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PAPER

Synthesis of allenamides by Pd-catalyzed coupling of 3-alkoxycarbonyloxy ynamides or 1-alkoxycarbonyloxy allenamides with arylboronic acids†

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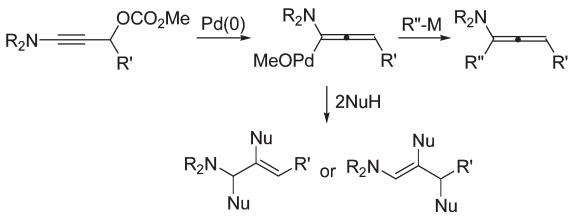
An efficient palladium-catalyzed method is reported for the synthesis of multi-substituted allenamides by Suzuki–Miyaura cross-coupling reaction between easily prepared 3-alkoxycarbonyloxy ynamides or 1-alkoxycarbonyloxy allenamides and arylboronic acids.

Introduction

Allenes represent a versatile functional group that has been widely investigated because of its high reactivity.[1] Allenamides, a special class of functionalized allenes, have recently received much attention in the synthetic community.[2] Various nitrogen-containing building blocks including nitrogen heterocycles were successfully synthesized from allenamides.[3] However, there are only a few methods to prepare allenamides, such as sigmatropic rearrangement of propargylic imidates,[4] base-catalyzed isomerization of propargylic amides,[5] and recently reported copper-catalyzed coupling of allenyl halides with amides.[6] From the view of the types and locations of substituents and availability of starting materials, more efficient strategies are still needed.

Since Tsuji's first report in 1985,[7] the palladium-catalyzed reaction of propargylic carbonates has become a powerful tool for constructing different kinds of allene, alkene, alkyne, and enyne derivatives.[8] Ynamides, an important subclass of alkynes, have emerged as important synthons in modern organic synthesis in the past 15 years.[9] An array of synthetic targets, including enamides,[10] amidines,[11] 2-amidofuran,[12] and amidocyclobutenes,[13] have been constructed from ynamides. We are recently interested in transition metal catalyzed reactions of alkynes, especially ynamides.[14] Enlightened by the chemistry of propargylic carbonates, we expect that in the presence of a Pd(0) catalyst, 3-alkoxycarbonyloxy ynamides would react with the organometallic reagents or nucleophiles to afford nitrogen substituted allenes or alkenes *via* allenylpalladium intermediates (Scheme 1). Considering ynamides can be easily prepared since the copper-catalyzed amides cross-coupling reaction was established,[15] we anticipate that this strategy might be an efficient route to construct allenamides. Herein, we report a novel reaction



Scheme 1

for the synthesis of allenamides *via* Pd-catalyzed coupling reaction of 3-alkoxycarbonyloxy ynamides with arylboronic acids.

Results and discussion

3-Alkoxycarbonyloxy ynamides were prepared from amides and alkynyl bromides in moderate to good yield by Hsung's method[15a–d,16] (Table 1).

Interestingly, the reaction gave 1-alkoxycarbonyloxy allenamides **2** as main products when R^2 and R^3 were both alkyl groups, and expected ynamides were not found (Scheme 2). Probably due to the high steric hindrance, spontaneous sigmatropic rearrangement occurred after 3-alkoxycarbonyloxy ynamides were formed under the conditions of coupling reaction. Fortunately, we were able to obtain single crystals of **2a**, which unambiguously confirmed the proposed structure *via* X-ray diffraction study[17] (Fig. 1).

Subsequently, reaction conditions were screened for the coupling reaction of 3-alkoxycarbonyloxy ynamides and arylboronic acid. $Pd(PPh_3)_4$ proved to be the best catalyst, and $Pd(OAc)_2$, $PdCl_2(PPh_3)_2$, and $Pd_2(dba)_3{\cdot}CHCl_3$ were not effective. The reaction proceeds well in dioxane, though other common solvents such as toluene and THF could also be used. The temperature is important for this reaction: at 100 °C the reaction runs smoothly, while lowering the temperature results in lower yield. Thus the reaction conditions were chosen as: ynamide 1.0 equiv.,

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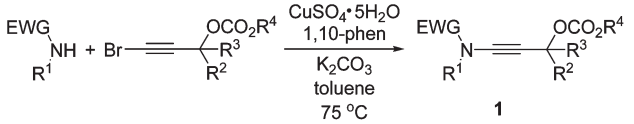
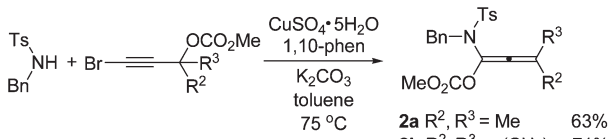
Table 1 Synthesis of 3-alkoxycarbonyloxy ynamides **1**[a]



Entry	EWG	R^1	R^2	R^3	R^4	Yield (%)
1	Ts	Bn	H	H	Me	59 (**1a**)
2	Ts	Bn	H	Me	Me	67 (**1b**)
3	Ts	Bn	H	H	*n*-Pr	52 (**1c**)
4	Ms	Bn	H	H	*n*-Pr	50 (**1d**)
5			H	H	Me	45 (**1e**)

[a] Unless otherwise specified, the reaction was carried out using amide (1.0 equiv.), alkynyl bromide (1.1 equiv.), $CuSO_4{\cdot}5H_2O$ (0.1 equiv.), 1,10-phen (0.2 equiv.), and K_2CO_3 (2.0 equiv.) in toluene at 75 °C under N_2.



Scheme 2

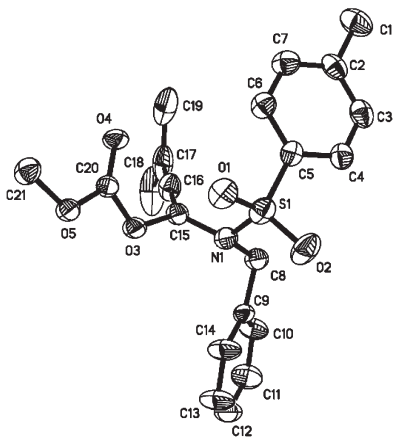


Fig. 1 ORTEP representation of **2a**.

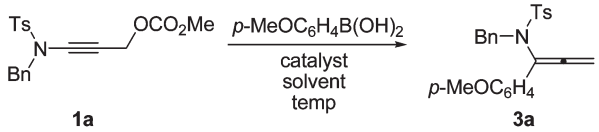
arylboronic acid 1.5 equiv., $Pd(PPh_3)_4$ 0.05 equiv. in dioxane at 100 °C for 30 min (Table 2).

1-Alkoxycarbonyloxy allenamide **2** could also undergo a coupling reaction under the same conditions and gave the corresponding allenamide in high yield. As far as we know, this is the first report that allenyl carbonate participates in a Suzuki–Miyaura reaction (Scheme 3).

With the optimized reaction conditions in hand, the scope of this Pd-catalyzed reaction was further investigated, and the results are summarized in Table 3.

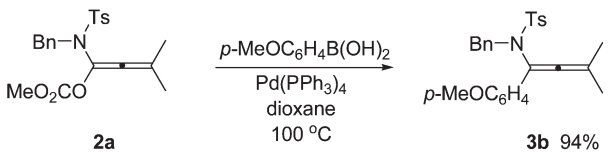
Various arylboronic acids gave good results, either with an electron-donating or electron-withdrawing group. Both 3-

Table 2 Optimization of the reaction conditions[a]



Entry	Catalyst	Solvent	Temp (°C)	Time (h)	Yield of **3a** (%)
1	$Pd(OAc)_2$	Dioxane	100	1	NR[b]
2	$PdCl_2(PPh_3)_2$	Dioxane	100	1	NR[b]
3	$Pd_2(dba)_3{\cdot}CHCl_3$	Dioxane	100	1	NR[b]
4	$Pd(PPh_3)_4$	Dioxane	100	0.5	75
5	$Pd(PPh_3)_4$	THF	65	3	57
6	$Pd(PPh_3)_4$	Toluene	100	0.5	33
7	$Pd(PPh_3)_4$	Dioxane	rt	3	ND[c]
8	$Pd(PPh_3)_4$	Dioxane	60	3	66

[a] Unless otherwise specified, the reaction was carried out using **1a** (1.0 equiv.), arylboronic acid (1.5 equiv.), and catalyst (0.05 equiv.) under N_2. [b] No reaction. [c] Not determined. The reaction was too slow to observe.



Scheme 3

alkoxycarbonyloxy ynsulfonamides **1** and 1-alkoxycarbonyloxy allensulfonamides **2** underwent the coupling reaction well to afford di-, tri-, and tetrasubstituted allensulfonamides **3**. However, oxazolidinone **1e** failed to produce any allenamide. The structures of all these products were confirmed with the help of spectral and analytical data, and the structure of **3a** was further established by X-ray diffraction analysis[18] (Fig. 2).

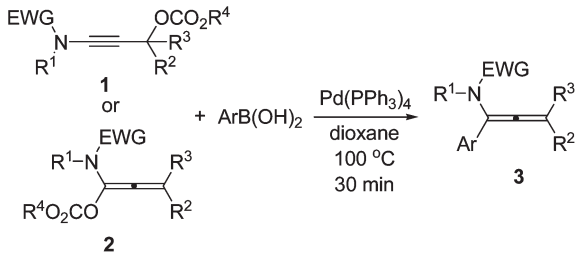
Interestingly, a cyclic product was obtained when 2-hydroxyphenylboronic acid was used. It is reasonable to propose that spontaneous cyclization occurred after allenamide was formed to afford 4-amino-2*H*-chromene **4** (Scheme 4).

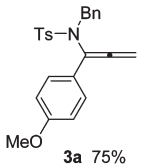
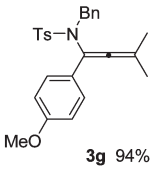
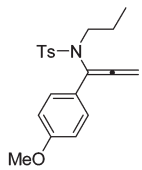
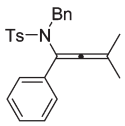
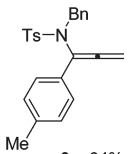
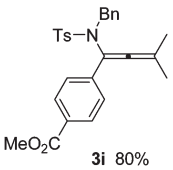
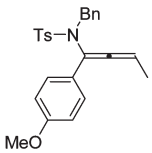
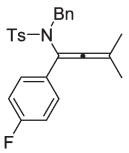
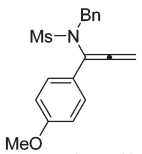
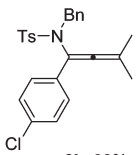
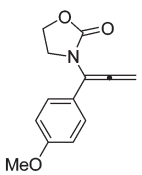
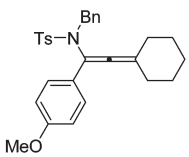
The following plausible mechanism was proposed for the coupling-reaction as shown in Scheme 5: (i) 3-alkoxycarbonyloxy ynamide **1** or 1-alkoxycarbonyloxy allenamide **2** (may be interconverted to **1** at 100 °C) reacts with Pd(0) to afford the intermediate **4**; (ii) subsequently, transmetalation reaction with arylboronic acid gives **5**; (iii) finally, reductive elimination gives the product allenamide **3**.

Conclusions

In summary, we have described an efficient palladium-catalyzed method for the synthesis of multi-substituted allenamides by Suzuki–Miyaura cross-coupling reaction between 3-alkoxycarbonyloxy ynamides or 1-alkoxycarbonyloxy allenamides and arylboronic acids.

Table 3 Synthesis of allenamides **3**[a]



Entry	1/2	Product, yield (%)	Entry	1/2	Product, yield (%)
1	**1a**	 **3a** 75%	7	**2a**	 **3g** 94%
2	**1c**	 **3b** 49%	8	**2a**	 **3h** 86%
3	**1a**	 **3c** 64%	9	**2a**	 **3i** 80%
4	**1b**	 **3d** 82%	10	**2a**	 **3j** 82%
5	**1d**	 **3e** 40%	11	**2a**	 **3k** 90%
6	**1e**	 **3f** 0%	12	**2b**	 **3l** 93%

[a] Unless otherwise specified, the reaction was carried out using **1a** (1.0 equiv.), arylboronic acid (1.5 equiv.), and catalyst (0.05 equiv.) under N_2.

Experimental

General

All reactions were performed under a N_2 atmosphere. All solvents were purified and dried according to standard methods prior to use. All ^1H NMR and ^{13}C NMR spectra were measured in $CDCl_3$ with TMS as the internal standard. Chemical shifts are expressed in ppm and *J* values are given in Hz.

General procedures for synthesis of 3-alkoxycarbonyloxy ynamides 1 and 1-alkoxycarbonyloxy allenamides 2[15c]

To a mixture of an amide (1.0 equiv.), K_2CO_3 (2.0 equiv.), $CuSO_4{\cdot}5H_2O$ (0.10 equiv.), and 1,10-phenanthroline (0.20 equiv.) in a reaction vial was added a solution of a respective 1-bromoalkyne (1.1 equiv.) in toluene. The reaction mixture was capped and heated at 75 °C while being monitored with TLC

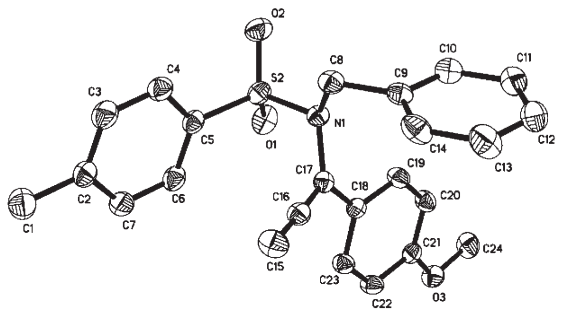
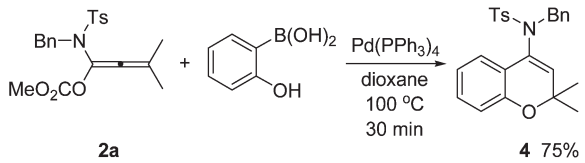
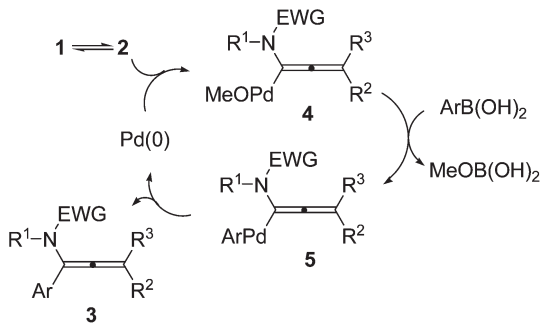


Fig. 2 ORTEP representation of **3e**.



Scheme 4



Scheme 5

analysis. Upon reaction completion, the mixture was filtered over a plug of silica gel (washed with ethyl acetate), and the filtrate was concentrated. The residue was purified by flash chromatography (eluent: hexane–ethyl acetate = 9 : 1–6 : 1) to afford **1** or **2**.

1a Yield: 59%. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (2H, d, J = 8.4 Hz), 7.26–7.31 (7H, m), 4.78 (2H, s), 4.49 (2H, s), 3.77 (3H, s), 2.43 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1, 144.9, 134.5, 134.2, 129.8, 128.7, 128.6, 128.4, 127.7, 81.2, 86.3, 56.2, 55.4, 55.1, 21.7; IR (film, cm^{-1}): 2957, 2247, 1755, 1361, 1261, 1168, 544; HRMS (m/z) Calcd for $C_{19}H_{19}NNaO_5S$ (M + Na)$^+$: 396.0882, Found: 396.0876.

1b Yield: 67%. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (2H, d, J = 8.0 Hz), 7.26–7.31 (7H, m), 5.53 (1H, t, J = 6.8 Hz), 4.52 (1H, d, J = 13.6 Hz), 4.42 (1H, d, J = 13.6 Hz), 3.75 (3H, s), 2.43 (3H, s), 1.40 (3H, d, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.7, 144.8, 134.4, 134.2, 129.7, 128.9, 128.5, 128.4, 127.8, 79.6, 70.1, 64.9, 55.4, 54.8, 21.7, 21.2; IR (film, cm^{-1}): 2956, 2247, 1749, 1367, 1264, 1170, 1090, 545; HRMS (m/z) Calcd for $C_{20}H_{21}NNaO_5S$ (M + Na)$^+$: 410.1038, Found: 410.1030.

1c Yield: 52%. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (2H, d, J = 8.0 Hz), 7.33 (2H, d, J = 8.0 Hz), 4.86 (2H, s), 4.10 (2H, t, J = 6.8 Hz), 3.26 (2H, t, J = 7.2 Hz), 2.44 (3H, s), 1.63–1.70 (4H, m), 0.95 (3H, t, J = 7.6 Hz), 0.88 (3H, t, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.7, 144.7, 134.6, 129.8, 127.6, 80.8, 69.9, 65.6, 56.0, 53.0, 22.0, 21.7, 21.2, 10.8, 10.2; IR (film, cm^{-1}): 2969, 2246, 1747, 1365, 1258, 1172, 581; HRMS (m/z) Calcd for $C_{17}H_{23}NNaO_5S$ (M + Na)$^+$: 376.1195, Found: 376.1182.

1d Yield: 50%. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.41 (5H, m), 4.85 (2H, s), 4.62 (2H, s), 4.11 (2H, d, J = 6.8 Hz), 2.87 (3H, s), 1.70 (2H, m), 0.96 (3H, d, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.7, 134.4, 128.9, 128.87, 128.81, 80.7, 70.0, 66.8, 55.9, 55.7, 39.2, 22.0, 10.2; IR (film, cm^{-1}): 2970, 2247, 1747, 1360, 1258, 1165, 929, 539; HRMS (m/z) Calcd for $C_{15}H_{19}NNaO_5S$ (M + Na)$^+$: 348.0882, Found: 348.0877.

1e Yield: 45%. Solid, mp: 106–108 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.89 (2H, s), 4.44 (2H, t, J = 8.0 Hz), 3.92 (2H, t, J = 8.0 Hz), 3.79 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.9, 155.2, 77.5, 66.0, 63.2, 55.9, 55.1, 46.6; IR (KBr, cm^{-1}): 3442, 2263, 1758, 1428, 1258, 1117, 754; HRMS (m/z) Calcd for $C_8H_9NNaO_5$ (M + Na)$^+$: 222.0378, Found: 222.0373.

2a Yield: 63%. Solid, mp: 101–103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (2H, d, J = 8.4 Hz), 7.29–7.33 (7H, m), 4.40 (2H, s), 3.74 (3H, s), 2.44 (3H, s), 1.53 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.2, 153.0, 143.9, 135.5, 135.2, 129.5, 128.5, 128.4, 128.1, 127.8, 117.4, 113.4, 55.2, 53.1, 21.6, 20.7; IR (KBr, cm^{-1}): 2930, 1763, 1275, 1170, 1153, 669; HRMS (m/z) Calcd for $C_{21}H_{23}NNaO_5S$ (M + Na)$^+$: 424.1188, Found: 424.1195.

2b Yield: 71%. Solid, mp: 95–97 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (2H, d, J = 8.4 Hz), 7.24–7.33 (7H, m), 4.40 (2H, s), 3.75 (3H, s), 2.43 (3H, s), 1.84–1.92 (4H, m), 1.40–1.52 (4H, m), 1.22–1.27 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.6, 153.0, 143.8, 135.6, 134.9, 129.4, 128.4, 128.3, 128.2, 127.7, 120.2, 117.2, 55.1, 53.4, 31.4, 27.1, 25.5, 21.6; IR (KBr, cm^{-1}): 2928, 1765, 1277, 1169, 1149, 670; HRMS (m/z) Calcd for $C_{24}H_{27}NNaO_5S$ (M + Na)$^+$: 464.1508, Found: 464.1503.

General procedures for synthesis of allenamides 3 and 4

A vial was charged with **1** or **2** (0.5 mmol), arylboronic acid (0.75 mmol) and $Pd(PPh_3)_4$ (28.9 mg, 0.025 mmol). The vial was evacuated under high vacuum and backfilled with N_2. Dioxane (3 mL) was next added and the solution was stirred at 100 °C for 30 min. Upon reaction completion, the mixture was concentrated and the residue was purified by flash chromatography on silica gel (eluent: hexane–ethyl acetate = 9 : 1–6 : 1) to afford **3** or **4**.

3a Yield: 75%. Solid, mp: 164–166 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (2H, d, J = 8.4 Hz), 7.21–7.34 (9H, m), 6.78 (2H, d, J = 8.4 Hz), 5.01 (2H, s), 4.40 (2H, s), 3.76 (3H, s), 2.46 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.5, 159.2, 143.7, 135.5, 134.1, 129.4, 129.2, 128.3, 128.2, 127.8, 127.2, 126.6, 113.6, 112.7, 84.9, 55.3, 54.5, 21.6; IR (KBr, cm^{-1}): 3447, 2971, 1607, 1509, 1347, 1251, 1165, 598; HRMS (m/z) Calcd for $C_{24}H_{23}NNaO_3S$ (M + Na)$^+$: 428.1296, Found: 428.1300.

3b Yield: 49%. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (2H, d, J = 8.0 Hz), 7.49 (2H, d, J = 8.8 Hz), 7.29 (2H, d, J = 8.0 Hz), 6.89 (2H, d, J = 8.8 Hz), 5.00 (2H, s), 3.81 (3H, s),

3.22 (2H, t, J = 7.2 Hz), 2.43 (3H, s), 1.50–1.56 (2H, m), 0.89 (3H, t, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.9, 159.3, 143.5, 134.3, 129.2, 128.1, 127.2, 126.9, 113.8, 112.7, 84.9, 55.3, 52.9, 21.6, 21.4, 11.4; IR (film, cm^{-1}): 3447, 2969, 1606, 1508, 1340, 1246, 1165, 837; HRMS (m/z) Calcd for $C_{20}H_{23}NNaO_3S$ (M + Na)$^+$: 380.1296, Found: 380.1294.

3c Yield: 64%. Solid, mp: 165–167 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (2H, d, J = 8.0 Hz), 7.22–7.34 (9H, m), 7.07 (2H, d, J = 8.0 Hz), 5.03 (2H, s), 4.41 (2H, s), 2.47 (3H, s), 2.29 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.7, 143.7, 137.5, 135.5, 134.0, 131.4, 129.4, 129.2, 128.9, 128.3, 128.2, 127.9, 125.9, 113.0, 85.0, 54.5, 21.7, 21.2; IR (KBr, cm^{-1}): 3447, 3036, 1342, 1160, 1067, 814, 661; HRMS (m/z) Calcd for $C_{24}H_{23}NNaO_3S$ (M + Na)$^+$: 412.1347, Found: 412.1355.

3d Yield: 82%. Solid, mp: 141–143 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (2H, d, J = 8.0 Hz), 7.19–7.34 (9H, m), 6.79 (2H, d, J = 8.8 Hz), 5.47 (1H, t, J = 6.8 Hz), 4.47 (1H, d, J = 13.6 Hz), 4.36 (1H, d, J = 13.6 Hz), 3.76 (3H, s), 2.46 (3H, s), 1.49 (3H, d, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.7, 159.0, 143.6, 135.8, 134.3, 129.4, 129.0, 128.33, 128.27, 127.8, 127.3, 113.5, 111.8, 96.4, 55.3, 54.4, 21.7, 14.0; IR (KBr, cm^{-1}): 3440, 2917, 1607, 1510, 1348, 1248, 1164, 594; HRMS (m/z) Calcd for $C_{25}H_{25}NNaO_3S$ (M + Na)$^+$: 442.1453, Found: 442.1448.

3e Yield: 40%. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.36 (7H, m), 6.84 (2H, d, J = 8.8 Hz), 5.41 (2H, s), 4.57 (2H, s), 3.78 (3H, s), 2.84 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.5, 159.6, 135.6, 129.4, 128.5, 128.2, 127.4, 125.4, 114.0, 112.1, 84.8, 55.3, 53.7, 38.6; IR (film, cm^{-1}): 2933, 1725, 1606, 1510, 1336, 1250, 1149, 835; HRMS (m/z) Calcd for $C_{18}H_{19}NNaO_3S$ (M + Na)$^+$: 352.0983, Found: 352.0976.

3g Yield: 94%. Solid, mp: 136–138 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (2H, d, J = 8.0 Hz), 7.23–7.37 (9H, m), 6.83 (2H, d, J = 8.8 Hz), 4.49 (2H, s), 3.77 (3H, s), 2.45 (3H, s), 1.56 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.8, 158.9, 143.5, 136.3, 134.9, 129.4, 128.8, 128.6, 128.4, 128.1, 127.7, 127.5, 113.5, 109.8, 106.6, 55.3, 54.3, 21.6, 20.2; IR (KBr, cm^{-1}): 3440, 2924, 1600, 1517, 1341, 1155, 1034; HRMS (m/z) Calcd for $C_{26}H_{27}NNaO_3S$ (M + Na)$^+$: 456.1609, Found: 456.1605.

3h Yield: 86%. Solid, mp: 145–147 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (2H, d, J = 8.4 Hz), 7.44 (2H, d, J = 7.6 Hz), 7.20–7.38 (10H, m), 4.52 (2H, s), 2.47 (3H, s), 1.59 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.6, 143.6, 136.3, 136.2, 135.1, 129.5, 128.8, 128.4, 128.2, 128.1, 127.8, 127.2, 126.3, 109.9, 106.6, 54.3, 21.7, 20.1; IR (KBr, cm^{-1}): 3445, 3031, 1597, 1350, 1167, 767, 662, 598; HRMS (m/z) Calcd for $C_{25}H_{25}NNaO_2S$ (M + Na)$^+$: 426.1504, Found: 426.1498.

3i Yield: 80%. Solid, mp: 153–155 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (2H, d, J = 8.4 Hz), 7.43 (2H, d, J = 8.4 Hz), 7.19–7.40 (9H, m), 4.44 (2H, s), 3.88 (3H, s), 2.46 (3H, s), 1.57 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.5, 167.0, 143.6, 141.1, 135.8, 134.8, 129.4, 129.3, 128.8, 128.5, 128.4, 128.2, 127.8, 126.0, 109.5, 107.2, 54.4, 52.0, 21.6, 19.9; IR (KBr, cm^{-1}): 3416, 1716, 1343, 1274, 1174, 1101, 665; HRMS (m/z) Calcd for $C_{27}H_{27}NNaO_4S$ (M + Na)$^+$: 484.1558, Found: 484.1545.

3j Yield: 82%. Solid, mp: 167–169 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (2H, d, J = 8.0 Hz), 7.23–7.34 (9H, m), 6.90–6.94 (2H, m), 4.44 (2H, s), 2.45 (3H, s), 1.55 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.1, 163.3, 160.8, 143.6, 136.0, 134.9, 132.3, 132.2, 129.4, 128.9, 128.3, 128.2, 127.8, 127.78, 127.73, 115.0, 114.8, 109.3, 106.9, 54.4, 21.6, 20.1; IR (KBr, cm^{-1}): 3448, 2964, 1598, 1507, 1340, 1158, 589; HRMS (m/z) Calcd for $C_{25}H_{24}FNNaO_2S$ (M + Na)$^+$: 444.1409, Found: 444.1403.

3k Yield: 90%. Solid, mp: 144–146 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (2H, d, J = 8.0 Hz), 7.17–7.34 (11H, m), 4.42 (2H, s), 2.46 (3H, s), 1.54 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.3, 143.6, 135.9, 134.9, 134.6, 132.8, 129.4, 128.7, 128.4, 128.2, 128.1, 127.8, 127.4, 109.3, 107.2, 54.4, 21.6, 20.0; IR (KBr, cm^{-1}): 3441, 2923, 1488, 1337, 1164, 1090, 673, 549; HRMS (m/z) Calcd for $C_{25}H_{24}ClNNaO_2S$ (M + Na)$^+$: 460.1114, Found: 460.1108.

3l Yield: 93%. Solid, mp: 119–121 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (2H, d, J = 8.4 Hz), 7.21–7.34 (9H, m), 6.81 (2H, d, J = 8.8 Hz), 4.46 (2H, s), 3.77 (3H, s), 2.45 (3H, s), 1.84–1.98 (4H, m), 1.47–1.59 (4H, m), 1.28–1.35 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.9, 158.8, 143.4, 136.3, 134.6, 129.4, 128.8, 128.7, 128.3, 128.2, 127.6, 127.3, 113.5, 113.4, 109.5, 55.3, 54.5, 31.1, 27.5, 25.7, 21.6; IR (KBr, cm^{-1}): 3447, 2926, 2914, 1606, 1510, 1342, 1159, 1038; HRMS (m/z) Calcd for $C_{29}H_{31}NNaO_3S$ (M + Na)$^+$: 496.1922, Found: 496.1918.

4 Yield: 75%. Solid, mp: 109–111 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (2H, d, J = 8.4 Hz), 7.22–7.31 (7H, m), 7.05–7.08 (2H, m), 6.70–6.78 (2H, m), 5.05 (1H, s), 4.59 (2H, s), 2.43 (3H, s), 1.27 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.5, 143.8, 135.63, 135.57, 131.8, 131.4, 129.8, 129.5, 129.4, 128.3, 128.1, 128.0, 124.0, 120.6, 119.9, 116.4, 76.6, 53.9, 27.2, 21.6; IR (KBr, cm^{-1}): 3447, 2972, 1637, 1451, 1352, 1163, 760, 661; HRMS (m/z) Calcd for $C_{25}H_{25}NNaO_3S$ (M + Na)$^+$: 442.1453, Found: 442.1447.

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Notes and references

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16 Amides such as *N*-benzylbenzamide and *N*-phenylacetamide did not give any 3-alkoxycarbonyloxy yne-amides.

17 Crystal data for **2a**: $C_{21}H_{23}NO_5S$, MW = 401.46, triclinic, space group $P\bar{1}$, final *R* indices [$I > 2\sigma(I)$], $R_1 = 0.0510$, w$R_2 = 0.1459$; *R* indices (all data), $R_1 = 0.1179$, w$R_2 = 0.1939$; $a = 10.8478(12)$ Å, $b = 11.5786(13)$ Å, $c = 17.841(2)$ Å, $\alpha = 80.352(2)$, $\beta = 80.707(2)$, $\gamma = 76.854(2)$, $V = 2133.5(4)$ Å^3, $T = 296(2)$ K, $Z = 4$. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Centre, CCDC 898714.

18 Crystal data for **3e**: $C_{48}H_{48}N_2O_7S_2$, MW = 829.00, triclinic, space group $P\bar{1}$, final *R* indices [$I > 2\sigma(I)$], $R_1 = 0.0481$, w$R_2 = 0.1476$; *R* indices (all data), $R_1 = 0.0620$, w$R_2 = 0.1682$; $a = 10.1299(6)$ Å, $b = 15.3763(9)$ Å, $c = 15.9530(9)$ Å, $\alpha = 61.7910(10)$, $\beta = 76.5350(10)$, $\gamma = 86.7540(10)$, $V = 2125.4(2)$ Å^3, $T = 296(2)$ K, $Z = 2$. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Centre, CCDC 898715.