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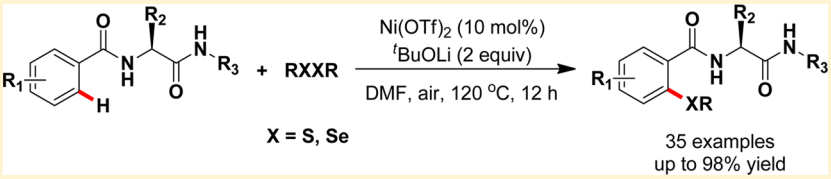
Nickel-Catalyzed *ortho*-C-H Thiolation of *N*-Benzoyl α-Amino Acid Derivatives

Feng Gao, Wei Zhu, Dengyou Zhang, Shuangjie Li, Jiang Wang, and Hong Liu*

CAS Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zuchongzhi Road, Shanghai 201203, China

Supporting Information



ABSTRACT: We developed the first nickel-catalyzed direct *ortho*-thiolation of *N*-benzoyl α-amino acid derivatives. This novel strategy showed wide generality, functional tolerance, and high regioselectivity. In addition, dipeptide derivatives were also compatible with this transformation system, providing a potential protocol for the direct modification of peptide derivatives.

INTRODUCTION

Functionalized amino acid derivatives have been widely employed as useful substrates in medicinal chemistry and the pharmaceutical industry for their broad biological activities[1] and facile membrane permeability.[2] Among them, *ortho*-thio-substituted *N*-benzoyl α-amino acid derivatives are frequently found as building blocks in bioactive compounds (Figure 1).[3] Traditionally, the construction of such scaffolds is achieved by cross coupling reactions between aryl-halides and thiol/disulfides, suffering from harsh reaction conditions, low substrate scopes, and prefunctionalization of the substrates.[4] Thus, there remains the need to develop efficient and environmentally friendly synthetic methods to elaborate amino acid derivatives.

In recent decades, transition-metal-catalyzed direct C−H functionalization has made great progress, in which diverse transformations and good regioselectivity have been realized with the assistance of various directing groups.[5] Very recently, environmentally friendly and inexpensive amino acid moieties have been employed as novel directing groups in C−H activation for the direct modification of amino acid derivatives. Chatani reported an elegant work of *ortho*-C(sp^2)−H arylation/alkylation using α-amino ester moieties as bidentate directing groups (Scheme 1A).[6] By the employment of a similar strategy, direct C(sp^3)−H functionalization of the amino acid derivatives has been accomplished by Yu's[7] and Hong's groups.[8] Mostly, these protocols demonstrated the formation of C−C bonds via C−H cleavage using palladium as the catalyst. Recently, nickel catalysts in C−H activation reactions have attracted increasing attention owing to their abundance, low cost, and relatively lower toxicity.[9,10] Given the importance of *ortho*-thio-substituted *N*-benzoyl α-amino acid derivatives, we proposed the construction of such privileged frameworks via nickel-catalyzed direct C−H activation. Herein, we report the first example of nickel-catalyzed C−H thiolation of *N*-benzoyl α-amino acid as well as dipeptide derivatives (Scheme 1B).

RESULTS AND DISCUSSION

To verify the hypothesis, we initiated our studies by investigating the reaction with a series of *N*-benzoyl α-amino acid derivatives. The treatment of **1a** with disulfide **2a** in the presence of nickel catalyst and base afforded desired thiolated product **3a** in 76% yield (Table 1, entries 1−5), whereas other substrates were not effective. This result suggested that bis-NH of amides was essential for the nickel-catalyzed C−H activation. The optimization of nickel salts revealed that $Ni(OTf)_2$ was the most effective catalyst for providing product **3a**, giving a yield of 93% (entries 6−10). Further screening determined that ^{t}BuOLi was the best base (entries 11−13). The efficiency of the reaction was also significantly affected by different solvents (entries 14−18) with DMF being identified as optimal. No desired product was obtained in nonpolar or protonic solvents, and the use of DMSO resulted in a dramatically decrease in yield.

With the optimized reaction conditions in hand, we investigated the scope of *N*-benzoyl α-amino acid derivatives. Generally, this thiolation reaction tolerated various substituents on both the aromatic ring and α-amino acid moieties and generated the desired products in moderate to high yields (Table 2). Benzamides bearing a large group in the *ortho*-position, such as trifluoromethyl and phenyl groups, gave moderate yields, probably due to the steric hindrance, whereas halogen could be tolerated well under standard conditions (**3b**−**3d**). When *meta*-substituted benzamides were employed, the C−H bond thiolation took place at the less sterically hindered position irrespective of the electronic nature of the substituents (**3e**−**3g**). The unsubstituted and *para*-substituted benzamides afforded a mixture of mono- and dithiolated products, and exclusive dithiolated products were obtained in good yields by increasing

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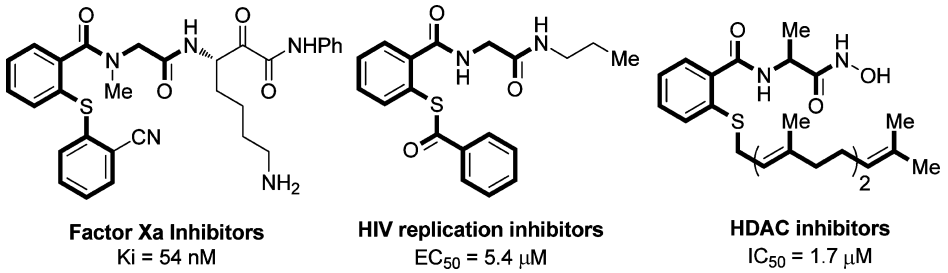
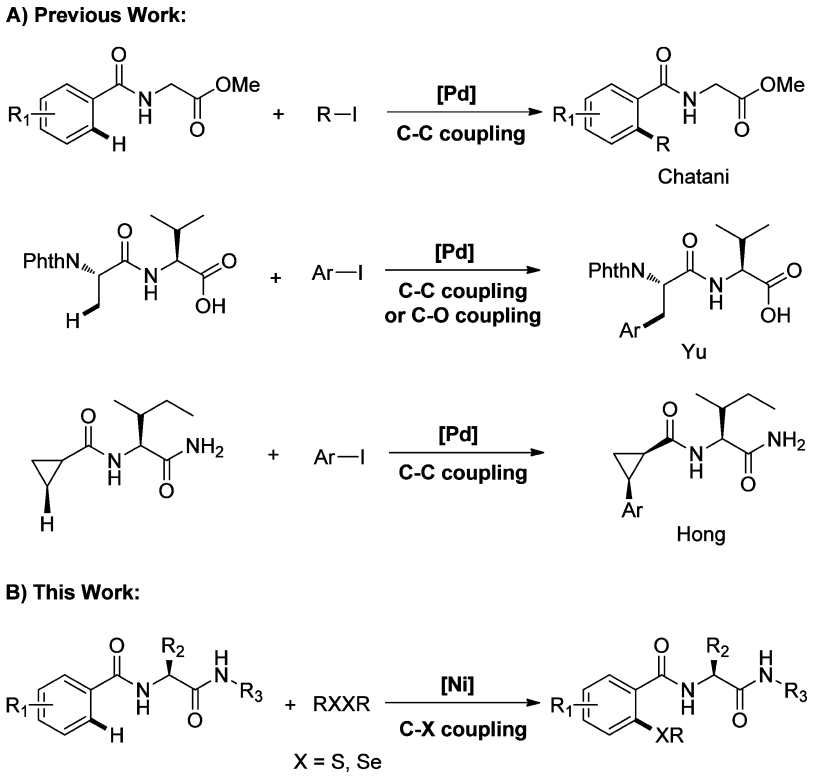


Figure 1. Bioactive *ortho*-thio-substituted *N*-benzoyl α-amino acid derivatives.

Scheme 1. Nickel-Catalyzed C(sp^2)−H Thiolation



the amounts of disulfide, nickel catalyst, and base (**3h**−**3j**). Multisubstituted benzamide derivative and naphthamide provided the desired products in high yields (**3k** and **3l**). Furthermore, heterocycles were also compatible with the optimal conditions (**3m** and **3n**). Next, the reaction efficiency of different α-amino acid moieties was evaluated. Cyclic amino acid derivatives proceeded smoothly and produced the corresponding products in high yields (**3o** and **3p**). Substrates bearing natural α-amino acid moieties, such as alanine, valine, leucine, and phenylalanine worked well under the standard conditions (**3q**−**3t**). Notably, the chirality at the α-position of valine was not influenced after the transformation (97% ee). In addition, dipeptide derivatives (**1u** and **1v**) were also effective substrates, indicating that the reaction system could be a potential strategy for direct modification of peptides. Importantly, the C(sp^2)-H thiolation was carried out on a gram scale without any additives to afford **3a** in 90% yield (Scheme 2).

Next, the scope of disulfides was tested further (Table 3). In general, various disulfides and diselanes proceeded smoothly to provide the corresponding products. The introduction of an electron-donating group at the para or meta position of diphenyl disulfides had no influence on the yield (**4b**, **4c**, and **4f**), whereas *meta*-nitro-substituted diphenyl disulfides gave a relatively lower yield (**4h**). Contrastingly, halogen-substituted diphenyl disulfides produced the corresponding products in excellent yields, guaranteeing further transformation (**4d** and **4g**). *Ortho*-substituted disulfide could also furnish the product with a slightly decreased yield, probably because of interference with the oxidative addition process (**4i**). Importantly, heteroaromatic disulfide and diphenyl diselanes were also compatible with the reaction conditions, delivering the products in moderate to good yields (**4j**−**4m**). Unfortunately, no desired thiolated product was observed when dibenzyldisulfane and dipropyldisulfane were applied (**4n** and **4o**).

To understand the reaction mechanism, we first performed a radical scavenger experiment (Scheme 3A). The results revealed that the reaction efficiency was not affected by TEMPO (1 equiv), indicating that it likely did not involve a single-electron transfer (SET) process. Furthermore, an intermolecular competition experiment between **1f** and **1g** was carried out, and the substrate bearing an electron-withdrawing substituent reacted with higher relative rate (Scheme 3B), which suggested that C−H bond cleavage might be influenced by its acidity. A detailed mechanism remains to be elucidated.

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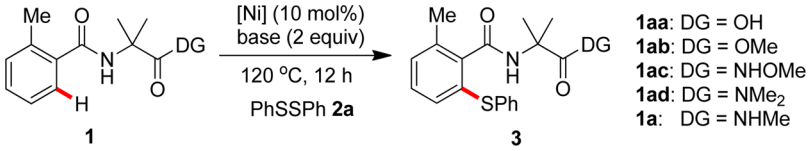
J. Org. Chem. 2016, 81, 9122−9130

Table 1. Optimization of Reaction Conditions[a]



entry	DG	[Ni]	base	solvent	yield (%)
1	**1aa**	$NiCl_2$	^{t}BuOLi	DMF	trace
2	**1ab**	$NiCl_2$	^{t}BuOLi	DMF	trace
3	**1ac**	$NiCl_2$	^{t}BuOLi	DMF	trace
4	**1ad**	$NiCl_2$	^{t}BuOLi	DMF	trace
5	**1a**	$NiCl_2$	^{t}BuOLi	DMF	76
6	**1a**	$NiBr_2$	^{t}BuOLi	DMF	80
7	**1a**	NiI_2	^{t}BuOLi	DMF	88
8	**1a**	$Ni(acac)_2$	^{t}BuOLi	DMF	81
9	**1a**	$Ni(OAc)_2$	^{t}BuOLi	DMF	82
10	**1a**	$Ni(OTf)_2$	^{t}BuOLi	DMF	93
11	**1a**	$Ni(OTf)_2$	^{t}BuONa	DMF	88
12	**1a**	$Ni(OTf)_2$	^{t}BuOK	DMF	84
13	**1a**	$Ni(OTf)_2$	Na_2CO_3	DMF	trace
14	**1a**	$Ni(OTf)_2$	^{t}BuOLi	DMSO	18
15	**1a**	$Ni(OTf)_2$	^{t}BuOLi	toluene	trace
16	**1a**	$Ni(OTf)_2$	^{t}BuOLi	DCE	trace
17	**1a**	$Ni(OTf)_2$	^{t}BuOLi	Dioxane	trace
18	**1a**	$Ni(OTf)_2$	^{t}BuOLi	^{t}AmylOH	trace

[a]Reaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol), [Ni] (10 mol %), base (2 equiv), and solvent (1 mL) in air at 120 °C.

CONCLUSIONS

In conclusion, we developed the first nickel-catalyzed direct *ortho*-thiolation of *N*-benzoyl α-amino acid derivatives. This method is widely applicable and shows high functional tolerance and high regioselectivity. Dipeptide derivatives were also compatible, representing a potential protocol for the direct modification of peptide derivatives. It also provides a straightforward approach for the construction of *ortho*-thio-substituted *N*-benzoyl α-amino acid derivatives, which are identified as privileged scaffolds with wide potential bioactivities in pharmaceuticals. Therefore, this modified strategy will be of importance to medicinal chemists.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, the reagents (chemicals) were purchased from commercial sources and used without further purification. Water was deionized before used. Analytical thin layer chromatography (TLC) was HSGF 254 (0.15−0.2 mm thickness). Compound spots were visualized by UV light (254 nm). Column chromatography was performed on silica gel FCP 200−300. NMR spectra were run on a 400 or 500 MHz instrument. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Low- and high-resolution mass spectra (LRMS and HRMS) were measured on a spectrometer.

General Procedure for the Preparation of Substrates 1a−v. To a mixture of 2-((*tert*-butoxycarbonyl)amino)-2-methylpropanoic acid (25.00 g, 123.01 mmol) and HOBt (18.28 g, 135.31 mmol) in 200 mL of DCM were added TEA (56.27 mL, 405.93 mmol) followed by the addition of EDCI (25.94 g, 135.31 mmol). The resulting mixture was stirred for 10 min, and then methanamine hydrochloride (8.31 g, 123.01 mmol) was added. The reaction was stirred overnight. The mixture was diluted with DCM, and the organic layer was washed with saturated sodium carbonate and brine, dried over anhydrous Na_2SO_4, and concentrated under vacuum to give a white solid (23.10 g, 87%).

To a mixture of *tert*-butyl (2-methyl-1-(methylamino)-1-oxopropan-2-yl)carbamate (23.10 g, 106.81 mmol) in 150 mL of dioxane was added dropwise a solution of HCl in dioxane (4 N, 150 mL) at 0 °C. The reaction was stirred at room temperature for 3 h. Then, the mixture was concentrated under vacuum to give the crude product as a white solid (15.80 g, 97%).

To an ice-cooled solution of 2-amino-*N*,2-dimethylpropanamide hydrochloride (1.50 g, 9.83 mmol) in 40 mL of DCM were added TEA (4.09 mL, 29.48 mmol) followed by the dropwise addition of the corresponding benzoyl chloride (1.08 mmol). The resulting mixture was stirred at room temperature for 6 h. Then, the reaction was quenched by water and extracted with DCM. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under vacuum. The residue was purified by silica gel column to afford the title compound as a white solid.

General Procedure for Nickel-Catalyzed *ortho*-C-H Thiolation of *N*-Benzoyl α-Amino Derivatives. A Schlenk tube equipped with a magnetic stir bar was charged with $Ni(OTf)_2$ (7.1 mg, 10 mol %), ^{t}BuOLi (32.1 mg, 0.40 mmol), substrate **1** (0.20 mmol), and disulfide **2** (0.4 mmol) and then capped with a septa. One milliliter of DMF was charged to the vial via syringe, and then the resulting mixture was stirred in a preheated oil bath at 120 °C for 12 h. After the reaction was completed, the solvent was removed under vacuum, and the residue was purified by silica gel column (PE/EA = 2:3) to afford the desired thiolated product.

Analytical Characterization Data of Products. *2-Methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)-6-(phenylthio)-benzamide (**3a**).* Compound **3a** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 64 mg, 93% yield. Mp: 144−146 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.47 (s, 1H), 7.37−7.20 (m, 8H), 7.13 (dd, J = 7.5, 0.8 Hz, 1H), 2.56 (d, J = 4.7 Hz, 3H), 2.30 (s, 3H), 1.41 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 174.3, 167.1, 141.2, 135.9, 135.7, 130.8, 130.6, 130.1, 129.9, 129.41, 129.37, 127.1, 56.6, 26.1, 25.0, 18.8. LRMS (ESI) $[M + H]^+$ found: 343.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{19}H_{22}O_2N_2NaS$: 365.1294; found: 365.1288. Anal. Calcd for $C_{19}H_{22}O_2N_2S$: C, 66.64; H, 6.48; N, 8.18. Found: C, 66.46; H, 6.51; N, 8.18.

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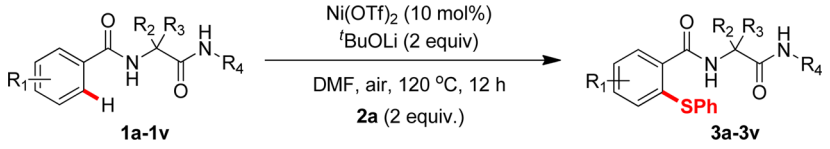
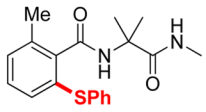
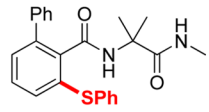
Table 2. Scope of *N*-Benzoyl α-Amino Acid Derivatives[a]



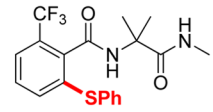
1a-1v **3a-3v**



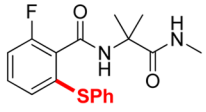
3a, 93%



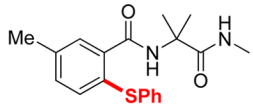
3b, 64%[b]



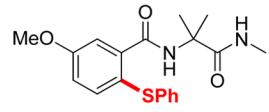
3c, 41%



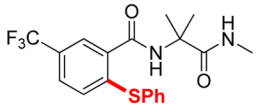
3d, 58%[b]



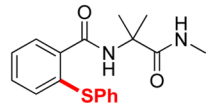
3e, 71%



3f, 74%

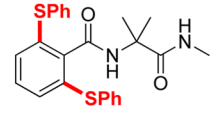


3g, 75%

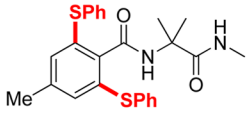


3h, 80%

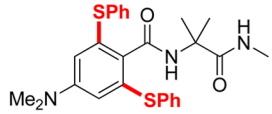
(mono:di = 1:1.4)



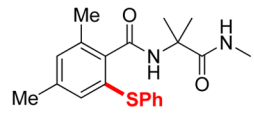
3h', 76%[c]



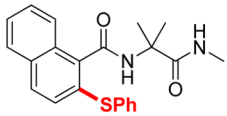
3i, 76%[c]



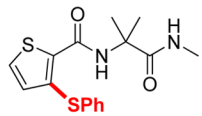
3j, 77%[c]



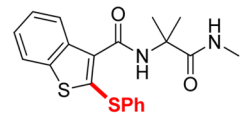
3k, 85%



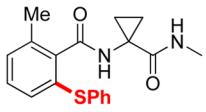
3l, 87%



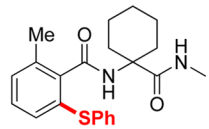
3m, 35%[b]



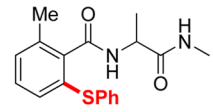
3n, 79%



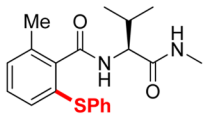
3o, 90%



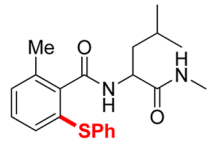
3p, 80%



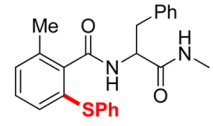
3q, 73%



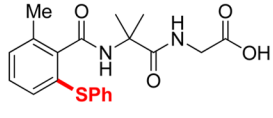
3r, 81% (97% ee)[d]



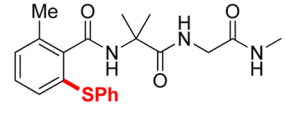
3s, 76%



3t, 54%



3u, 67%[e]



3v, 30%[e]

[a]Reaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol), $Ni(OTf)_2$ (10 mol %), ^tBuOLi (0.4 mmol), and DMF (1 mL) in air at 120 °C. [b]For 15 h. [c]Compound **2a** (0.6 mmol), $Ni(OTf)_2$ (15 mol %), and ^tBuOLi (0.6 mmol). [d]At 100 °C. [e]$Ni(OTf)_2$ (20 mol %) and ^tBuOLi (0.6 mmol).

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Scheme 2. Gram-Scale C(sp²)−H Thiolation

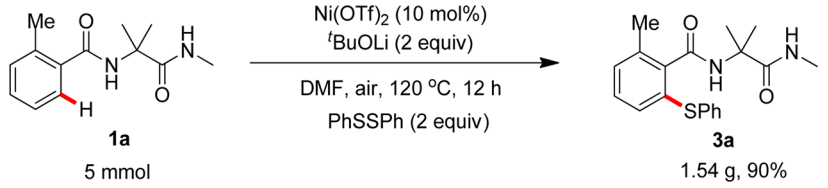
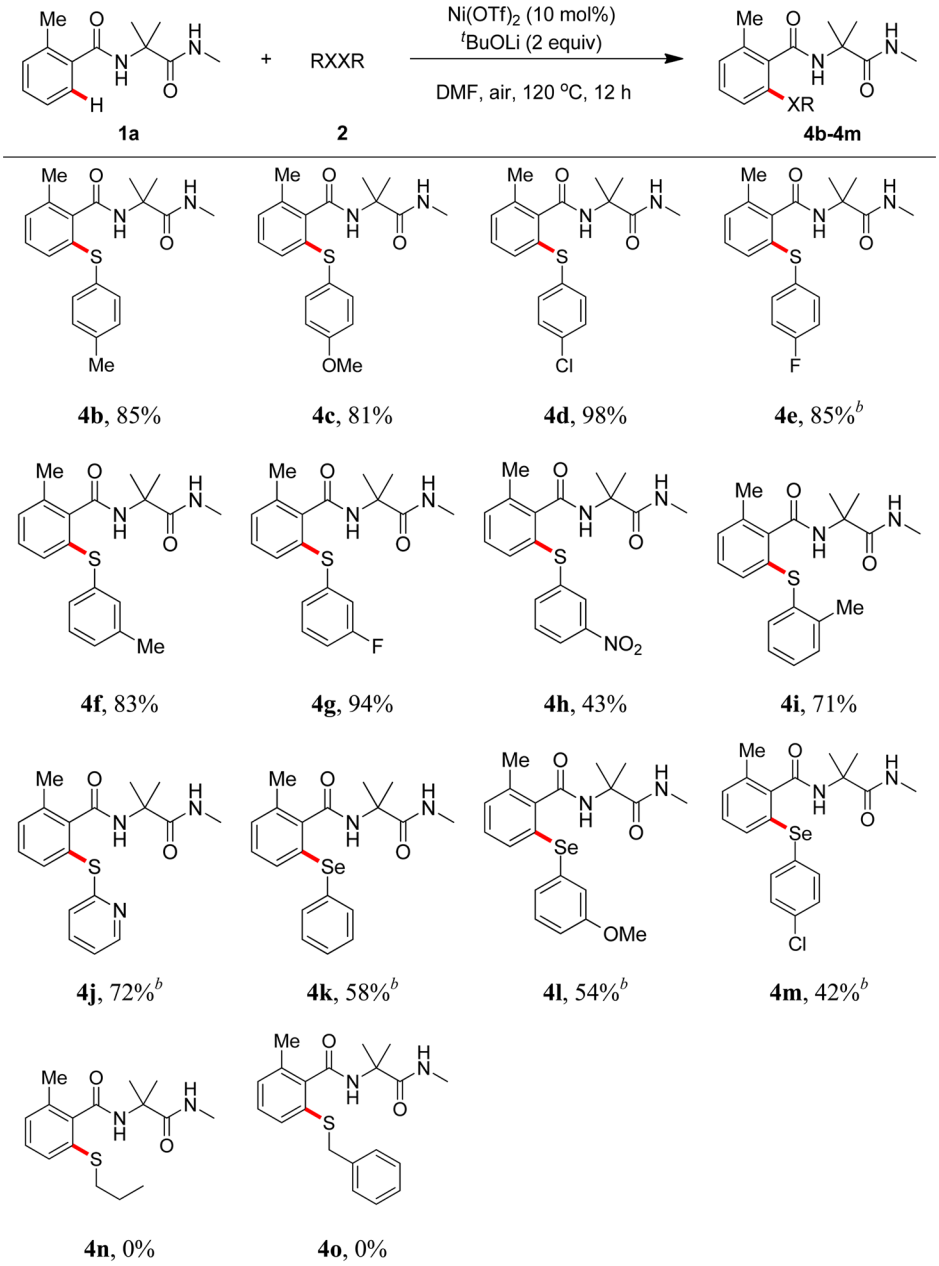


Table 3. Scope of Disulfides[a]



[a]Reaction conditions: **1a** (0.2 mmol), **2** (0.4 mmol), $Ni(OTf)_2$ (10 mol %), ^tBuOLi (2 equiv), and DMF (1 mL) in air at 120 °C. [b]For 18 h.

*N-(2-Methyl-1-(methylamino)-1-oxopropan-2-yl)-3-(phenylthio)-[1,1′-biphenyl]-2-carboxamide (**3b**).* Compound **3b** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 52 mg, 64% yield. Mp: 174−176 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 8.36 (s, 1H), 7.49−7.37 (m, 10H), 7.36−7.29 (m, 2H), 7.27 (d, J = 7.8 Hz, 1H), 6.65 (q, J = 4.7 Hz, 1H), 2.44 (d, J = 4.7 Hz, 3H), 1.17 (s, 6H). ^{13}C {^1H} NMR (125 MHz, DMSO-d_6) δ 174.0, 166.5, 140.0, 139.42, 139.39, 134.9, 132.3, 131.3, 131.1, 129.51, 129.49, 129.1, 128.8, 128.0, 127.6, 56.7, 25.9, 24.6. LRMS (ESI) $[M + H]^+$ found: 405.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{24}H_{24}O_2N_2NaS$: 427.1451; found: 427.1445.

*N-(2-Methyl-1-(methylamino)-1-oxopropan-2-yl)-2-(phenylthio)-6-(trifluoromethyl)benzamide (**3c**).* Compound **3c** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H

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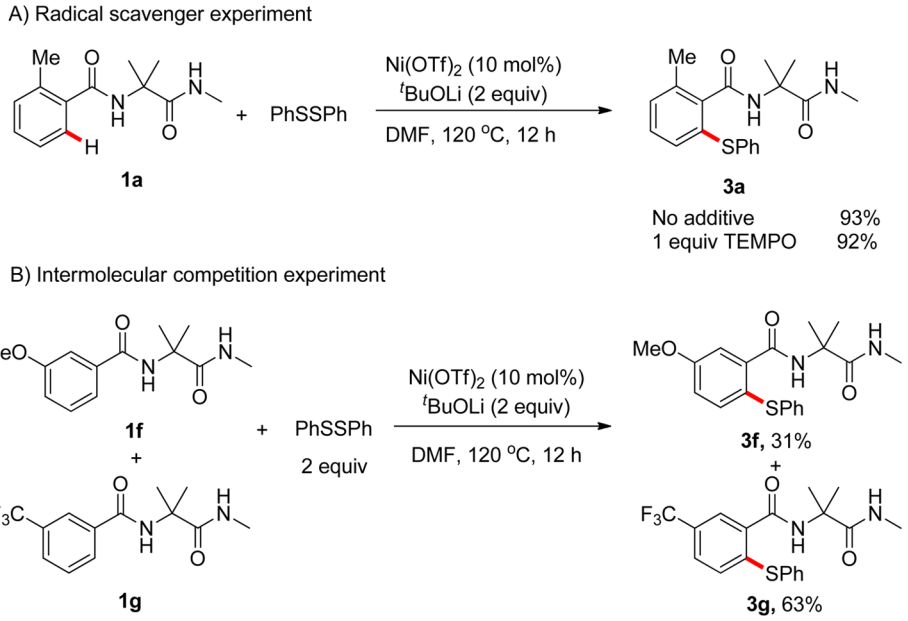
Scheme 3. Mechanistic Investigations



thiolation of *N*-benzoyl α-amino derivatives. White solid, 32 mg, 41% yield. Mp: 166−168 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.68 (s, 1H), 7.74 (d, J = 7.5 Hz, 1H), 7.62−7.51 (m, 2H), 7.49−7.38 (m, 4H), 7.38−7.33 (m, 1H), 7.27 (d, J = 4.2 Hz, 1H), 2.58 (d, J = 4.5 Hz, 3H), 1.45 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, MeOD) δ 176.9, 167.7, 138.1, 137.5, 137.2, 135.2, 133.2, 131.3, 130.8, 128.6, 129.0 (q, J = 31.8 Hz), 126.5 (q, J = 4.7 Hz), 125.0 (q, J = 273.7 Hz), 59.1, 26.6. LRMS (ESI) [M + H]$^+$ found: 397.0. HRMS (ESI) [M + Na]$^+$ calcd for $C_{19}H_{19}O_2N_2F_3NaS$: 419.1012; found: 419.1006.

*2-Fluoro-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)-6-(phenylthio)benzamide (**3d**).* Compound **3d** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 40 mg, 58% yield. Mp: 163−166 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.68 (s, 1H), 7.44−7.33 (m, 6H), 7.25−7.16 (m, 2H), 6.99 (d, J = 7.8 Hz, 1H), 2.59 (d, J = 4.6 Hz, 3H), 1.43 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 173.8, 162.3, 158.5 (d, J = 247.7 Hz), 135.1 (d, J = 4.0 Hz), 133.9, 131.7, 131.0 (d, J = 8.8 Hz), 129.6, 128.0, 127.8 (d, J = 20.5 Hz), 127.4, 114.5 (d, J = 11.0 Hz), 56.8, 26.1, 25.0. LRMS (ESI) [M + H]$^+$; found: 347.0. HRMS (ESI) [M + Na]$^+$ calcd for $C_{18}H_{19}O_2N_2FNaS$: 369.1043; found: 369.1042.

*5-Methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)-2-(phenylthio)benzamide (**3e**).* Compound **3e** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 49 mg, 71%. Mp: 149−152 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.33 (s, 1H), 7.46 (d, J = 1.2 Hz, 1H), 7.42 (q, J = 4.6 Hz, 1H), 7.37−7.32 (m, 2H), 7.32−7.24 (m, 3H), 7.19 (dd, J = 8.0, 1.3 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 2.56 (d, J = 4.6 Hz, 3H), 2.33 (s, 3H), 1.39 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 174.2, 167.0, 139.1, 136.8, 135.7, 132.1, 130.85, 130.79, 129.5, 129.4, 128.8, 127.2, 56.4, 26.1, 25.1, 20.4. LRMS (ESI) [M + H]$^+$ found: 343.0. HRMS (ESI) [M + Na]$^+$ calcd for $C_{19}H_{22}O_2N_2NaS$: 365.1294; found: 365.1292.

*5-Methoxy-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)-2-(phenylthio)benzamide (**3f**).* Compound **3f** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 53 mg, 74% yield. Mp: 162−165 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.35 (s, 1H), 7.40 (q, J = 4.5 Hz, 1H), 7.33−7.26 (m, 3H), 7.23−7.17 (m, 4H), 7.02 (dd, J = 8.7, 2.9 Hz, 1H), 3.82 (s, 3H), 2.55 (d, J = 4.6 Hz, 3H), 1.35 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 174.1, 166.7, 159.1, 142.4, 137.2, 135.9, 129.2, 128.9, 126.3, 121.4, 116.0, 113.9, 56.5, 55.6, 26.1, 25.0. LRMS (ESI) [M + H]$^+$ found: 359.0. HRMS (ESI) [M + H]$^+$ calcd for $C_{19}H_{23}O_3N_2S$: 359.1424; found: 359.1422.

*N-(2-Methyl-1-(methylamino)-1-oxopropan-2-yl)-2-(phenylthio)-5-(trifluoromethyl)benzamide (**3g**).* Compound **3g** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 59 mg, 75% yield. Mp: 162−163 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.67 (s, 1H), 8.06 (d, J = 1.4 Hz, 1H), 7.68−7.62 (m, 2H), 7.56−7.44 (m, 5H), 6.99 (d, J = 8.4 Hz, 1H), 2.60 (d, J = 4.6 Hz, 3H), 1.44 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 173.9, 165.6, 142.7, 135.6, 134.2, 131.9, 130.1, 129.3, 128.4, 126.6 (q, J = 3.5 Hz), 125.5 (q, J = 32.3 Hz), 125.2 (q, J = 3.5 Hz), 125.1 (q, J = 272.5 Hz), 56.6, 26.2, 25.2. LRMS (ESI) [M + H]$^+$ found: 396.9. HRMS (ESI) [M + Na]$^+$ calcd for $C_{19}H_{19}O_2N_2F_3NaS$: 419.1012; found: 419.1007.

*N-(2-Methyl-1-(methylamino)-1-oxopropan-2-yl)-2-(phenylthio)-benzamide (**3h**).* Compound **3h** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 22 mg, 34% yield (**3h** plus **3h′**; 80% total yield). Mp: 117−120 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.37 (s, 1H), 7.63 (dd, J = 7.4, 1.7 Hz, 1H), 7.46 (q, J = 4.6 Hz, 1H), 7.42−7.28 (m, 7H), 7.06 (dd, J = 7.7, 1.2 Hz, 1H), 2.58 (d, J = 4.6 Hz, 3H), 1.41 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 174.2, 166.9, 137.9, 134.5, 134.3, 132.1, 130.5, 130.2, 129.6, 128.3, 127.8, 126.4, 56.5, 26.1, 25.1. LRMS (ESI) [M + H]$^+$ found: 329.0. HRMS (ESI) [M + Na]$^+$ calcd for $C_{18}H_{20}O_2N_2NaS$: 351.1138; found: 351.1139.

*N-(2-Methyl-1-(methylamino)-1-oxopropan-2-yl)-2,6-bis(phenylthio)benzamide (**3h′**).* Compound **3h′** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 66 mg, 76% yield. Mp: 174−177 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.70 (s, 1H), 7.44−7.36 (m, 8H), 7.36−7.29 (m, 3H), 7.23−7.16 (m, 3H), 2.55 (d, J = 4.7 Hz, 3H), 1.43 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 174.1, 165.6, 142.3, 134.5, 133.0, 131.8, 131.1, 130.3, 129.5, 127.7, 57.0, 25.9, 25.0. LRMS (ESI) [M + H]$^+$ found: 436.9. HRMS (ESI) [M + Na]$^+$ calcd for $C_{24}H_{24}O_2N_2NaS_2$: 459.1171; found: 459.1167. Anal. Calcd for $C_{24}H_{24}O_2N_2S_2$: C, 66.02; H, 5.54; N, 6.42. Found: C, 64.20; H, 5.38; N, 6.22.

*4-Methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)-2,6-bis(phenylthio)benzamide (**3i**).* Compound **3i** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 68 mg, 76% yield. Mp: 204−206 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.59 (s, 1H), 7.42−7.35 (m, 8H), 7.34−7.26 (m, 2H), 7.17 (q, J = 4.2 Hz, 1H), 7.10 (s, 2H), 2.52 (d, J = 4.7 Hz, 3H), 2.16 (s, 3H), 1.40 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 174.2, 165.8, 140.6, 140.2, 134.9, 133.0, 132.3, 130.6, 129.5, 127.5, 56.9, 25.8, 25.0, 20.4. LRMS (ESI) [M + H]$^+$

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J. Org. Chem. 2016, 81, 9122−9130

found: 451.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{25}H_{26}O_2N_2NaS_2$: 473.1328; found: 473.1325.

*4-(Dimethylamino)-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)-2,6-bis(phenylthio)benzamide (**3j**).* Compound **3j** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 74 mg, 77% yield. Mp: 188−190 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.37 (s, 1H), 7.47−7.34 (m, 8H), 7.32−7.25 (m, 2H), 7.16 (q, J = 4.8 Hz, 1H), 6.56 (s, 2H), 2.74 (s, 6H), 2.51 (d, J = 4.8 Hz, 3H), 1.35 (s, 6H). ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 174.3, 166.1, 150.6, 135.5, 132.6, 131.4, 130.1, 129.3, 127.1, 115.6, 56.7, 39.5, 25.8, 24.9. LRMS (ESI) $[M + H]^+$ found: 480.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{26}H_{29}O_2N_3NaS_2$: 502.1593; found: 502.1581.

*2,4-Dimethyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)-6-(phenylthio)benzamide (**3k**).* Compound **3k** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 61 mg, 85% yield. Mp: 180−182 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.36 (s, 1H), 7.35−7.27 (m, 4H), 7.27−7.22 (m, 2H), 7.07 (s, 1H), 7.00 (s, 1H), 2.55 (d, J = 4.6 Hz, 3H), 2.27 (s, 3H), 2.22 (s, 3H), 1.40 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 174.2, 167.2, 138.9, 138.8, 136.2, 135.4, 131.3, 130.8, 129.8, 129.6, 129.2, 126.8, 56.5, 25.9, 25.0, 20.5, 18.6. LRMS (ESI) $[M + H]^+$ found: 357.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{20}H_{24}O_2N_2NaS$: 379.1451; found: 379.1445.

*N-(2-Methyl-1-(methylamino)-1-oxopropan-2-yl)-2-(phenylthio)-1-naphthamide (**3l**).* Compound **3l** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 66 mg, 87% yield. Mp: 165−167 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.78 (s, 1H), 8.05 (d, J = 8.3 Hz, 1H), 8.05 (d, J = 8.3 Hz, 1H), 7.94 (d, J = 7.6 Hz, 1H), 7.67−7.54 (m, 2H), 7.46 (q, J = 4.8 Hz, 1H), 7.42−7.23 (m, 6H), 2.64 (d, J = 4.6 Hz, 3H), 1.50 (s, 6H). ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 174.1, 166.5, 138.9, 135.4, 132.0, 130.5, 130.2, 129.5, 129.3, 128.1, 127.8, 127.4, 127.2, 126.9, 125.5, 56.8, 26.1, 25.1. LRMS (ESI) $[M + H]^+$ found: 379.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{22}H_{22}O_2N_2NaS$: 401.1294; found: 401.1284.

*N-(2-Methyl-1-(methylamino)-1-oxopropan-2-yl)-3-(phenylthio)-thiophene-2-carboxamide (**3m**).* Compound **3m** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. Colorless oil, 23 mg, 35% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.52 (s, 1H), 7.77 (d, J = 5.2 Hz, 1H), 7.74 (q, J = 4.5 Hz, 1H), 7.42−7.29 (m, 5H), 6.86 (d, J = 5.2 Hz, 1H), 2.60 (d, J = 4.5 Hz, 3H), 1.44 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 174.1, 159.6, 136.7, 134.4, 132.0, 130.9, 130.3, 129.7, 129.6, 127.7, 56.8, 26.2, 24.6. LRMS (ESI) $[M + H]^+$ found: 335.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{16}H_{18}O_2N_2NaS_2$: 357.0702; found: 357.0692.

*N-(2-Methyl-1-(methylamino)-1-oxopropan-2-yl)-2-(phenylthio)-benzo[b]thiophene-3-carboxamide (**3n**).* Compound **3n** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 61 mg, 79% yield. Mp: 186−189 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.52 (s, 1H), 7.95−7.89 (m, 2H), 7.53−7.33 (m, 8H), 2.61 (d, J = 4.6 Hz, 3H), 1.48 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 174.1, 162.5, 139.7, 137.5, 136.2, 135.3, 134.4, 130.7, 129.6, 128.2, 125.4, 125.1, 123.4, 122.2, 56.7, 26.2, 25.1. LRMS (ESI) $[M + H]^+$ found: 385.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{20}H_{20}N_2O_2NaS_2$: 407.0858; found: 407.0855.

*2-Methyl-N-(1-(methylcarbamoyl)cyclopropyl)-6-(phenylthio)-benzamide (**3o**).* Compound **3o** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 61 mg, 90% yield. Mp: 183−186 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.05 (s, 1H), 7.38−7.19 (m, 9H), 2.60 (d, J = 4.8 Hz, 3H), 2.25 (s, 3H), 1.34−1.29 (m, 2H), 1.02−0.96 (m, 2H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 171.2, 168.9, 141.2, 135.7, 135.4, 131.4, 130.2, 129.8, 129.7, 129.5, 129.4, 127.0, 34.2, 26.1, 18.6, 15.7. LRMS (ESI) $[M + H]^+$ found: 341.0. HRMS (ESI) $[M + H]^+$ calcd for $C_{19}H_{21}O_2N_2S$: 341.1318; found: 341.1315.

*2-Methyl-N-(1-(methylcarbamoyl)cyclohexyl)-6-(phenylthio)-benzamide (**3p**).* Compound **3p** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 61 mg, 80% yield. Mp: 165−168 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.30 (s, 1H), 7.37−7.21 (m, 8H), 7.15 (d, J = 7.3 Hz, 1H), 2.54 (d, J = 4.6 Hz, 3H), 2.36 (s, 3H), 2.16 (s, 1H), 2.12 (s, 1H), 1.72−1.62 (m, 2H), 1.61−1.42 (m, 5H), 1.26−1.12 (m, 1H). ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 174.3, 167.7, 141.7, 136.2, 135.7, 131.1, 130.3, 130.0, 129.8, 129.3, 129.2, 126.7, 60.1, 31.7, 25.8, 25.0, 21.1, 19.2. LRMS (ESI) $[M + H]^+$ found: 383.0. HRMS (ESI) $[M + H]^+$ calcd for $C_{22}H_{27}O_2N_2S$: 383.1788; found: 383.1789. Anal. Calcd for $C_{22}H_{26}O_2N_2S$: C, 69.08; H, 6.85; N, 7.32. Found: C, 68.74; H, 6.91; N, 7.17.

*2-Methyl-N-(1-(methylamino)-1-oxopropan-2-yl)-6-(phenylthio)-benzamide (**3q**).* Compound **3q** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 48 mg, 73% yield. Mp: 162−164 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.52 (d, J = 7.5 Hz, 1H), 7.67 (q, J = 4.5 Hz, 1H), 7.36−7.29 (m, 4H), 7.29−7.22 (m, 2H), 7.20 (d, J = 7.4 Hz, 1H), 7.07 (d, J = 7.6 Hz, 1H), 4.46−4.37 (m, 1H), 2.59 (d, J = 4.6 Hz, 3H), 2.28 (s, 3H), 1.24 (d, J = 7.1 Hz, 3H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 172.2, 167.0, 140.8, 135.8, 135.5, 131.2, 130.5, 130.0, 129.4, 129.3, 129.2, 127.0, 48.4, 25.5, 18.9, 17.9. LRMS (ESI) $[M + H]^+$ found: 328.9. HRMS (ESI) $[M + H]^+$ calcd for $C_{18}H_{21}O_2N_2S$: 329.1318; found: 329.1317. Anal. Calcd for $C_{18}H_{20}O_2N_2S$: C, 65.83; H, 6.14; N, 8.53. Found: C, 66.43; H, 6.22; N, 8.33.

*2-Methyl-N-(3-methyl-1-(methylamino)-1-oxobutan-2-yl)-6-(phenylthio)benzamide (**3r**).* Compound **3r** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 61 mg, 85% yield. Mp: 140−143 °C. $[\alpha]_D^{20}$ −65.4 (c 0.220, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.42 (d, J = 8.7 Hz, 1H), 7.78 (q, J = 4.6 Hz, 1H), 7.35−7.29 (m, 4H), 7.28−7.21 (m, 2H), 7.18 (d, J = 7.4 Hz, 1H), 7.05 (d, J = 7.6 Hz, 1H), 4.23 (dd, J = 8.3, 7.8 Hz, 1H), 2.59 (d, J = 4.6 Hz, 3H), 2.25 (s, 3H), 2.06−1.97 (m, 1H), 0.89 (d, J = 4.9 Hz, 3H), 0.88 (d, J = 4.9 Hz, 3H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 171.1, 167.5, 141.1, 136.0, 135.3, 131.3, 130.5, 130.0, 129.25, 129.21, 129.0, 127.0, 58.6, 29.9, 25.4, 19.4, 19.0, 18.5. LRMS (ESI) $[M + H]^+$ found: 357.0. HRMS (ESI) $[M + H]^+$ calcd for $C_{20}H_{25}O_2N_2S$: 357.1631; found: 357.1628.

*2-Methyl-N-(4-methyl-1-(methylamino)-1-oxopentan-2-yl)-6-(phenylthio)benzamide (**3s**).* Compound **3s** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 56 mg, 76% yield. Mp: 178−180 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.53 (d, J = 8.1 Hz, 1H), 7.71 (q, J = 4.5 Hz, 1H), 7.34−7.27 (m, 4H), 7.27−7.22 (m, 2H), 7.20 (d, J = 7.3 Hz, 1H), 7.08 (d, J = 7.5 Hz, 1H), 4.46−4.37 (m, 1H), 2.57 (d, J = 4.6 Hz, 3H), 2.27 (s, 3H), 1.76−1.62 (m, 1H), 1.59−1.50 (m, 1H), 1.44−1.36 (m, 1H), 0.86 (d, J = 6.5 Hz, 3H), 0.83 (d, J = 6.6 Hz, 3H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 172.2, 167.4, 141.1, 136.0, 135.4, 130.9, 130.3, 130.2, 129.4, 129.2, 129.1, 126.9, 51.2, 40.4, 25.5, 24.1, 23.1, 21.2, 18.9. LRMS (ESI) $[M + H]^+$ found: 371.0. HRMS (ESI) $[M + H]^+$ calcd for $C_{21}H_{27}O_2N_2S$: 371.1788; found: 371.1785.

*2-Methyl-N-(1-(methylamino)-1-oxo-3-phenylpropan-2-yl)-6-(phenylthio)benzamide (**3t**).* Compound **3t** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 44 mg, 54% yield. Mp: 193−195 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.69 (d, J = 8.3 Hz, 1H), 7.74 (q, J = 4.4 Hz, 1H), 7.40−7.24 (m, 7H), 7.24−7.14 (m, 4H), 7.11 (d, J = 7.5 Hz, 1H), 7.02 (d, J = 7.7 Hz, 1H), 4.68 (td, J = 10.4, 4.6 Hz, 1H), 3.08 (dd, J = 13.8, 4.4 Hz, 1H), 2.83 (dd, J = 13.8, 10.6 Hz, 1H), 2.58 (d, J = 4.6 Hz, 3H), 1.90 (s, 3H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 171.2, 167.4, 140.6, 138.0, 135.8, 135.4, 131.4, 130.6, 129.8, 129.3, 129.2, 129.1, 128.0, 127.1, 126.2, 54.3, 37.1, 25.5, 18.4. LRMS (ESI) $[M + H]^+$ found: 405.0. HRMS (ESI) $[M + H]^+$ calcd for $C_{24}H_{23}O_2N_2S$: 403.1486; found: 403.1495.

*2-(3-Methyl-2-(2-methyl-6-(phenylthio)benzamido)butanamido)acetic Acid (**3u**).* Compound **3u** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 52 mg, 67% yield. Mp: 183−186 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.58 (br, 1H), 8.50 (s, 1H), 7.63 (t, J = 5.5 Hz, 1H), 7.36−7.19 (m, 7H), 7.10 (d, J = 7.4 Hz, 1H), 3.73 (d, J = 5.5 Hz, 2H), 2.31 (s, 3H), 1.44 (s, 6H). ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 174.0, 171.1, 167.2, 140.8, 135.8, 135.7, 131.0,

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J. Org. Chem. 2016, 81, 9122−9130

130.4, 129.6, 129.32, 129.26, 127.1, 56.5, 41.1, 24.8, 18.8. LRMS (ESI) $[M-H]^-$ found: 385.1. HRMS (ESI) $[M + Na]^+$ calcd for $C_{20}H_{22}O_4N_2NaS$: 409.1192; found: 409.1183.

*2-Methyl-N-(3-methyl-1-((2-(methylamino)-2-oxoethyl)amino)-1-oxobutan-2-yl)-6-(phenylthio)benzamide (**3v**).* Compound **3v** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 24 mg, 30% yield. Mp: 168−172 °C. ^{1}H NMR (400 MHz, MeOD) δ 7.41−7.08 (m, 8H), 3.80 (s, 2H), 2.50 (s, 3H), 2.41 (s, 3H), 1.54 (s, 6H). ^{13}C $\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 173.8, 169.0, 168.3, 140.3, 135.83, 135.78, 130.9, 130.6, 129.9, 129.7, 129.5, 129.3, 126.9, 56.4, 42.9, 25.3, 24.8, 18.7. LRMS $[M + H]^+$ found 400.0. HRMS (ESI) $[M + H]^+$ calcd for $C_{21}H_{26}O_3N_3S$: 400.1689; found: 400.1679.

*2-Methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)-6-(p-tolylthio)benzamide (**4b**).* Compound **4b** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 61 mg, 85% yield. Mp: 98−102 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.50 (s, 1H), 7.38−7.12 (m, 7H), 7.02 (d, J = 7.5 Hz, 1H), 2.57 (d, J = 4.4 Hz, 3H), 2.29 (s, 3H), 2.28 (s, 3H), 1.43 (s, 6H). ^{13}C $\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ 174.2, 167.1, 140.3, 137.2, 135.4, 132.0, 131.6, 131.4, 130.1, 129.5, 129.2, 129.1, 56.6, 26.0, 25.0, 20.6, 18.7. LRMS (ESI) $[M + H]^+$ found: 357.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{20}H_{24}O_2N_2NaS$: 379.1451; found: 379.1440.

*2-((4-Methoxyphenyl)thio)-6-methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)benzamide (**4c**).* Compound **4c** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 60 mg, 81% yield. Mp: 88−91 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.51 (s, 1H), 7.44−7.38 (m, 2H), 7.34 (q, J = 4.3 Hz, 1H), 7.21−7.16 (m, 1H), 7.11 (d, J = 7.5 Hz, 1H), 7.00−6.94 (m, 2H), 6.91 (d, J = 7.8 Hz, 1H), 3.76 (s, 3H), 2.60 (d, J = 4.7 Hz, 3H), 2.28 (s, 3H), 1.46 (s, 6H). ^{13}C $\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 174.2, 167.1, 159.5, 139.1, 135.1, 134.7, 133.8, 129.0, 128.4, 128.0, 124.4, 115.2, 56.6, 55.3, 26.0, 25.0, 18.6. LRMS (ESI) $[M + H]^+$ found: 373.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{20}H_{24}O_3N_2NaS$: 395.1400; found: 395.1389.

*2-((4-Chlorophenyl)thio)-6-methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)benzamide (**4d**).* Compound **4d** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 74 mg, 98% yield. Mp: 173−176 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.48 (s, 1H), 7.41−7.36 (m, 2H), 7.33−7.23 (m, 5H), 7.19 (dd, J = 7.3, 1.2 Hz, 1H), 2.56 (d, J = 4.7 Hz, 3H), 2.31 (s, 3H), 1.40 (s, 6H). ^{13}C $\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ 174.1, 166.9, 141.7, 135.8, 135.4, 131.6, 131.3, 131.2, 130.3, 129.6, 129.4, 129.2, 56.5, 26.0, 25.0, 18.7. LRMS (ESI) $[M + H]^+$ found: 377.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{19}H_{21}O_2N_2ClNaS$: 399.0904; found: 399.0897.

*2-((4-Fluorophenyl)thio)-6-methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)benzamide (**4e**).* Compound **4e** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 61 mg, 85% yield. Mp: 138−140 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.51 (s, 1H), 7.41 (dd, J = 8.6, 5.3 Hz, 2H), 7.30 (q, J = 4.6 Hz, 1H), 7.27−7.23 (m, 1H), 7.23−7.18 (m, 3H), 7.09 (d, J = 7.7 Hz, 1H), 2.58 (d, J = 4.6 Hz, 3H), 2.30 (s, 3H), 1.43 (s, 6H). ^{13}C $\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ 174.1, 167.0, 161.6 (d, J = 245.4 Hz), 140.7, 135.6, 133.3 (d, J = 8.3 Hz), 131.3, 131.0 (d, J = 2.9 Hz), 130.1, 129.6, 129.3, 116.4 (d, J = 23.4 Hz), 56.6, 26.0, 25.0, 18.7. LRMS (ESI) $[M + H]^+$ found: 361.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{19}H_{21}O_2N_2FNaS$: 383.1200; found: 383.1190.

*2-Methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)-6-(m-tolylthio)benzamide (**4f**).* Compound **4f** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 59 mg, 83% yield. Mp: 156−158 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.46 (s, 1H), 7.30−7.15 (m, 5H), 7.15−7.04 (m, 3H), 2.57 (d, J = 4.5 Hz, 3H), 2.30 (s, 3H), 2.26 (s, 3H), 1.41 (s, 6H). ^{13}C $\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ 174.6, 167.5, 141.4, 139.2, 136.0, 135.8, 131.4, 131.2, 130.9, 130.1, 129.7, 128.4, 128.0, 57.0, 26.5, 25.5, 21.3, 19.2. LRMS (ESI) $[M + H]^+$ found: 357.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{20}H_{24}O_2N_2NaS$: 379.1451; found: 379.1444.

*2-((3-Fluorophenyl)thio)-6-methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)benzamide (**4g**).* Compound **4g** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 68 mg, 94% yield. Mp: 177−180 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.46 (s, 1H), 7.38−7.29 (m, 3H), 7.27 (dd, J = 7.1, 1.4 Hz, 1H), 7.22 (q, J = 4.6 Hz, 1H), 7.09 (d, J = 7.9 Hz, 1H), 7.04 (ddd, J = 17.4, 9.1, 2.1 Hz, 2H), 2.56 (d, J = 4.6 Hz, 3H), 2.32 (s, 3H), 1.39 (s, 6H). ^{13}C $\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 174.1, 166.9, 162.3 (d, J = 246.5 Hz), 142.2, 139.4 (d, J = 7.9 Hz), 135.9, 132.1, 130.9 (d, J = 8.7 Hz), 130.8, 129.5, 128.6, 124.8, 115.4 (d, J = 23.6 Hz), 113.4 (d, J = 21.2 Hz), 56.5, 26.0, 24.9, 18.7. LRMS (ESI) $[M + H]^+$ found: 361.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{19}H_{21}O_2N_2FNaS$: 383.1200; found: 383.1191.

*2-Methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)-6-((3-nitrophenyl)thio)benzamide (**4h**).* Compound **4h** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 33 mg, 43% yield. Mp: 202−204 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.46 (s, 1H), 8.03 (ddd, J = 8.1, 2.2, 1.0 Hz, 1H), 7.95−7.92 (m, 1H), 7.65 (ddd, J = 8.1, 1.6, 1.1 Hz, 1H), 7.61−7.56 (m, 1H), 7.41−7.34 (m, 3H), 7.24 (q, J = 4.6 Hz, 1H), 2.56 (d, J = 4.6 Hz, 3H), 2.34 (s, 3H), 1.38 (s, 6H). ^{13}C $\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 174.0, 166.7, 148.2, 142.6, 139.8, 136.18, 134.4, 132.4, 131.3, 130.4, 129.7, 127.6, 122.3, 121.1, 56.5, 26.0, 24.9, 18.8. LRMS (ESI) $[M + H]^+$ found: 388.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{19}H_{21}O_4N_3NaS$: 410.1145; found: 410.1133.

*2-Methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)-6-(o-tolylthio)benzamide (**4i**).* Compound **4i** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 51 mg, 71% yield. Mp: 91−94 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.39 (s, 1H), 7.29 (d, J = 7.3 Hz, 1H), 7.27−7.20 (m, 3H), 7.20−7.15 (m, 3H), 6.87 (d, J = 7.4 Hz, 1H), 2.57 (d, J = 4.7 Hz, 3H), 2.32 (s, 3H), 2.31 (s, 3H), 1.42 (s, 6H). ^{13}C $\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 174.1, 166.9, 140.1, 138.1, 135.5, 134.1, 131.7, 131.1, 130.5, 129.2, 129.1, 128.8, 127.6, 126.9, 56.5, 25.9, 24.9, 20.0, 18.7. LRMS (ESI) $[M + H]^+$ found: 357.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{20}H_{24}O_2N_2NaS$: 379.1451; found: 379.1441.

*2-Methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)-6-(pyridin-2-ylthio)benzamide (**4j**).* Compound **4j** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 49 mg, 72% yield. Mp: 84−87 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.37 (d, J = 3.9 Hz, 1H), 8.26 (s, 1H), 7.64 (ddd, J = 10.8, 4.5 Hz, 1.4 Hz 1H), 7.50−7.44 (m, 1H), 7.43−7.37 (m, 2H), 7.24 (q, J = 4.4 Hz, 1H), 7.14 (dd, J = 6.9, 5.1 Hz, 1H), 6.93 (d, J = 8.1 Hz, 1H), 2.55 (d, J = 4.6 Hz, 3H), 2.32 (s, 3H), 1.31 (s, 6H). ^{13}C $\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 174.0, 166.8, 160.1, 149.2, 143.4, 137.4, 136.1, 134.0, 131.6, 129.5, 125.9, 121.4, 120.4, 56.4, 26.0, 24.8, 18.8. LRMS (ESI) $[M + H]^+$ found: 344.0. HRMS (ESI) $[M + Na]^+$ calcd for $C_{18}H_{21}O_2N_3NaS$: 366.1247; found: 366.1238.

*2-Methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)-6-(phenylselanyl)benzamide (**4k**).* Compound **4k** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 45 mg, 58% yield. Mp: 107−109 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.44 (s, 1H), 7.49 (br, 2H), 7.32 (br, 4H), 7.27−7.12 (m, 3H), 2.60 (d, J = 3.9 Hz, 3H), 2.31 (s, 3H), 1.44 (s, 6H). ^{13}C $\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 174.1, 167.5, 141.2, 135.5, 132.9, 131.4, 130.8, 129.5, 129.3, 127.7, 127.6, 56.6, 25.9, 25.0, 19.0. LRMS (ESI) $[M + H]^+$ found: 390.9. HRMS (ESI) $[M + Na]^+$ calcd for $C_{19}H_{22}O_2N_2NaSe$: 413.0739; found: 413.0728.

*2-((3-Methoxyphenyl)selanyl)-6-methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)benzamide (**4l**).* Compound **4l** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 45 mg, 54% yield. Mp: 144−147 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (dd, J = 6.5, 2.1 Hz, 1H), 7.22−7.15 (m, 3H), 7.08 (s, 1H), 6.94−6.89 (m, 2H), 6.80−6.76 (m, 1H), 5.95 (s, 1H), 3.75 (s, 3H), 2.82 (d, J = 4.8 Hz, 3H), 2.37 (s, 3H), 1.52 (s, 6H). ^{13}C $\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 174.5,

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J. Org. Chem. 2016, 81, 9122−9130

168.8, 160.4, 141.3, 136.3, 133.6, 132.9, 130.8, 130.6, 130.0, 126.2, 123.9, 117.3, 113.1, 58.3, 55.5, 26.5, 25.5, 19.5. LRMS (ESI) $[M + H]^+$ found: 420.9. HRMS (ESI) $[M - H]^-$ calcd for $C_{20}H_{23}O_3N_2Se$: 419.0879; found: 419.0833.

*2-((4-Chlorophenyl)selanyl)-6-methyl-N-(2-methyl-1-(methylamino)-1-oxopropan-2-yl)benzamide (**4m**).* Compound **4m** was prepared as described in the general procedure for nickel-catalyzed *ortho*-C-H thiolation of *N*-benzoyl α-amino derivatives. White solid, 36 mg, 42% yield. Mp: 86−89 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.45 (s, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 3.6 Hz, 1H), 7.26−7.18 (m, 3H), 2.60 (d, *J* = 4.0 Hz, 3H), 2.32 (s, 3H), 1.43 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 174.0, 167.5, 141.6, 135.6, 134.2, 132.4, 131.9, 130.0, 129.9, 129.44, 129.38, 126.9, 56.6, 26.0, 25.0, 19.0. LRMS (ESI) $[M + H]^+$ found: 424.9. HRMS (ESI) $[M - H]^-$ calcd for $C_{19}H_{20}O_2N_2ClSe$: 423.0384; found: 423.0386.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01702.

Copies of ^{1}H and ^{13}C NMR spectra and LC−MS and HPLC experimental data (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: hliu@simm.ac.cn.

Notes

The authors declare no competing financial interest.

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