

Combining Oxidative N-Heterocyclic Carbene Catalysis with Click Chemistry: A Facile One-Pot Approach to 1,2,3-Triazole Derivatives

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Abstract: A combination of the oxidative N-heterocyclic carbine catalysis and click chemistry has been explored for the direct, one-pot synthesis of 1,2,3-triazole derivatives from aromatic aldehydes. This procedure was found to be very efficient and a variety of 1,2,3-triazole derivatives could be accessed through their corresponding propargyl esters in moderate-to-good yields under mild conditions.

Introduction

The inimitable reactivity of N-heterocyclic carbenes (NHCs) towards carbonyl groups has led to the discovery of new organocatalytic C–C bond-forming reactions in recent years.^[1] Apart from the classic umpolung reaction,^[1,2] the potential of NHCs has been explored in redox reactions,^[3] transesterifications,^[4] cycloadditions,^[5] and CO₂-fixation reactions,^[6] as well as in combination with photoredox catalysts,^[7] cascade catalysis,^[8] and in co-operative catalysis.^[9] Recently, oxidative NHC catalysis,^[10] an interesting sub-area of NHC catalysis, was uncovered for the construction of carbon–heteroatom bonds, by employing a NHC in combination with an external oxidant. This remarkable method was successfully applied to fundamental transformations, such as esterification,^[11] amidation,^[12] and lactone-ring-formation reactions.^[13]

Recently, we developed an efficient organocatalytic route for the direct conversion of aromatic aldehydes into aryl esters by using aryl boronic acids under oxidative NHC-catalyzed conditions.^[14] Although aryl esters were obtained in excellent yields, this method did not allow us to access aliphatic esters because aliphatic boronic acids did not react with the aldehydes under the optimized reaction conditions. Consequently, we became interested in developing a competent method for the synthesis of aliphatic esters, in particular, propargyl esters, because these esters could be derivatized in a straightforward manner to afford worthwhile compounds by using click chemistry^[15] or gold catalysis.^[16] Until

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now, only one report has appeared in the literature for the direct transformation of cinnamaldehyde into its corresponding propargyl ester by using NHC as a catalyst under oxidative conditions.^[17] However, the desired propargyl ester was only formed in 11 % yield at room temperature (45 % yield at 70 °C). Surprisingly, there are no reports on the direct NHC-catalyzed conversion of aromatic aldehydes into their corresponding propargyl esters. Based on these observations, we considered it worthwhile to develop a method for the synthesis of propargyl esters under oxidative NHC conditions and to elaborate those esters into their 1,2,3-triazole derivatives by using click chemistry in one pot (Scheme 1).^[18]



Scheme 1. Proposed one-pot approach to 1,2,3-triazole derivatives.

Results and Discussion

Before exploring the one-pot process for the synthesis of 1,2,3-triazoles, we considered it necessary to optimize the first step, that is, the formation of the propargyl ester. Thus, we performed optimization studies for the first step by using *para*-chlorobenzaldehyde (1) and propargyl bromide (2) under oxidative NHC-catalyzed conditions. All of the reactions were conducted in an open atmosphere to ensure that sufficient oxygen was available for the oxidation reaction to take place. The results of the optimization studies are shown in Table 1.

A variety of NHCs (4-8) were used for this transformation. After careful screening, NHC 7 was found to be the

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Table 1. Optimization studies.

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[a] Reaction conditions: 0.1 M solution of compound 1 in solvent, RT= 32-35 °C. [b] Yield of isolated product. N.R. = no reaction; DME = 1,2-dimethoxyethane; DCE = 1,2-dichloroethane.

DMF

DCE

1,4-dioxane

15

15

25

54

DBU

DBU

DBU

best catalyst and the conditions shown in Table 1, entry 4 were found to be the optimal conditions for this transformation. Next, because this particular oxidative esterification had not previously been reported, we examined the scope of this reaction with a variety of aldehydes and the results are summarized in Table 2.

A range of propargyl esters of aromatic acids could be readily accessed in good yields by using this method. Electron-poor aldehydes (9d-9f) reacted at faster rates than electron-rich aldehydes (9h) and benzaldehyde (9c). To our surprise and in contrast to a literature report, cinnamaldehyde gave its corresponding propargyl ester in 72% yield under the standard conditions; of course, our reaction conditions were slightly different to those in the previous report.^[17] This method also worked efficiently for the reactions of aliphatic aldehydes, such as dihydrocinnamaldehyde (9j) and cyclohexane carboxaldehyde (9k), and the corresponding esters were obtained in moderate yields. The scope of the reaction was extended to internal (91-9n) and secondary propargyl bromides (90). In all of those cases, the required propargyl esters were isolated in satisfactory yields. Encouraged by these results in the formation of the propargyl esters, we shifted our attention towards developing a one-pot procedure for the synthesis of 1,2,3-triazole derivatives^[19] from aldehydes by combining the oxidative NHC catalysis with copper-catalyzed click chemistry. Standardization experiments were performed by using benzyl azide and a copper catalyst, which were added immediately into the reaction mixture after the first step was complete (by TLC); the results are summarized in Table 3.

Table 2. Substrate scope in oxidative esterification reaction of aldehydes with propargyl bromide.[a]



[a] Reaction conditions: 0.1 M solution of the aldehyde in THF, RT = 32-35 °C.

Table 3. Optimization studies of one pot reaction.

CI	O H	7 DBL T then Cu Ph0	Br (1.5 equiv (15 mol%) J (1.5 equiv) HF, Air, RT J ₂ O (20 mol%), CH ₂ N ₃ , RT		Ph N=N
Entry ^[a]	Azide	[equiv]	Solvent	<i>t</i> [h] (steps 1+2)	Yield [%] ^[b]
1 ^[c]	1.3		THF/H ₂ O	3+10	49
2 ^[c]	1.5		THF/H ₂ O	3+6	55
3 ^[c]	2		THF/H ₂ O	3+3	60
4	1.5		THF	3+16	65
5	2		THF	3+12	78
6 ^[d]	2		THF	3+24	65
7 ^[e]	2		THF	3+10	44

[a] Reaction conditions: 0.1 M solution of compound 1 in THF, RT=32-35°C. [b] Yield of isolated product over two steps. [c] Water (1 mL) was added with the copper catalyst. [d] CuI (20 mol%) was used instead of Cu₂O. [e] CuSO₄·5H₂O (10 mol %) and sodium ascorbate (20 mol %) were used instead of Cu2O.

From the optimization studies, it was clear that the desired 1,2,3-triazole derivatives were formed under all of the reaction conditions that were tested (Table 3). However, the highest yield of compound 10 was obtained when two equivalents of the azide and 20 mol% of Cu₂O were used (Table 3, entry 5); thus, these conditions were employed as

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the standard conditions. No product was observed without a copper catalyst. These optimized conditions were investigated for the synthesis of a wide range of substituted 1,2,3-triazoles from a variety of aromatic aldehydes and azides (Table 4).

The scope of this one-pot method was also determined, as shown in Table 4, and 1,2,3-triazole derivatives were obtained in moderate-to-good yields in a regioselective manner. Electron-poor aldehydes (11d, 11e, and 11g), except for para-nitrobenzaldehyde (11 f), were transformed into the desired products at relatively faster rates than electron-rich aldehydes (11h–11j). This method was also employed for converting few heteroaromatic aldehydes into their corresponding 1,2,3triazole derivatives in moderate vields (11k and 11l). As well as benzyl azide, this method was also found to be equally effective for aromatic and other azides (11q-11x).

Since the NHC-catalyzed oxidation of aldehydes into their respective acids is precedented in the literature,^[20] we anticipated that the first step in our method proceeded through the initial formation of the corresponding acid, followed by alkylation with propargyl bromide. To confirm this assumption, some experiments were performed. In one experiment, Table 4. Substrate scope in the one-pot synthesis of 1,2,3-triazole derivatives.^[a]



[a] Reaction conditions: 0.1 M solution of the aldehyde in THF, RT = 32-35 °C.

para-chlorobenzaldehyde was treated with a catalytic amount of compound **7** and 1,8-diazabicyclo[5.4.0]undec-7ene (DBU, 1.5 equiv) in air, thereby affording the isolated product (*para*-chlorobenzoic acid) in 80% yield within 3 h. In another experiment, *para*-chlorobenzoic acid was treated with propargyl bromide (1.5 equiv) in the presence of DBU (1.5 equiv) and the propargyl ester **3** was formed in almost quantitative yield within 5 h. Based on these observations, we strongly believe that the reaction proceeds through the oxidation of the aldehyde into the corresponding acid, followed by propargylation.

Another interesting point was observed during the standardization of this method. As shown in Table 2, benzaldehyde was converted into its propargyl ester 9c in 60% yield; at the same time, under one-pot reaction conditions, benzaldehyde gave 1,2,3-triazole derivative **11a** in 60% overall yield. This result clearly implies that the triazole-formation step is almost quantitative in this case. However, when propargyl ester **9c** was directly treated with Cu₂O and benzyl azide in the absence of compound **7**, the product **11a** was only obtained in 60% yield, even after 28 h (Scheme 2). The reaction rate and the yield of compound **11a** were increased by the addition of 15 mol% of compound **7** to the reaction mixture (Scheme 2).

Based on these observations, we presume that the NHC also influences the triazole-formation step, probably through the formation of a complex with the copper catalyst, thereby increasing its catalytic activity.^[21]

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Scheme 2. Formation of 1,2,3-triazoles under different conditions. Reaction conditions: 0.1 M solution of compound **9c** in THF, RT = 32–35 °C.

Conclusions

In conclusion, a one-pot synthesis of 1,2,3-triazole derivatives was achieved by combining oxidative N-heterocyclic carbene catalysis with click chemistry. This method was utilized for the synthesis of a diverse range of 1,2,3-triazole derivatives from aldehydes under mild reaction conditions. Because one-pot syntheses are an integral part of making chemistry more sustainable, we believe that this method will find some applications in the near future.

Experimental Section

General Methods

Most of the reagents and starting materials were purchased from commercial sources and used as received. NHC precursor **8** was prepared according to a literature procedure.^[22] All of the organic azides were prepared according to a literature procedure.^[23] ¹H and ¹³C spectra were recorded in CDCl₃ on a 400 MHz Bruker FT-NMR spectrometer equipped with a PIKE MIRacle ATR. Chemical shifts are reported in parts per million relative to TMS. High-resolution mass spectroscopy was performed on a Waters Q-TOF Premier-HAB213 spectrometer. FTIR spectra were recorded on a Brucker FTIR spectrometer. Thin-layer chromatography was performed on Merck silica gel 60 F₂₅₄ TLC plates by using EtOAc/hexanes as an eluent. Column chromatography was performed on silica gel (100–200 mesh).

General Procedure for the NHC-Catalyzed Aerobic Oxidation of Aryl Aldehydes with Propargyl Bromide

The aromatic aldehyde (1 mmol) was added to a suspension of NHC 7 (0.15 mmol) and DBU (1.5 mmol) in THF (10 mL) at RT (32–35 °C) and the mixture was stirred for 30 min. Propargyl bromide (80% solution in toluene, 1.5 mmol) was added to the reaction mixture in a dropwise manner and the resulting suspension was stirred until most of the aldehyde had been consumed (by TLC). The suspension was then filtered, washed with EtOAc (20 mL), and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (EtOAc/hexanes).

General Procedure for the NHC-Catalyzed One-Pot Synthesis of 1,2,3-Triazole Derivatives

The aromatic aldehyde (1 mmol) was added to a suspension of NHC 7 (0.15 mmol) and DBU (1.5 mmol) in THF (10 mL) at room temperature ($32-35^{\circ}C$) and the mixture was stirred for 30 min. Propargyl bromide (80% solution in toluene, 1.5 mmol) was added in a dropwise manner and the resulting suspension was stirred until most of the aldehyde had been consumed (by TLC). Cu₂O (0.2 mmol) and the azide (2 mmol) were added to the reaction and stirring was continued until most of the propargyl ester that had formed during the first step had been consumed. The precipitate was then filtered, washed with EtOAc (20 mL), and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (EtOAc/hexanes).

Prop-2-yn-1-yl-4-chlorobenzoate (3)^[24]

82% Yield; colorless oil; ¹H NMR (400 MHz, CDCl₃): δ =8.00 (d, *J*= 8.72 Hz, 2H), 7.42 (d, *J*=8.72 Hz, 2H), 4.92 (d, *J*=2.48 Hz, 2H), 2.53 ppm (t, *J*=2.48 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ =165.0, 139.9, 131.2, 128.8, 127.8, 77.5, 75.2, 52.7 ppm; FTIR: $\tilde{\nu}$ =3299 (≡CH), 2131 (C≡C), 1722 cm⁻¹ (C=O).

Prop-2-yn-1-yl-4-bromobenzoate (9a)^[25]

85% Yield; colorless oil; ¹H NMR (400 MHz, CDCl₃): δ =7.93 (d, *J*= 8.72 Hz, 2H), 7.59 (d, *J*=8.72 Hz, 2H), 4.92 (d, *J*=2.48 Hz, 2H), 2.53 ppm (t, *J*=2.48 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ =165.1, 131.8, 131.3, 128.6, 128.3, 77.5, 75.3, 52.7 ppm; FTIR: $\tilde{\nu}$ =3297 (≡CH), 2130 (C≡C), 1721 cm⁻¹ (C=O).

Prop-2-yn-1-yl-4-phenylbenzoate (9b)

72% Yield; white solid; M.p. 106–107°C; ¹H NMR (400 MHz, CDCl₃): δ =8.14 (d, *J*=8.60 Hz, 2 H), 7.68 (d, *J*=8.60 Hz, 2 H), 7.64–7.61 (m, 2 H), 7.50–7.45 (m, 2 H), 7.43–7.38 (m, 1 H), 4.95 (d, *J*=2.48 Hz, 2 H), 2.54 ppm (t, *J*=2.48 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃): δ =165.7, 146.1, 139.9, 130.4, 129.0, 128.3, 128.1, 127.3, 127.1, 77.8, 75.0, 52.5 ppm; FTIR: $\bar{\nu}$ = 3250 (=CH), 2121 (C=C), 1713 cm⁻¹ (C=O); HRMS (ESI): *m*/*z* calcd for C₁₆H₁₃O₂: 237.0915 [*M*+H]⁺; found: 237.0916.

Prop-2-yn1-ylbenzoate (9c)^[24]

60% Yield; colorless oil; ¹H NMR (400 MHz, CDCl₃): δ = 8.09–8.06 (m, 2H), 7.61–7.56 (m, 1H), 7.48–7.43 (m, 2H), 4.93 (d, *J*=2.44 Hz, 2H), 2.52 ppm (t, *J*=2.48 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ =165.8, 133.4, 129.8, 129.4, 128.5, 77.7, 75.0, 52.5 ppm; FTIR: $\tilde{\nu}$ =3296 (≡CH), 2130 (C≡C), 1720 cm⁻¹ (C=O).

Prop-2-yn-1-yl-4-cyanobenzoate (9d)^[25]

75 % Yield; white solid; M.p. 96–97 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.18 (d, *J*=8.72 Hz, 2H), 7.76 (d, *J*=8.72 Hz, 2H), 4.96 (d, *J*=2.48 Hz, 2H), 2.55 ppm (t, *J*=2.48 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 164.2, 133.2, 132.3, 130.3, 117.9, 116.8, 77.2, 75.7, 53.2 ppm; FTIR: $\tilde{\nu}$ = 3267 (=CH), 2360 (C=N), 2230 (C=C), 1728 cm⁻¹ (C=O).

Methyl prop-2-yn-1-ylterephthalate $(9e)^{[26]}$

75% Yield; white solid; M.p. 88–89°C; ¹H NMR (400 MHz, CDCl₃): δ = 8.08–8.03 (m, 4H), 4.88 (d, J=2.48 Hz, 2H), 3.95 (s, 3H), 2.48 ppm (t, J=2.48 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ =166.2, 165.0, 134.3, 133.1, 129.8, 129.6, 77.2, 75.4, 52.9, 52.5 ppm; FTIR: $\tilde{\nu}$ =3248 (\equiv CH), 2130 (C \equiv C), 1720 cm⁻¹ (C=O).

Prop-2-yn-1-yl-4-nitrobenzoate $(9f)^{[24]}$

60% Yield; pale-yellow solid; M.p. 96–97°C; ¹H NMR (400 MHz, CDCl₃): δ =8.31 (d, J=9.04 Hz, 2H), 8.23 (d, J=9.04 Hz, 2H), 4.97 (d, J=2.48 Hz, 2H), 2.56 ppm (t, J=2.48 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ =164.0, 150.8, 134.7, 131.0, 123.7, 77.4, 75.8, 53.3 ppm; FTIR: $\tilde{\nu}$ =3288 (=CH), 2132 (C=C), 1720 (C=O) 1608, 1523 cm⁻¹.

Prop-2-yn-1-yl-4-trifluoromethoxybenzoate $(9g)^{[27]}$

71% Yield; colorless oil; ¹H NMR (400 MHz, CDCl₃): δ = 8.14–8.10 (m, 2H), 7.29–7.26 (m, 2H), 4.93 (d, *J*=2.48 Hz, 2H), 2.53 ppm (t, *J*= 2.48 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ =164.6, 152.9 (d, *J*(C,F)= 2.0 Hz), 131.9, 127.8, 120.3 (q, *J*(C,F)=257 Hz), 120.3, 77.4, 75.3, 52.7 ppm; FTIR: $\tilde{\nu}$ =3306 (=CH), 2132 (C=C), 1727 cm⁻¹ (C=O).

Prop-2-yn-1-yl-3,4-methylenedioxybenzoate (9h)

60% Yield; off-white solid; M.p. 59–60°C; ¹H NMR (400 MHz, CDCl₃): δ =7.68 (dd, *J*=8.20, 1.68 Hz, 1 H), 7.48 (d, *J*=1.68 Hz, 1 H), 6.84 (d, *J*= 8.20 Hz, 1 H), 6.04 (s, 2 H), 4.88 (d, *J*=2.44 Hz, 2 H), 2.52 ppm (t, *J*= 2.45 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃): δ =165.2, 152.0, 147.8, 125.8, 123.3, 109.7, 108.1, 101.9, 77.8, 75.0, 52.4 ppm; FTIR: $\tilde{\nu}$ =3245 (=CH), 2128 (C=C), 1708 cm⁻¹ (C=O); HRMS (ESI): *m*/*z* calcd for C₁₁H₉O₄: 205.0501 [*M*+H]⁺; found: 205.0504.

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Prop-2-yn-1-ylcinnamate (9i)[24]

72% Yield; colorless oil; ¹H NMR (400 MHz, CDCl₃): δ =7.75 (d, *J*=16.0 Hz, 1 H), 7.55–7.51 (m, 2 H), 7.41–7.38 (m, 3 H), 6.47 (d, *J*=16.0 Hz, 1 H), 4.82 (d, *J*=2.48 Hz, 2 H), 2.52 ppm (t, *J*=2.48 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃): δ =166.1, 146.0, 134.2, 130.6, 129.0, 128.2, 117.0, 77.8, 74.9, 52.1 ppm; FTIR: $\tilde{\nu}$ =3293 (=CH), 2129 (C=C), 1712 cm⁻¹ (C=O).

Prop-2-yn-1-yl-3-phenylpropanoate (9j)[24]

56 % Yield; colorless oil; ¹H NMR (400 MHz, CDCl₃): δ = 7.32–7.28 (m, 2H), 7.23–7.20 (m, 3H), 4.69 (d, *J* = 2.48 Hz, 2H), 2.98 (t, *J* = 7.56 Hz, 2H), 2.69 (t, *J* = 7.56 Hz, 2H), 2.48 ppm (t, *J* = 2.48 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 172.2, 140.3, 128.7, 128.4, 126.5, 77.8, 75.0, 52.1, 35.7, 30.9 ppm; FTIR: $\tilde{\nu}$ = 3288 (=CH), 2126 (C=C), 1740 cm⁻¹ (C=O).

$Prop-2-yn-1-ylcyclohexanecarboxylate (9k)^{[28]}$

48% Yield; colorless oil; ¹H NMR (400 MHz, CDCl₃): δ =4.66 (d, *J*=2.48, 2 H), 2.45 (t, *J*=2.48 Hz, 1 H), 2.38–2.31 (m, 1 H), 1.93–1.25 ppm (m, 10 H), ¹³C NMR (100 MHz, CDCl₃): δ =175.4, 78.1, 74.8, 51.8, 43.0, 29.0, 25.8, 25.5 ppm; FTIR: $\tilde{\nu}$ =3292 (=CH), 2131 (C=C), 1736 cm⁻¹ (C=O).

But-2-yn-1-ylbenzoate (91)[29]

78% Yield; colorless oil; ¹H NMR (400 MHz, CDCl₃): δ =8.09–8.06 (m, 2H), 7.59–7.55 (m, 1H), 7.47–7.42 (m, 2H), 4.89 (q, *J*=2.44 Hz, 2H), 1.88 ppm (t, *J*=2.44 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ =166.1, 133.3, 129.9, 129.8, 128.5, 83.4, 73.4, 53.4, 3.8 ppm; FTIR: $\tilde{\nu}$ =2240 (C=C), 1721 cm⁻¹ (C=O).

Pent-2-yn-1-ylbenzoate (**9***m*)^[30]

82% Yield; colorless oil; ¹H NMR (400 MHz, CDCl₃): δ =8.09–8.06 (m, 2H), 7.59–7.54 (m, 1H), 7.46–7.42 (m, 2H), 4.91 (t, *J*=2.20 Hz, 2H), 2.26 (qt, *J*=7.54, 2.20 Hz, 2H), 1.15 ppm (t, *J*=7.54 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ =166.1, 133.2, 130.2, 129.9, 128.5, 89.1, 73.5, 53.4, 13.7, 12.6 ppm; FTIR: $\tilde{\nu}$ =2242 (C=C), 1721 cm⁻¹ (C=O).

3-Phenylprop-2-yn-1-ylbenzoate (9n)^[31]

60% Yield; colorless oil; ¹H NMR (400 MHz, CDCl₃): δ = 8.13–8.10 (m, 2H), 7.60–7.56 (m, 2H), 7.50–7.44 (m, 5H), 7.34–7.33 (m, 1H), 5.17 ppm (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 166.1, 133.4, 132.1, 130.0, 129.9, 128.9, 128.6, 128.4, 122.3, 86.7, 83.2, 53.5 ppm; FTIR: $\tilde{\nu}$ = 2130 (C=C), 1722 cm⁻¹ (C=O).

4-Phenylbut-3-yn-2-ylbenzoate (90)[31]

58% Yield; colorless oil; ¹H NMR (400 MHz, CDCl₃): δ =8.13–8.10 (m, 2H), 7.60–7.56 (m, 1H), 7.49–7.44 (m, 4H), 7.33–7.29 (m, 3H), 5.95 (q, *J*=6.68 Hz, 1H), 1.73 ppm (d, *J*=6.68 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ =165.7, 133.3, 132.0, 130.1, 129.9, 128.7, 128.5, 128.4, 127.8, 87.6, 84.9, 61.5, 21.8 ppm; FTIR: $\tilde{\nu}$ =2229 (C=C), 1722 cm⁻¹ (C=O).

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-4-chlorobenzoate (10)

78% Yield; pale-yellow solid; M.p. 114–115°C; ¹H NMR (400 MHz, CDCl₃): δ =7.95 (d, *J*=8.64 Hz, 2H), 7.60 (s, 1H), 7.40–7.35 (m, 5H), 7.31–7.27 (m, 2H), 5.53 (s, 2H), 5.43 ppm (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ =165.6, 143.1, 139.7, 134.3, 131.2, 129.2, 128.9, 128.8, 128.2, 128.1, 123.9, 58.2, 54.3 ppm; FTIR: $\tilde{\nu}$ =1719 cm⁻¹; HRMS (ESI): *m/z* calcd for C₁₇H₁₄ClN₃O₂: 350.0673 [*M*+Na]⁺; found: 350.0678.

(1-Benzyl-1H-1,2,3-triazol-4-yl) methyl-benzoate $(11 a)^{[32]}$

60% Yield; white solid; M.p. 122–123°C; ¹H NMR (400 MHz, CDCl₃): δ =8.02 (dd, *J*=8.48, 1.40 Hz, 2H), 7.61 (s, 1H), 7.57–7.53 (m, 1H), 7.43–7.34 (m, 5H), 7.31–7.27 (m, 2H), 5.53 (s, 2H), 5.44 ppm (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ =166.5, 143.4, 134.4, 133.2, 129.8, 129.7, 129.2, 128.9, 128.4, 128.2, 123.9, 58.1, 54.3 ppm; FTIR: $\tilde{\nu}$ =1710 cm⁻¹.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-[1,1'-biphenyl]-4-carboxylate (11b)

60% Yield; golden-yellow solid; M.p. 153–154°C; ¹H NMR (400 MHz, CDCl₃): δ = 8.11 (d, *J* = 8.56 Hz, 2H), 7.66 (d, *J* = 8.59 Hz, 2H), 7.65–7.62

(m, 3 H), 7.51–7.46 (m, 2 H), 7.44–7.37 (m, 4 H), 7.35–7.30 (m, 2 H), 5.56 (s, 2 H), 5.50 ppm (s, 2 H); ¹³C NMR (100 MHz, CDCl₃): δ =166.4, 145.9, 143.4, 139.9, 134.4, 130.3, 129.2, 129.0, 128.9, 128.4, 128.2, 128.2, 127.3, 127.1, 123.9, 58.1, 54.3 ppm; FTIR: $\tilde{\nu}$ =1714 cm⁻¹; HRMS (ESI): *m/z* calcd for C₂₃H₂₀N₃O₂: 370.1555 [*M*+H]⁺; found: 370.1551.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-4-bromobenzoate (11c)

80% Yield; white solid; M.p. 114–115°C; ¹H NMR (400 MHz, CDCl₃): δ =7.87 (d, *J*=8.64 Hz, 2 H), 7.60 (s, 1 H), 7.55 (d, *J*=8.64 Hz, 2 H), 7.41–7.36 (m, 3 H), 7.30–7.27 (m, 2 H), 5.53 (s, 2 H), 5.43 ppm (s, 2 H); ¹³C NMR (100 MHz, CDCl₃): δ =165.8, 143.0, 134.3, 131.8, 131.3, 129.2, 128.9, 128.6, 128.4, 128.2, 123.9, 58.2, 54.3 ppm; FTIR: $\tilde{\nu}$ =1730 cm⁻¹; HRMS (ESI): *m/z* calcd for C₁₇H₁₅BrN₃O₂: 372.0347 [*M*+H]⁺; found: 372.0343.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-4-cyanobenzoate (11 d)

62% Yield; pale-orange solid; M.p. 131–32°C; ¹H NMR (400 MHz, CDCl₃): δ =8.12 (d, J=8.60 Hz, 2H), 7.71 (d, J=8.60 Hz, 2H), 7.60 (s, 1H), 7.41–7.35 (m, 3H), 7.32–7.265 (m, 2H), 5.53 (s, 2H), 5.46 ppm (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ =164.8, 142.6, 134.2, 133.5, 132.2, 130.3, 129.2, 129.0, 128.2, 124.0, 118.0, 116.6, 58.6, 54.3 ppm; FTIR: $\tilde{\nu}$ = 2231, 1719 cm⁻¹; HRMS (ESI): *m*/*z* calcd for C₁₈H₁₅N₄O₂: 319.1195 [*M*+H]⁺; found: 319.1197.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-methylterephthalate (11e)

70% Yield; off-white solid; M.p. 140–141°C¹; ¹H NMR (400 MHz, CDCl₃): δ =8.08 (s, 4H), 7.62 (s, 1H), 7.40–7.36 (m, 3H), 7.30–7.28 (m, 2H), 5.54 (s, 2H), 5.46 (s, 2H), 3.94 ppm (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ =166.2, 165.7, 142.9, 134.3, 134.1, 133.5, 129.8, 129.6, 129.2, 128.9, 128.2, 124.0, 58.4, 54.3, 52.5 ppm; FTIR: $\tilde{\nu}$ =2231, 1716 cm⁻; HRMS (ESI): *m*/*z* calcd for C₁₈H₁₇N₃O₄: 352.1297 [*M*+H]⁺; found: 352.1299.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-4-nitrobenzoate (11f)

57% Yield; pale-yellow solid; M.p. 140–141 °C; ¹H NMR (400 MHz, CDCl₃): δ =7.88 (d, *J*=8.64 Hz, 2H), 7.60 (s, 1H), 7.55 (d, *J*=8.68 Hz, 2H), 7.41–7.34 (m, 3H), 7.31–7.27 (m, 2H), 5.53 (s, 2H), 5.43 ppm (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ =164.6, 150.7, 135.1, 134.2, 130.9, 129.2, 129.0, 128.2, 123.6, 77.3, 58.8, 54.6, 54.4 ppm; FTIR: $\tilde{\nu}$ =1719, 1519, 1347 cm⁻¹; HRMS (ESI): *m/z* calcd for C₁₇H₁₅N₄O₄: 339.1093 [*M*+H]⁺; found: 339.1092.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-4-(trifluoromethoxy)benzoate (11g)

70% Yield; pale-yellow solid; M.p. 110–111°C; ¹H NMR (400 MHz, CDCl₃): δ =8.06 (d, *J*=8.96 Hz, 2H), 7.60 (s, 1H), 7.41–7.34 (m, 3H), 7.31–7.23 (m, 4H), 5.53 (s, 2H) 5.44 ppm (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ =165.3, 152.8, 143.0, 134.3, 131.8, 129.3, 129.2, 128.9, 128.2, 128.1, 123.9, 120.3, 58.3, 54.3 ppm; FTIR: $\tilde{\nu}$ =1719 cm⁻¹; HRMS (ESI): *m*/*z* calcd for C₁₈H₁₅F₃N₃O₃: 378.1065 [*M*+H]⁺; found: 378.1067.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-4-ethylbenzoate (11 h)

54% Yield; pale-yellow solid; M.p. 98–99°C; ¹H NMR (400 MHz, CDCl₃): δ =7.93 (d, *J*=8.32 Hz, 2H), 7.60 (s, 1H), 7.40 –7.35 (m, 3H), 7.30–7.26 (m, 2H), 7.23 (d, *J*=8.32 Hz, 2H), 5.52 (s, 2H), 5.43 (s, 2H), 2.68 (q, *J*=7.64 Hz, 2H), 1.23 ppm (t, *J*=7.64 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ =166.5, 150.2, 143.5, 134.4, 129.9, 129.2, 128.9, 128.2, 127.9, 127.2, 123.8, 57.9, 54.3, 29.0, 15.2 ppm; FTIR: $\tilde{\nu}$ =1702 cm⁻¹; HRMS (ESI): *m/z* calcd for C₁₈H₁₆N₃O₄: 322.1555 [*M*+H]⁺; found: 322.1552.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-4-(tert-butyl)benzoate (11 i)

59% Yield; pale-yellow solid; M.p. 98–99°C; ¹H NMR (400 MHz, CDCl₃): δ =7.95 (d, J=8.64 Hz, 2H), 7.60 (s, 1H), 7.43 (d, J=8.64 Hz, 2H), 7.40–7.35 (m, 3H), 7.29–7.26 (m, 2H), 5.52 (s, 2H), 5.43 (s, 2H), 1.32 ppm (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ =166.5, 156.9, 143.5, 134.4, 129.6, 129.2, 128.9, 128.2, 126.9, 125.4, 123.8, 57.9, 54.3, 35.1,

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31.1 ppm; FTIR: $\tilde{\nu}$ =1708 cm⁻¹; HRMS (ESI): *m*/*z* calcd for C₂₁H₂₄N₃O₂: 350.1868 [*M*+H]⁺; found: 350.1862.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-benzo[d][1,3]dioxole-5-carboxylate (11j)

60% Yield; off-white solid; M.p. 148–149°C; ¹H NMR (400 MHz, CDCl₃): δ =7.63 (dd, *J*=8.20, 1.72 Hz, 1H), 7.59 (s, 1H), 7.44 (d, *J*= 1.68 Hz, 1 H), 7.41- 7.35 (m, 3 H), 7.30–7.27 (m, 2 H), 6.81 (d, *J*=8.12 Hz, 1 H), 6.02 (s, 2 H), 5.52 (s, 2 H), 5.40 ppm (s, 2 H); ¹³C NMR (100 MHz, CDCl₃): δ =165.8, 151.8, 147.7, 143.4, 134.4, 129.2, 128.9, 128.2, 125.7, 123.8, 123.7, 109.6, 108.0, 101.8, 58.0, 54.3 ppm; FTIR: $\tilde{\nu}$ =1711 cm⁻¹; HRMS (ESI): *m*/*z* calcd for C₁₈H₁₆N₃O₄: 338.1141 [*M*+H]⁺; found: 338.1142.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-thiophene-2-carboxylate (11k)

48% Yield; off-white solid; M.p. 85–86°C; ¹H NMR (400 MHz, CDCl₃): δ=7.78 (dd, J=3.78, 1.24 Hz, 1H), 7.61 (s, 1H), 7.55 (dd, J=5.0, 1.24 Hz, 1H), 7.40–7.34 (m, 3H), 7.30–7.26 (m, 2H), 7.07 (dd, J=5.0, 3.80 Hz, 1H), 5.52 (s, 2H), 5.41 ppm (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ=162.1, 143.2, 134.4, 133.9, 133.2, 132.9, 129.2, 128.9, 128.2, 127.8, 124.0, 58.2, 54.3 ppm; FTIR: $\tilde{\nu}$ =1707 cm⁻¹; HRMS (ESI): *m*/*z* calcd for C₁₅H₁₄N₃O₂S: 300.0806 [*M*+H]⁺; found: 300.0804.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-furan-2-carboxylate (111)

48 % Yield; pale-brown solid; M.p. 84–85 °C; ¹H NMR (400 MHz, CDCl₃): δ = 7.62 (s, 1H), 7.55 (s, 1H), 7.39–7.34 (m, 3H), 7.28–7.26 (m, 2H), 7.17–7.16 (m, 1H), 6.48–6.47 (m, 1H), 5.51 (s, 2H), 5.40 ppm (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 158.5, 146.7, 144.1, 143.0, 134.3, 129.2, 128.9, 128.2, 124.1, 118.6, 111.9, 57.9, 54.3 ppm; FTIR: $\tilde{\nu}$ = 1702 cm⁻¹; HRMS (ESI): *m*/*z* calcd for C₁₅H₁₄N₃O₃: 284.1035 [*M*+H]⁺; found: 284.1034.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methylcinnamate (11 m)

65% Yield; white solid; M.p. 123–124°C; ¹H NMR (400 MHz, CDCl₃): δ=7.69 (d, *J*=16.00 Hz, 1 H), 7.58 (s, 1 H), 7.52 –7.47 (m, 2 H), 7.41–7.35 (m, 6H), 7.30 –7.27 (m, 2 H), 6.42 (d, *J*=16.04 Hz, 1 H), 5.53 (s, 2 H), 5.33 ppm (s, 2 H); ¹³C NMR (100 MHz, CDCl₃): δ =166.8, 145.6, 134.4, 134.2, 130.5, 129.2, 128.9, 128.9, 128.2, 128.2, 123.7, 117.5, 77.2, 57.7, 54.3 ppm; FTIR: $\tilde{\nu}$ =1715 cm⁻¹; HRMS (ESI): *m*/*z* calcd for C₁₉H₁₈N₃O₂: 320.1399 [*M*+H]⁺; found: 320.1399.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-3-chlorobenzoate (11n)

78% Yield; pale-orange solid; M.p. 104–105 °C; ¹H NMR (400 MHz, CDCl₃): δ =7.99 (t, *J*=1.84 Hz, 1H), 7.91–7.89 (m, 1H), 7.60 (s, 1H), 7.51 (ddd, *J*=8.0, 2.20, 1.84 Hz, 1H), 7.40–7.26 (m, 6H), 5.53 (s, 2H), 5.44 ppm (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ =165.3, 143.0, 134.6, 134.3, 133.2, 131.4, 129.8, 129.7, 129.2, 128.9, 128.2, 127.9, 123.9, 58.4, 54.3 ppm; FTIR: $\tilde{\nu}$ =1721 cm⁻¹; HRMS (ESI): *m/z* calcd for C₁₇H₁₅ClN₃O₂: 328.0853 [*M*+H]⁺; found: 328.0855.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-3-fluorobenzoate (11 o)

73% Yield; white solid; M.p. 126–127°C; ¹H NMR (400 MHz, CDCl₃): δ =7.83–7.80 (m, 1H), 7.71–7.68 (m, 1H), 7.60 (s, 1H), 7.42–7.35 (m, 4H), 7.31–7.22 (m, 3H), 5.53 (s, 2H), 5.45 ppm (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ =165.3 (d, *J*(C,F)=2.9 Hz), 162.5 (d, *J*(C,F)=245.7 Hz), 163.7, 143.0, 134.3, 131.9 (d, *J*(C,F)=8 Hz), 130.1 (d, *J*(C,F)=7 Hz), 129.2, 128.9, 128.2, 125.5 (d, *J*(C,F)=3 Hz), 123.9, 120.3 (d, *J*-(C,F)=21 Hz), 116.6 (d, *J*(C,F)=24 Hz), 58.4, 54.3 ppm; FTIR: $\tilde{\nu}$ = 1716 cm⁻¹; HRMS (ESI): *m*/*z* calcd for C₁₇H₁₅FN₃O₂: 328.0853 [*M*+H]⁺; found: 328.0855.

(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl-2-fluorobenzoate (11p)

62% Yield; pale-yellow oil; ¹H NMR (400 MHz, CDCl₃): δ =7.94–7.90 (m, 1H), 7.63 (s, 1H), 7.54–7.48 (m, 1H), 7.40–7.26 (m, 5H), 7.20–7.09 (m, 2H), 5.53 (s, 2H), 5.45 ppm (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ =164.0 (d, *J*(C,F)=3 Hz), 162.1 (d, *J*(C,F)=259.0 Hz), 143.2, 134.9 (d, *J*(C,F)=9 Hz), 134.4, 132.2, 129.2, 128.9, 128.2, 124.0, 123.9 (d, *J*(C,F)=7 Hz), 118.2, 117.0 (d, *J*(C,F)=22 Hz), 58.4, 54.3 ppm; FTIR: $\tilde{\nu}$ =

(1-(4-Methoxybenzyl)-1H-1,2,3-triazol-4-yl)methyl-4-chlorobenzoate (11 q)

55% Yield; off-white solid; M.p. 119–120°C; ¹H NMR (400 MHz, CDCl₃): δ =7.96 (d, J=8.60 Hz, 2H), 7.56 (s, 1H), 7.38 (d, J=8.60 Hz, 2H), 7.24 (d, J=8.64 Hz, 2H), 6.89 (d, J=8.64 Hz, 2H), 5.46 (s, 2H), 5.41 (s, 2H), 3.80 ppm (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ =165.6, 160.0, 143.0, 139.7, 131.2, 129.8, 128.7, 128.2, 126.3, 123.7, 114.5, 58.2, 55.4, 53.9 ppm; FTIR: $\tilde{\nu}$ =1716 cm⁻¹; HRMS (ESI): *m/z* calcd for C₁₇H₁₅ClN₃O₃: 358.0958 [*M*+H]⁺; found: 358.0965.

(1-(4-Methylbenzyl)-1H-1,2,3-triazol-4-yl)methyl-4-chlorobenzoate (11r)

67% Yield; pale-yellow solid; M.p. 110–111 °C; ¹H NMR (400 MHz, CDCl₃): δ =7.95 (d, J=8.64 Hz, 2H), 7.57 (s, 1H), 7.38 (d, J=8.64 Hz, 2H), 7.18 (s, 4H), 5.48 (s, 2H), 5.42 (s, 2H) 2.35 ppm (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ =165.6, 143.0, 139.7, 138.9, 131.3, 131.2, 129.9, 128.7, 128.3, 128.2, 123.8, 58.2, 54.1, 21.2 ppm; FTIR: $\tilde{\nu}$ =1719 cm⁻¹; HRMS (ESI): *m*/*z* calcd for C₁₇H₁₅ClN₃O₂: 342.1009 [*M*+H]⁺; found: 342.1008.

(1-(4-(Methoxycarbonyl)benzyl)-1H-1,2,3-triazol-4-yl)methyl-4-chlorobenzoate (**11s**)

82% Yield; off-white solid; M.p. 175–176°C; ¹H NMR (400 MHz, CDCl₃): δ =8.03 (d, *J*=8.38 Hz, 2H), 7.94 (d, *J*=8.68 Hz, 2H), 7.64 (s, 1H), 7.39 (d, *J*=8.68 Hz, 2H), 7.32 (d, *J*=8.42 Hz, 2H), 5.58 (s, 2H), 5.44 (s, 2H), 3.91 ppm (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ =166.4, 165.6, 143.4, 139.8, 139.1, 131.2, 130.7, 130.4, 128.8, 128.1, 127.9, 124.1, 58.2, 53.8, 52.4 ppm; FTIR: $\tilde{\nu}$ =1723, 1709 cm⁻¹; HRMS (ESI): *m/z* calcd for C₁₉H₁₇ClN₃O₄: 386.0907 [*M*+H]⁺; found: 386.0901.

(1-(4-(Trifluoromethoxy)benzyl)-1H-1,2,3-triazol-4-yl)methyl-4-chlorobenzoate (11 t)

80% Yield; pale-brown solid; M.p. 155–156°C; ¹H NMR (400 MHz, CDCl₃): δ =7.95 (d, J=8.68 Hz, 2H), 7.64 (s, 1H), 7.39 (d, J=8.72 Hz, 2H), 7.32 (d, J=8.72 Hz, 2H), 7.23–7.21 (m, 2H) 5.53 (s, 2H) 5.44 ppm (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ =165.6, 149.5, 143.3, 139.8, 133.0, 131.1, 129.7, 128.8, 128.1, 124.0, 121.6, 119.1, 58.1, 53.4 ppm; FTIR: $\tilde{\nu}$ = 1712 cm⁻¹; HRMS (ESI): *m/z* calcd for C₁₈H₁₄ClF₃N₃O₃: 412.0676 [*M*+H]⁺; found: 412.0678.

(1-(4-Methoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl-4-chlorobenzoate (11 u)

52% Yield; pale-yellow solid; M.p. 132–133 °C; ¹H NMR (400 MHz, CDCl₃): δ =8.04 (s, 1 H), 8.00 (d, *J*=8.72 Hz, 2 H), 7.65 (d, *J*=9.08 Hz, 2 H), 7.41 (d, *J*=8.72 Hz, 2 H), 7.02 (d, *J*=9.08 Hz, 2 H), 5.54 (s, 2 H), 3.87 ppm (s, 3 H); ¹³CNMR (100 MHz, CDCl₃): δ =165.7, 160.0, 143.2, 139.8, 131.2, 128.8, 128.2, 122.5, 122.3, 114.8, 77.2, 58.2, 55.7 ppm; FTIR: $\tilde{\nu}$ =1714 cm⁻¹; HRMS (ESI): *m/z* calcd for C₁₇H₁₅ClN₃O₃: 344.0802 [*M*+H]⁺; found: 344.0808.

(1-(p-Tolyl)-1H-1,2,3-triazol-4-yl)methyl-4-chlorobenzoate (11v)

69% Yield; pale-brown solid; M.p. 73–74°C; ¹H NMR (400 MHz, CDCl₃): δ =8.09 (s, 1H), 7.98 (d, *J*=8.68 Hz, 2H), 7.60 (d, *J*=8.44 Hz, 2H), 7.39 (d, *J*=8.68 Hz, 2H), 7.30 (d, *J*=8.08 Hz, 2H), 5.53 (s, 2H), 2.41 ppm (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ =165.7, 139.8, 139.2, 134.6, 131.2, 130.3, 129.3, 128.8, 128.2, 122.4, 120.6, 58.2, 21.1 ppm; FTIR: $\tilde{\nu}$ =1708 cm⁻¹; HRMS (ESI): *m/z* calcd for C₁₇H₁₅ClN₃O₂: 328.0853 [*M*+H]⁺; found: 328.0850.

(1-Mesityl-1H-1,2,3-triazol-4-yl)methyl-4-chlorobenzoate (11w)

65% Yield; pale-yellow solid; M.p. 132–133 °C; ¹H NMR (400 MHz, CDCl₃): δ =8.00 (d, J=8.68 Hz, 2H), 7.74 (s, 1H), 7.40 (d, J=8.68 Hz, 2H), 6.98 (s, 2H), 5.56 (s, 2H), 2.34 (s, 3H), 1.94 ppm (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ =165.6, 142.5, 140.2, 139.7, 135.0, 133.2, 131.2, 129.1, 128.8, 128.2, 125.9, 58.4, 21.1, 17.3 ppm; FTIR: $\tilde{\nu}$ =1730 cm⁻¹;

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HRMS (ESI): m/z calcd for $C_{19}H_{19}ClN_3O_2$: 356.1166 $[M+H]^+$; found: 356.1162.

(1-Phenyl-1H-1,2,3-triazol-4-yl)methyl-4-chlorobenzoate (11x)

60% Yield; pale-brown solid; M.p. 84–85°C; ¹H NMR (400 MHz, CDCl₃): δ =8.14 (s, 1H), 7.98 (d, *J*=8.72 Hz, 2H), 7.74–7.72 (m, 2H), 7.54–7.49 (m, 2H), 7.46–7.42 (m, 1H), 7.44 (d, *J*=8.72 Hz, 2H), 5.54 ppm (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ =165.7, 143.4, 139.8, 131.2, 129.8, 129.3, 129.0, 128.8, 128.1, 122.4, 120.6, 58.2 ppm; FTIR: $\tilde{\nu}$ =1718 cm⁻¹; HRMS (ESI): *m/z* calcd for C₁₆H₁₃ClN₃O₂: 314.0696 [*M*+H]⁺; found: 314.0693.

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- a) P. C. Chiang, J. W. Bode, N-Heterocyclic Carbenes: From Laboratory Curiosities to Efficient Synthetic Tools; In RSC Catalysis series;
 S. Díez-González, Ed.; Royal Society of Chemistry: Cambridge,
 2010, pp. 339–445; b) S. P. Nolan, N-Heterocyclic Carbenes in Synthesis; Wiley-VCH, Weinheim, 2006.
- [2] For reviews, see: a) D. Enders, O. Niemeier, A. Henseler, Chem. Rev. 2007, 107, 5606-5655; b) V. Nair, S. Vellalath, B. P. Babu, Chem. Soc. Rev. 2008, 37, 2691-2698; c) E. M. Phillips, A. Chan, K. A. Scheidt, Aldrichimica Acta 2009, 42, 55-66; d) J. R. deAlaniz, T. Rovis, Synlett 2009, 1189-1207; e) J. L. Moore, T. Rovis, Top. Curr. Chem. 2009, 291, 77-144; f) P. C. Chiang, J. W. Bode, TCI MAIL 2011, 149, 2-17; g) V. Nair, R. S. Menon, A. T. Biju, C. R. Sinu, R. R. Paul, A. Jose, V. Sreekumar, Chem. Soc. Rev. 2011, 40, 5336-5346; h) A. T. Biju, N. Kuhl, F. Glorius, Acc. Chem. Res. 2011, 44, 1182-1195; i) H. U. Vora, T. Rovis, Aldrichimica Acta 2011, 44, 3-11; j) Z. Rong, W. Zhang, G. Yang, S. You, Curr. Org. Chem. 2012, 41, 3511-3522.
- [3] For recent examples, see: a) K. Y. Chow, J. W. Bode, J. Am. Chem. Soc. 2004, 126, 8126-8127; b) N. T. Reynolds, J. R. deAlaniz, T. Rovis, J. Am. Chem. Soc. 2004, 126, 9518-9519; c) A. Chan, K. A. Scheidt, Org. Lett. 2005, 7, 905-908; d) S. S. Sohn, J. W. Bode, Org. Lett. 2005, 7, 3873-3876; e) S. S. Sohn, J. W. Bode, Angew. Chem. 2006, 118, 6167-6170; Angew. Chem. Int. Ed. 2006, 45, 6021-6024; f) K. Zeitler, Org. Lett. 2005, 8, 637-640; g) G. Li, Y. Li, L. Dai, S. You, Org. Lett. 2007, 9, 3519-3521; h) J. Kaeobamrung, J. Mahatthananchai, P. Zheng, J. W. Bode, J. Am. Chem. Soc. 2010, 132, 8810-8812.
- [4] a) G. A. Grasa, R. Kissling, S. P. Nolan, Org. Lett. 2002, 4, 3583–3586; b) G. A. Grasa, T. Güveli, R. Singh, S. P. Nolan, J. Org. Chem. 2003, 68, 2812–2819; c) G. W. Nyce, T. Glauser, E. F. Connor, A. Möck, R. M. Waymouth, J. L. Hedrick, J. Am. Chem. Soc. 2003, 125, 3046–3056.
- [5] a) M. He, J. R. Struble, J. W. Bode, J. Am. Chem. Soc. 2006, 128, 8418–8420; b) M. He, G. J. Uc, J. W. Bode, J. Am. Chem. Soc. 2006, 128, 15088–15089; c) J. Kaeobamrung, M. C. Kozlowski, J. W. Bode, Proc. Natl. Acad. Sci. USA 2010, 107, 20661–20665; d) S. J. Ryan, L. Candish, D. W. Lupton, J. Am. Chem. Soc. 2011, 133, 4694–4697; e) S. J. Ryan, A. Stasch, M. N. Paddon-Row, D. W. Lupton, J. Org. Chem. 2012, 77, 1113–1124; f) S. E. Allen, J. Mahatthananchai, J. W. Bode, M. C. Kozlowski, J. Am. Chem. Soc. 2012, 134, 12098–12103.
- [6] a) H. Zhou, W. Z. Zhang, C. H. Liu, J. P. Qu, X. B. Lu, J. Org. Chem. 2008, 73, 8039–8044; b) Y. Kayaki, M. Yamamoto, T. Ikariya, Angew. Chem. 2009, 121, 4258–4261; Angew. Chem. Int. Ed. 2009,

48, 4194-4197; c) X. Liu, C. Cao, Y. Li, P. Guan, L. Yang, Y. Shi, Synlett **2012**, 1343-1348.

- [7] T. Rovis, D. A. DiRocco, J. Am. Chem. Soc. 2012, 134, 8094-8097.
- [8] L. Candish, D. W. Lupton, Chem. Sci. 2012, 3, 380-383.
- [9] a) For reviews, see: D. T. Cohen, K. A. Scheidt, *Chem. Sci.* 2012, *3*, 53-57; b) D. E. A. Raup, B. Cardinal-David, D. Holte, K. A. Scheidt, *Nat. Chem.* 2010, *2*, 766-771; c) B. Cardinal-David, D. E. A. Raup, K. A. Scheidt, *J. Am. Chem. Soc.* 2010, *132*, 5345-5347; d) X. Zhao, D. A. DiRocco, T. Rovis, *J. Am. Chem. Soc.* 2011, *133*, 12466-12469; e) N. T. Patil, *Angew. Chem.* 2011, *123*, 1797-1799; *Angew. Chem. Int. Ed.* 2011, *50*, 1759-1761; f) R. S. Reddy, J. N. Rosa, L. F. Veiros, S. Caddick, P. M. P. Gois, *Org. Biomol. Chem.* 2011, *9*, 3126-3129.
- [10] For a recent review, see: C. E. I. Knappke, A. Imami, A. Jacobi von Wangelin, *ChemCatChem* 2012, 4, 937–941.
- [11] a) B. E. Maki, K. A. Scheidt, Org. Lett. 2008, 10, 4331-4334; b) J. Guin, S. D. Sarkar, S. Grimme, A. Studer, Angew. Chem. 2008, 120, 8855-8858; Angew. Chem. Int. Ed. 2008, 47, 8727-8730; c) C. Noonan, L. Baragwanath, S. J. Connon, Tetrahedron Lett. 2008, 49, 4003-4006; d) M. Yoshida, Y. Katagiri, W. B. Zhu, K. Shishido, Org. Biomol. Chem. 2009, 7, 4062-4066; e) B. E. Maki, A. Chan, E. M. Phillips, K. A. Scheidt, Tetrahedron 2009, 65, 3102-3109; f) S. Goswami, A. Hazra, Chem. Lett. 2009, 38, 484-485; g) S. D. Sarkar, S. Grimme, A. Studer, J. Am. Chem. Soc. 2010, 132, 1190-1191; h) Y. C. Xin, S. H. Shi, D. D. Xie, X. P. Hui, P. F. Hu, Eur. J. Org. Chem. 2011, 6527-6531; i) E. E. Finney, K. A. Ogawa, A. J. Boydston, J. Am. Chem. Soc. 2012, 134, 12374-12377; j) J. J. Meng, M. Gao, Y. P. Wei, W. Q. Zhang, Chem. Asian J. 2012, 7, 872-875.
- [12] S. De Sarkar, A. Studer, Org. Lett. 2010, 12, 1992–1995.
- [13] a) C. A. Rose, K. Zeitler, Org. Lett. 2010, 12, 4552–4555; b) S. De Sarkar, A. Studer, Angew. Chem. 2010, 122, 9452–9455; Angew. Chem. Int. Ed. 2010, 49, 9266–9269; c) J. H. Park, S. V. Bhilare, S. W. Youn, Org. Lett. 2011, 13, 2228–2231.
- [14] P. Arde, B. T. Ramanjaneyulu, V. Reddy, A. Saxena, R. V. Anand, Org. Biomol. Chem. 2012, 10, 848–851.
- [15] For reviews, see: a) H. C. Kolb, M. G. Finn, K. B. Sharpless, Angew. Chem. 2001, 113, 2056–2075; Angew. Chem. Int. Ed. 2001, 40, 2004– 2021; b) M. Meldal, C. W. Tornøe, Chem. Rev. 2008, 108, 2952– 3015; c) For special issues on click chemistry, see: Chem. Soc. Rev. 2010, 39, 1231–1405; Chem. Asian J. 2011, 6, 2565–2847; d) W. H. Binder, R. Sachsenhofer, Macromol. Rapid Commun. 2007, 28, 15– 54; e) J. F. Lutz, Angew. Chem. 2007, 119, 1036–1043; Angew. Chem. Int. Ed. 2007, 46, 1018–1025; f) H. C. Kolb, K. B. Sharpless, Drug Discovery Today 2003, 8, 1128–1137; g) J. E. Moses, A. D. Moorhouse, Chem. Soc. Rev. 2007, 36, 1249–1262; h) S. K. Mamidyala, M. G. Finn, Chem. Soc. Rev. 2010, 39, 1252–1261; i) D. S. Pedersen, A. Abell, Eur. J. Org. Chem. 2011, 2399–2411.
- [16] For recent reviews, see: a) D. J. Gorin, F. D. Toste, Nature 2007, 446, 395–403; b) A. S. K. Hashmi, Chem. Rev. 2007, 107, 3180–3211; c) K. Hashmi, A. Stephen, Angew. Chem. 2005, 117, 7150–7154; Angew. Chem. Int. Ed. 2005, 44, 6990–6993; d) G. L. Hamilton, E. J. Kang, M. Mba, F. D. Toste, Science 2007, 317, 496–499; e) P. Garcia, M. Malacria, C. Aubert, V. Gandon, L. Fensterbank, ChemCatChem 2010, 2, 493–497; f) A. S. Dudnik, N. Chernyak, V. Gevorgyan, Aldrichimica Acta 2010, 43, 37–46; g) A. S. K. Hashmi, M. Bührle, Aldrichimica Acta 2010, 43, 27–33; h) M. Bandini, Chem. Soc. Rev. 2011, 40, 1358–1367; i) H. A. Wegner, M. Auzias, Angew. Chem. 2011, 123, 8386–8397; Angew. Chem. Int. Ed. 2011, 50, 8236–8247; j) A. Corma, A. Leyva-Pérez, M. J. Sabater, Chem. Rev. 2011, 111, 1657–1712; k) N. T. Patil, Chem. Asian J. 2012, 7, 2186–2194.
- [17] B. Maji, S. Vedachalam, X. Ge, S. Cai, X. W. Liu, J. Org. Chem. 2011, 76, 3016–3023.
- [18] For recent reviews on sequential catalysis by using two different catalysts, see: a) Z. Shao, H. Zhang, *Chem. Soc. Rev.* 2009, *38*, 2745–2755; b) C. Zhong, X. Shi, *Eur. J. Org. Chem.* 2010, 2999–3025; c) J. Zhou, *Chem. Asian J.* 2010, *5*, 422–434; d) S. Piovesana, D. M. S. Schietroma, M. Bella, *Angew. Chem.* 2011, *123*, 6340–6357; *Angew. Chem. Int. Ed.* 2011, *50*, 6216–6232; e) C. C. J. Loh, D. Enders,

Chem. Asian J. 2013, 00, 0-0

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Chem. Eur. J. 2012, 18, 10212-10225; f) N. T. Patil, V. S. Shinde, B. Gajula, Org. Biomol. Chem. 2012, 10, 211-224.

- [19] a) A. K. Feldman, B. Colasson, V. Folkin, Org. Lett. 2004, 6, 3897–3899; b) K. Barral, A. D. Moorhouse, J. E. Moses, Org. Lett. 2007, 9, 1809–1811.
- [20] a) P. C. Chiang, J. W. Bode, Org. Lett. 2011, 13, 2422–2425; b) Y. Li,
 W. Du, W. P. Deng, Tetrahedron 2012, 68, 3611–3615.
- [21] For NHC-Cu-catalyzed click chemistry, see: a) S. Díez-González, A. Correa, L. Cavallo, S. P. Nolan, *Chem. Eur. J.* 2006, *12*, 7558–7564;
 b) T. Nakamura, T. Terashima, K. Ogata, S. Fukuzawa, *Org. Lett.* 2011, *13*, 620–623.
- [22] D. Enders, K. Breuer, U. Kallfass, T. Balensiefer, Synthesis 2003, 1292-1295.
- [23] a) J. Shen, R. Woodward, J. P. Kedenburg, X. Liu, M. Chen, L. Fang, D. Sun, P. G. Wang, *J. Med. Chem.* **2008**, *51*, 7417; b) J. Anderson, U. Madsen, F. Björkling, X. Liang, *Synlett* **2005**, 2209.
- [24] A. K. Chakraborti, B. Singh, S. V. Chankeshwara, A. R. Patel, J. Org. Chem. 2009, 74, 5967–5974.

- [25] V. P. Raj, A. Sudalai, Tetrahedron Lett. 2005, 46, 8303-8306.
- [26] S. Punna, S. Meunier, M. G. Finn, Org. Lett. 2004, 6, 2777-2779.
- [27] P. Hofmeister, R. Buerstinghaus, H. Adolphi, U.S. patent, US4642368, **1987**.
- [28] B. S. Zoser, U. S. patent, US0265269, 2007.
- [29] R. N. Ram, V. K. Soni, D. K. Gupta, *Tetrahedron* 2012, 68, 9068– 9075.
- [30] X.-F. Wu, H. Neumann, M. Beller, Chem. Commun. 2011, 47, 7959–7961.
- [31] L. X. Alvarez, M. L. Christ, A. B. Sorokin, *Appl. Catal. A* 2007, 325, 303–308.
- [32] B. R. Buckley, S. E. Dann, H. Heaney, E. C. Stubbs, Eur. J. Org. Chem. 2011, 770–776.

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NHCs click into place: A one-pot synthesis of 1,2,3-triazoles has been developed by combining oxidative N-heterocyclic carbene catalysis with click chemistry. A range of 1,2,3-triazoles were prepared in moderate-to-good yields under mild conditions.

Click Chemistry

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Combining Oxidative N-Heterocyclic Carbene Catalysis with Click Chemistry: A Facile One-Pot Approach to 1,2,3-Triazole Derivatives