EurJOC
European Journal of Organic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Synthesis of 2-(1,2,3-Triazolyl)benzamide Derivatives via Copper(I)-Catalyzed Multicomponent Reaction

Authors: Juthanat Kaeobamrung, Abdulhakim Hayeebueraheng, Benyapa Kaewmee, and Vatcharin Rukachaisirikul

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201701316

Link to VoR: http://dx.doi.org/10.1002/ejoc.201701316

Supported by
ACES Asian Chemical Editorial Society

WILEY-VCH

10.1002/ejoc.201701316

WILEY-VCH

Synthesis of 2-(1,2,3-Triazolyl)benzamide Derivatives via Copper(I)-Catalyzed Multicomponent Reaction

Abdulhakim Hayeebueraheng, Benyapa Kaewmee, Vatcharin Rukachaisirikul and Juthanat Kaeobamrung*

Dedication ((optional))

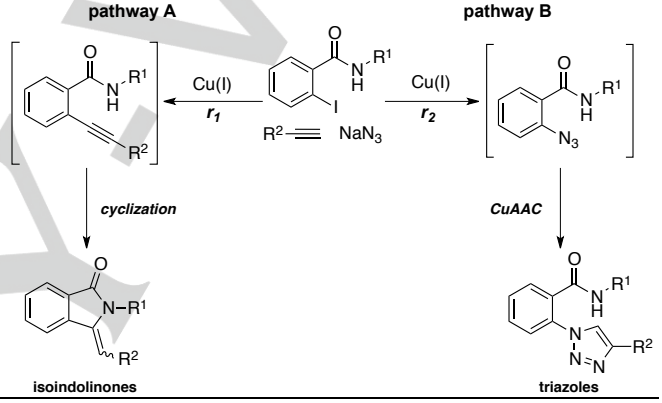
Abstract: The copper-catalyzed multicomponent reaction of 2-iodobenzamides, NaN_3 and terminal alkynes for the synthesis of 2-(1,2,3,-triazolyl)benzamide derivatives was achieved in a one-step process and short period of time under mild reaction condition. The transformations consisted of C(aryl)-N bond formation and azide-alkyne cycloadditon. The absence of an external base was found to be crucial in determining the preferred reaction pathway.

Introduction

Multicomponent reactions (MCRs) have been received a great attention from synthetic chemists because they allow us to access to both diversity and complexity of organic molecules from simple starting materials in a single reaction step. With adequate reaction designs, a very high level of efficiency can be obtained while avoiding isolation and purification of reaction intermediates. Moreover, unstable reactive intermediate can also be incorporated in MCRs.[1]

1,4-Disubstituted 1,2,3-triazoles are one of the important heterocyclic molecules. They show a vast spectrum of biological properties.[2] Furthermore, they also display unique properties in chemical and material sciences.[3] Due to their wide range of utilities, the methodologies in synthesis of this class of molecules have been consistently developed especially after the classical copper-catalyzed azide-alkyne cycloaddition (CuAAC) was independently introduced by Sharpless and Meldal.[4] But to our knowledge, only a few examples of copper-catalyzed multicomponent reactions for the synthesis of 1,4-disubstituted 1,2,3-triazoles have been reported especially from arylhalides, NaN_3 and alkynes due to unstable aryl azides. However, an elegant Cu-catalyzed MCRs was introduced by the Huang and Wen research groups in 2014.[5] They utilized a diaryliodonium, NaN_3 and terminal alkynes to construct the triazolophenanthridines core structures under mild reaction conditions. Fokin and co-workers reported the synthesis of 1,4-disubstituted 1,2,3-triazoles via copper-catalyzed one-pot reactions of aryliodides, NaN_3 and terminal alkynes.[6] In their case, pure products were obtained from filtration. However, stirring reaction overnight was required. Recently, Jiang and Zhang groups achieved 1,4-disubstituted 1,2,3-triazoles in a short period of reaction time via a two-step reaction process proceeding in one-pot.[7] Their protocol relied on the combination of CuI and DBU to catalyze reaction of aryliodides, NaN_3 and terminal alkynes.

Scheme 1. Possible reaction pathways of copper-catalyzed MCR



The copper-catalyzed MCR of aryliodides, NaN_3 and terminal alkynes for the synthesis of 1,4-disubstituted 1,2,3-triazoles with one-step reaction in short period of time still remained a challenge task. Therefore, we alternatively envision that 2-iodobenzamides would serve as a good aryliodide for the copper-catalyzed MCR with NaN_3 and terminal alkynes. The 2-iodobenzamides have often been used in copper-catalyzed coupling reactions with various coupling partners because the secondary amide moiety functions as a directing group, coordinating to the copper catalyst and allowing the coupling to occur smoothly and rapidly.[8] Significantly, 2-iodobenzamides were also known to react efficiently with terminal alkynes via copper-catalyzed domino process to form the corresponding isoindolinones[9] (Scheme 1, pathway A). We wish to explore whether we could develop the copper-catalyzed MCR in which 2-iodobenzamides first reacted with NaN_3 to form the arylazide intermediates. With the terminal alkynes remaining in the reaction, CuAAC followed to achieve 1,4-disubstituted 1,2,3-triazoles (Scheme 1, pathway B). Herein, we demonstrate a copper-catalyzed multicomponent domino reaction of 2-iodobenzamides, NaN_3 and terminal alkynes to obtain 2-(1,2,3-triazolyl)benzamides under simple preparation and mild reaction condition.

Results and Discussion

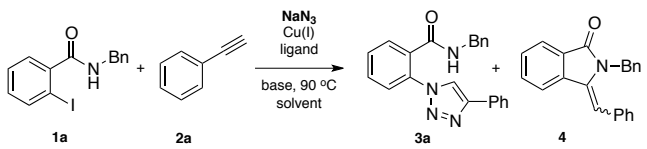
We began our investigation by selecting the reaction of *N*-

[a] Department of Chemistry and Center of Excellence for Innovation in Chemistry,
Prince of Songkla University
15 Kanjanavanit Road, Kohong, Hat-Yai, Songkhla 90112, Thailand
E-mail: juthanat.k@psu.ac.th

Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate))

benzyl-2-iodobenzamide, NaN_3 and phenylacetylene as our reaction model.

Table 1. Optimization reactions of triazole formation[a]



entry	Cu	ligand	base	solvent	yield[b]
1	CuBr	DMEDA	Cs_2CO_3	DMSO	trace[c]
2	CuBr	1,10-phenanthroline	Cs_2CO_3	DMSO	trace
3	CuBr	1,2-diaminocyclohexane	Cs_2CO_3	DMSO	35[d](52)[e]
4	CuBr	L-proline	Cs_2CO_3	DMSO	44 (39)
5	CuBr	2,2'-bipyridine	Cs_2CO_3	DMSO	trace
6	CuBr	picolinic acid	Cs_2CO_3	DMSO	trace
7	CuBr	-	Cs_2CO_3	DMSO	trace
8	CuBr	L-proline	K_3PO_4	DMSO	32 (38)
9	CuBr	L-proline	K_2CO_3	DMSO	43 (31)
10	CuBr	L-proline	$NaHCO_3$	DMSO	66 (22)
11	CuBr	L-proline	-	DMSO	66 (12)
12	CuI	L-proline	-	DMSO	61 (14)
13	Cu_2O	L-proline	-	DMSO	53 (9)
14	$Cu(OAc)_2$	L-proline	-	DMSO	49 (10)
15	CuBr	L-proline	-	DMF	57 (9)
16	CuBr	L-proline	-	MeCN	39 (15)
17	CuBr	L-proline	-	DMSO:H_2O (2:1)	73 (8)
18	CuBr	L-proline	-	DMSO:H_2O (2:1) (0.4M)	82 (5)
19	CuBr	L-proline	-	DMSO:H_2O (2:1) (1.0M)	70 (trace)
20	CuBr	L-proline	-	DMSO:H_2O (1:1) (1.0M)	63 (trace)

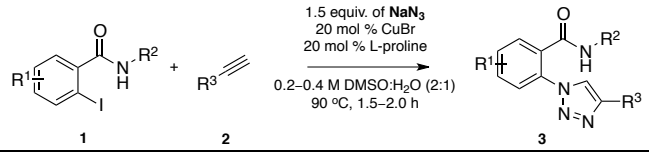
[a]Reaction conditions: all reactions were performed with 0.5 mmol of **1a**, 20 mol % of Cu salt, 1.5 equiv. of sodium azide and 1.5 equiv. of **2a** in 0.2 M of solvent for 1.5 h under air in a sealed tube. [b]Isolated yield. [c]Integration of ^{1}H NMR of the crude reaction mixture. [d]Yield of triazole. [e]Yield of isoindolinone.

A variety of common ligands, such as DMEDA, 1,10-phenanthroline, 1,2-diaminocyclohexane, L-proline, 2,2'-bipyridine, picolinic acid and no ligand were explored (entries 1–7). We found that 1,2-diaminocyclohexane and L-proline were two ligands that gave the desired triazole product in 35% and 44%. However, both reactions also gave the isoindolinone side-product in 52% and 39%, respectively (entries 3 and 4). L-proline was selected as a ligand for the reaction. Next, we tried to reduce the formation of the isoindolinone byproduct. Therefore, we considered the two reaction pathways for the formation of desired triazole **3a** and undesired isoindolinone **4** (Scheme 1).[10] We found that two factors had to be considered in order to increase the yield of **3a**. The first was that the rate ($\mathbf{r_1}$) of isoindolinone formation had to be decreased. The second was increasing the rate ($\mathbf{r_2}$) of azidation. With these in mind, we hypothesized that the formation of Cu(I) acetylene complex could be slowed by using weak base, resulting in the decrease of $\mathbf{r_1}$. Consequently, a variety of weak bases, such as K_3PO_4, K_2CO_3, $NaHCO_3$ and no base were added to the reaction. K_3PO_4 gave **3a** and **4** in 32% and 38% (entry 8). Similar result was found with K_2CO_3, 43% and 31% of **3a** and **4**, respectively (entry 9). Delightfully, the yield of **3a** was dramatically increased when $NaHCO_3$ was used. The reaction gave 66% of **3a** and 22% of **4** (entry 10). Surprisingly, with no base the reaction occurred smoothly to give the same yield 66% of **3a**, and the yield of **4** was diminished to 12% (entry 11). The results suggested that with no base the isoindolinone pathway was greatly decreased, allowing the azidation to predominate. The common copper salt was also one of our variables. CuI, Cu_2O and $Cu(OAc)_2$ were individually subjected to the reaction, resulting the triazole in 61%, 53% and 49% respectively (entries 12–14). Others common polar solvents were also subjected to our optimization. DMF gave quite moderate yield of triazole, 57% (entry 15). Low yield of triazole, 39%, was observed when MeCN was used (entry 16). Next, we try to increase the rate of azidation reaction by increasing a solubility of NaN_3 (Scheme 1). We found that the yield of triazole significantly increased to 73% with 2:1 ratio of DMSO and H_2O (entry 17). The yield was slightly increased to 82% when we increased the molarity of reaction to 0.4 M (entry 18). However, with 1.0 M of reaction concentration the yield diminished to 70% (entry 19). An attempt to increase product yield with high concentration by changing the ratio of solvents to 1:1 DMSO:H_2O failed. These results suggested that the solubility was crucial in our reaction. This condition led to 63% yield of the triazole (entry 20). It is worth noting that 20 mol % of CuBr was required in order to give the best product yield and avoid the formation of aniline byproduct.

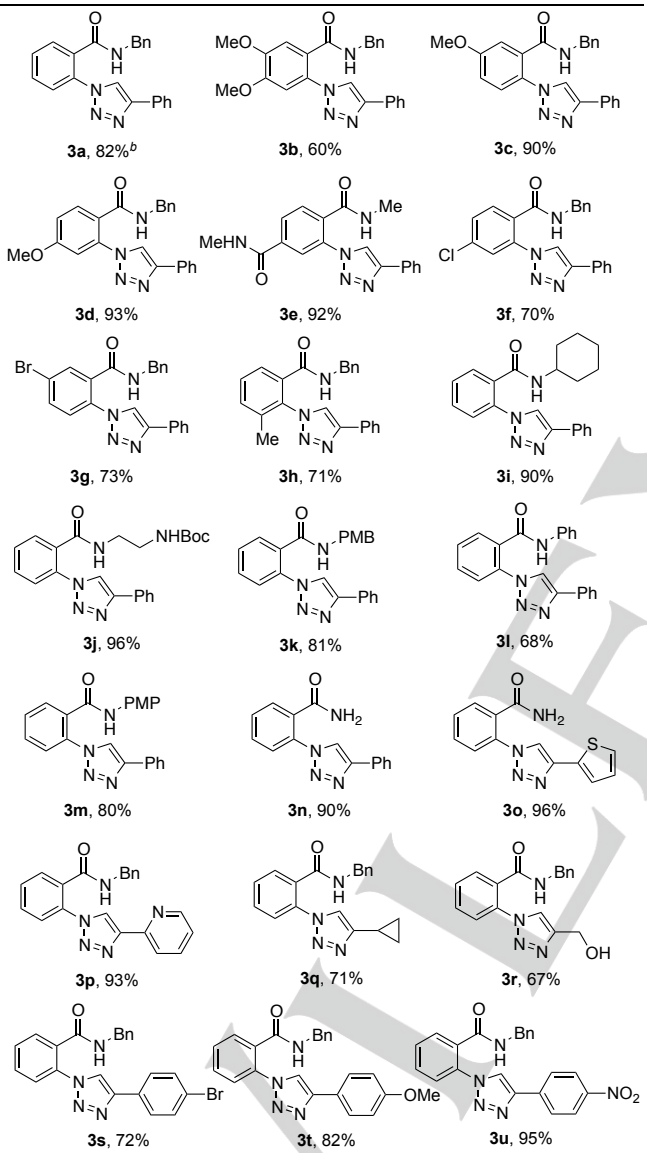
With our established optimal conditions, we next explored the scope of 2-iodobenzamides and terminal alkynes for the synthesis of 2-(1,2,3-triazolyl)benzamide derivatives (Table 2). It was found that 2-iodobenzamides bearing both electron-donating and electron-withdrawing groups were applicable in this reaction. However, the reaction of benzamides bearing two methoxy substituents gave a moderate yield, 60% (**3b**). Different result was found with one methoxy substituent. The reaction of 2-iodo-5-methoxybenzamide resulted in an excellent yield, 90% (**3c**). Likewise, the triazole was obtained in 93% from 2-iodo-4-methoxybenzamide (**3d**). These results suggested that the level of electron density of 2-iodobenzamides partially impacted the reaction. Having another amide functionality on the benzamide provided high yield, 92% (**3e**). 2-Iodobenzamides with halide atom were also compatible with the reaction yielding the triazoles in 70% and 73% yields from chlorine and bromine respectively (**3f** and **3g**). Steric environment near the iodine atom affected the reaction, resulting product in 71% yield from 2-iodo-3-methylbenzamide (**3h**). Other substituents on nitrogen of amides were also subjected into our substrate scope. With alkyl substituents, the reactions provided good to excellent yields of triazoles (**3a**, **3i**, **3j** and **3k**). The yield was significantly diminished to 68% when the *N*-phenyl benzamides was used (**3l**). On the other hand, increasing electron density by introducing a methoxy substituent resulted in the product yield of 80% for the reaction of *N*-(4-methoxyphenyl)benzamide (**3m**).

Based on these results, the Lewis basicity of nitrogen amide must have played a role in the reaction. The excellent yield of triazole, 90%, was obtained from the reaction of naked amide (**3n**).

Table 2. The synthesis of 2-(1,2,3-triazolyl)benzamide derivatives[a]



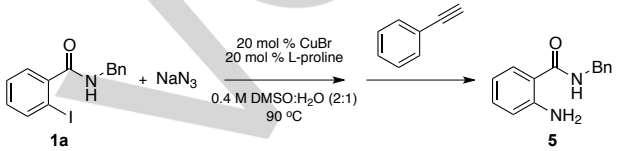
1 2 3



[a]Reaction conditions: 0.5 mmol of **1** and 1.5 equiv. of **2** under air in a sealed tube. [b]Isolated yield.

Our multicomponent reaction was also applicable to a variety of terminal alkynes including aryl or alkyl. It is worth to note that heterocycle-tethered acetylenes (2-thiophene and 2-pyridine moieties) provided excellent yields, 96% and 93%, respectively (**3o** and **3p**). Good yield of trizole, 71%, was obtained from ethynylcyclopropane (**3q**). Satisfactorily, the reaction of unprotected alcohol gave desired triazole in good yield, 67% (**3r**). High to excellent yields of triazoles were obtained from bromo, methoxy and nitro substituents (**3s**, **3t** and **3u**). In short, a broad range of substituents of phenylacetylene was suitable in our reaction.

Interestingly, we found that the desired triazole was not obtained when the reaction was carried out via two-step procedure in one-pot manner by adding phenylacetylene after 2-iodobenzamide was completely consumed (monitoring by thin layer chromatography). The result suggested that the generated aryl azide decomposed to a corresponding amine in the presence of copper under our reaction condition prior to undergoing CuAAC with phenylacetylene (Scheme 2).

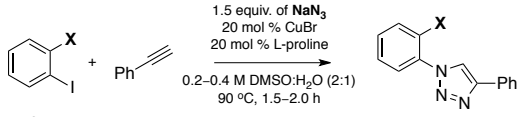


1a 5

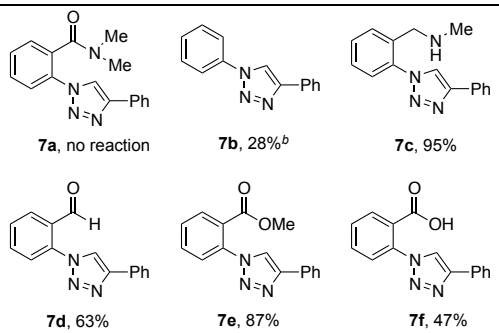
Scheme 2. Two-step process reaction in one-pot manner

The generations of aniline from NaN_3 and aryl halide derivatives in the presence of copper salt have been reported by several research groups; for example, Li and Chen research groups took this phenomenon to synthesize quinazolinones[11] from 2-iodobenzamide, NaN_3 and aldehydes. Singh and co-worker utilized the *in-situ* generated 2-aminobenzaldehydes from 2-bromobenzaldehydes and NaN_3 followed by condensation reaction to achieve the corresponding quinolines in multicomponent manner.[12] Our finding emphasized one of the greatest aspects of multicomponent reactions: the utilization of unstable intermediate.

Table 3. 1,2,3-Triazoles formation from other directing groups[a]



6 7



[a]Reaction conditions: 0.5 mmol of **6** and 1.5 equiv. of phenylacetylene under air in a sealed tube. [b]Isolated yield.

Next, we explored other functional groups *ortho* to the iodine (Table 3). Although we did not exhaustively explore all the functionalities, we have found that the directing group

significantly affected our copper-catalyzed multicomponent reaction. Firstly, when we modified the 2-iodobenzamide from secondary amide to tertiary amide, no reaction occurred. We observed only the amide starting material from the ^{1}H NMR spectrum of the crude reaction mixture (**7a**). Presumably, the weaker coordination ability and steric hindrance of the tertiary amide obstructed our reaction. Without any directing group, the reaction of iodobenzene provided the triazole in low yield, 28% (**7b**). An excellent yield, 95%, was obtained when having secondary amine as directing group (**7c**). The aldehyde functionality was also applicable to the reaction. The reaction of 2-iodobenzaldehye gave moderate yield, 63% (**7d**). Fortunately, the ester group provided a high yield of the corresponding triazole in 87% (**7e**). These results significantly suggested that the level of Lewis basicity crucially impacted the multicomponent reaction. On the other hand, having the acid functionality diminished the yield of product to 47% (**7f**).

Conclusions

We have demonstrated a simple and efficient protocol to synthesize 2-(1,2,3-triazolyl)benzamides under mild reaction condition and in short period of time. Our multicomponent catalytic procedure offers an alternative tool for utilizing aryl azides to form corresponding triazoles via a one-pot click-reaction without the need of purification of the intermediary and semi-stable aryl azides. The solubility of sodium azide and also the absence of an external base tremendously shift the reaction paradigm to the desired triazole formations by increasing the rate of copper-catalyzed azide coupling over that of terminal alkyne coupling. Furthermore, the concentration of our reaction and the Cu catalyst loading also played a crucial role to carry out the click-reaction over the generation of side-product aromatic amines from the *in situ* generated azides.

Experimental Section

General Information. Commercially available reagents and solvents for reactions, analytical reagent (AR.) grade, were used without purification from commercial source. Solvents for extraction and column chromatography were distilled at their boiling point ranges prior to use. Thin-layer chromatography (TLC) was performed on silica gel 60 GF_{254} (Merck) and were visualized by fluorescence quenching under UV light. Column chromatography was performed on SiliaFlash® G60 (70-230 Mesh). ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were recorded on a 300 MHz Bruker FTNMR Ultra Shield spectrometer using tetramethylsilane (TMS) as an internal standard. Chemical shifts are expressed in parts per million (ppm) downfield from TMS (δ 0.00) and coupling constants are reported as Hertz (Hz). Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; m, multiplet. High-resolution mass spectra (HRMS) were recorded in ESI mode using TOF mass spectrometer. Infrared spectra (IR) were measured on a Perkin Elmer Spectrum GX FT-IR system and recorded on wavenumber (cm^{-1}).

Synthesis of Starting Materials. 2-Iodobenzamides were prepared according to the literature procedure.[13] A flame-dried round bottom flask was charged with 1.0 equiv of 2- iodobenzoic acid in CH_2Cl_2 (0.3 M) and DMF (2 drops), followed by the addition of 1.25 equiv of oxalyl chloride at 0 ºC. The reaction mixture was allowed to stir at room temperature for 4 h. After that, the mixture was evaporated to dryness. The prepared acid chloride was dissolved in CH_2Cl_2 (0.3 M). The solution of benzylamine (1.5 equiv) and triethylamine (3.0 equiv) was added at 0 ºC. The reaction mixture was allowed to stir at room temperature for 15 h. The reaction mixture was quenched with sat. NH_4Cl and extracted with CH_2Cl_2. The organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography.

General Procedure for the Synthesis of 2-(1,2,3-triazolyl)benzamide derivatives. A dried flask was charged with 2-iodobenzamide (**1a**) (0.5 mmol), commercially available phenylacetylene (0.75 mmol), sodium azide (0.75 mmol), CuBr 20 mol%, and L-proline 20 mol% in DMSO:H_2O (1.7:0.8 mL). The reaction mixture was allowed to stir at 90 °C for 2 h. After completion of reaction, the reaction mixture was cooled to room temperature. Quenched with saturated NH_4Cl, extracted with EtOAc and washed with brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to afford crude residue. The desired product was isolated by column chromatography over silica gel using ethyl acetate/hexanes as eluent.

^{1}H and ^{13}C Spectral Data of the new 2-iodobenzamides.

***N*-Benzyl-2-iodo-5-methoxybenzamide (1c).** Prepared according to the synthesis of starting material. Yield: 75%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 4.4 Hz, 1H), 7.42–7.30 (m, 5H), 7.00 (d, *J* = 1.5 Hz, 1H), 6.69 (dd, *J* = 1.5, 4.4 Hz, 1H), 6.03 (brs, 1H), 4.65 (d, *J* = 2.8 Hz, 2H), 3.79 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.0, 159.6, 144.1, 140.5, 139.5, 128.7, 127.9, 127.3, 117.4, 114.7, 82.3, 56.0, 43.0; IR (thin film) v 3855, 3736, 2958, 2862, 2343, 1698, 1522, 1053 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. for $C_{15}H_{14}INO_2$ 389.9967, found 390.0021.

2-Iodo-*N*^{1},*N*^{4}-dimethylterephthalamide (1e) Prepared according to the synthesis of starting material. Yield: 85%. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.58 (d, *J* = 3.0 Hz, 1H), 8.34 (d, *J* = 3.0 Hz, 1H), 8.26 (s, 1H), 7.83 (d, *J* = 9.0 Hz), 7.36 (d, *J* = 9.0 Hz), 2.76–2.73 (m, 6H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.4, 165.0, 145.8, 137.9, 136.5, 128.2, 127.2, 94.0, 26.8, 26.5; IR (thin film) v 3850, 3736, 3275, 2963, 2343, 1648, 1542 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. For $C_{10}H_{11}IN_2O_2$ 340.9763, found 340.9762.

***tert*-Butyl-2-(2-iodobenzamido)ethylcarbamate (1j).** Prepared according to the synthesis of starting material. Yield: 88%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.9 Hz, 1H), 7.37–7.27 (m, 2H), 7.10–7.05 (m, 1H), 6.59 (brs, 1H), 5.11 (brs, 1H), 3.58–3.52 (m, 2H), 3.41–3.38 (m, 2H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 156.8, 142.0, 139.8, 131.1, 128.1, 128.0, 92.5, 79.8, 40.9, 40.1, 28.4; IR (thin film) v 3318, 2976, 2930, 1693, 1640, 1253, 1015, 751 cm^{-1}; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{14}H_{19}IN_2O_3$ 413.0338, found 413.0338.

^{1}H and ^{13}C Spectral Data of the Products.

***N*-Benzyl-2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzamide (3a)**. Prepared according to general procedure from *N*-benzyl-2-iodobenzamide[13] (**1a**) and phenylacetylene (**2a**). Yield 145.3 mg (82%) as light yellow solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.93 (t, *J* = 5.8 Hz, 1H), 8.70 (s, 1H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.59–7.52 (m, 4H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.26 (t, *J* = 7.1 Hz, 1H), 7.11–7.06 (m, 5H), 4.23 (d, *J* = 5.8 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.6, 146.9, 139.4, 134.6, 133.5, 131.2, 130.9, 130.1, 129.4, 129.3, 128.6 (128.64), 128.6 (128.56), 127.2, 126.1, 125.8, 123.2,

42.9; IR (thin film) v 3409, 2940, 2838, 1654, 1644, 1414, 1022 cm^{-1}. HRMS (ESI) $[M+H]^+$ calcd. for $C_{22}H_{18}N_4O$ 355.1559, found 355.1558.

***N*-Benzyl-4,5-dimethoxy-2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzamide (3b).** Prepared according to general procedure from *N*-benzyl-2-iodo-4,5-dimethoxybenzamide[8c] (**1b**) and phenylacetylene (**2a**). Yield 124.3 mg (60%) as light yellow solid. ^1H NMR (300 MHz, DMSO-d_6) δ 8.82 (t, *J* = 5.7 Hz, 1H), 8.74 (s, 1H), 7.89 (d, *J* = 7.7 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.39–7.34 (m, 1H), 7.25–7.20 (m, 7H), 4.31 (d, *J* = 5.7 Hz, 2H), 3.90 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.3, 150.3, 149.3, 146.6, 139.3, 130.8, 129.4, 128.6 (128.64), 128.6 (128.55), 128.0, 127.5, 127.2, 125.7, 125.5, 123.5, 111.7, 110.1, 56.6, 56.5, 43.0; IR (thin film) v 3775, 3033, 2892, 2746, 1588, 1039, 956 cm^{-1}. HRMS (ESI) $[M+H]^+$ calcd. for $C_{24}H_{22}N_4O_3$ 415.1770, found 415.1770.

***N*-Benzyl-5-methoxy-2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzamide (3c)**. Prepared according to general procedure from *N*-benzyl-2-iodo-5-methoxybenzamide (**1c**) and phenylacetylene (**2a**). Yield 172.9 mg (90%) as white solid. ^1H NMR (300 MHz, DMSO-d_6) δ 9.01 (t, *J* = 5.8 Hz, 1H), 8.73 (s, 1H), 7.89 (d, *J* = 8.6 Hz, 2H), 7.61 (d, *J* = 8.6 Hz, 1H), 7.49 (t, *J* = 7.3 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.26–7.18 (m, 7H), 4.33 (d, *J* = 5.8 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.2, 160.0, 146.6, 139.3, 134.8, 131.0, 129.4, 128.6, 128.5, 127.9, 127.7, 127.5, 127.2, 125.7, 123.5, 116.1, 114.4, 56.4, 42.9; IR (thin film) v 3775, 3072, 2758, 1588, 1179, 1039, 957 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. for $C_{23}H_{20}N_4O_2$ 407.1484, found 407.1484.

***N*-Benzyl-4-methoxy-2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzamide (3d)**. Prepared according to general procedure from N-benzyl-2-iodo-4-methoxybenzamide[14] (**1d**) and phenylacetylene (**2a**). 178.8 mg (93%) as white solid. ^1H NMR (300 MHz, DMSO-d_6) δ 8.90 (t, *J* = 5.7 Hz, 1H), 8.82 (s, 1H), 7.89 (d, *J* = 7.5 Hz, 2H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.40–7.35 (m, 1H), 7.26–7.22 (m, 7H), 4.31 (d, *J* = 5.7 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 161.4, 148.2, 137.2, 135.2, 130.9, 129.9, 128.9, 128.6, 128.5, 127.8, 127.5, 125.9, 124.8, 122.1, 115.9, 111.7, 55.9, 44.3; IR (thin film) v 3288, 1638, 1612, 1277, 1165, 1031 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. for $C_{23}H_{20}N_4O_2$ 407.1484, found 407.1485.

***N*^{1},*N*^{4}-Dimethyl-2-(4-phenyl-1H-1,2,3-triazol-1-yl)terephthalamide (3e)**. Prepared according to general procedure from *N*^{1},*N*^{4}-dimethyl-2-iodoterephthalamide (**1e**) and phenylacetylene (**2a**). Yield 154.3 mg (92%) as yellow solid. ^1H NMR (300 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.71 (d, *J* = 4.4 Hz, 1H), 8.51 (d, *J* = 4.4 Hz, 1H), 8.11–8.04 (m, 2H), 7.94 (d, *J* = 7.7 Hz, 2H), 7.73 (d, *J* = 7.9 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 7.40–7.36 (m, 1H), 2.82 (d, *J* = 4.4 Hz, 3H), 2.65 (d, *J* = 4.4 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.5, 165.2, 147.0, 136.8, 135.4, 134.5, 130.7, 129.6, 129.5, 128.7, 128.5, 125.8, 124.5, 123.0, 26.8, 26.5; IR (thin film) v 3776, 3073, 2884, 2746, 1588, 1169, 957 cm^{-1}. HRMS (ESI) $[M+H]^+$ calcd. $C_{18}H_{17}N_5O_2$ 336.1460, found 336.1460.

***N*-Benzyl-4-chloro-2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzamide (3f)**. Prepared according to general procedure from *N*-benzyl-4-chloro-2-iodobenzamide[8c] (**1f**) and phenylacetylene (**2a**). Yield 136.1 mg (70%) as light yellow solid. ^1H NMR (300 MHz, DMSO-d_6) δ 9.08 (t, *J* = 5.8 Hz, 1H), 8.91 (s, 1H), 7.91–7.88 (m, 3H), 7.77–7.69 (m, 2H), 7.50 (t, *J* = 7.7 Hz, 2H), 7.41–7.36 (m, 1H), 7.22–7.18 (m, 5H), 4.33 (d, *J* = 5.8 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.0,147.1, 139.0, 135.5, 135.3, 132.0, 131.0, 130.5, 130.0, 128.8, 128.7, 127.6, 127.3, 125.8, 123.1, 43.0; IR (thin film) v 3778, 3694, 3068, 2883, 1587, 1118, 951 cm^{-1}. HRMS (ESI) $[M+H]^+$ calcd. for $C_{22}H_{17}ClN_4O$ 389.1169, found 389.1169.

***N*-Benzyl-5-bromo-2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzamide (3g)**. Prepared according to general procedure from *N*-benzyl-5-bromo-2-iodobenzamide[8c] (**1g**) and phenylacetylene (**2a**). Yield 158.1 mg (73%) as white solid. ^1H NMR (300 MHz, DMSO-d_6) δ 9.15 (t, *J* = 5.8 Hz, 1H), 8.84 (s, 1H), 7.95–7.88 (m, 4H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.40–7.35 (m, 1H), 7.22–7.18 (m, 5H), 4.33 (d, *J* = 5.8 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.3, 147.1, 138.9, 134.9, 134.1, 133.7, 131.9, 130.4, 129.5, 128.8, 128.7, 128.1, 127.6, 127.3, 125.8, 123.0, 122.9, 43.1; IR (thin film) v 3790, 3090, 2879, 1599, 1128, 956 cm^{-1}. HRMS (ESI) $[M+H]^+$ calcd. for $C_{22}H_{17}BrN_4O$ 433.0664, found 433.0664.

***N*-Benzyl-3-methyl-2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzamide (3h)**. Prepared according to general procedure from *N*-benzyl-2-iodo-3-methylbenzamide[8c] (**1h**) and phenylacetylene (**2a**). Yield 130.8 mg (71%) as light yellow solid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.89–7.86 (m, 2H), 7.62–7.60 (m, 1H), 7.53–7.45 (m, 4H), 7.42–7.37 (m, 1H), 7.15–7.10 (m, 3H), 7.04–7.00 (m, 2H), 6.26 (brs, 1H), 4.29 (d, *J* = 5.8 Hz, 2H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ; 166.1, 148.1, 137.1, 136.5, 135.0, 133.0, 132.8, 130.6, 129.9, 128.9, 128.6, 128.5, 127.7, 126.9, 125.9, 122.7, 44.2, 17.4; IR (thin film) v 3776, 3697, 2884, 1588, 1169, 957 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. for $C_{23}H_{20}N_4O$ 391.1535, found 391.1535.

***N*-Cyclohexyl-2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzamide (3i)**. Prepared according to general procedure from *N*-cyclohexyl-2-iodobenzamide[15] (**1i**) and phenylacetylene (**2a**). Yield 155.9 mg (90%) as yellow solid. ^1H NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.85 (d, *J* = 7.7 Hz, 2H), 7.70–7.68 (m, 1H), 7.58–7.53 (m, 3H), 7.47–7.42 (m, 2H), 7.39–7.34 (m, 1H), 5.97 (d, *J* = 7.6 Hz, 1H), 3.77–3.74 (m, 1H), 1.75–1.71 (m, 2H), 1.58–1.48 (m, 2H), 1.31–1.19 (m, 3H), 1.09–0.91 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 148.1, 133.8, 133.4, 130.8, 130.1, 130.0, 129.3, 128.9, 128.5, 126.2, 125.9, 122.1, 48.9, 32.4, 25.3, 24.6; IR (thin film) v 3776, 3697, 3073, 2888, 1588, 1162, 956 cm^{-1}. HRMS (ESI) $[M+H]^+$ calcd. for $C_{21}H_{22}N_4O$ 347.1872, found 347.1872.

***tert*-Butyl-2-(2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzamido)ethylcarbamate (3j)**. Prepared according to general procedure from *tert*-butyl 2-(2-iodobenzamido)ethylcarbamate (**1j**) and phenylacetylene (**2a**). Yield 195.6 mg (96%) as yellow solid. ^1H NMR (300 MHz, DMSO-d_6) δ 8.87 (s, 1H), 8.52 (brs, 1H), 7.92 (d, *J* = 7.6 Hz, 2H), 7.67–7.64 (m, 4H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.38–7.33 (m, 1H), 6.78 (brs, 1H), 3.13–3.09 (m, 2H), 3.00–2.98 (m, 2H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.6, 156.1, 146.9, 134.6, 133.3, 131.2, 130.9, 129.9, 129.4, 128.5, 125.9, 125.8, 123.1, 78.2, 28.8; IR (thin film) v 3776, 3158, 2840, 1598, 1111, 964 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. for $C_{22}H_{25}N_5O_2$ 430.1855, found 430.2070.

***N*-(4-Methoxybenzyl)-2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzamide (3k)**. Prepared according to general procedure from 2-iodo-*N*-(4-methoxybenzyl)benzamide[16] (**1k**) and phenylacetylene (**2a**). Yield 155.7 mg (81%) as pale solid. ^1H NMR (300 MHz, DMSO-d_6) δ 8.94 (t, *J* = 5.7 Hz, 1H), 8.77 (s, 1H), 7.88 (d, *J* = 7.6 Hz, 2H), 7.68–7.65 (m, 4H), 7.48 (t, *J* = 7.4 Hz, 2H), 7.39–7.36 (m, 1H), 7.09 (d, *J* = 8.4 Hz, 2H), 6.73 (d, *J* = 8.4 Hz, 2H), 4.24 (d, *J* = 5.7 Hz, 2H), 3.65 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 159.0, 148.1, 133.9, 132.9, 131.1, 130.1, 130.0, 129.3, 129.1, 128.9, 128.5, 126.3, 125.9, 122.0, 114.0, 55.1, 43.7; IR (thin film) v 3775, 3073, 2888, 1588, 1162, 1040, 956 cm^{-1}. HRMS (ESI) $[M+H]^+$ calcd. For $C_{23}H_{20}N_4O_2$ 385.1665, found 385.1664.

***N*-Phenyl-2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzamide (3l)**. Prepared according to general procedure from 2-iodo-*N*-phenylbenzamide[8c] (**1l**) and phenylacetylene (**2a**). Yield 115.7 mg (68%) as white solid. ^1H NMR (300 MHz, $CDCl_3$) δ 8.20 (brs, 1H), 8.13 (s, 1H), 7.85–7.78 (m, 3H), 7.61–7.58 (m, 2H), 7.55–7.50 (m, 1H), 7.44–7.34 (m, 5H), 7.27–7.22 (m,

2H), 7.10–7.05 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 138.2, 134.2, 133.0, 130.7, 130.1, 129.5, 129.1, 128.7, 125.7, 125.4, 124.3, 121.6, 120.3; IR (thin film) ν 3776, 3639, 3074, 2884, 1588, 1118, 964 cm^{-1}. HRMS (ESI) $[M+H]^+$ calcd. For $C_{21}H_{16}N_4O$ 341.1402, found 341.1402.

***N*-(4-Methoxyphenyl)-2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzamide (3m)**. Prepared according to general procedure from 2-iodo-*N*-(4-methoxyphenyl)benzamide[17] (**1m**) and phenylacetylene (**2a**). Yield 148.2 mg (80%) as white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.93–7.83 (m, 4H), 7.67–7.57 (m, 3H), 7.48–7.43 (m, 2H), 7.40–7.30 (m, 3H), 6.81 (d, *J* = 9.0 Hz, 2H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 156.7, 148.2, 133.9, 132.8, 131.2, 130.5, 129.9, 129.4, 128.9, 128.5, 125.9, 122.3, 121.9, 114.0, 55.4; IR (thin film) ν 3736, 2343, 1648, 1603, 1509, 1234, 1032 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. For $C_{22}H_{18}N_4O_2$ 393.1327, found 393.1425.

2-(4-Phenyl-1H-1,2,3-triazol-1-yl)benzamide (3n). Prepared according to general procedure from 2-iodobenzamide[8c] (**1n**) and phenylacetylene (**2a**). Yield 118.9 mg (90%) as light yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.90–7.88 (m, 2H), 7.82–7.79 (m, 1H), 7.65–7.60 (m, 2H), 7.57–7.54 (m, 1H), 7.48–7.43 (m, 2H), 7.40–7.35 (m, 1H), 6.00 (brs, 1H), 5.69 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 148.2, 134.0, 132.0, 131.5, 129.8, 129.4, 129.0, 128.6, 126.3, 125.9, 122.0; IR (thin film) ν 3775, 3663, 3073, 2884, 1588, 1161, 956 cm^{-1}. HRMS (ESI) $[M+H]^+$ calcd. for $C_{15}H_{12}N_4O$ 265.1089, found 265.1089.

2-(4-(Thiophen-2-yl)-1H-1,2,3-triazol-1-yl)benzamide (3o). Prepared according to general procedure from 2-iodobenzamide (**1n**) and commercially available 2-ethynylthiophene. Yield 129.7 mg (96%) as brown solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.75 (s, 1H), 7.92 (brs, 1H), 7.67–7.65 (m, 4H), 7.56 (d, *J* = 5.0 Hz, 1H), 7.49 (d, *J* = 3.5 Hz, 1H), 7.46 (brs, 1H), 7.16–7.14 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.3, 142.2, 134.3, 133.8, 133.1, 131.1, 130.2, 129.2, 128.4, 126.2, 124.9, 122.5; IR (thin film) ν 3775, 3696, 3072, 2892, 2746, 1588, 956 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. for $C_{13}H_{10}N_4OS$ 293.0473, found 293.0472.

***N*-Benzyl-2-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)benzamide (3p)**. Prepared according to general procedure from from *N*-benzyl-2-iodobenzamide (**1a**) and commercially available 2-ethynylpyridine. Yield 165.2 mg (93%) as brown solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.03 (t, *J* = 5.8 Hz, 1H), 8.82 (s, 1H), 8.64 (d, *J* = 4.1 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.95 (t, *J* = 7.5 Hz, 1H), 7.73–7.67 (m, 4H), 7.40 (t, *J* = 5.1 Hz, 1H), 7.18–7.15 (m, 5H), 4.33 (d, *J* = 5.8 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.6, 150.2, 150.1, 147.8, 139.3, 137.8, 134.4, 133.5, 131.2, 130.3, 129.3, 128.6, 127.6, 127.2, 126.3, 124.9, 123.7, 120.2, 42.9; IR (thin film) ν 3775, 3697, 3052, 2884, 2760, 1588, 956 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. for $C_{21}H_{17}N_5O$ 378.1331, found 378.1332.

***N*-Benzyl-2-(4-cyclopropyl-1H-1,2,3-triazol-1-yl)benzamide (3q)**. Prepared according to general procedure from N-benzyl-2-iodobenzamide (**1a**) and commercially available 2-ethynylpyridine. Yield 113.0 mg (71%) as white solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.96 (t, *J* = 5.7 Hz, 1H), 8.01 (s, 1H), 7.64–7.55 (m, 4H), 7.33–7.20 (m, 5H), 4.32 (d, *J* = 5.7 Hz, 2H), 2.01–1.92 (m, 1H), 0.97–0.91 (m, 2H), 0.78–0.73 (m, 2H); ^{13}C NMR (75 MHz,$CDCl_3$) δ 166.3, 150.7, 137.2, 134.1, 132.7, 131.0, 129.9, 129.3, 128.7, 127.8, 127.6, 126.3, 122.2, 44.2, 8.0, 6.6,; IR (thin film) ν 3724 2966 2866 2360 1665 1522 1053 1031cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. For $C_{19}H_{18}N_4O$ 341.1378, found 341.1377.

***N*-Benzyl-2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)benzamide (3r)**. Prepared according to general procedure from *N*-benzyl-2-iodobenzamide (**1a**) and commercially available prop-2-yn-1-ol. Yield 103.3 mg (67%) as light yellow solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.90 (t, *J* = 5.8 Hz, 1H), 8.17 (s, 1H), 7.68–7.59 (m, 4H), 7.33–7.28 (m, 2H), 7.25–7.21 (m, 3H), 5.32 (t, *J* = 5.6 Hz, 1H), 4.57 (d, *J* = 5.5 Hz, 2H), 4.33 (d, *J* = 5.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6) δ 166.7, 148.6, 139.2, 134.6, 133.3, 130.8, 129.5, 129.1, 128.5, 127.7, 127.1, 125.7, 124.0, 55.5, 43.1; IR (thin film) ν 3775, 3663, 3073, 2883, 1588, 1161, 956 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. for $C_{17}H_{16}N_4O_2$ 331.1171, found 331.1172.

***N*-Benzyl-2-(4-(4-bromophenyl)-1H-1,2,3-triazol-1-yl)benzamide (3s)**. Prepared according to general procedure from *N*-benzyl-2-iodobenzamide (**1a**) and commercially available 1-bromo-4-ethynylbenzene. Yield 155.9 mg (72%) as light yellow solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.06 (t, *J* = 5.8 Hz, 1H), 8.90 (s, 1H), 7.87 (d, *J* = 9.0 Hz, 2H), 7.72–7.65 (m, 6H), 7.27–7.19 (m, 5H), 4.34 (d, *J* = 5.8 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.5, 145.8, 139.4, 134.5, 133.5, 132.4, 131.2, 130.2, 130.1, 129.4, 128.6, 127.7, 127.6, 127.2, 126.2, 121.5, 42.9; IR (thin film) ν 3774, 3696, 3073, 2883, 1588, 1159, 956 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. for $C_{22}H_{17}BrN_4O$ 455.0483, found 455.0484.

2-(4-(4-Methoxyphenyl)-1H-1,2,3-triazol-1-yl)benzamide (3t). Prepared according to general procedure from *N*-benzyl-2-iodobenzamide (**1a**) and commercially available 1-ethynyl-4-methoxybenzene. Yield 157.6 mg (82%) as yellow solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.02 (t, *J* = 5.8 Hz, 1H), 8.69 (s, 1H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.67–7.63 (m, 4H), 7.20–7.17 (m, 5H), 7.04 (d, *J* = 8.4 Hz, 2H), 4.32 (d, *J* = 5.8 Hz, 2H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.7, 159.6, 146.8, 139.4, 134.7, 133.5, 131.1, 130.0, 129.3, 128.7, 127.6, 127.2, 126.0, 123.4, 122.2, 114.8, 55.7. 42.9; IR (thin film) ν 3780, 3696, 3073, 2879, 1586, 1162, 956 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. for $C_{23}H_{20}N_4O_2$ 407.1484, found 407.1484.

***N*-benzyl-2-(4-(4-nitrophenyl)-1H-1,2,3-triazol-1-yl)benzamide (3u)**. Prepared according to general procedure from *N*-benzyl-2-iodobenzamide (**1a**) and commercially available 1-ethynyl-4-nitrobenzene. Yield 189.7 mg (95%) as light yellow solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.13 (s, 1H), 9.08 (t, *J* = 5.8 Hz, 1H), 8.37 (d, *J* = 8.7 Hz, 2H), 8.18 (d, *J* = 8.7 Hz, 2H), 7.72–7.70 (m, 4H), 7.26–7.17 (m, 5H), 4.34 (d, *J* = 5.8 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.4, 147.2, 144.9, 139.4, 137.3, 134.4, 133.5, 131.3, 130.4, 129.4, 128.6, 127.6, 127.2, 126.6, 126.3, 125.4, 124.9, 42.9; IR (thin film) ν 3784, 3696, 3072, 2884, 1586, 1039, 956 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. for $C_{22}H_{17}N_5O_3$ 422.1229, found 422.1276.

1,4-Diphenyl-1H-1,2,3-triazole (7b). Prepared according to general procedure from commercially available iodobenzene and phenylacetylene (**2a**). Yield 31.0 mg (28%) as light yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.93 (d, *J* = 7.5 Hz, 2H), 7.81 (d, *J* = 7.8 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 4H), 7.39 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 129.8, 129.0, 128.8, 128.5, 125.9, 120.6, 117.6. Other data was identical to the literature values.[18]

***N*-Methyl-1-(2-(4-phenyl-1H-1,2,3-triazol-1-yl)phenyl)methanamine (7c)**. Prepared according to general procedure from 1-(2-iodophenyl)-*N*-methylmethanamine[19] and phenylacetylene. Yield 125.6 mg (95%) as yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.92 (d, *J* = 7.3, 2H), 7.59 (d, *J* = 7.2 Hz, 1H), 7.54−7.52 (m, 2H), 7.51−7.47 (m, 4H), 7.40−7.35 (m, 1H) 3.61 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.9, 136.4, 132.9, 131.9, 130.1, 129.9, 129.0, 128.9, 128.7, 128.5, 125.8, 125.4, 121.7, 50.9, 35.1; IR (thin film) ν 1498, 1228, 1033, 989, 763, 689 cm^{-1}. HRMS (ESI) $[M+H]^+$ calcd. for $C_{16}H_{16}N_4$ 265.1453, found 265.1453.

2-(4-Phenyl-1H-1,2,3-triazol-1-yl)benzaldehyde (7d). Prepared according to general procedure from 2-iodobenzaldehyde and phenylacetylene. Yield 78.5 mg (63%) as yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.20 (s, 1H), 8.13 (dd, *J* = 6.2, 1.5 Hz, 1H), 7.94–7.91 (m, 2H), 7.83–7.77 (m, 1H), 7.71–7.66 (m, 1H), 7.61–7.58 (m, 1H), 7.51–7.48 (m, 2H), 7.46–7.42 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.5, 134.7, 130.1, 129.6, 129.1, 128.8, 125.4, 121.5; IR (thin film) v 3776, 3700, 3072, 2888, 1586, 1039, 957 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. For $C_{15}H_{11}N_3O$ 272.0800, found 272.0800.

Methyl 2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzoate (7e). Prepared according to general procedure from methyl 2-iodobenzoate and phenylacetylene. Yield 121.5 mg (87%) as white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 8.02 (dd, *J* = 7.5, 1.5, 1H), 7.92 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.70–7.59 (m, 2H), 7.55 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.38 (d, *J* = 7.5 Hz, 1H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 147.6, 136.1, 132.8, 131.3, 130.3, 129.9, 128.9, 128.4, 127.6, 126.6, 126.1, 125.9, 121.4, 52.7; IR (thin film) v 3560, 3134, 2949, 1731, 1489, 1294, 1268, 1125 cm^{-1}. HRMS (ESI) $[M+Na]^+$ calcd. for $C_{16}H_{13}N_3O_2$ 302.0905, found 302.0905.

2-(4-phenyl-1H-1,2,3-triazol-1-yl)benzoic acid (7f). Prepared according to general procedure from 2-iodobenzoic acid and phenylacetylene. Yield 62.3 mg (47%) as white solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.31 (brs, 1H). 9.00 (s, 1H), 7.94 (m, 3H), 7.78 (m, 1H), 7.70 (t, *J* = 3.8 Hz, 2H), 7.48 (t, *J* = 3.8 Hz, 2H), 7.37 (m, Hz, 1H), ^{13}C NMR (75 MHz, DMSO-d_6) δ 167.0, 146.8, 136.0, 133.0, 131.0, 130.9, 130.5, 129.5, 129.1, 128.5, 127.8, 125.4, 123.5. Other data was identical to the literature values.[18]

Acknowledgements ((optional))

This work was supported by the Thailand Research Fund for a research grant (MRG5980246). Further support was generously provided by The Center of Excellence for Innovation in Chemistry (PERCH-CIC) for A. H.. B. K. also is a graduate fellow of Development of Science and Technology Talents Project (DPST). We also thank Dr. Jessada Mahatthananchai for helpful discussions.

Keywords: Multicomponent reactions • Copper-catalyzed azide-alkynes cycloadditon • 1,2,3-Triazole • C-N bond formation • click chemistry

[1] For selected reviews, see: (a) de Graaff, C.; Ruijter, E.; Orru, R. V. A. *Chem. Soc. Rev.* **2012**, *41*, 3969; (b) Dömling, A.; Ugi, I. *Angew. Chem. Int. Ed.* **2000**, *39*, 3168; (c) Touré, B. B.; Hall, D. G. *Chem. Rev.* **2009**, *109*, 4439; (d) Granem, B. *Acc. Chem. Res.*, **2009**, *42*, 463; (e) Tietze, L. F.; Kinzel, T.; Brazel, C. C. *Acc. Chem. Res.* **2009**, *42*, 367; (f) Rotstein, B. H.; Zaretsky, S.; Rai, V.; Yudin, A. K. *Chem. Rev.* **2014**, *114*, 8323.

(2) (a) Tron, G. C.; Pirali, T.; Billington, R. A.; Canonico, P. L.; Sorba, G.; Genazzani, A. A. *Med. Res. Rev.* **2008**, *28*, 278; (b) Brik, A.; Alexandratos, J.; Lin, Y.-C.; Elder, J. H.; Olson, A. J.; Wlodawer, A.; Goodsell, D. S.; Wong, C.-H. *ChemBioChem* **2005**, *6*, 1; (c) Genin, M.; Allwine, D. A.; Anderson, D. J.; Barbachyn, M. R.; Emmert, D. E.; Garmon, S. A.; Graber, D. R.; Grega, D. C.; Hester, J. B.; Hutchinson, D. K.; Morris, J.; Reischer, R. J.; Ford, C. W.; Zurenko, G. E.; Hamel, J. C.; Schaadt, R. D.; Stapert, D.; Yagi, B. H. *J. Med. Chem.* **2000**, *43*, 953; (d) Kallander, L. S.; Lu, Q.; Chen, W.; Tomaszek, T.; Yang, G.; Tew, D.; Meek, T. D.; Hofmann, G. A.; Schulz-Pritchard, C. K.; Smith, W. W.; Janson, C. A.; Ryan, M. D.; Zhang, G.-F.; Johanson, K. O.; Kirkpatrick, R. B.; Ho, T. F.; Fisher, P. W.; Mattern, M. R.; Johnson, R. K.; Hansbury, M. J.; Winkler, J. D.; Ward, K. W.; Veber, D. F.; Thompson, S. K. *J. Med. Chem.* **2005**, *48*, 5644; (e) Vatmurge, N. S.; Hazra, B. G.; Pore, V. S.; Shirazi, F.; Deshpande, M. V.; Kadreppa, S.; Chattopadhyay, S.; Gonnade, R. G. *Org. Biomol. Chem.* **2008**, *6*, 3823; (f) Pedersen, D. S.; Abell, A. *Eur. J. Org. Chem.* **2011**, 2399; (g) Pokorski, J. K.; Miller Jenkins, L. M.; Feng, H.; Durell, S. R.; Bai, Y.; Appella, D. H. *Org. Lett.* **2007**, *9*, 2381; (h) Moorhouse, A. D.; Santos, A. M.; Gunaratnam, M.; Moore, M.; Neidle, S.; Moses, J. E. *J. Am. Chem. Soc.* **2006**, *128*, 15972.

(3) (a) Ryu, E.-H.; Zhao, Y. *Org. Lett.* **2005**, *7*, 1035; (b) Gill, M. V.; Arévalo M. J.; López, O. *Synthesis* **2007**, 1589; (c) Wu, P.; Malkoch, M.; Hunt, J. N.; Vestberg, R.; Kaltgrad, E.; Finn, M. G.; Fokin, V. V.; Sharpless, K. B.; Hawker, C. J. *Chem. Commun.* **2005**, *48*, 5775.

(4) (a) Hassan, S.; Müller, T. J. J. *Adv. Synth. Catal.* **2015**, *357*, 617; (b) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2001**, *40*, 2004; (c) Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057; (c) Schreiner, E.; Wilcke, T.; Müller, T. J. J. *Synlett.* **2016**, *27*, 379; (d) Barral, K.; Moorhouse, A. D., Moses, J. E. *Org. Lett.* **2007**, *9*, 1809; (e) Kacprzak, K. *Synlett* **2005**, 943.

(5) Liu, Z.; Zhu, D.; Luo, B.; Zhang, N.; Liu, Q.; Hu, Y.; Pi, R.; Huang, P.; Wen, S. *Org. Lett.* **2014**, *16*, 5600.

(6) Feldman, A. K.; Colasson, B.; Fokin, V. V. *Org. Lett.* **2004**, *6*, 3897.

(7) Jiang, Y.; Li, X.; Zhao, Y.; Jia, S.; Li, M.; Zhao, Z.; Zhang, R.; Li, W.; Zhang, W. *RSC Adv.* **2016**, *6*, 110102.

(8) For selected examples, see: (a) Diao, X.; Xu, L.; Zhu, W.; Jiang, Y.; Wang, H.; Guo, Y.; Ma, D. *Org. Lett.* **2011,** *13*, 6422; (b) Xu, W.; Jin, Y.; Liu, H.; Jiang, Y.; Fu, H. *Org. Lett.* **2011**, *13*, 1274; (c) Songsichan, T.; Promsuk, J.; Rukachaisirikul, V.; Kaeobamrung, J. *Org. Biomol. Chem.* **2014**, *12*, 4571; (d) Nozawa-Kumada, K.; Kadokawa, J.; Kameyama, T.; Kondo, Y. *Org. Lett.* **2015**, *17*, 4479; (e) Kotipalli, T.; Kavala, V.; Janreddy, D.; Bandi, V.; Kuo, C.-W.; Yao, C.-F. *Eur. J. Org. Chem.* **2016,** 1182.

(9) (a) Li, L.; Wang, M.; Zhang, X.; Jiang, Y.; Ma, D. *Org. Lett.* **2009**, *11*, 1309. (b) Zhang, L.; Zhang, Y.; Wang, X.; Shen, J. *Molecules* **2013**, *18*, 654.

(10) (a) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 51; (b) Jin, L.; Hao, W.; Xu, J.; Sun, N.; Hu, B.; Shen, Z.; Mo, W.; Hu, X. *Chem. Commun.*, **2017**, *53*, 4124; (c) Liu, L.; Wu, Y.; Wang, Z.; Zhu, J.; Zhao, Y. *J. Org. Chem.* **2014**, *79*, 6816.

(11) Li, T.; Chen, M.; Yang, L.; Xiong, Z.; Wang, Y.; Li, F.; Chen, D. *Tetrahedron* **2016**, *72*, 868.

(12) Anand, N.; Chanda, T.; Koley, S.; Chowhury, S.; Singh, M. S. *RSC Adv.* **2015**, *5*, 7654.

(13) Kitching, M. O.; Hurst, T. E.; Snieckus, V. *Angew. Chem. Int. Ed.* **2012**, *51*, 2925.

(14) Yao, B.; Wang, Q.; Zhu, J. *Angew. Chem. Int. Ed.* **2013**, *52*, 12992.

(15) Pacuta, J. A.; Scianowski, J.; Aleksandrzak, B. K. *RSC Adv.* **2014**, *4*, 48959.

(16) Iqbal, N.; Cho, J. E. *Adv. Synth. Catal.* **2015**, *357*, 2187.

(17) Miyura, T.; Hiruga, K.; Toyoshima, T.; Yamauchi, M.; Murakami, M. *Chem. Lett.* **2012**, *41*, 798.

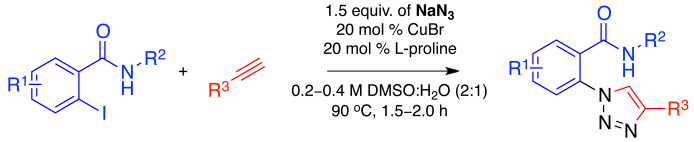
(18) Barral, K.; Moorhouse, D. A.; Moses, E. J. *Org. Lett.*, **2007**, *9*, 1809.

(19) Kihara, M.; Ikeuchi, M.; Jinno, K.; Kashimoto, M.; Kobayashi, Y.; Nagao, Y. *Tetrahedron* **1993**, *5*, 1017.

Entry for the Table of Contents (Please choose one layout)

Layout 2:

FULL PAPER



- broad substrate scope
- 21 examples; 60–90% yield
- no addition of base
- one-step process

The synthesis of 2-(1,2,3-triazolyl)benzamides was accomplished via copper(I)-catalyzed multicomponent reaction of 2-iodobenzamides, NaN_3 and terminal alkynes in short period of time. One-step reaction process in one-pot manner was required. No addition of base was crucial in determining the preferred pathway.

*A. Hayeebueraheng, B. Kaewmee, V. Rukachaisirikul, J. Kaeobamrung**

Page No. – Page No.

Title Synthesis of 2-(1,2,3-Triazolyl)benzamide Derivatives via Copper(I)-Catalyzed Multicomponent Reaction