (4H, m). ^{13}C NMR δ 115.7, 117.2, 117.3, 125.2, 127.4 (1C, q, J = 270.8 Hz), 129.1, 132.5 (1C, q, J = 32.4 Hz), 134.4, 134.9, 143.5, 151.3, 197.7. HRMS [M + H^+] found *m/z* 266.0919, calcd for $C_{14}H_{11}F_3NO$ 266.0787.

2-[3,5-bis-(trifluoromethyl)benzoyl]aniline 1c: ^{1}H NMR δ 6.15 (2H, bs), 6.53 (1H, m), 6.66 (1H, d, J = 8.3 Hz), 7.21 (2H, m), 7.93 (1H, s), 7.97 (2H, s). ^{13}C NMR δ 116.0, 116.6, 117.2. 123.0 (1C, q, J = 271.2 Hz), 124.3 (1C, m), 128.9, 131.8 (1C, q, J = 33.6 Hz), 133.8, 135.3, 142.0, 151.6, 195.3. HRMS [M + H^+] found *m/z* 334.0643, calcd for $C_{15}H_{10}F_6NO$ 334.0661.

Condensation of phenone module 1a-c and bromoacetyl bromide yielding *N*-(2-benzoylphenyl)-2-bromo-acetamides 2a-c. General Procedure: A solution of bromoacetyl bromide (104.64 mmol) in acetonitrile (2 mL/1 g) was slowly added to a slurry of phenone module **1a-c** (102.32 mmol) and potassium carbonate 70.71 g (511.6 mmol) in acetonitrile (240 mL). The reaction was stirred at ambient temperature (room temperature water bath) for 1 h, and upon completion (monitored by TLC), the acetonitrile was evaporated under vacuum. Water (200 mL) was then added to the crude mixture and extracted with dichloromethane (200 mL) three times. The organic portions were combined, dried and concentrated under vacuum to afford the corresponding α-bromoamide product **2a-2** in 98% yield and greater than 99% chemical purity.

***N*-(2-benzoyl-phenyl)-2-bromo-acetamide 2a:** [12a-b] M.p. 71.7 °C. ^{1}H NMR δ 4.20 (2H, s), 7.15 (1H, m), 7.43−7.53 (2H, m), 7.53−7.63 (3H, m), 7.63−7.75 (2H, m), 8.61 (1H, dd, J = 8.80, 1.17 Hz), 11.6 (1H, bs). ^{13}C NMR δ 43.0, 121.3, 122.9, 124.0, 128.1, 129.8, 132.4, 133.3, 133.9, 138.1, 139.0, 165.1, 198.8. HRMS [M + Na^+] found *m/z* 339.9955, calcd for $C_{15}H_{12}BrNNaO_2$ 339.9949. mp 105.8 °C.

***N*-(2-(4-(1,1,1-trifluoromethyl)-benzoyl-phenyl)-2-bromoacetamide 2b:** M.p. 67.3 °C. ^{1}H NMR δ 4.03 (2H, s), 7.17 (1H, td, J = 8.1, 0.6 Hz), 7.54 (1H, dd, J = 8.1, 1.8 Hz), 7.65 (1H, td, J = 8.4,

1.2 Hz), 7.75–7.88 (4H, m), 8.69 (1H, dd, $J = 8.1$, 0.6 Hz), 11.50 (1H, s). ^{13}C NMR δ 121.8, 123.2, 123.3, 125.4, 125.5, 125.6, 130.1, 130.3, 133.5, 134.0 (1C, q, $J = 32.85$ Hz), 134.9, 139.9, 141.6, 165.1, 198.2. ^{19}F NMR δ −63.08. HRMS [M + Na^+] found *m/z* 407.9932, calcd for $C_{16}H_{11}BrF_3NNaO_2$ 407.9817.

***N*-(2-(3,5-di(1,1,1-trifluoromethyl)-benzoyl)-phenyl)-2-bromoacetamide 2c:** M.p. 58.2 °C. ^{1}H NMR δ 4.04 (2H, s), 7.22 (2H, m), 7.49 (1H, dd, $J = 7.2$, 1.2 Hz), 7.70 (1H, td, $J = 8.7$, 1.2 Hz), 8.11 (1H, s), 8.17 (2H, s), 8.66 (1H, d, $J = 8.7$ Hz), 11.37 (1H, s). ^{13}C NMR δ 29.4, 122.1, 122.8 (2C, q, $J = 271.28$ Hz), 125.8, 129.8, 132.5 (2C, q, $J = 75.25$ Hz), 132.6, 133.0, 135.5, 140.0, 140.41, 165.1, 196.1. ^{19}F NMR δ −62.92. HRMS [M + Na^+] found *m/z* 475.9710, calcd for $C_{17}H_{10}BrF_6NNaO_2$ 475.9691.

Alkylation of Secondary Amines With *N*-(2-benzoylphenyl)-2-bromo-acetamide 2a-c, yielding the corresponding *N*-(2-benzoylphenyl)-2-dialkylamino-acetamide 3a-c, 4a-c. General Procedure. To a slurry of *N*-(2-benzoylphenyl)-2-bromo-acetamide **2a-c** (1 eq.) and potassium carbonate (1.2 eq.) in acetonitrile (10 mL/1 g of *N*-(2-benzoylphenyl)-2-bromo-acetamide) was added the corresponding secondary amine (1.1 eq.). The reaction was allowed to proceed for 2 h at 60-70 °C (monitored by TLC) before the reaction mixture was concentrated under vacuum. Water was added to the viscous liquid, followed by extraction with dichloromethane. The organic portions were combined, dried with magnesium sulfate, and concentrated in a vacuum to afford the corresponding *N*-(2-benzoylphenyl)-2-dialkylamino-acetamide **3a-c, 4a-c** in nearly quantitative yield and high chemical purity >99%.

***N*-(2-benzoylphenyl)-2-dibutylamino-acetamide 3a:** [12b-c] ^{1}H NMR δ 0.78 (6H, t, $J = 7.5$ Hz), 1.25 (4H, s, $J = 7.5$ Hz), 1.46 (4H, p, $J = 7.5$ Hz), 2.51 (4H, t, $J = 7.5$ Hz), 3.17 (2H, s), 7.09 (1H, dt, $J = 8.1$, 1.2 Hz), 7.45–7.61 (4H, m), 7.77 (1H, d, $J = 8.7$ Hz), 8.63 (1H, d, $J = 8.7$ Hz), 11.38 (1H, bs). ^{13}C NMR δ 14.2, 20.8, 29.5, 55.7, 59.9, 122.0, 122.5, 126.1, 128.5, 130.3, 132.3, 132.8, 133.3, 138.6, 139.0, 172.3, 197.9. HRMS [M + H^+] found *m/z* 367.2251, calcd for $C_{23}H_{31}N_2O_2$ 367.2380.

***N*-(2-(4-trifluoromethyl-benzoyl)-phenyl)-2-dibutylamino-acetamide 3b:** ^{1}H NMR δ 0.83 (3H, t, $J = 7.2$ Hz), 1.29 (4H, s, $J = 7.2$ Hz), 1.45–1.55 (4H, m), 2.56 (4H, t, $J = 7.2$ Hz), 3.22 (2H, s), 7.13 (1H, td, $J = 7.5$, 0.6 Hz), 7.46 (1H, dd, $J = 7.5$, 1.8 Hz), 7.61 (1H, td, $J = 8.4$, 1.5 Hz), 7.77 (2H, d, $J = 8.4$ Hz), 7.89 (2H, d, $J = 8.7$ Hz), 8.69 (1H, d, $J = 8.7$ Hz), 11.56 (1H, s). ^{13}C NMR δ 14.0, 20.5, 55.4, 59.7, 121.9, 122.4, 125.1, 125.3, 125.4, 125.5, 130.1, 132.3, 133.8 (1C, q, $J = 32.3$ Hz), 134.0, 139.3, 141.7, 172.2, 196.6. HRMS [M + Na^+] found *m/s* 457.2078, calcd for $C_{24}H_{29}F_3N_2NaO_2$ 457.2073.

***N*-(2-(3,5-bis-(trifluoromethyl)-benzoyl)-phenyl)-2-dibutylamino-acetamide 3c:** ^{1}H NMR δ 0.85 (6H, t, $J = 7.2$ Hz), 1.31 (4H, s, $J = 7.2$ Hz), 1.47–1.57 (4H, m), 2.58 (4H, t, $J = 7.5$ Hz), 3.23 (2H, s), 7.19 (1H, td, $J = 7.2$, 0.9 Hz), 7.42 (1H, dd, $J = 6.3$, 0.9 Hz), 7.67 (1H, td, $J = 8.7$, 1.5 Hz), 8.13 (1H, s), 8.24 (2H, s), 8.69 (1H, dd, $J = 8.7$, 0.9 Hz), 11.49 (1H, s). ^{13}C NMR δ 14.0, 20.6, 29.4, 55.5, 59.7, 122.3, 122.7, 122.9 (2C, q, $J = 271.28$ Hz), 124.1, 125.6, 125.7, 129.8, 131.9, 132.1 (2C, q, $J = 33.75$ Hz), 134.5, 139.4, 140.4, 172.2, 194.5. ^{19}F NMR δ −161.74. HRMS [M + H^+] found *m/s* 503.2115, calcd for $C_{25}H_{29}F_6N_2O_2$ 503.2129.

***N*-(2-benzoylphenyl)-2-piperidyl-acetamide 4a:** [12a-b] M.p. 111.5 °C. ^{1}H NMR δ 1.40–1.50 (2H, m), 1.72 (4H, m), 2.50 (4H, m), 3.09 (2H, s), 7.09 (1H, dd, $J = 7.82$, 7.32 Hz), 7.40–7.65 (5H, m), 7.70–7.80 (2H, m), 8.63 (1H, dd, $J = 8.31$, 1.10 Hz), 11.5 (1H, bs). ^{13}C NMR δ 23.8, 25.8, 54.9, 63.1, 121.4, 121.9, 125.0, 127.9, 129.7, 132.1, 132.1, 132.9, 138.1, 138.7, 170.4, 197.1. HRMS [M + Na^+] found *m/z* 345.1472, calcd for $C_{20}H_{22}N_2NaO_2$ 345.1579.

***N*-(2-(4-trifluoromethylbenzoyl)-phenyl)-2-piperidyl-acetamide 4b:** M.p. 123.8 °C. ^{1}H NMR δ 1.36–1.43 (2H, m), 1.64 (4H, m), 2.44 (4H, t, $J = 5.4$ Hz), 3.03 (2H, s), 7.02 (1H, t, $J = 7.6$ Hz), 7.37 (1H, d, $J = 7.6$ Hz), 7.51 (1H, t, $J = 8.4$ Hz), 7.67 (2H, d, $J = 8.2$ Hz), 7.78 (2H, d, $J = 8.2$ Hz), 8.61 (1H, d, $J = 8.4$ Hz). ^{13}C NMR δ 23.8, 25.9, 55.1, 63.3, 121.8, 122.3, 124.3, 125.2, 125.3, 125.4, 125.5, 130.1, 132.7, 133.7 (1C, q, $J = 32.5$ Hz), 134.2, 139.6, 141.8, 171.04, 196.7. HRMS [M + H^+] found *m/s* 391.1631, calcd for $C_{21}H_{22}F_3N_2O_2$ 391.1628.

***N*-(2-(3,5-bis-(trifluoromethyl)-benzoyl)-phenyl)-2-piperidyl-acetamide 4c:** M.p. 93.5 °C. ^{1}H NMR δ 1.43 (2H, m), 1.66 (4H, m), 2.46 (4H, t, $J = 5.1$ Hz), 3.04 (2H, s), 7.07 (1H, t, $J = 7.7$ Hz), 7.32 (1H, d, $J = 7.7$ Hz), 7.56 (1H, t, $J = 8.4$ Hz), 8.01 (1H, s), 8.11 (2H, s), 8.61 (1H, d, $J = 8.4$ Hz). ^{13}C NMR δ 23.8, 25.9, 55.1, 63.2, 121.1, 122.2, 122.6, 123.5, 124.7, 129.7, 132.0 (2C, q, $J = 33.4$ Hz), 132.3, 134.7, 139.8, 140.6, 171.1, 194.6. HRMS [M + H^+] found *m/s* 459.1505, calcd for $C_{22}H_{21}F_6N_2O_2$ 459.1502.

Synthesis of the Ni(II) complexes of glycine Schiff bases with *N*-(2-benzoylphenyl)-2-alkylamino-acetamides 3a-c, 4a-c. General Procedure. A solution of potassium hydroxide (10 eq.) in methanol (7 mL/1 g of KOH) was added to a suspension of *N*-(2-benzoylphenyl)-2-alkylamino-acetamides **3a-c, 4a-c** (1 eq.), glycine (5 eq.), nickel nitrate hexahydrate (2 eq.) in methanol (10 mL/1 g of **3a-c, 4a-c**) at 60-70 °C. Upon complete consumption of the *N*-(2-benzoylphenyl)-2-alkylamino-acetamides **3a-c, 4a-c**, monitored by TLC, the reaction mixture was poured over slurry of ice and 5% acetic acid. After the complete precipitation, product **5a-c, 6a-c** was filtered and dried, in an low temp oven (50 °C) overnight. The product was obtained in high chemical yield (99%) and high chemical purity without further purification.

Ni(II) Complex of Glycine Schiff Base with *N*-(2-benzoylphenyl)-2-dibutylamino-acetamide 5a: [12a-b] M.p. 174.9 °C. ^{1}H NMR δ 1.08 (6H, t, $J = 7.2$ Hz), 1.44–1.64 (4H, m), 2.17–2.37 (4H, m), 2.86 (2H, dt, $J = 12.6$, 4.5 Hz), 3.04–3.17 (2H, m), 3.38 (2H, s), 3.74 (2H, m), 6.80 (1H, m), 6.90 (1H, dd, $J = 8.1$, 1.8 Hz), 7.08–7.11 (2H, m), 7.36 (1H, m), 7.51–7.57 (3H, m), 8.70 (1H, d, $J = 8.4$ Hz). ^{13}C NMR δ 14.3, 21.0, 29.3, 60.5, 61.5, 62.2, 121.4, 124.5, 125.5, 126.2, 129.8, 132.8, 133.8, 135.0, 142.8, 172.0, 177.5, 179.0. HRMS [M + H^+] found *m/s* 480.1779, calcd for $C_{25}H_{31}N_3NaNiO_3$ 480.1792.

Ni(II) Complex of Glycine Schiff Base with *N*-(2-(4-trifluoromethylbenzoyl)-phenyl)-2-dibutylamino-acetamide 5b: M.p. 167.2 °C. ^{1}H NMR δ 1.09 (6H, t, $J = 7.5$ Hz), 1.55 (4H, s, $J = 7.5$ Hz), 2.22–2.38 (4H, m), 2.85–2.93 (2H, m), 3.11–3.17 (2H, m), 3.39 (2H, s), 3.70 (2H, s), 6.82 (2H, m), 7.29 (2H, d, $J = 7.2$ Hz), 7.39 (1H, m), 7.85 (2H, d, $J = 8.1$ Hz), 8.73 (1H, d, $J = 8.7$ Hz). ^{13}C NMR δ 121.3, 124.5, 124.6, 126.7, 127.0 (2C, q, $J = 58.0$ Hz), 131.9, 133.2, 138.3, 142.9, 170.1, 176.8, 179.0. ^{19}F NMR δ −161.7. HRMS [M + Na^+] found *m/s* 570.1329, calcd for $C_{26}H_{30}F_3N_3NaO_3$ 570.1485.

Ni(II) Complex of Glycine Schiff Base with *N*-(2-(3,5-bis-(trifluoromethyl)-benzoyl)-phenyl)-2-dibutylamino-acetamide 5c: M.p. 153.6 °C. ^{1}H NMR δ 1.05 (6H, t, $J = 7.2$ Hz), 1.51 (4H, s, $J = 7.2$ Hz), 2.17–2.32 (4H, m), 2.81–2.89 (2H, m), 3.10–3.17 (2H, m), 3.32 (2H, s), 3.65 (2H, s), 6.64 (1H, d, $J = 8.1$ Hz), 6.81 (1H, td, $J = 6.9$, 1.2 Hz), 7.36 (1H, td, $J = 6.9$, 1.5 Hz), 7.63 (2H, s), 8.06 (1H, s), 8.74 (1H, d, $J = 8.7$ Hz). ^{13}C NMR δ 14.01, 20.75, 29.20, 60.47, 61.35, 61.81, 121.52, 123.91, 124.04, 124.32, 124.74, 126.50, 132.67, 133.28, 133.44, 133.74, 136.73, 143.32, 168.00, 176.24, 179.04. ^{19}F NMR δ −161.9. HRMS [M + H^+] found *m/s* 616.1918, calcd for $C_{27}H_{30}F_6N_3NiO_3$ 616.1540.

Ni(II) Complex of Glycine Schiff Base with *N*-(2-benzoylphenyl)-2-piperidyl-acetamide 6a: [12a-b] M.p. 243.4 °C (decomp.). ^{1}H NMR δ 1.36–1.80 (6H, m), 3.08–3.22 (2H, m), 3.28–3.43 (2H, m), 3.66 (2H, s), 3.70 (2H, s), 6.78 (1H, ddd, $J = 8.30$, 6.96, 1.10 Hz), 6.87 (1H, dd, $J = 8.30$, 1.71 Hz), 7.00–7.06 (2H, m), 7.33 (1H, ddd, $J = 8.66$, 6.84, 1.71 Hz), 7.46–7.58 (3H, m), 8.53 (1H, dd, $J = 8.66$, 1.10 Hz). ^{13}C NMR δ 19.7, 22.8, 55.8, 60.5, 61.0, 120.9, 124.0, 125.0, 125.5, 129.2, 132.1, 133.0, 134.2, 142.0, 171.4, 176.4, 176.7. HRMS [M + Na^+] found *m/s* 458.1283, calcd for $C_{22}H_{23}N_3NaNiO_3$ 458.0991.

Ni(II) Complex of Glycine Schiff Base with *N*-(2-(4-trifluoromethylbenzoyl)-phenyl)-2-piperidyl-acetamide 6b: M.p. >250 °C (decomp). ^{1}H NMR δ 1.35–1.70 (6H, m), 3.09 (2H, d, J = 13.1 Hz), 3.30 (2H, t, J = 12.4 Hz), 3.57 (4H, s), 6.71 (2H, m), 7.15 (2H, d, J = 7.8 Hz), 7.27 (1H, t, J = 6.4 Hz), 7.73 (2H, d, J = 7.9 Hz), 8.52 (1H, d, J = 8.6 Hz). ^{13}C NMR δ 19.9, 22.9, 56.1, 60.8, 61.2, 121.4, 122.1, 124.6, 124.8, 125.6, 126.7, 132.0 (1C, q, J = 33.0 Hz), 132.6, 132.7, 138.2, 142.7, 170.3, 176.6, 177.0. HRMS [M + H$^+$] found *m/s* 504.1015, calcd for $C_{23}H_{23}F_3N_3NiO_3$ 504.1040.

Ni(II) Complex of Glycine Schiff Base with *N*-(2-(3,5-bis-(trifluoromethyl)-benzoyl)-phenyl)-2-piperidyl-acetamide 6c: M.p. M.p. >250 °C (decomp). ^{1}H NMR δ 1.37–1.68 (6H, m), 3.11 (2H, d, J = 13.2 Hz), 3.31 (2H, t, J = 12.5 Hz), 3.56 (2H, s), 3.57 (2H, s), 6.57 (1H, d, J = 7.8 Hz), 6.76 (1H, t, J = 7.8 Hz), 7.32 (1H, t, J = 8.1 Hz), 7.51 (2H, s), 7.99 (1H, s), 8.54 (1H, d, J = 8.1 Hz). ^{13}C NMR δ 19.4, 22.8, 56.2, 60.8, 61.4, 120.7, 127.7, 133.9, 124.3, 124.9, 126.4, 132.5, 133.3, 133.6 (2C, q, J = 34.0 Hz), 136.6, 143.2, 168.2, 176.0, 177.1. HRMS [M + H$^+$] found *m/s* 572.0917, calcd for $C_{24}H_{22}F_6N_3NiO_3$ 572.0913.

Phase transfer alkylation of Ni(II) Complexes of glycine Schiff Base with *N*-(2-benzoyl-phenyl)-2-dibutylamino-acetamide 5a-c with benzyl bromide or methyl iodide. General Procedure: To a solution of **5a-c** in CH_2Cl_2 (1 mL/g) at room temperature was added tetrapropylammonium bromide (0.15 eq.), 30% sodium hydroxide solution (1 mL/mL CH_2Cl_2), and benzyl bromide or methyl iodide (1.2 equivalents). The resultant mixture was rigorously stirred at room temperature for 1 h. To the resulting slurry, additional water and CH_2Cl_2 was added and the water was extracted several times with CH_2Cl_2. The organic layer was dried with $MgSO_4$, filtered, and evaporated in vacuum to yield a crystalline compound **7a-f**.

Ni(II) Complex of Phenylalanine Schiff Base with *N*-(2-benzoylphenyl)-2-dibutylamino-acetamide 7a: [12b] M.p. 159.7 °C. ^{1}H NMR δ 0.92 (3H, t, J = 5.7 Hz), 0.98 (3H, t, J = 5.7 Hz), 1.16–1.31 (4H, m), 1.41 (1H, s, J = 2.4 Hz), 1.52 (1H, s, J = 2.4 Hz), 1.89–2.00 (2H, m), 2.08–2.19 (2H, m), 2.69 (1H, m), 2.75 (1H, ABX, J = 10.2, 3.9 Hz), 2.81 (1H, AB, J = 12.0 Hz), 3.04 (1H, ABX, J = 10.2, 3.9 Hz), 3.38 (1H, AB, J = 12.0 Hz), 4.12 (1H, q, J = 5.4 Hz), 6.79 (2H, d, J = 2.7 Hz), 7.05 (1H, dd, J = 5.4, 0.6 Hz), 7.30–7.33 (2H, m), 7.43–7.45 (2H, m), 7.51–7.57 (6H, m), 8.45 (1H, dd, J = 6.6, 0.6 Hz). ^{13}C NMR δ 13.9, 14.1, 20.4, 20.8, 23.5, 29.4, 39.3, 54.9, 57.9, 63.7, 71.4, 121.2, 123.7, 127.0, 127.3, 127.7, 128.9, 129.1, 129.2, 130.0, 131.5, 132.8, 133.7, 133.8, 136.3, 142.8, 170.7, 176.0, 178.1. HRMS [M + Na$^+$] found *m/s* 592.2239, calcd for $C_{32}H_{37}N_3NaNiO_3$ 592.2080.

Ni(II) Complex of Phenylalanine Schiff Base with *N*-(2-(4-trifluoromethylbenzoyl)-phenyl)-2-dibutylamino-acetamide 7b: M.p. 207.6 °C. ^{1}H NMR δ 0.93 (3H, t, J = 5.4 Hz), 0.98 (3H, t, J = 5.4 Hz), 1.17–1.54 (6H, m), 1.94–2.02 (2H, m), 2.11–2.20 (2H, m), 2.48 (1H, td, J = 9.3, 3.3 Hz), 2.71 (1H, m), 2.72 (1H, ABX, J = 10.2, 3.9 Hz), 2.83 (1H, AB, J = 12.0 Hz), 3.13 (1H, ABX, J = 10.2, 3.9 Hz), 3.42 (1H, AB, J = 12.0 Hz), 4.11 (1H, m), 6.67 (1H, dd, J = 6.3, 1.2 Hz), 6.81 (1H, td, J = 6.3, 0.9 Hz), 7.13 (1H, d, J = 6.0 Hz), 7.35 (1H, td, J = 5.4, 1.5 Hz), 7.40–7.43 (2H, m), 7.49 (1H, d, J = 6.3 Hz), 7.54–7.58 (3H, m), 7.77 (1H, d, J = 6.0 Hz), 7.84 (1H, d, J = 6.0 Hz), 8.49 (1H, dd, J = 5.4, 0.9 Hz). ^{13}C NMR δ 13.9, 14.0, 20.4, 20.8, 23.8, 29.4, 29.7, 55.1, 58.2, 63.6, 71.6, 121.3, 124.0, 125.2, 126.2, 126.3, 126.4, 127.8, 128.0, 128.3, 129.0, 131.4, 132.0 (1C, q, J = 32.9 Hz), 133.2, 133.3, 135.9, 137.3, 137.4, 143.1, 169.0, 176.3, 177.7. HRMS [M + H$^+$] found *m/s* 638.2449, calcd for $C_{33}H_{36}F_3N_3NiO_3$ 638.2135.

Ni(II) Complex of Phenylalanine Schiff Base with *N*-(2-(3,5-bis-(trifluoromethyl)-benzoyl)-phenyl)-2-dibutylamino-acetamide 7c: M.p. 145.7 °C. ^{1}H NMR δ 0.94 (3H, t, J = 5.4 Hz), 0.99 (3H, t, J = 5.4 Hz), 1.20–1.44 (6H, m), 2.01–2.05 (2H, m), 2.15–2.19 (2H, m), 2.47 (1H, td, J = 6.8, 1.2 Hz), 2.65 (1H, m), 2.67 (1H, ABX, J = 10.2, 3.9 Hz), 2.85 (1H, AB, J = 12.0 Hz), 3.24 (1H, ABX, J = 10.2, 3.9 Hz), 3.44 (1H, AB, J = 12.0 Hz), 4.01 (1H, t, J = 3.0 Hz), 6.51 (1H, dd, J = 6.3, 1.2 Hz), 6.83 (1H, td, J = 5.4, 1.2 Hz), 7.35–7.44 (4H, m), 7.82 (1H, s), 8.08 (1H, s), 8.54 (1H, dd, J = 6.6, 0.9 Hz). ^{13}C NMR δ 13.9, 14.0, 20.4, 20.8, 23.9, 29.4, 40.2, 55.3, 58.3, 63.5, 71.6, 121.5, 122.5 (2C, q, J = 203.7 Hz), 123.8, 123.9, 124.1, 124.2, 125.7, 127.5, 127.9, 128.0, 129.1, 131.2, 132.7, 132.8133.0, 133.2, 133.5, 135.3, 135.9, 143.4, 166.9, 176.2, 177.0. HRMS [M + H$^+$] found *m/s* 706.2025, calcd for $C_{34}H_{36}F_6N_3NiO_3$ 706.2009.

Ni(II) Complex of Alanine Schiff Base with *N*-(2-benzoylphenyl)-2-dibutylamino-acetamide 7d: M.p. 161.3 °C. ^{1}H NMR δ 1.04 (3H, t, J = 6.93 Hz), 1.06 (3H, t, J = 6.72 Hz), 1.41–1.57 (4H, m), 1.58 (3H, d, J = 7.05 Hz), 2.07 (1H, td, J = 11.8, 4.65 Hz), 2.22–2.30 (2H, m), 2.54 (1H, m), 2.73 (2H, m), 2.83 (1H, td, J = 12.2, 3.84 Hz), 3.07 (1H, AB, J = 16.8 Hz), 3.32 (1H, m), 3.81 (1H, AB, J = 16.8 Hz), 3.91 (1H, q, J = 7.05, 6.75 (2H, m), 7.01 (1H, d, J = 6.33 Hz), 7.24 (1H, m), 7.31 (1H, m), 7.50 (3H, m), 8.61 (1H, d, J = 11.3 Hz). ^{13}C NMR δ 13.9, 14.1, 20.7, 20.8, 21.4, 29.1, 29.2, 58.1, 61.7, 66.5, 121.1, 123.8, 126.4, 127.1, 127.6, 128.9, 129.1, 129.7, 132.6, 133.6, 142.4, 170.6, 177.9, 180.5. HRMS [M + H$^+$] found *m/s* 494.1923, calcd for $C_{26}H_{34}N_3NiO_3$ 494.1948.

Ni(II) Complex of Alanine Schiff Base with *N*-(2-(4-trifluoromethylbenzoyl)-phenyl)-2-dibutylamino-acetamide 7e: M.p. 233.4 °C. ^{1}H NMR δ 1.40 (3H, t, J = 7.32 Hz), 1.06 (3H, t, J = 7.29 Hz), 1.42–1.54 (4H, m), 1.60 (3H, d, J = 7.02 Hz), 2.09 (1H, td, J = 11.7, 4.70 Hz), 2.25 (2H, m), 2.53 (1H, m), 2.69–2.89 (3H, m), 3.06 (1H, m), 3.42 (1H, m), 3.80 (2H, m), 6.63 (1H, m), 6.77 (1H, m), 7.20 (1H, d, J = 7.95 Hz), 7.31 (1H, m), 7.44 (1H, d, J = 7.95 Hz), 7.80 (2H, m), 8.65 (1H, d, J = 8.70 Hz). ^{13}C NMR δ 13.9, 14.1, 20.7, 21.4, 21.5, 29.1, 29.2, 58.1, 61.6, 61.7, 66.5, 121.2, 123.4 (1C, q, J = 271.0 Hz), 124.0, 125.7, 127.8, 128.2, 132.0 (1C, q, J = 33.0 Hz), 133.0, 133.2, 137.3, 142.7, 168.9, 178.0, 179.9. HRMS [M + H$^+$] found *m/s* 562.1824, calcd for $C_{27}H_{33}F_3N_3NiO_3$ 562.1822.

Ni(II) Complex of Alanine Schiff Base with *N*-(2-(3,5-bis-(trifluoromethyl)-benzoyl)-phenyl)-2-dibutylamino-acetamide 7f: M.p. >250 °C (decomp.). ^{1}H NMR δ 1.04 (3H, t, J = 7.68 Hz), 1.06 (3H, t, J = 7.68 Hz), 1.43–1.54 (4H, m), 1.60 (3H, d, J = 7.02 Hz), 2.10 (1H, td, J = 11.8, 4.65 Hz), 2.27 (2H, m), 2.50 (1H, td, J = 12.2, 4.29 Hz), 2.70–2.91 (3H, m), 3.07 (1H, AB, J = 16.9 Hz), 3.37 (1H, m), 3.67 (1H, q, J = 7.02 Hz), 3.77 (1H, AB, J = 16.9 Hz), 6.50 (1H, d, J = 8.19 Hz), 6.80 (1H, m), 7.36 (1H, m), 7.56 (1H, s), 7.78 (1H, s), 8.07 (1H, s), 8.70 (1H, d, J = 8.7 Hz). ^{13}C NMR δ 13.9, 14.1, 20.7, 21.5, 21.6, 29.2, 29.3, 58.4, 61.6, 61.8, 66.6, 120.7, 122.5 (2C, q, J = 271.7 Hz), 124.3, 125.3, 127.3, 127.9, 132.7 (2C, q, J = 34.1 Hz), 132.8, 133.4, 135.8, 143.1, 166.8, 178.2, 179.3. HRMS [M + H$^+$] found *m/s* 630.1674, calcd for $C_{28}H_{32}F_6N_3NiO_3$ 630.1696.

The Michael addition of the oxazolidinone derived amides of unsaturated acids (*S*)-8a-d and nucleophilic glycine equivalent 6a-c. General Procedure. To a flask containing **6a-c** (0.10 g), 3-((*E*)-3-phenylacryloyl)oxazolidin-2-one **(S)-8a-d** (1.05 eq.) and 1.5 mL of DMF, DBU (15 mol%) was added to the reaction mixture, which was stirred at room temperature and monitored by TLC. After disappearance of starting glycine equivalent by TLC, the reaction mixture was poured into a beaker containing 100 mL ice water. After the ice had melted the corresponding product **9a-l**, was filtered from the aqueous solution and dried in an oven to afford the appropriate product in high chemical yields.

Ni(II) Complex of (2*S*,3*S*)-3-methyl-5-[(4′*S*)-4′-phenyl-2′-oxazolidinonyl)]glutamic acid Schiff Base with *N*-(2-benzoylphenyl)-2-piperidyl-acetamide 9a: [12a-b] M.p. 286.5 °C (decomp.). ^{1}H NMR δ 1.20–2.10 (6H, m), 1.95 (3H, d, J = 6.83 Hz), 2.59 (1H, m), 2.70–3.50 (5H, m), 3.40 (1H, m), 3.67 (1H, d, J = 16.6 Hz), 3.84 (1H, d, J = 16.6 Hz), 4.00 (1H, d, J = 5.13 Hz), 4.17 (1H, dd, J = 8.79, 3.17 Hz), 4.51 (1H, t, J = 8.79 Hz), 5.24 (1H, dd, J = 8.80, 3.18 Hz), 6.69–6.78 (2H, m), 6.94 (1H, bd, J = 7.33 Hz), 7.13–7.52 (10H, m), 8.57 (1H, d, J = 8.54 Hz). ^{13}C NMR δ 17.1, 19.3, 19.9, 22.8, 34.1, 38.8, 54.2, 56.8, 57.3, 60.6, 69.8, 73.5, 120.9, 123.1, 125.7, 126.5, 126.9, 127.9, 128.2, 128.6, 128.7, 128.7, 129.4, 132.4,

133.2, 133.7, 138.8, 142.2, 153.0, 170.0, 171.0, 175.8, 176.7. HRMS [M + Na^+] found *m/s* 689.1902, calcd for $C_{36}H_{38}N_4NaNiO_5$ 689.1886. $[\alpha]_D^{25}$ +2320 (*c* 0.105, CH_3Cl).

Ni(II) Complex of (2*S*,3*S*)-3-methyl-5-[(4′*S*)-4′-phenyl-2′-oxazolidinonyl)]glutamic acid Schiff Base with *N*-(2-(4-trifluoromethylbenzoyl)-phenyl)-2-piperidyl-acetamide 9b: M.p. 182.4 °C (decomp.). ^{1}H NMR δ 1.26–1.91 (7H, m), 2.27 (3H, d, *J* = 6.03 Hz), 2.32 (1H, m), 2.71 (1H, dd, *J* = 18.6, 4.02 Hz), 3.00–3.41 (4H, m), 3.69 (1H, AB, *J* = 16.5 Hz), 3.81 (1H, AB, *J* = 16.5 Hz), 3.95 (1H, d, *J* = 4.02 Hz), 4.20 (1H, dd, *J* = 8.80, 2.43 Hz), 4.55 (1H, t, *J* = 8.58 Hz), 5.12 (1H, dd, *J* = 8.25, 2.43 Hz), 6.62 (1H, m), 6.76 (1H, m), 7.11 (1H, m), 7.18 (2H, m), 7.28–7.38 (5H, m), 7.63 (1H, d, *J* = 8.01 Hz), 8.60 (1H, d, *J* = 8.58 Hz). ^{13}C NMR δ 17.3, 19.4, 20.0, 22.9, 33.6, 38.7, 54.4, 57.1, 57.3, 60.8, 70.0, 73.0, 121.3, 123.7, 123.8 (1C, q, *J* = 271.5 Hz), 126.1, 126.3, 126.4, 127.9, 128.6, 128.8, 129.0, 129.1, 131.8 (1C, q, *J* = 32.5 Hz), 133.1, 133.6, 137.1, 139.2, 142.8, 153.4, 169.9, 170.0, 176.3, 176.7. HRMS [M + H^+] found *m/s* 735.1937, calcd for $C_{36}H_{36}F_3N_4NiO_6$ 7351935. $[\alpha]_D^{25}$ +1604 (*c* 0.85, CH_3Cl).

Ni(II) Complex of (2*S*,3*S*)-3-methyl-5-[(4′*S*)-4′-phenyl-2′-oxazolidinonyl)]glutamic acid Schiff Base with *N*-(2-(3,5-bis-(trifluoromethyl)-benzoyl)-phenyl)-2-piperidyl-acetamide 9c: M.p. 193.8 °C (decomp.). ^{1}H NMR δ 1.33–2.10 (7H, m), 2.40 (3H, d, *J* = 6.93 Hz), 2.66 (1H, m), 2.96 (2H, m), 3.18 (1H, m), 3.34 (2H, m), 3.66 (2H, m), 4.08 (2H, m), 4.52 (1H, t, *J* = 8.79 Hz), 4.88 (1H, dd, *J* = 8.64, 3.06 Hz) 6.42 (1H, m), 6.71 (1H, m), 7.03 (2H, m), 7.20–7.31 (5H, m), 7.61 (1H, s), 6.76 (1H, s), 8.47 (1H, d, *J* = 8.58 Hz). ^{13}C NMR δ 17.1, 19.3, 20.0, 22.8, 33.2, 38.3, 54.5, 57.3, 57.5, 60.6, 69.9, 71.9, 121.5, 122.5 (1C, q, *J* = 275.2 Hz), 123.0 (1C, q, *J* = 275.2 Hz), 124.0, 124.8, 125.7, 126.3, 127.4, 128.3, 128.5, 128.9, 132.5 (1C, q, *J* = 33.4 Hz), 132.6 (1C, q, *J* = 33.4 Hz), 133.1, 133.3, 135.4, 139.3, 142.9, 153.4, 167.9, 169.8, 176.2, 176.5. HRMS [M + H^+] found *m/s* 803.1816, calcd for $C_{37}H_{35}F_6N_4NiO_6$ 803.1809. $[\alpha]_D^{25}$ +1467 (*c* 1.29, CH_3Cl).

Ni(II) Complex of (2*S*,3*R*)-3-isopropyl-5-[(4′*S*)-4′-phenyl-2′-oxazolidinonyl)]glutamic acid Schiff Base with *N*-(2-benzoylphenyl)-2-piperidyl-acetamide 9d: [12b] M.p. >190 °C (decomp.). ^{1}H NMR δ 0.25 (3H, d, *J* = 6.84 Hz), 0.88 (3H, d, *J* = 6.84 Hz), 1.20–1.84 (7H, m), 2.34 (1H, m), 2.51 (1H, dd, *J* = 19.0, 1.47 Hz) 2.92 (1H, m), 3.10 (1H, dd, *J* = 19.0, 10.0 Hz), 3.14 (1H, m), 3.26–3.45 (2H, m), 3.61 (1H, m), 3.64–3.76 (2H, m), 3.90–4.03 (2H, m), 5.32 (1H, dd, *J* = 6.14, 3.35 Hz), 6.79 (1H, ddd, *J* = 8.30, 6.96, 1.22 Hz), 6.87 (1H, dd, *J* = 8.30, 1.71 Hz), 7.12–7.59 (11H, m), 8.73 (1H, dd, *J* = 8.66, 1.22 Hz. ^{13}C NMR δ 15.6, 19.1, 19.8, 21.6, 22.9, 27.4, 31.5, 45.3, 53.7, 56.1, 57.2, 60.6, 70.5, 72.1, 121.1, 122.7, 125.3, 125.7, 127.8, 128.4, 128.8, 128.9, 129.1, 129.1, 129.7, 132.6, 133.3, 134.3, 139.0, 142.4, 153.5, 171.1, 172.3, 176.5, 178.0. HRMS [M + Na^+] found *m/s* 717.2361, calcd for $C_{38}H_{42}N_4NaNiO_6$ 717.2199. $[\alpha]_D^{25}$ +2187 (*c* 0.104, CH_3Cl).

Ni(II) Complex of (2*S*,3*R*)-3-isopropyl-5-[(4′*S*)-4′-phenyl-2′-oxazolidinonyl)]glutamic acid Schiff Base with *N*-(2-(4-trifluoromethylbenzoyl)-phenyl)-2-piperidyl-acetamide 9e: M.p. >190 °C (decomp.). ^{1}H NMR δ 0.46 (3H, d, *J* = 6.69 Hz), 0.92 (3H, d, *J* = 6.81 Hz), 1.36–1.79 (7H, m), 2.51 (1H, m), 2.80 (1H, m), 2.93 (1H, m), 3.16 (2H, m), 3.28–3.40 (2H, m), 3.58 (1H, m), 3.71 (1H, m), 3.94 (1H, m), 4.04 (1H, dd, *J* = 8.55, 1.98 Hz), 4.12 (1H, t, *J* = 8.45 Hz), 5.29 (1H, dd, *J* = 6.21, 3.25 Hz), 6.73 (1H, m), 6.81 (1H, m), 7.27 (2H, m), 7.31–7.43 (6H, m), 7.79 (2H, d, *J* = 8.22 Hz), 8.73 (1H, d, *J* = 8.61 Hz). ^{13}C NMR δ 16.0, 19.2, 19.9, 22.1, 22.9, 27.4, 31.3, 45.1, 54.1, 56.5, 57.4, 60.8, 70.5, 72.2, 121.6, 123.3, 123.5 (1C, q, *J* = 270.8 Hz), 125.7, 125.8, 126.4, 126.5, 128.6, 128.7, 129.2, 129.6, 132.1 (1C, q, *J* = 30.3 Hz), 133.3, 134.1, 137.3, 139.2, 142.9, 153.9, 170.0, 172.2, 176.9, 177.9. HRMS [M + H^+] found *m/s* 763.2255, calcd for $C_{38}H_{40}F_3N_4NiO_6$ 763.2248. $[\alpha]_D^{25}$ +1610 (*c* 0.65, CH_3Cl).

Ni(II) Complex of (2*S*,3*R*)-3-isopropyl-5-[(4′*S*)-4′-phenyl-2′-oxazolidinonyl)]glutamic acid Schiff Base with *N*-(2-(3,5-bis-(trifluoromethyl)-benzoyl)-phenyl)-2-piperidyl-acetamide 9f: M.p. >200 °C (decomp.). ^{1}H NMR δ 1.02 (3H, d, J = 7.14 Hz), 1.04 (3H, d, J = 7.54 Hz), 1.26–1.82 (7H, m), 2.31 (1H, m), 2.63 (1H, m), 2.99 (1H, m), 3.12–3.47 (3H, m), 3.72 (1H, AB, J = 16.4 Hz), 3.83 (2H, m), 3.97 (1H, m), 4.11 (1H, m), 4.45 (1H, t, J = 8.40 Hz), 5.10 (1H, m), 6.54 (1H, d, J = 8.22 Hz), 6.80 (1H, t, J = 7.35 Hz), 7.16 (2H, m), 7.37 (4H, m), 7.49 (1H, s), 7.67 (1H, s), 7.77 (1H, m), 8.65 (1H, d, J = 8.67 Hz). ^{13}C NMR δ 16.9, 19.3, 20.0, 22.8, 23.2, 26.9, 30.6, 43.6, 54.4, 56.8, 57.6, 60.7, 70.1, 70.9, 121.6, 123.7, 125.7, 125.9, 126.1 (1C, q, J = 272.3 Hz), 126.2, 126.5 (1C, q, J = 273.8 Hz), 127.5, 128.6, 129.0, 129.3, 132.6 (1C, q, J = 35.2 Hz), 132.8 (1C, q, J = 33.8 Hz), 133.4, 133.5, 135.6, 139.3, 143.1, 153.7, 168.1, 171.2, 176.5, 177.6. HRMS [M + H^+] found *m/s* 831.2107, calcd for $C_{39}H_{39}F_6N_4NiO_6$ 831.2122. $[\alpha]_D^{25}$ +1487 (*c* 0.45, CH_3Cl).

Ni(II) Complex of (2*S*,3*R*)-3-(2-trifluoromethylphenyl)-5-[(4′*S*)-4′-phenyl-2′-oxazolidinonyl)]glutamic acid Schiff Base with *N*-(2-benzoylphenyl)-2-piperidyl-acetamide 9g: [12b] M.p. >200 °C (decomp.). ^{1}H NMR δ 1.19–1.80 (7H, m), 2.50–2.74 (2H, m), 2.99 (1H, m), 3.29 (1H, m), 3.44 (1H, d, *J* = 16.1 Hz), 3.50–3.67 (2H, m), 4.13 (1H, dd, *J* = 8.79, 3.42 Hz), 4.23 (1H, m), 4.33 (1H, d, *J* = 4.89 Hz), 4.49 (1H, t, *J* = 8.79 Hz), 5.16 (1H, dd, *J* = 8.54, 3.42 Hz), 6.56 (1H, bs), 6.66–6.75 (2H, m), 6.94–7.20 (2H, m), 7.10–7.30 (6H, m), 7.40–7.57 (5H, m), 7.72 (1H, d, *J* = 7.62 Hz), 8.62 (1H, d, *J* = 8.55 Hz). ^{13}C NMR δ 19.5, 20.0, 22.9, 38.3, 40.7, 54.4, 55.7, 57.3, 60.4, 69.9, 74.0, 120.6122.6, 123.8 (q, *J* = 273.7 Hz), 125.4, 126.4, 126.4, 126.4 (q, *J* = 5.92 Hz), 127.2, 127.4, 127.9, 128.1, 128.6, 128.7, 129.0, 129.5, 129.8 (q, *J* = 29.4 Hz), 130.2, 132.0, 132.8, 133.1, 134.1, 138.0, 138.3, 142.8, 153.3, 168.6, 172.5, 175.3, 176.3. HRMS [M + Na^+] found *m/s* 819.1591, calcd for $C_{42}H_{39}F_3N_4NaNiO_5$ 819.1916. $[\alpha]_D^{25}$ +1810 (*c* 0.106, CH_3Cl).

Ni(II) Complex of (2*S*,3*R*)-3-(2-trifluoromethylphenyl)-5-[(4′*S*)-4′-phenyl-2′-oxazolidinonyl)]glutamic acid Schiff Base with *N*-(2-(4-trifluoromethylbenzoyl)-phenyl)-2-piperidyl-acetamide 9h: M.p. >200 °C (decomp.). ^{1}H NMR δ 1.26–1.75 (7H, m), 2.40 (1H, m), 2.56 (1H, m), 2.92 (1H, m), 3.24–3.38 (3H, m), 3.94 (2H, m), 4.17 (1H, dd, *J* = 8.76, 2.76 Hz), 4.27 (1H, m), 4.57 (1H, t, *J* = 8.61 Hz), 5.08 (1H, dd, *J* = 8.37, 2.65 Hz), 6.61 (1H, m), 6.73 (1H, m), 7.04 (2H, m), 7.26–7.31 (5H, m), 7.35 (1H, m), 7.53 (1H, m), 7.61 (1H, m), 7.76 (3H, m), 7.84 (1H, m), 8.58 (1H, d, *J* = 8.58 Hz). ^{13}C NMR δ 19.5, 19.9, 22.8, 38.1, 40.1, 54.7, 55.8, 57.2, 60.4, 70.1, 73.3, 120.9, 122.8, 123.7 (1C, q, *J* = 273.2 Hz), 124.9 (1C, q, *J* = 271.6 Hz), 125.6, 125.9, 126.2, 126.9, 127.9, 128.0, 128.4, 128.7, 128.9, 130.0 (1C, q, *J* = 30.9 Hz), 131.2, 131.7 (1C, q, *J* = 33.2 Hz), 131.9, 132.6, 133.3, 133.8, 136.9, 138.6, 138.7, 143.1, 153.5, 168.8, 171.4, 175.1, 176.6. HRMS [M + H^+] found *m/s* 865.1979, calcd for $C_{42}H_{37}F_6N_4NiO_6$ 865.1965. $[\alpha]_D^{25}$ +1143 (*c* 0.96, CH_3Cl).

Ni(II) Complex of (2*S*,3*R*)-3-(2-trifluoromethylphenyl)-5-[(4′*S*)-4′-phenyl-2′-oxazolidinonyl)]glutamic acid Schiff Base with *N*-(2-(3,5-bis-(trifluoromethyl)-benzoyl)-phenyl)-2-piperidyl-acetamide 9i: M.p. >167.5 °C. ^{1}H NMR δ 1.20–1.68 (7H, m), 2.17 (1H, m), 2.52 (2H, m), 2.93 (2H, m), 3.25 (2H, m), 3.53 (1H, m), 4.13 (1H, m), 4.16 (1H, dd, *J* = 8.79, 3.15 Hz), 4.41 (1H, d, *J* = 4.05 Hz), 4.63 (1H, t, *J* = 8.76 Hz), 4.97 (1H, dd, *J* = 8.58, 2.97 Hz), 6.51 (1H, m), 6.75 (1H, m), 7.05 (2H, m), 7.26–7.43 (6H, m), 7.71 (1H, s), 7.82 (1H, s), 7.99 (2H, m), 8.49 (1H, d, *J* = 8.61 Hz). ^{13}C NMR δ 19.6, 19.9, 22.8, 38.4, 39.1, 54.8, 56.0, 57.6, 60.4, 70.1, 72.2, 121.1, 123.2, 125.4, 126.1 (1C, q, *J* = 271.6), 126.3, 126.7 (1C, q, *J* = 273.1 Hz), 126.8, 126.9, 127.3, 127.9 (1C, q, *J* = 271.6), 128.1, 128.6, 128.9, 129.0 (1C, q, *J* = 30.1 Hz), 129.9 (1C, q, *J* = 30.1 Hz), 130.1, 131.9, 132.4 (1C, q, *J* = 33.7 Hz), 132.9, 133.3, 133.6, 135.3, 138.5, 138.8, 143.3, 153.5, 169.1, 169.2, 174.7, 177.0. HRMS [M + H^+] found *m/s* 933.1852, calcd for $C_{43}H_{36}F_9N_4NiO_6$ 933.1839. $[\alpha]_D^{25}$ +962 (*c* 1.12, CH_3Cl).

Ni(II) Complex of (2*S*,3*R*)-3-(2-methoxyphenyl)-5-[(4′*S*)-4′-phenyl-2′-oxazolidinonyl)]glutamic acid Schiff Base with *N*-(2-benzoylphenyl)-2-piperidyl-acetamide 9j: [12b] M.p. >190 °C

(decomp.). ^{1}H NMR δ 1.24–1.70 (7H, m), 2.00–2.20 (1H, m), 2.40 (1H, m), 2.83–3.05 (2H, m), 3.15–3.40 (1H, m), 3.24 (3H, s), 3.40 (1H, dd, J = 18.3, 8.54 Hz), 3.58 (1H, dd, J = 18.3 6.59 Hz), 4.03 (1H, m), 4.13 (1H, dd, J = 8.79, 3.42 Hz), 4.33 (1H, d, J = 4.64 Hz), 4.56 (1H, t, J = 8.79 Hz), 5.11 (1H, dd, J = 8.55, 3.42 Hz), 6.68–6.78 (2H, m), 6.93–7.02 (2H, m), 7.08 (1H, d, J = 8.05 Hz), 7.15–7.34 (8H, m), 7.40–7.61 (3H, m), 7.68 (1H, bd, J = 7.33 Hz), 8.37 (1H, d, J = 8.54 Hz). ^{13}C NMR δ 19.4, 19.7, 22.8, 35.5, 36.1, 54.5, 54.6, 55.2, 57.2, 60.0, 69.5, 73.4, 109.9, 120.5, 121.0, 122.8, 125.6, 126.7, 126.8, 127.8, 127.9, 128.4, 128.5, 128.7, 128.9, 129.3, 129.9, 131.9, 133.4, 133.6, 138.6, 142.1, 152.9, 158.0, 169.5, 171.3, 174.9, 176.7. HRMS [M + H$^+$] found *m/s* 759.2089, calcd for $C_{42}H_{42}N_4NaNiO_6$ 759.2251. $[\alpha]_D^{25}$ +1607 (*c* 0.097, CH_3Cl).

Ni(II) Complex of (2*S*,3*R*)-3-(2-methoxyphenyl)-5-[(4′*S*)-4′-phenyl-2′-oxazolidinonyl)]glutamic acid Schiff Base with *N*-(2-(4-trifluoromethylbenzoyl)-phenyl)-2-piperidyl-acetamide 9k: M.p. >200 °C (decomp.). ^{1}H NMR δ 1.20–1.33 (3H, m), 1.42–1.51 (2H, m), 1.61 (1H, m), 2.87–3.08 (3H, m), 3.25 (3H, s), 3.30 (1H, m), 3.99 (2H, m), 4.19 (2H, m), 4.59 (1H, t, J = 8.62 Hz), 5.06 (1H, m), 6.65 (1H, m), 6.76 (1H, m), 7.09 (3H, m), 7.29 (5H, m), 7.38 (2H, d, J = 7.98 Hz), 7.64 (3H, m), 7.81(1H, m), 8.40 (1H, d, J = 8.55 Hz). ^{13}C NMR δ 19.5, 19.8, 22.8, 35.0, 36.6, 54.7, 54.8, 55.4, 57.3, 60.1, 70.0, 73.0, 110.2, 120.9, 121.5, 123.3, 123.9 (1C, q, J = 270.8 Hz), 126.0, 126.5, 127.8, 128.2, 128.4, 128.9, 129.0, 129.2, 130.8, 131.7 (1C, q, J = 32.5 Hz), 132.6, 133.4, 137.5, 139.2, 142.6, 153.4, 158.1, 169.7, 170.2, 175.4, 176.9. HRMS [M + H$^+$] found *m/s* 827.2205, calcd for $C_{42}H_{40}F_3N_4NiO_7$ 827.2197. $[\alpha]_D^{25}$ +1232 (*c* 0.9242, CH_3Cl).

Ni(II) Complex of (2*S*,3*R*)-3-(2-methoxyphenyl)-5-[(4′*S*)-4′-phenyl-2′-oxazolidinonyl)]glutamic acid Schiff Base with *N*-(2-(3,5-bis-(trifluoromethyl)-benzoyl)-phenyl)-2-piperidyl-acetamide 9l: M.p. 227.3 °C. ^{1}H NMR δ 1.31 (3H, m), 1.48 (2H, m), 1.62 (1H, m), 1.88 (1H, bs), 2.07 (1H, d, J = 13.5 Hz), 2.38 (1H, m), 2.96 (3H, m), 3.26 (2H, m), 3.31 (3H, s), 3.72 (1H, m), 4.15 (1H, m), 4.30 (1H, d, J = 4.53 Hz), 4.62 (1H, t, J = 8.76 Hz), 4.97 (1H, dd, J = 8.55, 2.76 Hz), 6.56 (1H, m), 6.78 (1H, dd, J = 7.71, 7.53 Hz), 7.08 (2H, m), 7.14 (1H, d, J = 8.22 Hz), 7.28–7.35 (5H, m), 7.57 (1H, s), 7.65 (2H, m), 7.72 (1H, s), 7.80 (1H, s), 8.38 (1H, d, J = 8.38 Hz). ^{13}C NMR δ 19.4, 19.8, 22.8, 34.4, 36.6, 54.7, 54.8, 55.5, 57.7, 60.0, 69.9, 72.5, 110.3, 121.2, 121.8, 123.7, 124.0, 124.4, 125.7, 126.4, 127.0 (2C, q, J = 271.5 Hz), 127.9, 128.5, 128.9, 129.3, 130.8, 132.4 (2C, q, J = 33.5 Hz), 132.9, 135.8, 139.3, 142.9, 153.4, 157.8, 168.1, 169.9, 175.4, 176.8. HRMS [M + H$^+$] found *m/s* 895.2087, calcd for $C43H_{39}F_6N_4NiO_7$ 895.2071. $[\alpha]_D^{25}$ +1189 (*c* 0.88, CH_3Cl).

4.1. Competitive phase transfer benzylation or methylation of Ni(II) complexes of glycine Schiff Bases **5a-c**

A stock solution (approximately 0.06 M) was prepared for each complex **5a-c** in CD_2Cl_2. A mixture of two complexes for comparison was prepared by transferring equal amounts of each complex to an NMR tube. ^{1}H NMR was performed to ensure that the complexes were equimolar. Adjustments were made through appropriate quantities of the necessary solution until the mixture was equimolar. Solutions (approximately 0.3 M) were prepared of benzyl bromide and methyl iodide in CD_2Cl_2. An appropriate amount of the alkylating reagent solution was transferred to the equimolar complex mixture to achieve final solution that contains the alkylating reagent (0.9 eq.) and 1 equivalent of each complex. The contents of the NMR tube were transferred to a small reaction vessel and CH_2Cl_2 was used to dilute the mixture to approximately 2 mL of solution. A solution of tetrabutylammonium bromide in CH_2Cl_2 was prepared and the appropriate amount was transferred to the reaction mixture to achieve a 0.15 equivalents of the phase transfer catalyst, compared to the amount of each complex. The reaction vessel was purged with N_2 and approximately 2 mL of 30% aqueous potassium hydroxide was added. The reactions were allowed to react at room temperature with vigorous stirring for 2 h. An additional amount of water (10 mL) and CH_2Cl_2 (5 mL) were added. After diluting the reaction mixture the organic fraction is extracted and this procedure was repeated three times. The organic fractions were combined, dried with $MgSO_4$, filtered, and evaporated under vacuum which yielded the crude reaction mixture for further ^{1}H NMR analysis.

4.2. Competitive DBU catalyzed Michael Addition of oxazolidinone derived amides of unsaturated acids **8a-d** and nucleophilic glycine equivalents **6a-c**

A stock solution (approximately 0.06 M) was prepared for each complex **6a-c** in $CDCl_3$. A mixture of two complexes for comparison was prepared by transferring equal amounts of each complexes to an NMR tube. ^{1}H NMR was performed to ensure that the complexes were equimolar in solution. Adjustments were made through appropriate quantities of the necessary solution until the mixture was equimolar. Solutions (approximately 0.3 M) were prepared of Michael Acceptor **8a-d** in $CDCl_3$. An appropriate amount of the solution containing the Michael Acceptor was transferred to the equimolar complex mixture to achieve final solution that contains the Michael Acceptor (0.9 eq.) and 1 equivalent of each complex. The contents of the NMR tube were transferred to a small reaction vessel and the solvent was evaporated under vacuum. An aliquot of DMF was added to the reaction vessel, and the system was purged with N_2. An appropriate amount of a previously prepared DBU/DMF solution was added to the vessel to achieve a 0.15 equivalent of the DBU. The reactions were allowed to react at room temperature with vigorous stirring for 2 h. The reactions were quenched by pouring the reaction mixture over a solution of ice water to achieve a 20:1H_2O:DMF solution. After approximately 1 h, methylene chloride was added and the mixture was extracted. The water was washed with CH_2Cl_2 twice, and the combined organic fractions were washed with an additional amount of water. The resulting organic fraction was dried with $MgSO_4$, filtered, and evaporated under vacuum which yielded the crude reaction mixture for further ^{1}H NMR analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2020.131741.

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