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Nickel-Catalyzed Amidation of Aryl Alkynyl Acids with Tetraalkylthiuram Disulfides: A Facile Synthesis of Aryl Alkynyl Amides

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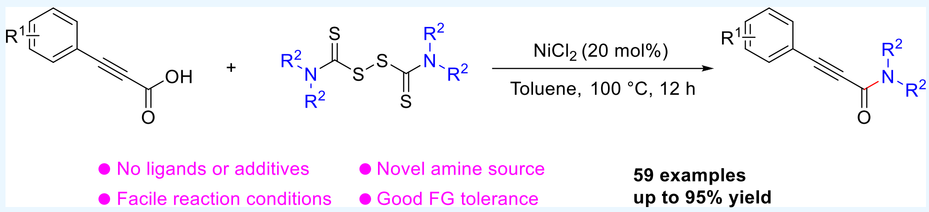

ABSTRACT: Nickel-catalyzed amidation of aryl alkynyl acids using tetraalkylthiuram disulfides as the amine source is described, affording a series of aryl alkynyl amides in good to excellent yields under mild conditions. This general methodology provides an alternative pathway for the synthesis of useful aryl alkynyl amides in an operationally simple manner, which shows its practical synthetic value in organic synthesis. The mechanism of this transformation was explored through control experiments and DFT calculations.

■ INTRODUCTION

Thiuram reagents constitute an important class of compounds that is known to have a wide range of biological activities.[1] As low-toxic, easy-to-prepare, and even commercially available organosulfur compounds, thiurams have also been extensively used in organic thiolation reactions[2] and thus exhibited its broad applications in modern organic synthesis. As a continuing research interest, our group also selected thiurams as interesting reagents for the development of new synthetic transformations.

Aryl alkynyl amide derivatives are attractive synthetic targets because of their significant biological activities.[3] This skeleton and their analogues also act as valuable intermediates in organic synthesis.[4] As a consequence, tremendous attention has been focused on the synthesis of aryl alkynyl amides, and a number of methods have been devised. Among the numerous approaches, the coupling reactions between a carbamoyl chloride and a terminal alkyne conducted by 1,4-diazabicyclo[2.2.2]octane (DABCO)[5] or Pd/Cu catalysts[6] had been commonly used (Scheme 1a). Moreover, *N*, *N*-dimethylformamide (DMF) or secondary amines were also proved to be common amidation reagents for their great efficiency on the synthesis of alkynyl amides by reacting with acids[7] or aldehydes[8] (Scheme 1b). Nevertheless, these documented methods respectively suffer from some drawbacks such as harsh reaction conditions and foul-smelling amines to inhibit the application of these procedures. Meanwhile, by using carbamoylsilane as a source of amine was feasible as well (Scheme 1c).[9] Moreover, the synthesis of alkynyl amides through one-pot three-component reactions had also been developed (Scheme 1d). For instance, Bhanage's group reported a route of highly effective Pd/C-catalyzed oxidative *N*-dealkylation/carbonylation of various aliphatic as well as cyclic tertiary amines with alkynes.[10] Shortly afterward, Lee and co-workers subsequently developed a method for the synthesis of alkynyl amides via the carbonylation of alkynoic acids and C−N activation of tertiary amines.[11] Very recently, efficient approaches under metal-free conditions also played a necessary role in the reaction of amidation.[12] Despite these advances, to the best of our knowledge, using thiuram reagents as amine sources to synthesize aryl alkynyl amides has not been precedented so far. As a continuation of this research program,[13] herein, we present a nickel-catalyzed amidation of aryl alkynyl acids with tetraalkylthiuram to synthesize aryl alkynyl amides (Scheme 1e).

■ RESULTS AND DISCUSSION

At the outset of our investigation, phenylpropiolic acid (**1a**) and tetramethylthiuram disulfide (TMTD, **2a**) were chosen as the model substrates to optimize the reaction conditions, and the results were summarized in Table 1. First, the effect of catalysts

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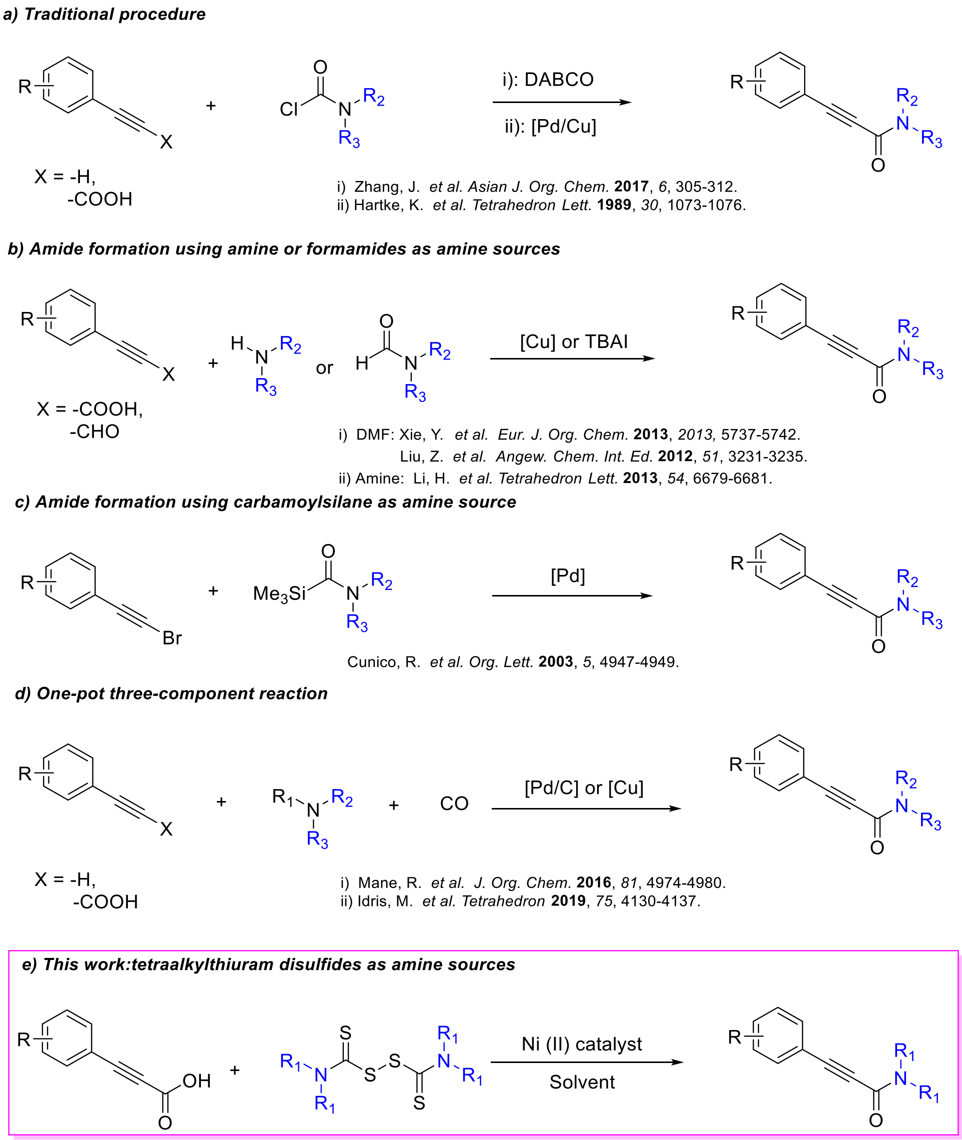
Scheme 1. Procedures for the Synthesis of Aryl Alkynyl Amides[a]



[a](a) Traditional procedure, (b) amide formation using amine or formamides as amine sources, (c) amide formation using carbamoylsilane as amine source, (d) one-pot three-component reaction, and (e) tetraalkylthiuram disulfides as amine sources.

has been studied. We were delighted to find that the reactions occurred, which afforded the corresponding product **3a** (*N*, *N*-dimethyl-3-phenylpropiolamide) in acceptable yields (26, 30, and 39%) using $CuBr_2$ (1 equiv), $CoBr_2$ (1 equiv), and $NiBr_2$ (1 equiv) as the catalysts (entries 1−3, Table 1). No desired product was detected when the reaction was carried out in the absence of metal catalysts, which indicated that the metal catalysts were necessary indeed to improve the reaction efficiency (entry 4, Table 1). Consequently, some other nickel salts such as $NiCl_2$, NiF_2, and $Ni(OAc)_2$ were further tested in the reaction, and $NiCl_2$ was proven to be superior to other nickel salts that could provide product **3a** in 80% yield (entry 5 vs entries 3, 6−7). An investigation of solvents showed that the solvent had an important influence on the reaction. The best yield (85%, entry 13) was given in the solvent of toluene. A substantially decreased reaction efficiency was observed when the reaction was conducted in 1,4-dioxane, THF (tetrahydrofuran), DCE (1,2-dichloorethaan), hexane, and CH_3CN (36−69%, entries 8−12). Particularly, the polar solvents such as DMF (*N*, *N*-dimethylformamide) and DMSO (dimethyl sulfoxide) showed an even worse performance in this process (trace: 16%, entries 14−15). Next, we evaluated the effect of reaction temperature, and 100 °C was determined as the optimized reaction temperature after a series of screening experiments (90% vs 41−85%, entry 17 vs entries 13, 16, and 18). Lowering the catalyst loading to 20 mol %, the reaction provided a similar yield of product **3a** (89% vs 90%, entry 19 vs entry 17). However, a continuous decrease of the catalyst loading caused an unsatisfactory result (76%, entry 20). Therefore, the catalyst loading of 20 mol % was chosen for further optimization. We also briefly screened the reaction time, and 12 h was found to be the best choice (89% vs 79−80%, entry 19 vs entries 21−22). Inert conditions proved to be not critical. When the reaction was run under nitrogen conditions, the product **3a** was obtained in a similar yield (84%, entry 23). After surveying a variety of parameters, we found that the optimized reaction conditions were identified as follows: 20 mol % of $NiCl_2$

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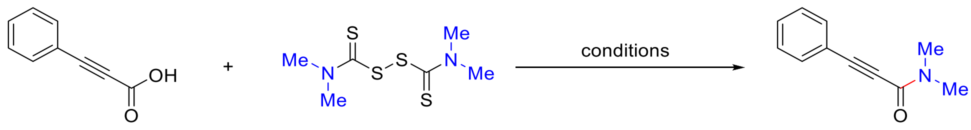
Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	solvent	catalyst loadings (equiv.)	temperature (°C)	yields of **3a** (%)[b]
1	$CuBr_2$	EtOAc	1	120	26
2	$CoBr_2$	EtOAc	1	120	30
3	$NiBr_2$	EtOAc	1	120	39
4		EtOAc	1	120	<5
5	$NiCl_2$	EtOAc	1	120	80
6	NiF_2	EtOAc	1	120	31
7	$Ni(OAc)_2$	EtOAc	1	120	21
8	$NiCl_2$	1,4-dioxane	1	120	43
9	$NiCl_2$	THF	1	120	69
10	$NiCl_2$	DCE	1	120	58
11	$NiCl_2$	hexane	1	120	61
12	$NiCl_2$	CH_3CN	1	120	36
13	$NiCl_2$	toluene	1	120	85
14	$NiCl_2$	DMF	1	120	16
15	$NiCl_2$	DMSO	1	120	trace
16	$NiCl_2$	toluene	1	140	41
17	$NiCl_2$	toluene	1	100	90
18	$NiCl_2$	toluene	1	80	77
19	$NiCl_2$	toluene	0.2	100	89
20	$NiCl_2$	toluene	0.1	100	76
21[c]	$NiCl_2$	toluene	0.2	100	80
22[d]	$NiCl_2$	toluene	0.2	100	79
23[e]	$NiCl_2$	toluene	0.2	100	84

[a]Reaction conditions: **1a** (0.10 mmol), **2a** (0.15 mmol), catalyst (1 equiv), solvent (1.0 mL), 120 °C, 12 h, under air. [b]Isolated yields. [c]Run for 18 h. [d]Run for 6 h. [e]Under N_2.

as the catalyst in toluene at 100 °C under air atmosphere for 12 h (entry 19).

With the optimal conditions in hand, the cross-coupling reactions of phenylpropiolic acid analogues and tetramethylthiuram disulfide (TMTD, **2a**) were first investigated, and the results were summarized in Table 2. Generally, the electron-donating groups (−Me, −OMe, −Et, −OEt, −*i*-Pr, and −*t*-Bu) and electron-withdrawing groups (−F, −Cl, −Br, $-CF_3$, and −CHO) were all compatible with this reaction, which afforded the corresponding products in moderate to excellent yields (**3a**−**3a′**, 37−95%). Electron-withdrawing groups seemed to be slightly more beneficial to the reaction than electron-donating groups. For example, 3-(*p*-tolyl)propiolic acid **1b** gave the corresponding product **3b** in 76% yield, while the bromo, chloro, and fluoro counterparts resulted in 86−93% yields of products **3n**−**3p**. Noteworthily, the bromo-substituted phenylpropiolic acid works well in this transformation, which makes this reaction particularly attractive for further transformation by transition-metal-catalyzed coupling reactions. The position of substituents may not significantly affect the yield of the reaction. *ortho*-, *meta*-, and *para*-Methyl- or methoxyl-substituted substrates worked well and gave the desired products in similar yields (**3b** vs **3h** and **3j**, 76% vs 83 and 87%). Interestingly, 3-(4-formylphenyl)propiolic acid **1y** was also the suitable substrate to check the reactivity of TMTD, and the desired product **3y** was formed in 37% yield. This protocol also exhibited good feasibility with 3-(thiophen-2-yl)propiolic acid **1z** and 3-(thiophen-3-yl)propiolic acid **1a′**, which provided the products **3z**−**3a′** in 37−64% yields. To our delight, benzoylformic acid could complete the reaction and afford the product **3b′** in 81% yield (Scheme 2).

We then investigated the substrate scope of tetraalkylthiuram disulfides. As shown in Table 3, *N*, *N*, *N*′, *N*′-tetraethylthiuram disulfide (TETD, **2b**) was initially examined. To our delight, it underwent these transformations smoothly and gave the products **4a**−**4w** in moderate yields (30−76%), respectively. In particular, this protocol was applicable indeed to 3-(thiophen-2-yl)propiolic acid and 3-(thiophen-3-yl)propiolic acid with **2b**, even though sharply lower yields were observed in these reactions (**4v**−**4w**, 31−46%). *N*, *N*, *N*′, *N*′-tetrabutylthiuram disulfide (TBTD, **2c**) also performed well to give the desired products **4x**−**4d′** with good yields (51−80%). These results greatly expanded the substrate scope of this reaction. It is worth noting that the longer chain-substituted tetraalkylthiuram disulfides sometimes performed better in these reactions (**3z**−**3a′** vs **4c′**−**4d′**), which indicated that the yields were occasionally modulated by the presence of different alkyl substituents on the tetraalkylthiuram disulfides. The reaction of phenylpropiolic acid with tetraisopropylthiuram disulfide has also been carried out in our lab, and probably because of the larger steric effect of isopropyl group, the tetraisopropylthiuram disulfide is proven to be invalid to this reaction.

Interestingly, tetramethylthiuram monosulfide (TMTM, **5**) is an active substrate to this amidation, and the corresponding product **3a** was obtained in 65% yield (Scheme 3a). Bis(pentamethylene)thiuram tetrasulfide (**6**) could also react

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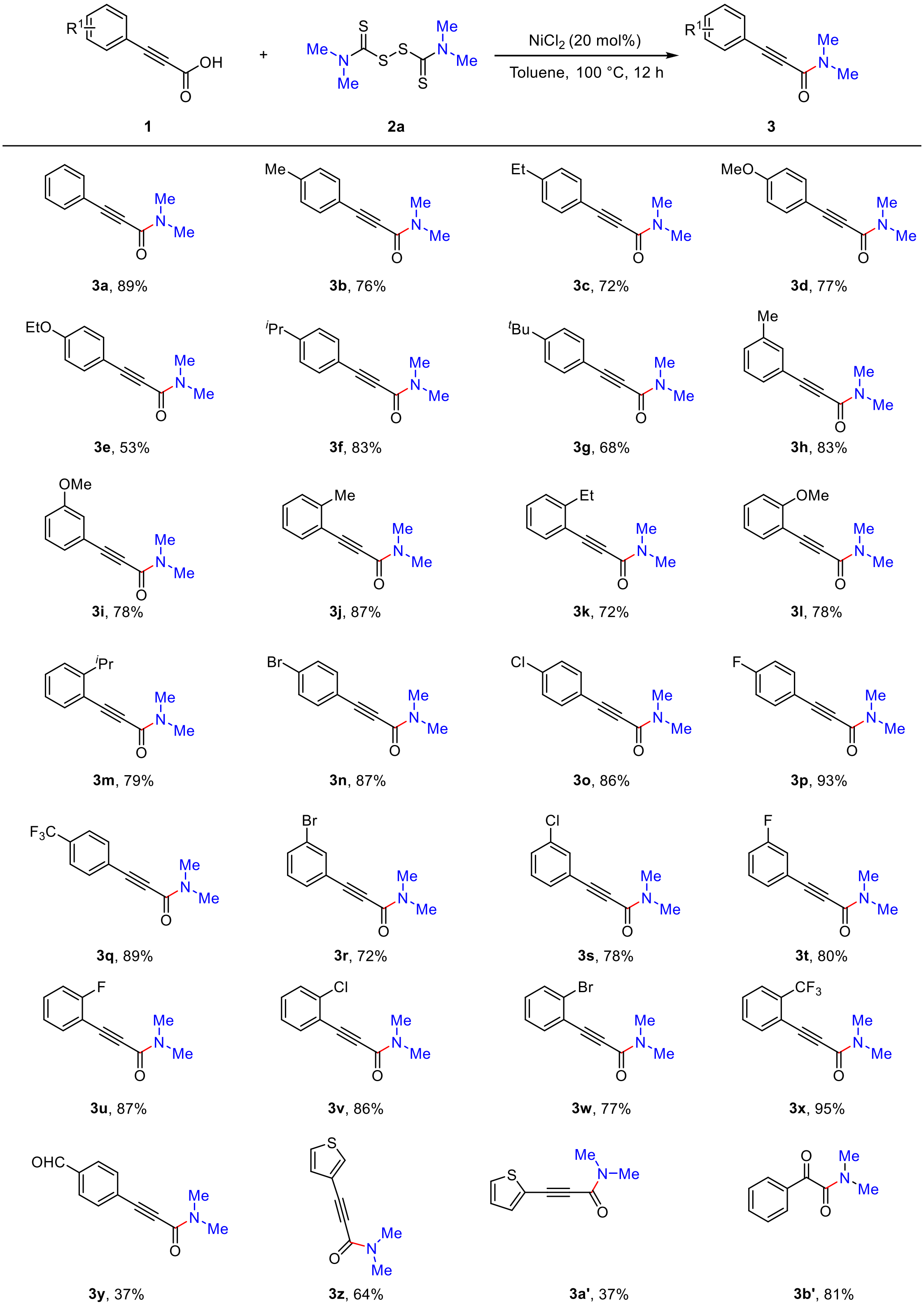
Table 2. Amidation of Aryl Alkynyl Acids with TMTD[a,b]



[a]Reaction conditions: **1** (0.10 mmol), **2** (0.15 mmol), $NiCl_2$ (20 mol %), toluene (1.0 mL), 100 °C, 12 h, under air. [b]Isolated yields.

with phenylpropiolic acid, which provided the product 7 in 78% yield (Scheme 3b).

To gain a deeply understanding of the reaction mechanism, DFT calculations were utilized. As shown in Scheme 4, TMTD (**2a**) prefers to dissociate into **B**, and the reaction Gibbs free energy is 7.30 kcal/mol. This reaction is supported by the investigation of Steudel's group.[14] **B** will combine with $NiCl_2$ spontaneously to form intermediate **C**, and the Gibbs free

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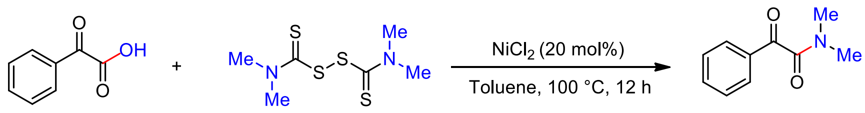
Scheme 2. Amidation of Benzoylformic Acid with TMTD[a,b]



1b' 2a 3b', 81%

[a]Reaction conditions: **1b′** (0.10 mmol), **2a** (0.15 mmol), $NiCl_2$ (20 mol%), toluene (1.0 mL), 100 °C, 12 h, under air. [b]Isolated yields.

energy would decrease to 35.28 kcal/mol. Then, **C** will form intermediate **D** via a transition state **TS1**, and the reaction Gibbs free energy would increase to 43.08 kcal/mol. Subsequently, **D** will form **E** via a transition state **TS2**, and the reaction Gibbs free energy would decrease to 6.85 kcal/mol. **E** will release CS_2 and Cl radical to form **F**, and the reaction Gibbs free energy would increase to 21.62 kcal/mol. The Ni atom of **F** will accept the lone pair electrons attached to the carbonyl group of **1a** to form **G**, and the reaction Gibbs free energy would slightly increase to 7.99 kcal/mol. **G** will form **H** via a transition state **TS3**, and the reaction Gibbs free energy would increase to 29.28 kcal/mol. Finally, **H** will release $NiCl_2$ and OH radical to form the product **3a**, and the reaction Gibbs free energy would slightly increase 3.89 to kcal/mol. Notably, the OH radical will combine with **B** to form **A**, and the reaction Gibbs free energy would decrease to 42.45 kcal/mol.

In order to further ascertain the mechanism, some control experiments were conducted, and the results were exhibited in Scheme 5. When 2 equiv of radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxyl (TEMPO), butylated hydroxyl toluene (BHT), or galvinoxyl free radical was added to the reaction of **1a** and **2a** under the standard conditions, a substantial decrease of the reaction efficiency was observed, illustrating that a radical process may exist in this reaction (Scheme 5a). Particularly, when quencher 1,1-diphenylethylene was added, the sulfur radical was captured to give **8**, which also indicated that a radical mechanism might be involved in this reaction (Scheme 5b).

Based on the mechanistic experiments and reported literatures,[2c,15] a plausible mechanism is outlined in Scheme 6. The reaction is presumed to involve a sulfur radical **A**, which is generated by the hemolysis of tetramethylthiuram disulfide under heat conditions, along with the release of by-product **H**. Sulfur radical **A** coordinates with $NiCl_2$ to form the intermediate **B**, which undergoes two steps rearrangement affording the Ni−N species **E**, CS_2, and chloride radical. The following coordination of intermediate **E** to substrate **1a** affords the Ni intermediate **F**. Then, another rearrangement process occurs to give the intermediate **G**, Finally, the dissociation of intermediate **G** produces the product **3a**, hydroxyl radical, and the regeneration of $NiCl_2$.

CONCLUSIONS

In summary, we have developed a mild and efficient amidation reaction of aryl alkynyl acids with tetraalkylthiuram disulfides via C−N cross-coupling. These processes gave a series of aryl alkynyl amides in mild conditions. This methodology is versatile and works well with a variety of aryl alkynyl acids and provides a straightforward way for the synthesis of aryl alkynyl amides. Investigation of the synthetic application and biological activities of these products are currently underway in our laboratory.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under an air atmosphere in a dried tube. All the reagents were obtained commercially and used without further purification. Silica gel was purchased from Qing Dao Hai Yang Chemical Industry Co. Analytical thin-layer chromatography (TLC) was performed on precoated silica gel F_{254} plates. Compounds were visualized by irradiation with UV light (254 nm).

^1H NMR and ^{13}C NMR spectral data were recorded by a BRUKER AVANCE III 400 MHz spectrometer (^1H 400 MHz, ^{13}C 100 MHz), using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. ^1H NMR spectral data are given as chemical shifts in ppm followed by multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), number of protons, and coupling constants. ^{13}C NMR chemical shifts are expressed in ppm. HRMS data were obtained using an AB SCIEX Triple TOF 5600+ high resolution mass spectrometer (USA). Infrared spectra were recorded with a Thermo Scientific Nicolet 6700 FT-IR spectrometer. The products listed below were determined by ^1H and ^{13}C NMR spectra. Melting points were measured on a microscopic apparatus and were uncorrected.

General Procedure for the Preparation of Aryl Alkynyl Acids. Aryl iodide (5 mmol) was added to the reaction tube and dissolved in 6 mL of DMSO, and a propionic acid solution (385 mg, 5.5 mmol dissolved in 6 mL of DMSO) was added dropwise. The reaction was incubated at room temperature for 16−19 h. After the reaction was completed, the reaction was quenched with saturated aqueous sodium bicarbonate, and the aqueous phase was washed twice with ethyl acetate. The aqueous phase was adjusted to pH = 2 with hydrochloric acid and extracted twice with dichloromethane. The organic phase was dried over anhydrous magnesium sulfate. The solvent was evaporated to dryness under reduced pressure, and the product was purified by column chromatography using ethyl acetate/petroleum ether as eluent to give **1b**−**1a′**.

General Procedure for the Reaction of Aryl Alkynyl Acids with Tetraalkylthiuram Disulfides. To a 10 mL tube, aryl alkynyl acids **1** (0.1 mmol) and tetraalkylthiuram disulfides **2** (0.15 mmol), $NiCl_2$ (0.02 mmol), and toluene (1.0 mL) were added under an air atmosphere. The resulting mixture was heated in a 100 °C oil bath with vigorous stirring for 12 h. Then, the reaction mixture was cooled to room temperature, quenched with a sat. NH_4Cl solution, and subsequently extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the solvent was evaporated under vacuum. The residue was purified by flash chromatography using petroleum ether/ethyl acetate as eluent affording **3** or **4** in 30−95% yields.

N,N-dimethyl-3-phenylpropiolamide (3a). Purification by column chromatography on silica gel (R_f = 0.37, petroleum ether/ethyl acetate = 3:1) yielded **3a** (15.5 mg, 89%) as a pale yellow solid; m. p. 99−101 °C; ^1H NMR (400 MHz, $CDCl_3$)

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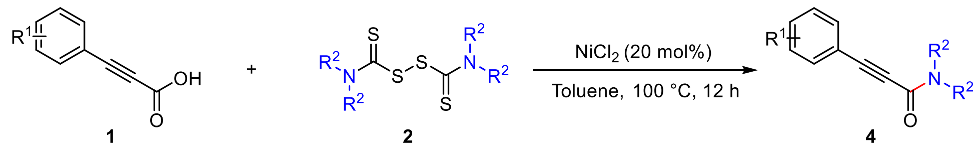
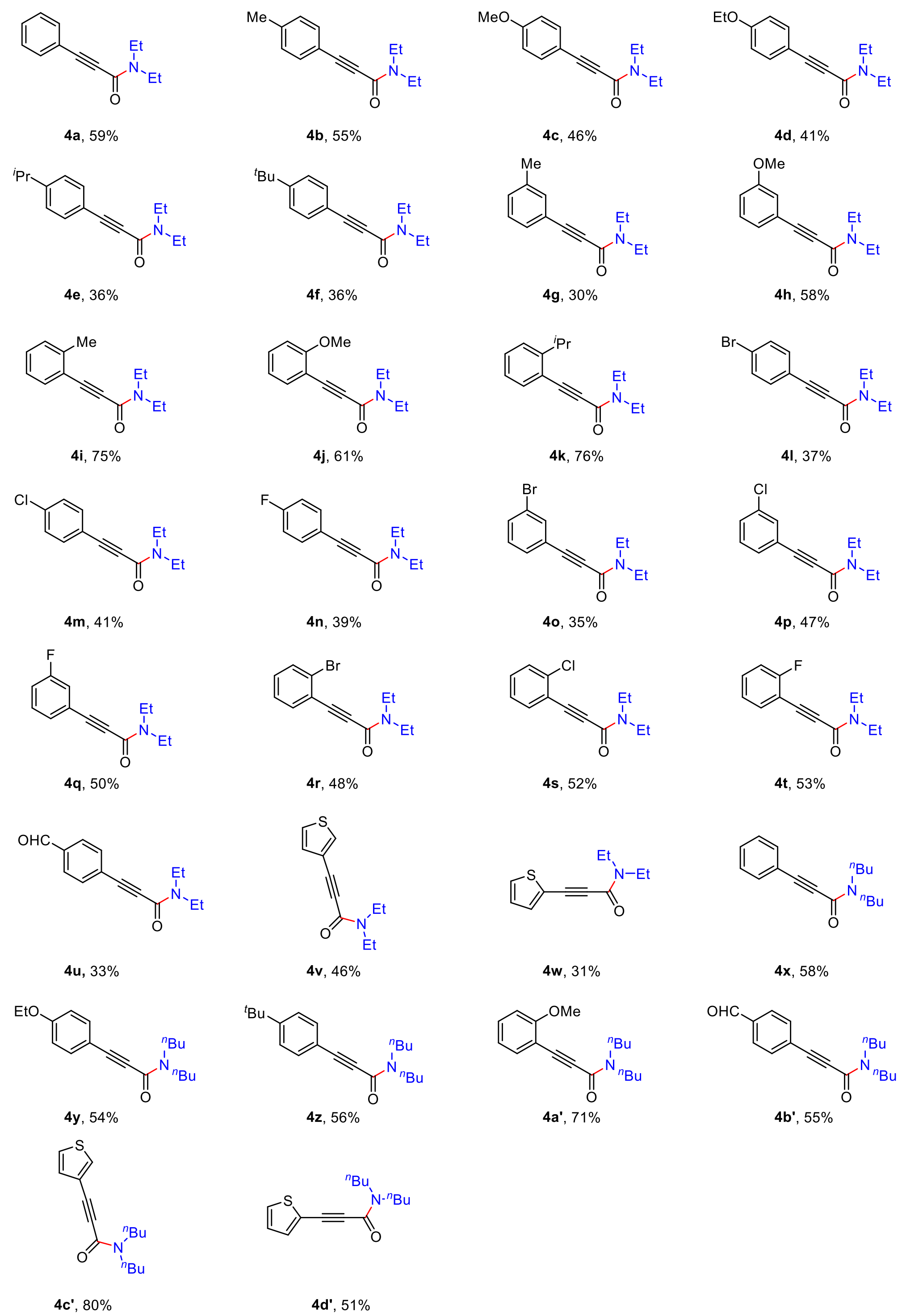
Table 3. Amidation of Aryl Alkynyl Acids with *N*,*N*,*N*′,*N*′-Tetraalkylthiuram Disulfides[a,b]





[a]Reaction conditions: **1** (0.10 mmol), **2** (0.15 mmol), $NiCl_2$ (20 mol %), Toluene (1.0 mL), 100 °C, 12 h, under air. [b]Isolated yields.

ppm: δ 7.58−7.52 (d, J = 6.7 Hz, 2H), 7.45−7.39 (m, 1H), 7.39−7.33 (m, 2H), 3.29 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.6, 132.3, 130.0, 128.5, 120.6, 90.1, 81.6, 38.4, 34.2; IR(KBr): 2928, 2219, 1622, 1491, 1397, 1278, 1180,

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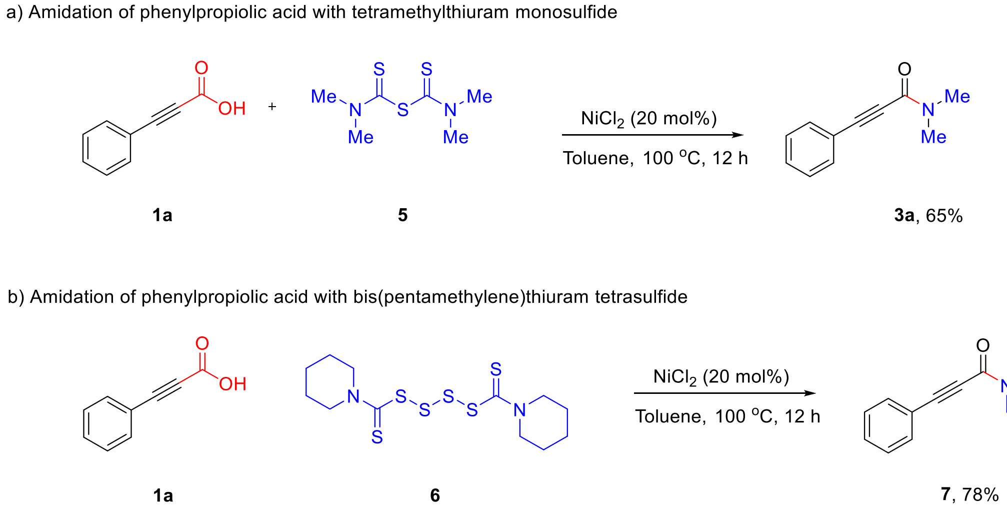
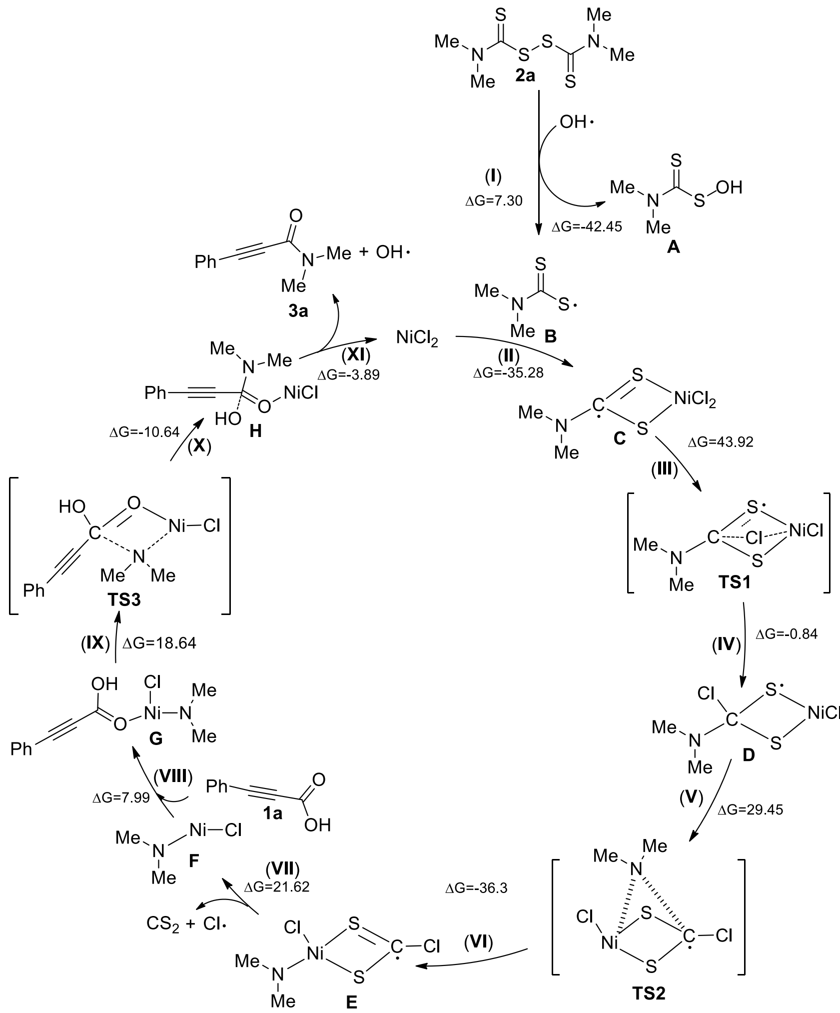
Scheme 3. Amidation of Phenylpropiolic Acid with Tetramethylthiuram Monosulfide (a) and Bis(pentamethylene)thiuram Tetrasulfide (b)



Scheme 4. Computational Reaction Mechanism



1137, 1065, 996, 765, 729, 692, 572, 531 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{11}NO$: $[M + H]^+$: 174.0919, found: 174.0908.

*N,N-dimethyl-3-(p-tolyl)propiolamide (**3b**).* Purification by column chromatography on silica gel (R_f = 0.33, petroleum ether/ethyl acetate = 3:1) yielded **3b** (14.2 mg, 76%) as a pale yellow solid; m. p. 79−81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.48−7.41 (d, J = 8.1 Hz, 2H), 7.20−7.13 (d, J = 7.9 Hz, 2H), 3.29 (s, 3H), 3.03 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.8, 140.5, 132.3, 129.3, 117.5, 90.6, 81.2, 38.4, 34.2, 21.6; IR(KBr): 3423, 2922, 2213, 1620, 1508, 1393,

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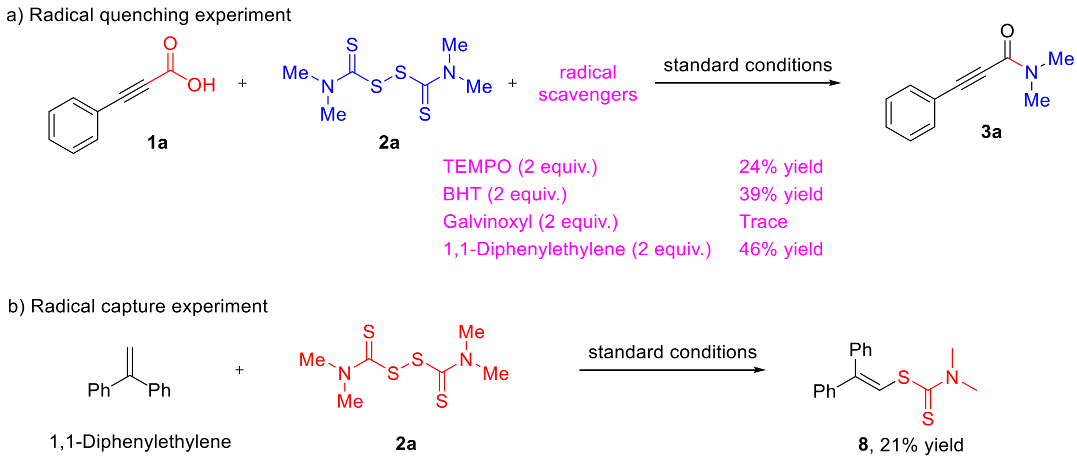
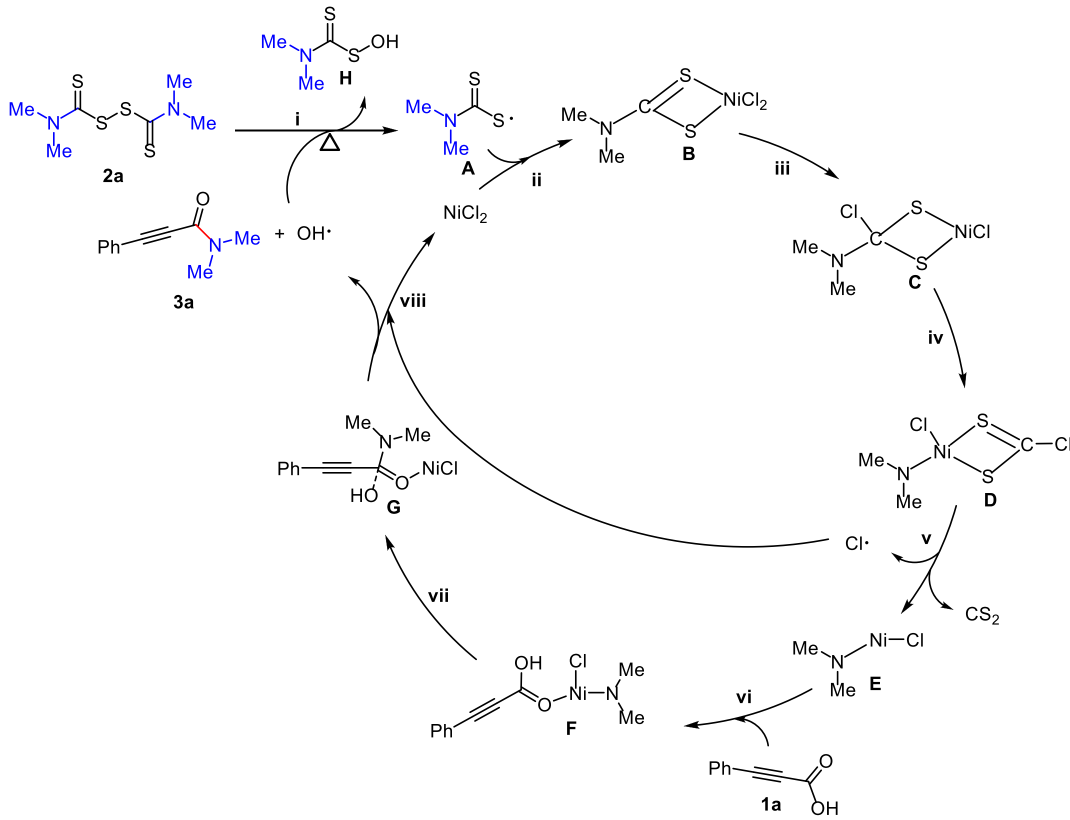
Scheme 5. Radical Quenching Experiment (a) and Radical Capture Experiment (b)



Scheme 6. Plausible Reaction Mechanism



1269, 1133, 1049, 968, 817, 731, 670, 530, 510 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}NO$: $[M + H]^+$: 188.1070, found: 188.1075.

3-(4-Ethylphenyl)-N,N-dimethylpropiolamide (**3c**). Purification by column chromatography on silica gel (R_f = 0.34, petroleum ether/ethyl acetate = 3:1) yielded **3c** (14.4 mg, 72%) as a pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.51–7.43 (d, J = 8.2 Hz, 2H), 7.23–7.16 (d, J = 8.2 Hz, 2H), 3.29 (s, 3H), 3.02 (s, 3H), 2.72–2.62 (q, J = 7.6 Hz, 2H), 1.28–1.19 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.8, 146.7, 132.4, 128.1, 117.7, 90.6, 81.2, 38.4, 34.2, 28.9, 15.2; IR(KBr): 3446, 2965, 2928, 2206, 1631, 1507, 1392, 1271, 1130, 1051, 833, 729 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{15}NO$: $[M + H]^+$: 202.1226, found: 202.1229.

3-(4-Methoxylphenyl)-N,N-dimethylpropiolamide (**3d**). Purification by column chromatography on silica gel (R_f = 0.36, petroleum ether/ethyl acetate = 3:1) yielded **3d** (15.6 mg, 77%) as a pale yellow solid; m. p. 82–84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.53–7.45 (dt, J = 8.9, 2.7 Hz, 2H), 6.92–6.84 (dt, J = 8.9, 2.7 Hz, 2H, 1H), 3.83 (s, 3H), 3.28 (s, 3H), 3.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.0, 154.9, 134.1, 114.2, 112.5, 90.7, 80.9, 55.4, 38.4, 34.2; IR(KBr): 2965, 2925, 2206, 1628, 1509, 1464, 1401, 1297, 1172, 1135, 1024, 837, 723, 671, 546 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}NO_2$: $[M + H]^+$: 204.1019, found: 204.1023.

3-(4-Ethoxylphenyl)-N,N-dimethylpropiolamide (**3e**). Purification by column chromatography on silica gel (R_f = 0.31, petroleum ether/ethyl acetate = 3:1) yielded **3e** (11.5 mg, 53%)

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as a yellow solid; m. p. 75−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.52−7.45 (dt, J = 8.8, 2.6 Hz, 2H), 6.90−6.82 (dt, J = 8.8, 2.6 Hz, 2H), 4.10−4.00 (q, J = 7.0 Hz, 2H), 3.28 (s, 3H), 3.02 (s, 3H), 1.47−1.38 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 160.4, 155.0, 134.1, 114.7, 112.3, 90.8, 80.8, 63.6, 38.4, 34.2, 14.7; IR(KBr): 2978, 2924, 2194, 1626, 1511, 1473, 1396, 1300, 1252, 1181, 1131, 1043, 847, 724, 683, 572 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{15}NO_2$: $[M + H]^+$: 218.1176, found: 218.1182.

*3-(4-Isopropylphenyl)-N,N-dimethylpropiolamide (**3f**).* Purification by column chromatography on silica gel (R_f = 0.35, petroleum ether/ethyl acetate = 3:1) yielded **3f** (17.9 mg, 83%) as a yellow solid; m. p. 60−62 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.52−7.44 (d, J = 8.3 Hz, 2H), 7.25−7.19 (d, J = 8.2 Hz, 2H), 3.28 (s, 3H), 3.03 (s, 3H), 2.98−2.84 (m, 1H), 1.28−1.21 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.8, 151.3, 132.4, 126.7, 117.9, 90.6, 81.1, 38.4, 34.2, 34.2, 23.7; IR(KBr): 2960, 2925, 2211, 1621, 1508, 1392, 1272, 1133, 1054, 843, 834, 729, 567 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}NO$: $[M + H]^+$: 216.1383, found: 216.1389.

*3-(4-(tert-Butyl)phenyl)-N,N-dimethylpropiolamide (**3g**).* Purification by column chromatography on silica gel (R_f = 0.42, petroleum ether/ethyl acetate = 3:1) yielded **3g** (15.6 mg, 68%) as a pale yellow solid; m. p. 84−86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.53−7.45 (dt, J = 8.6, 1.9 Hz, 2H), 7.42−7.34 (d, J = 8.6 Hz, 2H), 3.29 (s, 3H), 3.03 (s, 3H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.8, 153.5, 132.2, 125.5, 117.5, 90.6, 81.2, 38.4, 35.0, 34.2, 31.1; IR(KBr): 2968, 2926, 2204, 1624, 1506, 1395, 1267, 1135, 1104, 1058, 834, 730, 642, 568 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{19}NO$: $[M + H]^+$: 230.1539, found: 230.1546.

*N,N-Dimethyl-3-(m-tolyl)propiolamide (**3h**).* Purification by column chromatography on silica gel (R_f = 0.35, petroleum ether/ethyl acetate = 3:1) yielded **3h** (15.5 mg, 83%) as a yellow solid; m. p. 52−54 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.39−7.32 (d, J = 8.4 Hz, 2H), 7.29−7.19 (m, 2H), 3.29 (s, 3H), 3.03 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.7, 138.3, 132.8, 130.9, 129.5, 128.4, 120.4, 90.4, 81.3, 38.4, 34.2, 21.2; IR(KBr): 2924, 2218, 1629, 1490, 1395, 1283, 1130, 1065, 796, 729, 691, 582 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}NO$: $[M + H]^+$: 188.1070, found: 188.1063.

*3-(3-Methoxylphenyl)-N,N-dimethylpropiolamide (**3i**).* Purification by column chromatography on silica gel (R_f = 0.31, petroleum ether/ethyl acetate = 3:1) yielded **3i** (15.8 mg, 78%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.31−7.23 (t, J = 7.8 Hz, 1H), 7.17−7.10 (d, J = 7.6 Hz, 1H), 7.10−7.04 (s, 1H), 7.01−6.93 (dd, J = 8.3, 2.0 Hz, 1H), 3.81 (s, 3H), 3.29 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 159.3, 154.6, 129.6, 124.8, 121.5, 117.0, 116.7, 90.1, 81.3, 55.4, 38.4, 34.2; IR(KBr): 3435, 2919, 2217, 1627, 1454, 1392, 1230, 1258, 1171, 1126, 1046, 869, 728, 685, 575 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}NO_2$: $[M + H]^+$: 204.1019, found: 204.1017.

*N,N-Dimethyl-3-(o-tolyl)propiolamide (**3j**).* Purification by column chromatography on silica gel (R_f = 0.36, petroleum ether/ethyl acetate = 3:1) yielded **3j** (16.3 mg, 87%) as a pale yellow solid; m. p. 56−58 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.56−7.49 (d, J = 7.4 Hz, 1H), 7.35−7.26 (td, J = 7.6, 1.2 Hz, 1H), 7.26−7.23 (d, J = 7.6 Hz, 1H), 7.23−7.14 (t, J = 7.6 Hz, 1H), 3.31 (s, 3H), 3.04 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.8, 141.2, 132.9, 130.0, 129.7, 125.8, 120.5, 89.3, 85.4, 38.4, 34.2, 20.8; IR(KBr): 2922, 2202, 1626, 1486, 1396, 1269, 1198, 1136, 1109, 1057, 769, 728, 593, 556 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}NO$: $[M + H]^+$: 188.1070, found: 188.1064.

*3-(2-Ethylphenyl)-N,N-dimethylpropiolamide (**3k**).* Purification by column chromatography on silica gel (R_f = 0.42, petroleum ether/ethyl acetate = 3:1) yielded **3k** (14.5 mg, 72%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.57−7.50 (d, J = 7.3 Hz, 1H), 7.39−7.31 (t, J = 7.1 Hz, 1H), 7.30−7.23 (d, J = 7.6 Hz, 1H), 7.23−7.15 (t, J = 7.6 Hz, 1H), 3.30 (s, 3H), 3.04 (s, 3H), 2.91−2.75 (q, J = 7.6 Hz, 2H), 1.33−1.19 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.8, 147.3, 133.3, 130.2, 128.1, 125.8, 119.8, 89.1, 85.0, 38.3, 34.2, 27.7, 15.0; IR(KBr): 3436, 2929, 2204, 1631, 1494, 1448, 1393, 1267, 1138, 1112, 1051, 757, 730 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{15}NO$: $[M + H]^+$: 202.1226, found: 202.1223.

*3-(2-Methoxylphenyl)-N,N-dimethylpropiolamide (**3l**).* Purification by column chromatography on silica gel (R_f = 0.34, petroleum ether/ethyl acetate = 3:1) yielded **3l** (15.9 mg, 78%) as a yellow solid; m. p. 61−63 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.55−7.48 (dd, J = 7.6, 1.6 Hz, 1H), 7.42−7.33 (td, J = 8.4, 1.7 Hz, 1H), 6.97−6.93 (td, J = 7.6, 0.9 Hz, 1H), 6.93−6.88 (d, J = 8.4 Hz, 1H), 3.88 (s, 3H), 3.33 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.1, 154.9, 134.3, 131.6, 120.5, 110.7, 109.9, 86.9, 85.7, 55.8, 38.4, 34.1; IR(KBr): 3005, 2921, 2850, 2209, 1629, 1495, 1437, 1398, 1274, 1142, 1039, 1019, 767, 722, 546 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}NO_2$: $[M + H]^+$: 204.1019, found: 204.1012.

*3-(2-Isopropylphenyl)-N,N-dimethylpropiolamide (**3m**).* Purification by column chromatography on silica gel (R_f = 0.42, petroleum ether/ethyl acetate = 3:1) yielded **3m** (17 mg, 79%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.56−7.49 (dd, J = 7.7, 1.1 Hz, 1H), 7.42−7.34 (td, J = 7.8, 1.3 Hz, 1H), 7.34−7.28 (d, J = 7.0 Hz, 1H), 7.22−7.13 (td, J = 7.5, 1.3 Hz, 1H), 3.55−3.39 (m, 1H), 3.30 (s, 3H), 3.04 (s, 3H), 1.31−1.24 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.8, 151.6, 133.3, 130.3, 125.8, 125.1, 119.4, 89.2, 85.3, 38.3, 34.2, 31.7, 23.2; IR(KBr): 3435, 2926, 2202, 1630, 1484, 1446, 1392, 1266, 1133, 1052, 759, 729, 595, 584 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}NO$: $[M + H]^+$: 216.1383, found: 216.1381.

*3-(4-Bromophenyl)-N,N-dimethylpropiolamide (**3n**).* Purification by column chromatography on silica gel (R_f = 0.36, petroleum ether/ethyl acetate = 3:1) yielded **3n** (21.9 mg, 87%) as a pale yellow solid; m. p. 106−108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.54−7.48 (d, J = 8.5 Hz, 2H), 7.44−7.36 (d, J = 8.5 Hz, 2H), 3.28 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.4, 133.7, 131.9, 124.6, 119.6, 89.0, 82.5, 38.4, 34.2; IR(KBr): 2924, 2214, 1625, 1496, 1392, 1267, 1136, 1069, 1008, 839, 823, 727, 610, 527, 508 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{10}BrNO$: $[M + H]^+$: 252.0019, found: 252.0025.

*3-(4-Chlorophenyl)-N,N-dimethylpropiolamide (**3o**).* Purification by column chromatography on silica gel (R_f = 0.38, petroleum ether/ethyl acetate = 3:1) yielded **3o** (17.8 mg, 86%) as a pale yellow solid; m. p. 107−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.52−7.44 (d, J = 8.5 Hz, 2H), 7.39−7.31 (d, J = 8.5 Hz, 2H), 3.28 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.4, 136.3, 133.5, 129.0, 119.1, 89.0, 82.4, 38.4, 34.2; IR(KBr): 2922, 2211, 1626, 1587, 1485, 1394, 1268, 1129, 1078, 1011, 819, 728, 630, 528 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{10}ClNO$: $[M + H]^+$: 208.0524, found: 208.0531.

*3-(4-Fluorophenyl)-N,N-dimethylpropiolamide (**3p**).* Purification by column chromatography on silica gel (R_f = 0.39, petroleum ether/ethyl acetate = 3:1) yielded **3p** (17.7 mg, 93%) as a pale yellow solid; m. p. 64−66 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.59−7.50 (t, J = 7.1 Hz, 2H), 7.12−7.01 (tt, J =

8.6, 2.7 Hz, 2H), 3.29 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.5 (d, J = 250.8 Hz), 154.5, 134.5 (d, J = 8.6 Hz), 116.7 (d, J = 3.5 Hz), 116.0 (d, J = 22.0 Hz), 89.2, 81.4, 38.4, 34.2; IR(KBr): 3420, 2922, 2211, 1626, 1597, 1505, 1393, 1230, 1130, 1092, 970, 838, 728, 670, 527 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{10}FNO$: $[M + H]^+$: 192.0819, found: 192.0821.

N,N-Dimethyl-3-(4-(trifluoromethyl)phenyl)propiolamide (3q). Purification by column chromatography on silica gel (R_f = 0.36, petroleum ether/ethyl acetate = 3:1) yielded **3q** (21.5 mg, 89%) as a pale yellow solid; m. p. 95−97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.69−7.60 (m, 4H), 3.30 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 154.1, 132.6, 131.6 (q, J = 32.5 Hz), 125.5 (q, J = 3.8 Hz), 124.4 (d, J = 1.2 Hz), 123.6 (q, J = 270.8 Hz), 88.2, 83.3, 38.4, 34.2; IR(KBr): 3056, 2929, 2223, 1628, 1519, 1437, 1396, 1326, 1274, 1132, 1067, 1018, 970, 852, 729, 602, 580 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{10}F_3NO$: $[M + H]^+$: 242.0787, found: 242.0781.

3-(3-Bromophenyl)-N,N-dimethylpropiolamide (3r). Purification by column chromatography on silica gel (R_f = 0.31, petroleum ether/ethyl acetate = 3:1) yielded **3r** (18.2 mg, 72%) as a yellow solid; m. p. 42−44 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.72−7.66 (t, J = 1.6 Hz, 1H), 7.58−7.51 (dq, J = 8.1, 1.0 Hz, 1H), 7.51−7.42 (dt, J = 7.8, 1.2 Hz, 1H), 7.29−7.19 (t, J = 7.9 Hz, 1H), 3.29 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.2, 134.9, 133.1, 130.9, 130.0, 122.6, 122.3, 88.3, 82.5, 38.4, 34.2; IR(KBr): 2925, 2222, 1632, 1555, 1472, 1395, 1136, 1073, 787, 728, 679, 577 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{10}BrNO$: $[M + H]^+$: 252.0019, found: 252.0020.

3-(3-Chlorophenyl)-N,N-dimethylpropiolamide (3s). Purification by column chromatography on silica gel (R_f = 0.43, petroleum ether/ethyl acetate = 3:1) yielded **3s** (16.1 mg, 78%) as a yellow solid; m. p. 49−51 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.54−7.50 (t, J = 1.6 Hz, 1H), 7.46−7.42 (d, J = 7.6 Hz, 1H), 7.41−7.36 (d, J = 8.9 Hz, 1H), 7.33−7.26 (t, J = 7.9 Hz, 1H), 3.28 (s, 3H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.2, 134.4, 132.0, 130.5, 130.3, 129.8, 122.3, 88.4, 82.4, 38.4, 34.2; IR(KBr): 2927, 2211, 1635, 1559, 1474, 1318, 1272, 1137, 1059, 886, 860, 791, 730, 682, 576 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{10}ClNO$: $[M + H]^+$: 208.0524, found: 208.0525.

3-(3-Fluorophenyl)-N,N-dimethylpropiolamide (3t). Purification by column chromatography on silica gel (R_f = 0.40, petroleum ether/ethyl acetate = 3:1) yielded **3t** (15.3 mg, 80%) as a pale yellow solid; m. p. 57−59 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.39−7.29 (m, 2H), 7.29−7.20 (m, 1H), 7.19−7.07 (m, 1H), 3.29 (s, 3H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.7 (d, J = 246.0 Hz), 154.2, 130.2 (d, J = 8.5 Hz), 128.2 (d, J = 3.2 Hz), 122.4 (d, J = 9.4 Hz), 119.0 (d, J = 23.2 Hz), 117.4 (d, J = 21.0 Hz), 88.6 (d, J = 3.2 Hz), 82.1, 38.4, 34.2; IR(KBr): 3432, 2925, 2220, 1624, 1579, 1488, 1393, 1285, 1164, 1123, 986, 915, 870, 798, 728, 681, 576, 519 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{10}FNO$: $[M + H]^+$: 192.0819, found: 192.0822.

3-(2-Fluorophenyl)-N,N-dimethylpropiolamide (3u). Purification by column chromatography on silica gel (R_f = 0.39, petroleum ether/ethyl acetate = 3:1) yielded **3u** (16.6 mg, 87%) as a pale yellow solid; m. p. 75−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.60−7.52 (td, J = 7.5, 1.7 Hz, 1H), 7.46−7.36 (m, 1H), 7.22−7.07 (m, 2H), 3.31 (s, 3H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.3 (d, J = 252.4 Hz), 154.3, 134.2, 131.9 (d, J = 8.1 Hz), 124.2 (d, J = 3.9 Hz), 115.7 (d, J = 20.4 Hz), 109.4 (d, J = 15.3 Hz), 86.4 (d, J = 3.4 Hz), 83.4, 38.3, 34.2; IR(KBr): 2925, 2217, 1622, 1493, 1397, 1264, 1215, 1139, 1064, 771, 728, 688, 584, 474 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{10}FNO$: $[M + H]^+$: 192.0819, found: 192.0819.

3-(2-Chlorophenyl)-N,N-dimethylpropiolamide (3v). Purification by column chromatography on silica gel (R_f = 0.33, petroleum ether/ethyl acetate = 3:1) yielded **3v** (17.8 mg, 86%) as a pale yellow solid; m. p. 55−57 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.66−7.59 (dd, J = 7.6, 1.5 Hz, 1H), 7.46−7.41 (dd, J = 8.0, 0.9 Hz, 1H), 7.39−7.32 (td, J = 7.6, 1.6 Hz, 1H), 7.31−7.23 (td, J = 7.6, 1.2 Hz, 1H), 3.35 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.3, 136.8, 134.5, 131.0, 129.4, 126.7, 120.8, 86.4, 86.2, 38.4, 34.2; IR(KBr): 3066, 2926, 2854, 2207, 1628, 1473, 1395, 1265, 1164, 1138, 1060, 971, 736, 728, 581, 536 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{10}ClNO$: $[M + H]^+$: 208.0524, found: 208.0520.

3-(3-Bromophenyl)-N,N-dimethylpropiolamide (3w). Purification by column chromatography on silica gel (R_f = 0.36, petroleum ether/ethyl acetate = 3:1) yielded **3w** (19.5 mg, 77%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.65−7.59 (m, 2H), 7.35−7.30 (td, J = 7.5, 1.2 Hz, 1H), 7.30−7.24 (td, J = 7.5, 1.9 Hz, 1H), 3.37 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.3, 134.7, 132.6, 131.1, 127.3, 126.1, 123.1, 87.9, 85.5, 38.5, 34.3; IR(KBr): 3433, 2925, 2220, 1630, 1464, 1390, 1261, 1135, 1046, 753, 728, 655, 580 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{10}BrNO$: $[M + H]^+$: 252.0019, found: 252.0021.

N,N-Dimethyl-3-(2-(trifluoromethyl)phenyl)propiolamide (3x). Purification by column chromatography on silica gel (R_f = 0.33, petroleum ether/ethyl acetate = 3:1) yielded **3x** (22.9 mg, 95%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.80−7.73 (d, J = 7.3 Hz, 1H), 7.73−7.67 (d, J = 7.3 Hz, 1H), 7.61−7.48 (m, 2H), 3.28 (s, 3H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.1, 135.3, 131.9 (q, J = 29.0 Hz), 129.8, 126.0 (q, J = 5.0 Hz), 123.3 (q, J = 271.5 Hz), 118.9 (q, J = 2.0 Hz), 86.4, 85.1, 38.0, 34.3; IR(KBr): 3447, 2929, 2215, 1636, 1494, 1451, 1396, 1318, 1266, 1175, 1134, 1058, 767, 730, 650, 595 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{10}F_3NO$: $[M + H]^+$: 242.0787, found: 242.0784.

3-(4-Formylphenyl)-N,N-dimethylpropiolamide (3y). Purification by column chromatography on silica gel (R_f = 0.31, petroleum ether/ethyl acetate = 3:1) yielded **3y** (7.4 mg, 37%) as a yellow solid; m. p. 86−88 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 10.04 (s, 1H), 7.98−7.85 (dd, J = 6.6, 1.8 Hz, 2H), 7.73−7.67 (d, J = 7.4 Hz, 2H), 3.30 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 191.2, 154.0, 136.6, 132.8, 129.6, 126.6, 88.6, 84.5, 38.4, 34.3; IR(KBr): 3437, 2923, 2212, 1691, 1628, 1601, 1393, 1271, 1207, 1163, 1066, 824, 794, 726, 530 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{11}NO_2$: $[M + H]^+$: 202.0863, found: 202.0862.

N,N-Dimethyl-3-(thiophen-3-yl)propiolamide (3z). Purification by column chromatography on silica gel (R_f = 0.36, petroleum ether/ethyl acetate = 3:1) yielded **3z** (11.5 mg, 64%) as a dark yellow solid; m. p. 77−79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.69−7.64 (dd, J = 3.0, 1.2 Hz, 1H), 7.35−7.29 (dd, J = 5.0, 3.0 Hz, 1H), 7.23−7.17 (dd, J = 5.0, 1.1 Hz, 1H), 3.28 (s, 3H), 3.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.7, 132.0, 129.9, 125.9, 119.8, 85.6, 81.5, 38.4, 34.2; IR(KBr): 3081, 2925, 2211, 1620, 1488, 1390, 1262, 1198, 1130, 986, 869, 805, 727, 625, 585 cm^{-1}; HRMS (ESI) calcd. for C_9H_9NOS: $[M + H]^+$: 180.0478, found: 180.0481.

N,N-Dimethyl-3-(thiophen-2-yl)propiolamide (3a′). Purification by column chromatography on silica gel (R_f = 0.33, petroleum ether/ethyl acetate = 3:1) yielded **3a′** (6.7 mg, 37%) as a dark yellow solid; m. p. 50−52 °C; ^{1}H NMR (400 MHz,

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$CDCl_3$) ppm: δ 7.44−7.38 (m, 2H), 7.06−7.02 (dd, *J* = 4.9, 3.9 Hz, 1H), 3.27 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.5, 135.0, 129.9, 127.4, 120.3, 85.6, 83.9, 38.3, 34.2; IR(KBr): 3429, 2922, 2198, 1623, 1394, 1259, 1198, 1123, 1066, 737, 589 cm^{-1}; HRMS (ESI) calcd. for C_9H_9NOS: $[M + H]^+$: 180.0478, found: 180.0476.

*N,N-Dimethyl-2-oxo-2-phenylacetamide (**3b′**).* Purification by column chromatography on silica gel (R_f = 0.28, petroleum ether/ethyl acetate = 3:1) yielded **3b′** (14.4 mg, 81%) as a pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) ppm: δ 8.01−7.92 (m, 2H), 7.71−7.64 (t, *J* = 7.4 Hz, 1H), 7.58−7.42 (t, *J* = 7.6 Hz, 2H), 3.33−3.20 (s, 3H), 3.01−2.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 191.8, 167.0, 134.7, 133.1, 129.7, 129.0, 37.1, 34.0; IR(KBr): 3329, 2922, 1670, 1630, 1597, 1450, 1405, 1247, 1146, 994, 882, 726, 683, 643 cm^{-1}; HRMS (EI) calcd. for $C_{10}H_{12}NO_2$: $[M]^+$: 177.0784, found: 177.0783.

*N,N-Diethyl-3-phenylpropiolamide (**4a**).* Purification by column chromatography on silica gel (R_f = 0.33, petroleum ether/ethyl acetate = 3:1) yielded **4a** (11.8 mg, 59%) as a pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) ppm: δ 7.57−7.50 (d, *J* = 6.7 Hz, 2H), 7.45−7.39 (m, 1H), 7.39−7.32 (m, 2H), 3.72−3.62 (q, *J* = 7.1 Hz, 2H), 3.53−3.43 (q, *J* = 7.1 Hz, 2H), 1.32−1.23 (t, *J* = 7.2 Hz, 3H), 1.22−1.14 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.0, 132.3, 129.9, 128.5, 120.8, 89.0, 82.0, 43.6, 39.3, 14.4, 12.9; IR(KBr): 3438, 2974, 2219, 1624, 1489, 1426, 1380, 1286, 1136, 1072, 921, 733, 689, 531 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{15}NO$: $[M + H]^+$: 202.1226, found: 202.1227.

*N,N-Diethyl-3-(p-tolyl)propiolamide (**4b**).* Purification by column chromatography on silica gel (R_f = 0.35, hexane/ethyl acetate = 6:1) yielded **4b** (11.8 mg, 55%) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) ppm: δ 7.46−7.40 (d, *J* = 8.1 Hz, 2H), 7.20−7.13 (d, *J* = 7.9 Hz, 2H), 3.71−3.61 (q, *J* = 7.1 Hz, 2H), 3.53−3.43 (q, *J* = 7.1 Hz, 2H), 2.37 (s, 3H), 1.32−1.23 (t, *J* = 7.1 Hz, 3H), 1.22−1.14 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.2, 140.3, 132.3, 129.3, 117.7, 89.4, 81.5, 43.6, 39.3, 21.6, 14.4, 12.9; IR(KBr): 3434, 2974, 2204, 1626, 1509, 1425, 1289, 1219, 1135, 816, 733, 532 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}NO$: $[M + H]^+$: 216.1383, found: 216.1376.

*N,N-Diethyl-3-(4-methoxylphenyl)propiolamide (**4c**).* Purification by column chromatography on silica gel (R_f = 0.31, hexane/ethyl acetate = 6:1) yielded **4c** (10.6 mg, 46%) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) ppm: δ 7.52−7.44 (dt, *J* = 9.2, 2.4 Hz, 2H), 6.92−6.85 (dt, *J* = 9.5, 2.6 Hz, 2H), 3.83 (s, 3H), 3.71−3.61 (q, *J* = 7.1 Hz, 2H), 3.52−3.42 (q, *J* = 7.2 Hz, 2H), 1.32−1.23 (t, *J* = 7.1 Hz, 3H), 1.21−1.11 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 160.9, 154.3, 134.1, 114.2, 112.7, 89.5, 81.2, 55.4, 43.6, 39.3, 14.4, 12.9; IR(KBr): 3447, 2974, 2934, 2203, 1623, 1510, 1426, 1379, 1286, 1251, 1135, 1028, 833, 733, 660, 533 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}NO_2$: $[M + H]^+$: 232.1332, found: 232.1328.

*N,N-Diethyl-3-(4-ethoxyphenyl)propiolamide (**4d**).* Purification by column chromatography on silica gel (R_f = 0.31, hexane/ethyl acetate = 6:1) yielded **4d** (10.1 mg, 41%) as a dark yellow oil; ^1H NMR (400 MHz, $CDCl_3$) ppm: δ 7.51−7.43 (dt, *J* = 9.5, 2.7 Hz, 2H), 6.90−6.83 (dt, *J* = 9.5, 2.6 Hz, 2H), 4.10−3.98 (q, *J* = 7.0 Hz, 2H), 3.71−3.61 (q, *J* = 7.1 Hz, 2H), 3.52−3.42 (q, *J* = 7.2 Hz, 2H), 1.46−1.37 (t, *J* = 7.0 Hz, 3H), 1.32−1.24 (t, *J* = 7.1 Hz, 3H), 1.21−1.13 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 160.3, 154.3, 134.1, 114.6, 112.4, 89.6, 81.1, 63.6, 43.6, 39.2, 14.7, 14.4, 12.9; IR(KBr): 3447, 2978, 2933, 2202, 1624, 1509, 1425, 1379, 1205, 1173, 1134, 1042, 922, 828, 732 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{19}NO_2$: $[M + H]^+$: 246.1489, found: 246.1496.

*N,N-Diethyl-3-(4-isopropylphenyl)propiolamide (**4e**).* Purification by column chromatography on silica gel (R_f = 0.32, hexane/ethyl acetate = 6:1) yielded **4e** (8.8 mg, 36%) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) ppm: δ 7.51−7.43 (d, *J* = 8.2 Hz, 2H), 7.29−7.19 (d, *J* = 8.1 Hz, 2H), 3.71−3.58 (q, *J* = 7.1 Hz, 2H), 3.53−3.43 (q, *J* = 7.1 Hz, 2H), 2.99−2.85 (m, 1H), 1.32−1.27 (d, *J* = 7.2 Hz, 3H), 1.27−1.21 (d, *J* = 7.0 Hz, 6H), 1.21−1.15 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.2, 151.2, 132.4, 126.7, 118.0, 89.4, 81.5, 43.6, 39.3, 34.2, 23.7, 14.4, 12.9; IR(KBr): 3436, 2963, 2931, 2205, 1626, 1456, 1380, 1288, 1135, 1054, 833, 734, 563 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{21}NO$: $[M + H]^+$: 244.1696, found: 244.1691.

*3-(4-(tert-Butyl)phenyl)-N,N-diethylpropiolamide (**4f**).* Purification by column chromatography on silica gel (R_f = 0.33, hexane/ethyl acetate = 6:1) yielded **4f** (9.3 mg, 36%) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) ppm: δ 7.52−7.44 (dd, *J* = 6.6, 1.8 Hz, 2H), 7.42−7.33 (dd, *J* = 6.8, 1.9 Hz, 2H), 3.71−3.61 (q, *J* = 7.1 Hz, 2H), 3.53−3.43 (q, *J* = 7.2 Hz, 2H), 1.32 (s, 9H), 1.28−1.22 (m, 3H), 1.22−1.14 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.2, 153.4, 132.2, 125.5, 117.7, 89.3, 81.5, 43.6, 39.3, 35.0, 31.1, 14.4, 12.9; IR(KBr): 3435, 2969, 2205, 1626, 1425, 1380, 1220, 1173, 1066, 834, 734, 563 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{23}NO$: $[M + H]^+$: 258.1852, found: 258.1849.

*N,N-Diethyl-3-(m-tolyl)propiolamide (**4g**).* Purification by column chromatography on silica gel (R_f = 0.33, hexane/ethyl acetate = 6:1) yielded **4g** (6.5 mg, 30%) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) ppm: δ 7.38−7.30 (d, *J* = 6.4 Hz, 2H), 7.30−7.24 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.24−7.17 (m, 1H), 3.74−3.61 (q, *J* = 7.2 Hz, 2H), 3.54−3.41 (q, *J* = 7.1 Hz, 2H), 2.35 (s, 3H), 1.35−1.24 (t, *J* = 7.1 Hz, 3H), 1.22−1.07 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.1, 138.3, 132.8, 130.8, 129.5, 128.4, 120.6, 89.3, 81.6, 43.6, 39.3, 21.2, 14.4, 12.9; IR(KBr): 3434, 2974, 2212, 1627, 1425, 1331, 1293, 1219, 1132, 1095, 785, 733, 689, 580 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}NO$: $[M + H]^+$: 216.1383, found: 216.1379.

*N,N-Diethyl-3-(3-methoxylphenyl)propiolamide (**4h**).* Purification by column chromatography on silica gel (R_f = 0.32, hexane/ethyl acetate = 6:1) yielded **4h** (13.4 mg, 58%) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) ppm: δ 7.31−7.23 (t, *J* = 6.4 Hz, 1H), 7.20−7.10 (d, *J* = 7.6 Hz, 1H), 7.10−7.04 (d, *J* = 2.4 Hz, 1H), 7.00−6.84 (dd, *J* = 8.4, 2.6 Hz, 1H), 3.81 (s, 3H), 3.71−3.55 (q, *J* = 7.1 Hz, 2H), 3.53−3.40 (q, *J* = 7.2 Hz, 2H), 1.36−1.24 (m, 3H), 1.22−1.12 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR: 100 MHz, $CDCl_3$ 159.4, 154.0, 129.6, 124.8, 121.7, 117.1, 116.5, 88.9, 81.7, 55.4, 43.6, 39.3, 14.4, 12.9; IR(KBr): 3434, 2973, 2933, 2212, 1731, 1626, 1425, 1380, 1259, 1133, 1044, 786, 733, 685 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}NO_2$: $[M + H]^+$: 232.1332, found: 232.1331.

*N,N-Diethyl-3-(o-tolyl)propiolamide (**4i**).* Purification by column chromatography on silica gel (R_f = 0.34, hexane/ethyl acetate = 6:1) yielded **4i** (16.2 mg, 75%) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) ppm: δ 7.55−7.49 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.34−7.26 (td, *J* = 7.6, 1.3 Hz, 1H), 7.26−7.21 (d, *J* = 7.6 Hz, 1H), 7.21−7.13 (t, *J* = 7.6 Hz, 1H), 3.73−3.64 (q, *J* = 7.2 Hz, 2H), 3.54−3.44 (q, *J* = 7.2 Hz, 2H), 2.48 (s, 3H), 1.32−1.23 (t, *J* = 7.1 Hz, 3H), 1.23−1.15 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.1, 141.1, 133.0, 129.9, 129.7, 125.8, 120.6, 88.0, 85.8, 43.6, 39.4, 20.7, 14.5, 12.9; IR(KBr): 3458, 2974, 2204, 1624, 1455, 1422, 1379, 1282, 1220, 1140 ,1074, 948, 826,

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758, 593 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}NO$: [M + H]$^+$: 216.1383, found: 216.1381.

N,N-Diethyl-3-(2-methoxylphenyl)propiolamide (4j). Purification by column chromatography on silica gel (R_f = 0.31, hexane/ethyl acetate = 6:1) yielded **4j** (14.1 mg, 61%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.54−7.47 (dd, J = 7.6, 1.7 Hz, 1H), 7.42−7.33 (td, J = 7.9, 1.7 Hz, 1H), 6.97−6.91 (td, J = 7.5, 0.9 Hz, 1H), 6.91−6.87 (d, J = 8.4 Hz, 1H), 3.87 (s, 3H), 3.77−3.67 (q, J = 7.1 Hz, 2H), 3.53−3.43 (q, J = 7.1 Hz, 2H), 1.32−1.23 (t, J = 7.1 Hz, 3H), 1.22−1.14 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.2, 154.3, 134.2, 131.5, 120.5, 110.7, 110.1, 86.1, 85.6, 55.7, 43.6, 39.3, 14.4, 12.9; IR(KBr): 3453, 2973, 2205, 1623, 1491, 1424, 1277, 1139, 1046, 752, 732 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}NO_2$: [M + H]$^+$: 232.1332, found: 232.1332.

N,N-Diethyl-3-(2-isopropylphenyl)propiolamide (4k). Purification by column chromatography on silica gel (R_f = 0.33, hexane/ethyl acetate = 6:1) yielded **4k** (18.4 mg, 76%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.56−7.49 (dd, J = 7.7, 1.1 Hz, 1H), 7.42−7.34 (td, J = 7.8, 1.3 Hz, 1H), 7.34−7.27 (d, J = 6.8 Hz, 1H), 7.22−7.13 (td, J = 7.5, 1.4 Hz, 1H), 3.73−3.63 (q, J = 7.2 Hz, 2H), 3.54−3.48 (d, J = 7.2 Hz, 2H), 3.48−3.37 (m, 1H), 1.32−1.24 (m, 9H), 1.23−1.15 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.1, 151.5, 133.4, 130.3, 125.8, 125.1, 119.6, 87.9, 85.6, 43.6, 39.4, 31.8, 23.3, 14.5, 12.9; IR(KBr): 3455, 3062, 2968, 2872, 2203, 1625, 1424, 1314, 1220, 1137, 1033, 948, 812, 733, 594 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{21}NO$: [M + H]$^+$: 244.1696, found: 244.1694.

3-(4-Bromophenyl)-N,N-diethylpropiolamide (4l). Purification by column chromatography on silica gel (R_f = 0.35, hexane/ethyl acetate = 6:1) yielded **4l** (10.4 mg, 37%) as a yellow solid; m. p. 81−83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.55−7.48 (dt, J = 8.8, 2.2 Hz, 2H), 7.48−7.35 (dt, J = 8.8, 2.1 Hz, 2H), 3.70−3.60 (q, J = 7.2 Hz, 2H), 3.53−3.43 (q, J = 7.2 Hz, 2H), 1.32−1.23 (t, J = 7.2 Hz, 3H), 1.22−1.14 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 153.7, 133.7, 131.9, 124.5, 119.7, 87.8, 82.9, 43.6, 39.4, 14.4, 12.8; IR(KBr): 3432, 2977, 2933, 2208, 1617, 1480, 1431, 1290, 1218, 1139, 1061, 1007, 837, 732, 532 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{14}BrNO$: [M + H]$^+$: 280.0332, found: 280.0334.

3-(4-Chlorophenyl)-N,N-Diethylpropiolamide (4 M). Purification by column chromatography on silica gel (R_f = 0.34, hexane/ethyl acetate = 6:1) yielded **4 m** (9.6 mg, 41%) as a yellow solid; m. p. 56−58 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.52−7.43 (dt, J = 8.8, 2.2 Hz, 2H), 7.38−7.28 (dt, J = 8.8, 2.1 Hz, 2H), 3.70−3.60 (q, J = 7.2 Hz, 2H), 3.53−3.43 (q, J = 7.2 Hz, 2H), 1.32−1.23 (t, J = 7.2 Hz, 3H), 1.22−1.14 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 153.7, 136.2, 133.5, 128.9, 119.2, 87.8, 82.8, 43.6, 39.3, 14.4, 12.9; IR(KBr): 3438, 2981, 2936, 2210, 1615, 1484, 1431, 1317, 1298, 1219, 1141, 1088, 1011, 841, 733, 535 cm^{-1}; HRMS (ESI) calcd. For $C_{13}H_{14}ClNO$: [M + H]$^+$: 236.0837, found: 236.0834.

3-(4-Fluorophenyl)-N,N-diethylpropiolamide (4n). Purification by column chromatography on silica gel (R_f = 0.32, hexane/ethyl acetate = 6:1) yielded **4n** (8.6 mg, 39%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.53−7.49 (dt, J = 8.9, 2.2 Hz, 2H), 7.10−6.98 (t, J = 8.7 Hz, 2H), 3.70−3.55 (q, J = 7.1 Hz, 2H), 3.53−3.43 (q, J = 7.1 Hz, 2H), 1.33−1.24 (t, J = 7.2 Hz, 3H), 1.23−1.11 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.4 (d, J = 250.7 Hz), 153.9, 134.5 (d, J = 8.6 Hz), 116.9 (d, J = 3.0 Hz), 116.0 (d, J = 22.0 Hz), 88.0, 81.8, 43.6, 39.3, 14.4, 12.9; IR(KBr): 3435, 2974, 2221, 1626, 1507, 1427, 1289, 1236, 1136, 1076, 838, 733, 582, 534 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{14}FNO$: [M + H]$^+$: 220.1132, found: 220.1137.

3-(3-Bromophenyl)-N,N-diethylpropiolamide (4o). Purification by column chromatography on silica gel (R_f = 0.35, hexane/ethyl acetate = 6:1) yielded **4o** (9.8 mg, 35%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.69−7.64 (t, J = 1.6 Hz, 1H), 7.58−7.52 (dq, J = 8.1, 1.0 Hz, 1H), 7.52−7.44 (dt, J = 7.8, 1.1 Hz, 1H), 7.29−7.20 (t, J = 7.9 Hz 1H), 3.72−3.60 (q, J = 7.2 Hz, 2H), 3.54−3.43 (q, J = 7.1 Hz, 2H), 1.36−1.23 (t, J = 7.1 Hz, 3H), 1.23−1.14 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 153.5, 134.9, 133.0, 130.9, 130.0, 122.8, 122.3, 87.1, 82.9, 43.6, 39.4, 14.5, 12.8; IR(KBr): 3435, 2974, 2211, 1626, 1474, 1426, 1314, 1286, 1137, 1072, 783, 732, 679, 575 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{14}BrNO$: [M + H]$^+$: 280.0332, found: 280.0330.

3-(3-Chlorophenyl)-N,N-diethylpropiolamide (4p). Purification by column chromatography on silica gel (R_f = 0.33, hexane/ethyl acetate = 6:1) yielded **4p** (11.1 mg, 47%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.54−7.47 (t, J = 1.7 Hz, 1H), 7.45−7.41 (dt, J = 7.6, 1.3 Hz, 1H), 7.41−7.36 (dq, J = 8.2, 1.2 Hz, 1H), 7.33−7.28 (t, J = 7.8 Hz, 1H), 3.70−3.60 (q, J = 7.2 Hz, 2H), 3.53−3.43 (q, J = 7.2 Hz, 2H), 1.32−1.23 (t, J = 7.2 Hz, 3H), 1.22−1.14 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 153.6, 134.4, 132.0, 130.5, 130.2, 129.8, 122.5, 87.2, 82.8, 43.6, 39.4, 14.4, 12.8; IR(KBr): 3446, 2975, 2212, 1627, 1475, 1427, 1380, 1218, 1139, 1079, 784, 732, 680, 574 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{14}ClNO$: [M + H]$^+$: 236.0837, found: 236.0833.

3-(3-Fluorophenyl)-N,N-diethylpropiolamide (4q). Purification by column chromatography on silica gel (R_f = 0.34, hexane/ethyl acetate = 6:1) yielded **4q** (10.9 mg, 50%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.39−7.28 (m, 2H), 7.28−7.18 (m, 1H), 7.17−7.06 (m, 1H), 3.70−3.60 (q, J = 7.2 Hz, 2H), 3.53−3.43 (q, J = 7.2 Hz, 2H), 1.32−1.23 (t, J = 7.2 Hz, 3H), 1.23−1.14 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.3 (d, J = 245.9 Hz), 153.6, 130.2 (d, J = 8.6 Hz), 128.2 (d, J = 3.4 Hz), 122.6 (d, J = 9.4 Hz), 119.0 (d, J = 23.2 Hz), 117.3 (d, J = 21.0 Hz), 87.4 (d, J = 3.4 Hz), 82.5, 43.6, 39.4, 14.4, 12.8; IR(KBr): 3426, 2975, 2935, 2216, 1626, 1582, 1426, 1314, 1219, 1175, 1079, 1050, 965, 788, 733, 681, 576 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{14}FNO$: [M + H]$^+$: 220.1132, found: 220.1128.

3-(2-Bromophenyl)-N,N-diethylpropiolamide (4r). Purification by column chromatography on silica gel (R_f = 0.32, hexane/ethyl acetate = 6:1) yielded **4r** (13.4 mg, 48%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.67−7.57 (m, 2H), 7.37−7.29 (td, J = 7.5, 1.2 Hz, 1H), 7.29−7.20 (td, J = 7.4, 1.9 Hz, 1H), 3.82−3.72 (q, J = 7.1 Hz, 2H), 3.54−3.40 (q, J = 7.2 Hz, 2H), 1.33−1.26 (t, J = 7.1 Hz, 3H), 1.22−1.14 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 153.7, 134.8, 132.6, 131.0, 127.3, 126.0, 123.2, 86.8, 85.8, 43.6, 39.4, 14.6, 12.9; IR(KBr): 3436, 2973, 2211, 1626, 1473, 1380, 1273, 1140, 1048, 755, 732 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{14}BrNO$: [M + H]$^+$: 280.0332, found: 280.0327.

3-(2-Chlorophenyl)-N,N-diethylpropiolamide (4s). Purification by column chromatography on silica gel (R_f = 0.35, hexane/ethyl acetate = 6:1) yielded **4s** (12.2 mg, 52%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.66−7.59 (dd, J = 7.6, 1.6 Hz, 1H), 7.47−7.40 (dd, J = 8.1, 1.1 Hz, 1H), 7.40−7.33 (td, J = 7.5, 1.7 Hz, 1H), 7.33−7.23 (td, J = 7.6, 1.3 Hz, 1H), 3.79−3.69 (q, J = 7.1 Hz, 2H), 3.67−3.44 (q, J = 7.2 Hz, 2H), 1.33−1.24 (q, J = 7.3 Hz, 3H), 1.24−1.15 (q, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 153.7, 136.8, 134.5, 130.9, 129.4,

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126.7, 121.0, 86.5, 85.2, 43.6, 39.4, 14.5, 12.9; IR(KBr): 3434, 2973, 2211, 1624, 1475, 1380, 1259, 1139, 1058, 752, 732 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{14}ClNO$: $[M + H]^+$: 236.0837, found: 236.0838.

3-(2-Fluorophenyl)-N,N-diethylpropiolamide (4t). Purification by column chromatography on silica gel (R_f = 0.32, hexane/ethyl acetate = 6:1) yielded **4t** (11.7 mg, 53%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.60−7.51 (td, J = 7.5, 1.7 Hz, 1H), 7.46−7.35 (m, 1H), 7.20−7.06 (m, 2H), 3.74−3.63 (q, J = 7.2 Hz, 2H), 3.58−3.44 (q, J = 7.1 Hz, 2H), 1.32−1.24 (t, J = 7.1 Hz, 3H), 1.22−1.14 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.4 (d, J = 252.3 Hz), 153.6, 134.2, 131.8 (d, J = 8.0 Hz), 124.2 (d, J = 3.7 Hz), 115.7 (d, J = 20.4 Hz), 109.6 (d, J = 15.3 Hz), 86.8 (d, J = 3.3 Hz), 82.2, 43.7, 39.4, 14.4, 12.9; IR(KBr): 3437, 2974, 2219, 1628, 1492, 1426, 1365, 1267, 1138, 1072, 836, 758, 733 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{14}FNO$: $[M + H]^+$: 220.1132, found: 220.1135.

N,N-Diethyl-3-(4-formylphenyl)propiolamide (4u). Purification by column chromatography on silica gel (R_f = 0.31, hexane/ethyl acetate = 6:1) yielded **4u** (7.6 mg, 33%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 10.04 (s, 1H), 7.92−7.83 (d, J = 8.3 Hz, 2H), 7.74−7.66 (d, J = 8.2 Hz, 2H), 3.72−3.55 (q, J = 7.2 Hz, 2H), 3.54−3.45 (q, J = 7.2 Hz, 2H), 1.33−1.24 (m, 3H), 1.23−1.16 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 191.2, 153.4, 136.6, 132.8, 129.6, 126.8, 87.5, 84.9, 43.7, 39.4, 14.5, 12.8; IR(KBr): 3430, 2973, 2924, 1703, 1628, 1426, 1283, 1203, 1166, 1066, 828, 732, 608, 532 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{15}NO_2$: $[M + H]^+$: 230.1176, found: 230.1176.

N,N-Diethyl-3-(thiophen-3-yl)propiolamide (4v). Purification by column chromatography on silica gel (R_f = 0.32, hexane/ethyl acetate = 6:1) yielded **4v** (9.5 mg, 46%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.69−7.62 (dd, J = 3.0, 1.1 Hz, 1H), 7.35−7.28 (t, J = 4.0 Hz, 1H), 7.22−7.16 (dd, J = 5.0, 1.1 Hz, 1H), 3.70−3.60 (q, J = 7.1 Hz, 2H), 3.52−3.36 (q, J = 7.1 Hz, 2H), 1.31−1.23 (t, J = 7.1 Hz, 3H), 1.22−1.08 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.0, 131.8, 129.9, 125.8, 119.9, 84.4, 81.8, 43.5, 39.2, 14.4, 12.8; IR(KBr): 3434, 2214, 1619, 1427, 1358, 1276, 1130, 1094, 783, 732, 625 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{13}NOS$: $[M + H]^+$: 208.0791, found: 208.0785.

N,N-Diethyl-3-(thiophen-2-yl)propiolamide (4w). Purification by column chromatography on silica gel (R_f = 0.31, hexane/ethyl acetate = 6:1) yielded **4w** (6.4 mg, 31%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.48−7.37 (m, 2H), 7.08−7.00 (dd, J = 5.0, 4.0 Hz, 1H), 3.68−3.59 (q, J = 7.1 Hz, 2H), 3.59−3.40 (q, J = 7.1 Hz, 2H), 1.38−1.26 (d, J = 7.1 Hz, 3H), 1.20−1.14 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 153.8, 134.8, 129.7, 127.4, 120.5, 86.0, 82.7, 43.5, 39.3, 14.4, 12.9; IR(KBr): 3435, 2973, 2203, 1624, 1412, 1380, 1276, 1066, 1049, 738, 705 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{13}NOS$: $[M + H]^+$: 208.0791, found: 208.0790.

N,N-Dibutyl-3-phenylpropiolamide (4x). Purification by column chromatography on silica gel (R_f = 0.44, petroleum ether/ethyl acetate = 6:1) yielded **4x** (15.0 mg, 58%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.57−7.49 (d, J = 6.6 Hz, 2H), 7.44−7.38 (m, 1H), 7.38−7.31 (m, 2H), 3.64−3.56 (t, J = 7.4 Hz, 2H), 3.45−3.36 (t, J = 7.6 Hz, 2H), 1.70−1.61 (m, 2H), 1.61−1.51 (m, 2H), 1.46−1.37 (m, 2H), 1.37−1.28 (m, 2H), 1.02−0.96 (t, J = 6.4 Hz, 3H), 0.96−0.90 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.4, 132.3, 129.8, 128.5, 120.8, 89.2, 82.2, 48.9, 44.6, 31.0, 29.6, 20.2, 20.0, 13.9, 13.8; IR(KBr): 3436, 2960, 2872, 2213, 1625, 1490, 1422, 1378, 1265, 1138, 1051, 756, 733, 688, 530 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{23}NO$: $[M + H]^+$: 258.1852, found: 258.1853.

N,N-Dibutyl-3-(4-ethoxyphenyl)propiolamide (4y). Purification by column chromatography on silica gel (R_f = 0.32, hexane/ethyl acetate = 6:1) yielded **4y** (16.2 mg, 54%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.50−7.42 (dd, J = 6.9, 1.9 Hz, 2H), 6.90−6.82 (d, J = 8.8 Hz, 2H), 4.10−4.00 (q, J = 7.0 Hz, 2H), 3.63−3.55 (t, J = 7.4 Hz, 2H), 3.44−3.35 (t, J = 7.4 Hz, 2H), 1.72−1.60 (m, 2H), 1.60−1.50 (m, 2H), 1.46−1.41 (d, J = 7.0 Hz, 3H), 1.41−1.30 (m, 4H), 1.02−0.96 (d, J = 7.3 Hz, 3H), 0.96−0.91 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 160.3, 154.7, 134.0, 114.7, 112.5, 89.8, 81.4, 63.6, 48.9, 44.5, 31.0, 29.6, 20.2, 20.0, 14.7, 13.9; IR(KBr): 2958, 2931, 2872, 2208, 1625, 1509, 1422, 1378, 1250, 1138, 1114, 1043, 837, 732 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{27}NO_2$: $[M + H]^+$: 302.2115, found: 302.2113.

N,N-Dibutyl-3-(4-(tert-butyl)phenyl)propiolamide (4z). Purification by column chromatography on silica gel (R_f = 0.48, hexane/ethyl acetate = 6:1) yielded **4z** (17.6 mg, 56%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.51−7.43 (dd, J = 6.6, 1.8 Hz, 2H), 7.42−7.34 (dd, J = 6.7, 1.9 Hz, 2H), 3.67−3.56 (t, J = 7.4 Hz, 2H), 3.44−3.36 (t, J = 7.6 Hz, 2H), 1.71−1.61 (m, 2H), 1.61−1.50 (m, 2H), 1.43−1.38 (m, 2H), 1.38−1.33 (m, 2H), 1.32 (s, 9H), 1.01−0.96 (m, 3H), 0.96−0.90 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.6, 153.4, 132.1, 125.5, 117.8, 89.6, 81.7, 48.9, 44.6, 35.0, 31.1, 31.0, 29.6, 20.2, 20.0, 13.9; IR(KBr): 3435, 2959, 2871, 2211, 1628, 1504, 1421, 1364, 1296, 1208, 1105, 834, 731, 563 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{31}NO$: $[M + H]^+$: 314.2478, found: 314.2481.

N,N-Dibutyl-3-(2-methoxylphenyl)propiolamide (4a′). Purification by column chromatography on silica gel (R_f = 0.31, hexane/ethyl acetate = 6:1) yielded **4a′** (20.5 mg, 71%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.55−7.48 (dd, J = 7.6, 1.6 Hz, 1H), 7.41−7.33 (td, J = 7.6, 1.6 Hz, 1H), 6.97−6.91 (t, J = 7.5 Hz, 1H), 6.91−6.84 (d, J = 8.4 Hz, 1H), 3.87 (s, 3H), 3.71−3.60 (t, J = 7.5 Hz, 2H), 3.47−3.32 (t, J = 7.6 Hz, 2H), 1.72−1.61 (m, 2H), 1.61−1.50 (m, 2H), 1.46−1.37 (m, 2H), 1.37−1.29 (dt, J = 16.5, 6.8 Hz, 2H), 1.00−0.90 (dt, J = 11.6, 7.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.1, 154.7, 134.4, 131.4, 120.5, 110.6, 110.1, 86.3, 85.9, 55.6, 48.9, 44.5, 31.1, 29.6, 20.2, 20.0, 13.9, 13.9; IR(KBr): 2958, 2930, 2211, 1622, 1595, 1464, 1422, 1376, 1276, 1112, 1046, 1022, 937, 751, 732, 554 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{25}NO_2$: $[M + H]^+$: 288.1958, found: 288.1965.

N,N-Dibutyl-3-(4-formylphenyl)propiolamide (4b′). Purification by column chromatography on silica gel (R_f = 0.31, hexane/ethyl acetate = 6:1) yielded **4b′** (15.7 mg, 55%) as a dark yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 10.04 (s, 1H), 7.93−7.83 (dd, J = 6.6, 1.8 Hz, 2H), 7.71−7.64 (d, J = 8.2 Hz, 2H), 3.67−3.56 (t, J = 7.4 Hz, 2H), 3.46−3.37 (t, J = 7.6 Hz, 2H), 1.71−1.62 (m, 2H), 1.62−1.51 (m, 2H), 1.46−1.38 (m, 2H), 1.38−1.31 (m, 2H), 1.02−0.92 (dt, J = 11.1, 7.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 191.2, 153.8, 136.5, 132.7, 129.6, 126.9, 87.7, 85.2, 48.9, 44.7, 31.0, 29.5, 20.2, 20.0, 13.9, 13.8; IR(KBr): 3434, 2958, 1702, 1628, 1601, 1423, 1301, 1203, 1166, 1050, 829, 732 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{23}NO_2$: $[M + H]^+$: 286.1802, found: 286.1802.

N,N-Dibutyl-3-(thiophen-3-yl)propiolamide (4c′). Purification by column chromatography on silica gel (R_f = 0.41, hexane/ethyl acetate = 6:1) yielded **4c'** (21.1 mg, 80%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.66−7.61 (dd, J = 3.0, 1.1 Hz, 1H), 7.35−7.28 (dd, J = 5.0, 3.0 Hz, 1H), 7.21−7.15 (dd, J = 5.0, 1.1 Hz, 1H), 3.62−3.54 (t, J = 7.4 Hz, 2H), 3.44−3.35 (t, J =

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7.6 Hz, 2H), 1.71–1.60 (m 2H), 1.60–1.50 (m, 2H), 1.46–1.37 (m, 2H), 1.37–1.30 (m, 2H), 1.02–0.96 (d, J = 7.3 Hz, 3H), 0.96–0.91 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.4, 131.8, 129.9, 125.9, 120.0, 84.7, 82.1, 48.8, 44.6, 31.0, 29.6, 20.2, 20.0, 13.9, 13.8; IR(KBr): 3445, 2959, 2872, 2213, 1621, 1519, 1462, 1360, 1293, 1261, 1213, 1134, 1051, 871, 784, 733, 626 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{21}NOS$: $[M + H]^+$: 264.1417, found: 264.1410.

*N,N-Dibutyl-3-(thiophen-2-yl)propiolamide (**4d′**).* Purification by column chromatography on silica gel (R_f = 0.43, hexane/ethyl acetate = 6:1) yielded **4d′** (13.5 mg, 51%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.43–7.36 (t, J = 3.5 Hz, 2H), 7.07–6.98 (t, J = 4.4 Hz, 1H), 3.60–3.52 (t, J = 7.5 Hz, 2H), 3.44–3.31 (t, J = 7.6 Hz, 2H), 1.70–1.60 (m, 2H), 1.60–1.51 (m, 2H), 1.47–1.38 (m, 2H), 1.38–1.30 (m, 2H), 1.03–0.96 (t, J = 7.4 Hz, 3H), 0.96–0.90 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 154.2, 134.8, 129.7, 127.4, 120.6, 86.2, 82.9, 48.9, 44.6, 31.0, 29.6, 20.2, 20.0, 13.9, 13.8; IR(KBr): 3435, 2959, 2928, 2198, 1623, 1411, 1377, 1292, 1217, 1046, 729, 704 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{21}NOS$: $[M + H]^+$: 264.1417, found: 264.1411.

*3-Phenyl-1-(piperidin-1-yl)prop-2-yn-1-one (**7**).* Purification by column chromatography on silica gel (R_f = 0.42, hexane/ethyl acetate = 3:1) yielded **7** (16.7 mg, 78%) as a pale yellow solid; m. p. 112–114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.61–7.53 (m, 2H), 7.48–7.34 (m, 3H), 3.83–3.77 (t, J = 5.8 Hz, 2H), 3.72–3.46 (t, J = 5.6 Hz, 2H), 1.81–1.55 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 152.9, 132.3, 129.9, 128.5, 120.8, 90.2, 81.5, 48.2, 42.4, 26.5, 25.4, 24.6; IR(KBr): 2926, 2852, 2202, 1614, 1440, 1274, 1209, 1132, 1020, 850, 761, 692 cm^{-1}; HRMS (EI) calcd. for $C_{14}H_{15}NO$: $[M]^+$: 213.1148, found: 213.1138.

*2,2-Diphenylvinyl Dimethylcarbamodithioate (**8**).* Purification by column chromatography on silica gel (R_f = 0.35, petroleum ether/EtOAc = 10:1) yielded **8** (6.3 mg, 21%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 7.74 (s, 1H), 7.41–7.33 (m, 6H), 7.32–7.25 (m, 4H), 3.55 (s, 3H), 3.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 194.4, 142.0, 141.1, 139.8, 129.7, 128.4, 128.3, 128.0, 127.8, 127.6, 123.5, 45.4, 41.6 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{17}NS_2$: $[M + H]^+$: 300.0875, found: 300.0866.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.2c07353.

Experimental mechanistic studies; ^{1}H and ^{13}C NMR spectra of all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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