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Synthesis of α-Keto-1,2,3-triazoles Through Copper Iodide Catalyzed Oxygenation

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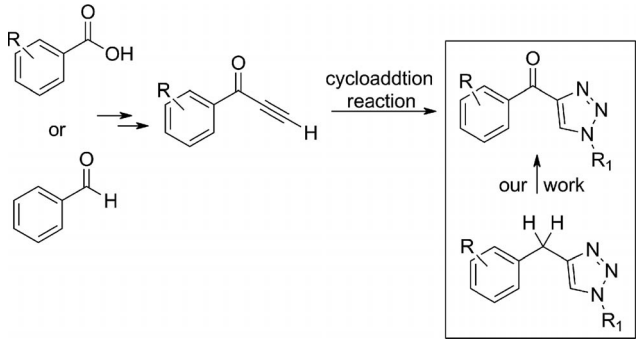
Benzyltriazoles have been catalytically oxidized by using CuI and *tert*-butyl hydroperoxide to yield phenyl(1*H*-1,2,3-triazol-4-yl)methanone derivatives in good yields at room temperature.

Introduction

Benzylic oxidation is one of the most important and useful reactions in organic chemistry.[1] The possibility of generating ketones is one of its greatest advantages because these compounds are used as building blocks for pharmaceuticals and agrochemicals.[2] Therefore several methods for benzylic oxidation have been developed during the last few years. In 2007, Nakanishi and Bolm reported benzylic oxidation reactions promoted by catalytic amounts of $FeCl_3$ and *tert*-butyl hydroperoxide (TBHP) as oxidant in pyridine as solvent at 80 °C,[3] Reddy and co-workers reported the oxidation of benzylic moieties by using TBHP and potassium iodide as catalyst (20 mol-%),[4] and recently, a selective oxidation of C(sp^3)–H bonds to C(sp^3)–O bonds in the presence of copper catalysts bearing quinoline-imine ligands with peresters as oxidants was described.[5]

In an ongoing project aimed at developing novel antituberculosis agents, we focused on the synthesis of α-ketotriazoles. We recently synthesized a series of benzyltriazoles that exert biological activities against InhA (also called 2-*trans*-enoyl-ACP reductase enzyme).[6,7] To create small libraries of families of compounds based on judiciously functionalized triazole frameworks, we decided to oxidize the benzylic moieties of these compounds. α-Ketotriazoles display various interesting biological activities and are found as building blocks in numerous biological molecules[8] and recently Sau and Hrdlicka used them for the synthesis of functionalized triazole-linked DNA as promising hybridization probes in nucleic acid chemistry and biotechnology.[9]

Ketotriazoles can be synthesized from ynones[10] through Sharpless–Fokin cycloaddition reactions (Scheme 1)[11] as well as by amine-catalyzed [3+2] cycloaddition reactions between carbonyl compounds and azides.[12]



Scheme 1. Synthetic routes to α-ketotriazoles.

In this context we wish to report herein our investigations on a copper-dependent method for the preparation of α-ketotriazoles directly from benzyltriazoles by employing catalytic amounts of copper iodide in the presence of TBHP (70% in water).

Results and Discussion

The starting materials (i.e., benzyltriazoles) are readily available by copper-catalyzed alkyne-azide cycloaddition (CuAAC) reaction.[11d] They were synthesized by click chemistry using $CuSO_4$ (0.2 equiv.) and sodium ascorbate (0.4 equiv.). When not commercial, the alkyne precursors were prepared in two steps from commercially available phenethyl alcohol derivatives. First, Dess–Martin oxidation of the corresponding alcohols followed by condensation with the Ohira–Bestmann reagent[13] provided the desired alkyne products in good yields.

The initial attempt to transform 1,4-dibenzyl-1*H*-1,2,3-triazole into the ketone was performed with potassium iod-

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ide in the presence of TBHP (70% in water) at room temperature with diphenylmethane, as described by Reddy and co-workers.[4] An average yield of 48% was obtained after several attempts (Table 1; entry 1). A control reaction was then performed with diphenylmethane as described previously,[4] which gave a yield similar to that published (70 vs. 78%). Slightly higher yields were obtained when the reaction was conducted at reflux with KI (0.1 or 0.3 equiv.; entries 3 and 4).

With our continuing interest in developing more convenient reactions catalyzed by copper, we investigated different copper sources. When copper(II) chloride was used as catalyst along with TBHP and/or 2,9-dimethyl-1,10-phenanthroline, the reaction outcome showed that the presence of TBHP is vital whereas the ligand had no important effect on the reaction (entries 5–7). In addition, no significant amounts of product were observed with copper chloride in the presence of DDQ as oxidant (entry 8). The source of copper, the reaction temperature, and solvent were critical.

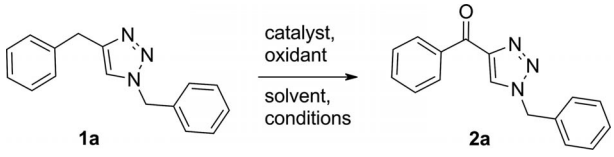
The presence of copper iodide and TBHP in MeCN at reflux afforded the desired product in only 51% yield (entry 9). Replacement of the aqueous TBHP (70 wt-% in water) with TBHP in organic solution (5 M in decane) led to a lower yield (33%; entry 10). After screening different solvents, acetonitrile proved to be the optimal solvent for the reaction, with CuI (0.1 equiv.) at room temperature and TBHP (4 equiv.) being the best system for oxidation (entry 14). The reaction was clean and the desired product was isolated in 81% yield. Extending the reaction time did not improve the yield (entry 15). Increasing the amount of CuI to 0.2 equiv. had no effect on the yield and the use of 2 equiv. of TBHP instead of 4 equiv. (as frequently reported in the literature) only slightly modified the yield of the product (74 vs. 81%). Finally, TBHP alone does not promote the reaction; the starting material was totally recovered (data not shown).

These reactions also indicated that the CuI/TBHP couple is more efficient than KI/TBHP in oxidizing benzyltriazoles. The use of $FeCl_2$ as catalyst in the presence of acetic acid and O_2 was also tested, as described by Maes and coworkers;[14] only traces of the desired product were detected (entry 16). However, when TBHP was used as oxidant in the presence of $FeCl_2$, the product was obtained in good yield (78%, entry 17). Heating the same reaction mixture at reflux led to the product with a slight improvement in both the conversion (>95%) and yield (82%; entry 18).

Finally, it is noteworthy that the reaction is completely chemoselective; no oxidation of the methylene group of the *N*-benzyl moiety was observed.

To evaluate the scope of the reaction, different triazoles were tested under the standard reaction conditions. All reactions were conducted for 20 h at room temperature in the presence of 10 mol-% CuI or at reflux in the presence of 10 mol-% $FeCl_2$. The catalysis was not sensitive to the nature of the substituent on the triazole. Triazole systems possessing remote aromatic groups at the 1-position led to good yields (entries 1–5) except in the case of the naphthylmethyl group (entry 6). In this case, the naphthyl derivative **1f** was only partially soluble and the reaction took more time, as shown by TLC. When a mixture containing 1,4- and 1,5-dibenzyltriazoles in a ratio of 1:4 was subjected to the oxidation reaction, the same ratio of products was obtained in 77% yield (entry 7), thereby revealing the ab-

Table 1. Screening of the reaction conditions for the oxidation of benzyltriazole.



Entry	Catalyst, oxidant	Solvent	Conditions	Yield[a] [%]
1	KI (0.1 equiv.), TBHP (4 equiv.)	MeCN	r.t., 20 h	48
2	KI (0.1 equiv.), TBHP (4 equiv.)	MeCN	r.t., 20 h	70[b] (78)[c]
3	KI (0.1 equiv.), TBHP (4 equiv.)	MeCN	reflux, 20 h	49
4	KI (0.3 equiv.), TBHP (4 equiv.)	MeCN	reflux, 20 h	53
5	$CuCl_2$ (0.1 equiv.), TBHP (4 equiv.)	MeCN	reflux, 20 h	25
6	$CuCl_2$ (0.1 equiv.), 2,9-dimethyl-1,10-phenanthroline (0.2 equiv.)	MeCN	reflux, 20 h	0
7	$CuCl_2$ (0.1 equiv.), TBHP (4 equiv.), 2,9-dimethyl-1,10-phenanthroline (0.2 equiv.)	MeCN	reflux, 20 h	23
8	$CuCl_2$ (0.1 equiv.), DDQ (1.5 equiv.)	MeCN	reflux, 20 h	14
9	CuI (0.1 equiv.), TBHP (4 equiv.)	MeCN	reflux, 20 h	51
10	CuI (0.1 equiv.), TBHP (4 equiv.)	MeCN	reflux, 20 h	33[d]
11	CuI (0.1 equiv.), TBHP (4 equiv.)	DMSO	80 °C, 20 h	37
12	CuI (0.1 equiv.), TBHP (4 equiv.)	DMF	reflux, 20 h	6
13	CuI (0.1 equiv.), TBHP (4 equiv.)	MeOH	reflux, 20 h	13
14	CuI (0.1 equiv.), TBHP (4 equiv.)	MeCN	r.t., 20 h	81
15	CuI (0.1 equiv.), TBHP (4 equiv.)	MeCN	r.t., 44 h	77
16	$FeCl_2$ (0.1 equiv.), AcOH, O_2 (balloon)	DMSO	100 °C, 24 h	0
17	$FeCl_2$ (0.1 equiv.), TBHP (4 equiv.)	MeCN	r.t., 20 h	78
18	$FeCl_2$ (0.1 equiv.), TBHP (4 equiv.)	MeCN	reflux, 20 h	82

[a] Isolated yields. [b] Reaction performed with diphenylmethane. [c] See ref.[4] [d] Reaction performed with TBHP in decane.

sence of regioselectivity. Triazole systems with alkyl substituents at the 1-position (entries 8–11) also afforded the oxidized products in good yields.

As shown in Table 2, the reaction is not sensitive to the electronic properties of substituents present on the phenyl ring of the benzyltriazoles as electron-donating and -withdrawing groups could be employed in the reaction (entries 12–14). We recently disclosed a copper-mediated oxidation of α-ketotriazoles to α,β-diketotriazoles with triazole as an effective intramolecular directing group.[10] This reaction was carried out with either copper chloride or iodide as catalyst in the presence of 2,9-dimethyl-1,10-phenanthroline, the use of copper iodide allowing shorter reaction times. By using the method we report here (i.e., CuI and TBHP), α-ketotriazole was oxidized to α,β-diketotriazole in only 16% yield (entry 15).

The use of $FeCl_2$ (0.1 equiv.) in the presence of TBHP (4 equiv.) at reflux was also tested in the oxidation reaction; similar (entries 1, 3, 6) or lower (entries 9, 12) yields were obtained in comparison with CuI.

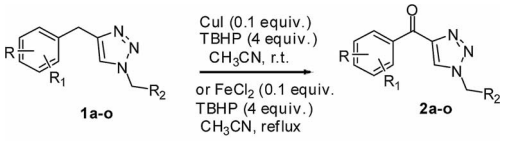
Again, no oxidation occurred on the benzylic moiety (when present) attached to the nitrogen atom of the triazole ring.

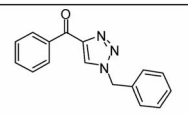
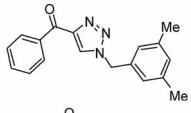
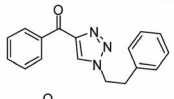
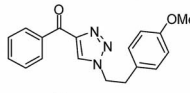
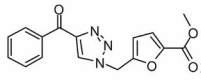
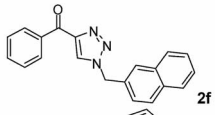
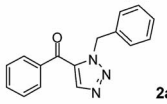
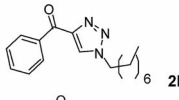
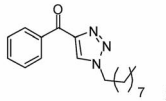
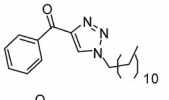
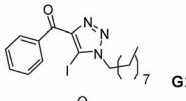
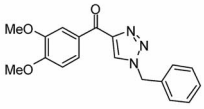
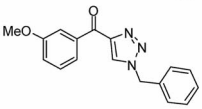
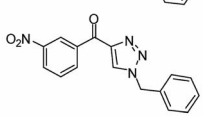
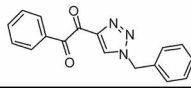
To gain an insight into the reaction mechanism, we also performed this reaction on four other starting compounds (Scheme 2). The oxidation reactions of diphenylmethane and 2- and 3-benzylpyridines were performed for comparison. A slightly better yield was obtained in the case of 3-benzylpyridine, but the difference is not sufficient to confirm the role of the nitrogen atom in the oxidation process. Finally, when the corresponding alcohol of the benzyltriazole system was used as the starting material, the alcohol was oxidized quantitatively to the corresponding ketone **4** (Scheme 2).

This last reaction is analogous to that reported by Sasson and co-workers in 1998 for the oxidation of allylic and benzylic alcohols to the respective ketones by using TBHP in the presence of $CuCl_2$ or CuCl under phase-transfer catalysis conditions.[15] Nikolaropoulos and co-workers in 2003 proposed a multistep process with the formation of a radical intermediate generated by the *tert*-butoxyl radical and the intermediate Cu^{II}–O–O–*t*Bu.[16] In 2007, Kirihara et al. reported the oxidation of thiols to disulfides with H_2O_2 in the presence of catalytic amounts of NaI.[17] They suggested the oxidation of iodide to the very reactive hypoiodous acid (I–OH). In 2011, Wan and co-workers reported the α-oxyacylation of ethers with carboxylic acids in the presence of iodide and TBHP.[18] They proposed a radical mechanism through a I_2/I^- redox process. In our hands, the presence of iodide was assessed by the typical green-brown solution after the addition of TBHP (4 equiv.) to a colorless solution of copper iodide in CH_3CN.

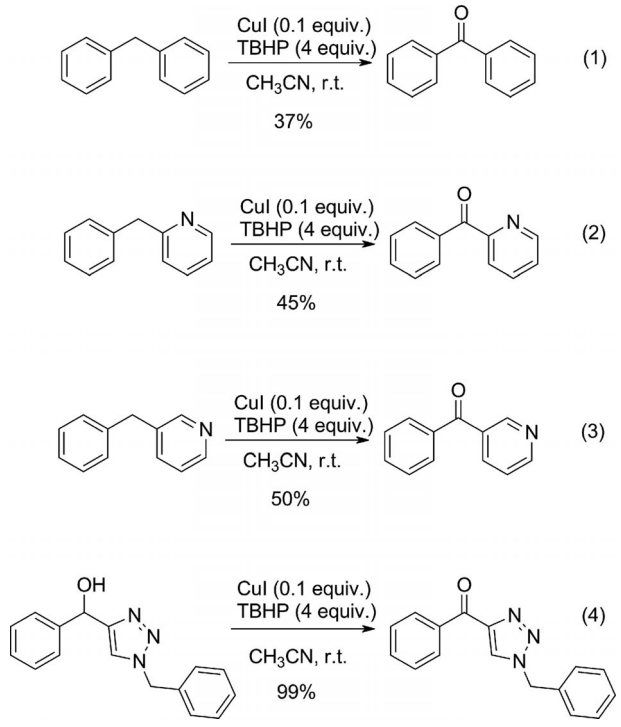
The results obtained with the TBHP–Cu^I system in this work can be explained by modifying the mechanisms proposed by Sasson et al. and earlier by Kochi,[19] who used a series of redox reactions to form benzylic *tert*-butyl peroxide, which decomposes to afford the ketone [Equations (a)–(e)].

Table 2. Scope of the CuI-catalyzed oxidation of benzylic triazoles.

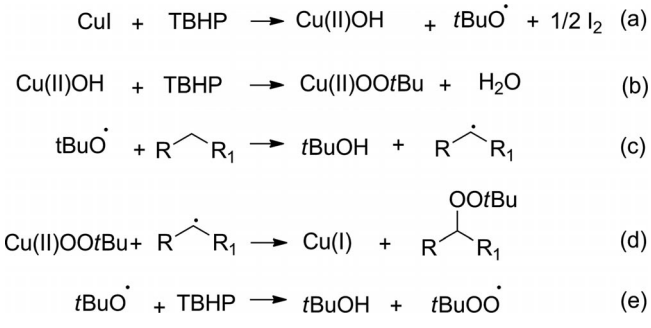


Entry	Product	Yield[a] % CuI/$FeCl_2$
1	 **2a**	81 / 82
2	 **2b**	64 / n.d.[c]
3	 **2c**	69 / 77
4	 **2d**	61 / n.d.[c]
5	 **2e**	71 / n.d.[c]
6	 **2f**	52 (46 h reaction) / 55
7	 **2a/2g** (80/20 : 1,4/1,5-triazoles)	77 (80/20) / n.d.[c]
8	 **2h**	79 / n.d.[c]
9	 **2i**	82 / 68
10	 **2j**	83 / n.d.[c]
11	 **G2k**	84 / n.d.[c]
12	 **2l**	83 / 67
13	 **2m**	81 / n.d.[c]
14	 **2n**	72 / n.d.[c]
15[b]	 **2o**	16 / n.d.[c]

[a] Yields of isolated compounds. [b] Synthesized from the corresponding α-ketotriazole. [c] Not determined.



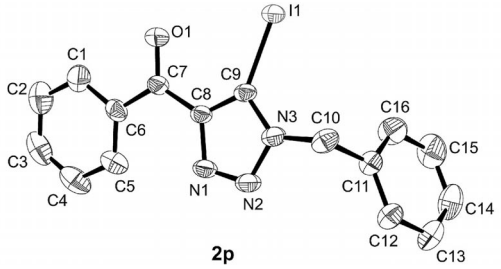
Scheme 2. Further copper-catalyzed oxidation reactions.



In the absence of copper, the *tert*-butoxyl radical can be generated by an I_2/I^- redox process, which can create both benzylic and *tert*-butoxyl radicals.[20]

In both cases (presence or absence of copper), 2 equiv. of *t*BuOOH are needed to generate the *t*BuO$^{\cdot}$ and *t*BuOO$^{\cdot}$ radicals.

Finally, benzoyltriazoles can be synthesized in a one-pot strategy, as shown in Scheme 3. In this one-pot synthesis, TBHP was added after 20 h to a stoichiometric CuI-promoted alkyne-azide cycloaddition reaction, as previously reported by us. Only a single, final purification step was then necessary for the production of α-ketotriazole. The oxidized 5-iodotriazole **2p** (characterized by ^{1}H and ^{13}C NMR, IR, and mass spectrometry) was identified as a by-product formed in 8% yield. Its structure was confirmed by single-crystal X-ray analysis.[21] It was gratifying to find that when a catalytic amount of CuI was used, triazole **2a** was obtained in 57% yield without any traces of **2p**.



2p

Conclusions

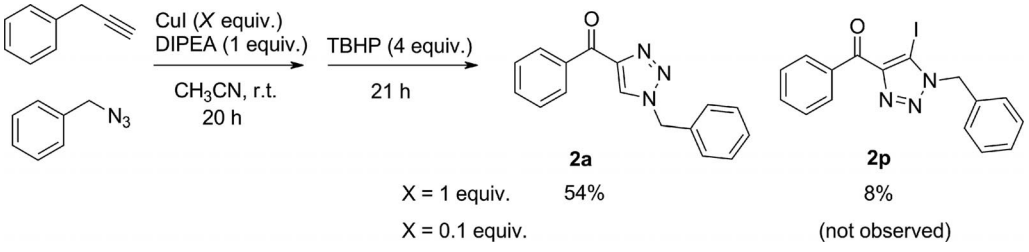
We have developed a catalytic copper iodide mediated method to oxidize benzylic triazoles to ketotriazoles in good yields. The insight gained from this method permitted a two-step, one-pot sequence from the corresponding alkyne and azide to afford α-ketotriazole in a good yield, again under catalytic copper iodide conditions. This method represents a useful access to α-keto-1,2,3-triazoles.

Experimental Section

General: All chemicals were obtained from Aldrich or Acros Organics and used without further purification. NMR spectra were recorded with a Bruker AC 300 spectrometer (^{1}H and ^{13}C NMR). ^{1}H NMR spectra were recorded at 300 MHz with $CDCl_3$ (δ = 7.26 ppm) as internal standard. ^{13}C NMR spectra were recorded at 75.0 MHz and resonances are referenced against the central line of the $CDCl_3$ triplet at δ = 77.0 ppm. Mass spectra were recorded with a ThermoQuest TSQ 7000 spectrometer and HRMS was performed with a ThermoFinnigan MAT 95 XL spectrometer using electrospray ionization (ESI). IR spectra were recorded with a Perkin–Elmer 1725 spectrometer.

Triazoles **1a–1o** were synthesized by copper-catalyzed alkyne–azide cycloaddition (CuAAC) reactions as described previously.[7]

Representative Procedure for the Synthesis of α-Ketotriazole Derivatives: A solution of 1,4-dibenzyl-1*H*-1,2,3-triazole (1.0 equiv., 0.281 mmol, 70.0 mg), *t*BuOOH (4.0 equiv., 1.124 mmol), and CuI



Scheme 3. One-pot synthesis of α-ketotriazole.

or $FeCl_2$ (0.1 equiv., 0.028 mmol) in solvent (1.0 mL) was stirred at room temperature or reflux, respectively, for 20 h. Ethyl acetate was added and the residue was washed with water (25 mL), extracted with ethyl acetate (50 mL), washed with brine (30 mL), and dried with $MgSO_4$. When DMSO or DMF was used as solvent, the extraction was carried out with diethyl ether. The solvent was removed under reduced pressure and the product isolated by flash chromatography (gradient, petroleum ether/ethyl acetate = 90:10 to 50:50). The product was obtained as a white solid.

(1-Benzyl-1*H*-1,2,3-triazol-4-yl)(phenyl)methanone (2a): White crystals, m.p. 116.5 °C, yield 81%. IR (neat): $\tilde{\nu}$ = 3120, 1638, 1518, 1230 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.47–8.35 (m, 2 H), 8.19 (s, 1 H), 7.66–7.56 (m, 1 H), 7.56–7.46 (m, 2 H), 7.37 (m, 5 H), 5.61 (s, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 185.7, 136.5, 133.7, 133.3, 130.6, 129.4, 129.2, 128.4, 54.5 ppm. HRMS (DCI/CH_4): calcd. for $C_{16}H_{14}N_3O$ 264.1137; found 264.1138.

[1-(3,5-Dimethylbenzyl)-1*H*-1,2,3-triazol-4-yl](phenyl)methanone (2b): White powder, m.p. 121.4 °C, yield 64%. IR (neat): $\tilde{\nu}$ = 3132, 1632, 1519, 1234 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.42 (d, J = 7.1 Hz, 2 H), 8.15 (s, 1 H), 7.61 (t, J = 7.4 Hz, 1 H), 7.51 (t, J = 7.3 Hz, 2 H), 7.02 (s, 1 H), 6.94 (s, 2 H), 5.52 (s, 2 H), 2.32 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 185.7, 148.3, 139.0, 136.5, 133.4, 133.2, 130.7, 130.5, 128.3, 128.2, 126.2, 54.4, 21.2 ppm. HRMS (DCI/CH_4): calcd. for $C_{18}H_{18}N_3O$ 292.1450; found 292.1450.

(1-Phenethyl-1*H*-1,2,3-triazol-4-yl)(phenyl)methanone (2c): White crystals, m.p. 124.1 °C, yield 69%. IR (neat): $\tilde{\nu}$ = 3120, 1637, 1526, 1237 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.61 (t, J = 7.4 Hz, 1 H), 7.51 (t, J = 7.5 Hz, 2 H), 7.13 (d, J = 7.8 Hz, 2 H), 4.69 (t, J = 7.2 Hz, 2 H), 3.28 (t, J = 7.2 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 185.6, 136.4, 133.2, 130.5, 129.0, 128.6, 128.3, 127.3, 51.9, 36.5 ppm. HRMS (DCI/CH_4): calcd. for $C_{17}H_{16}N_3O$ 278.1293; found 278.1307.

[1-(4-Methoxyphenethyl)-1*H*-1,2,3-triazol-4-yl](phenyl)methanone (2d): White crystals, m.p. 116.3 °C, yield 61%. IR (neat): $\tilde{\nu}$ = 3121, 1638, 1513, 1239 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.37 (d, J = 7.1 Hz, 2 H), 7.98 (br. s, 1 H), 7.61 (t, J = 7.4 Hz, 1 H), 7.50 (t, J = 7.4 Hz, 2 H), 7.02 (d, J = 8.6 Hz, 2 H), 6.83 (d, J = 8.7 Hz, 2 H), 4.65 (t, J = 7.1 Hz, 2 H), 3.78 (s, 3 H), 321 (t, J = 7.1 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 185.6, 158.8, 136.6, 133.2, 130.5, 129.6, 128.3, 114.3, 55.2, 52.1, 35.6 ppm. HRMS (DCI/CH_4): calcd. for $C_{18}H_{18}N_3O_2$ 308.1399; found 308.1405.

Methyl 5-[(4-Benzoyl-1*H*-1,2,3-triazol-1-yl)methyl]furan-2-carboxylate (2e): White crystals, m.p. 118.6 °C, yield 71%. IR (neat): $\tilde{\nu}$ = 3141, 1715, 1639, 1521, 1306, 1244 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.39 (d, J = 7.1 Hz, 2 H), 8.35 (s, 1 H), 7.61 (t, J = 7.3 Hz, 1 H), 7.51 (t, J = 7.4 Hz, 2 H), 7.15 (d, J = 3.5 Hz, 1 H), 6.59 (d, J = 3.5 Hz, 1 H), 5.69 (s, 2 H), 3.89 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 185.4, 158.5, 150.3, 148.4, 145.5, 136.3, 133.3, 130.5, 128.4, 118.7, 112.5, 52.2, 46.8, 26.4 ppm. HRMS (DCI/CH_4): calcd. for $C_{16}H_{14}N_3O_4$ 312.0984; found 312.0992.

[1-(Naphthalen-2-ylmethyl)-1*H*-1,2,3-triazol-4-yl](phenyl)methanone (2f): White crystals, m.p. 118.0 °C, yield 52%. IR (neat): $\tilde{\nu}$ = 3121, 3056, 1638, 1517, 1223 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.42 (d, J = 8.3 Hz, 2 H), 8.20 (s, 1 H), 7.86 (m, 4 H), 7.53 (m, 5 H), 7.40 (dd, J = 8.5, 1.8 Hz, 1 H), 5.76 (s, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 185.6, 136.5, 133.3, 133.2, 131.0, 130.6, 129.4, 128.4, 128.0, 127.9, 127.8, 127.0, 126.9, 125.3, 54.7 ppm. HRMS (DCI/CH_4): calcd. for $C_{20}H_{16}N_3O$ 314.1293; found 314.1306.

(1-Octyl-1*H*-1,2,3-triazol-4-yl)(phenyl)methanone (2h): White crystals, m.p. 36.1 °C, yield 79%. IR (neat): $\tilde{\nu}$ = 3128, 2925, 2855, 1638, 1519, 1236 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.55–8.34 (m, 2 H), 8.25 (s, 1 H), 7.75–7.38 (m, 3 H), 4.45 (t, J = 7.2 Hz, 2 H), 2.17–1.78 (m, 2 H), 1.48–1.18 (m, 10 H), 1.05–0.69 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 185.8, 136.6, 133.3, 130.6, 128.4, 50.7, 31.7, 30.2, 29.0, 28.9, 26.4, 14.1 ppm. HRMS (DCI/CH_4): calcd. for $C_{17}H_{24}N_3O$ 286.1919; found 286.1929.

(1-Nonyl-1*H*-1,2,3-triazol-4-yl)(phenyl)methanone (2i): White crystals, m.p. 47.3 °C, yield 82%. IR (neat): $\tilde{\nu}$ = 3126, 2925, 1634, 1522, 1240 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 843 (d, J = 7.1 Hz, 2 H), 8.25 (s, 1 H), 7.61 (t, J = 7.3 Hz, 1 H), 7.51 (t, J = 7.4 Hz, 2 H), 4.34 (t, J = 7.2 Hz, 2 H), 1.96 (m, 2 H), 1.25 (m, 12 H), 0.86 (t, J = 6.7 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 185.8, 148.1, 136.5, 133.2, 130.6, 128.4, 128.1, 50.6, 31.8, 30.1, 29.3, 29.1, 28.9, 26.4, 22.6, 14.1 ppm. HRMS (DCI/CH_4): calcd. for $C_{18}H_{26}N_3O$ 299.1998; found 299.2002.

(1-Dodecyl-1*H*-1,2,3-triazol-4-yl)(phenyl)methanone (2j): White solid, m.p. 49.8 °C, yield 83%. IR (neat): $\tilde{\nu}$ = 3127, 2921, 2849, 1633, 1525, 1241 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.44 (d, J = 7.1 Hz, 2 H), 8.26 (s, 1 H), 7.61 (t, J = 7.3 Hz, 1 H), 7.51 (t, J = 7.3 Hz, 2 H), 4.44 (t, J = 7.2 Hz, 2 H), 1.96 (m, 2 H), 1.25 (m, 18 H), 0.87 (t, J = 6.7 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 185.8, 136.6, 133.2, 130.6, 128.3, 50.7, 31.9, 30.1, 29.5, 29.4, 29.32, 29.29, 28.9, 26.4, 22.6, 14.1 ppm. HRMS (DCI/CH_4): calcd. for $C_{21}H_{32}N_3O$ 342.2545; found 342.2549.

(5-Iodo-1-nonyl-1*H*-1,2,3-triazol-4-yl)(phenyl)methanone (2k): Yellow powder, m.p. 49.8 °C, yield 84%. IR (neat): $\tilde{\nu}$ = 2925, 2855, 1645, 1472, 1228 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.32 (d, J = 7.1 Hz, 2 H), 7.60 (t, J = 7.3 Hz, 1 H), 7.50 (t, J = 7.4 Hz, 2 H), 4.48 (t, J = 7.4 Hz, 2 H), 1.96 (m, 2 H), 1.26 (m, 12 H), 0.87 (t, J = 6.7 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 185.6, 147.0, 136.6, 133.2, 130.7, 128.2, 84.5, 31.7, 29.7, 29.3, 29.1, 28.9, 26.3, 22.6, 14.0 ppm. HRMS (DCI/CH_4): calcd. for $C_{18}H_{25}N_3OI$ 426.1042; found 426.1056.

(1-Benzyl-1*H*-1,2,3-triazol-4-yl)(3,4-dimethoxyphenyl)methanone (2l): White crystals, m.p. 126.0 °C, yield 83%. IR (neat): $\tilde{\nu}$ = 3122, 1633, 1574, 1509, 1269 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.36 (dd, J = 8.5, 2.0 Hz, 1 H), 8.15 (s, 1 H), 7.98 (d, J = 2.0 Hz, 1 H), 7.39 (m, 3 H), 7.35 (m, 2 H), 6.96 (d, J = 8.6 Hz, 1 H), 5.60 (s, 2 H), 3.97 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 183.7, 153.6, 146.8, 133.7, 129.34, 129.30, 129.1, 128.4, 128.2, 126.2, 112.4, 110.1, 56.1, 56.0, 54.4 ppm. HRMS (DCI/CH_4): calcd. for $C_{18}H_{18}N_3O_3$ 324.1348; found 324.1353.

(1-Benzyl-1*H*-1,2,3-triazol-4-yl)(3-methoxyphenyl)methanone (2m): White crystals, m.p. 92.3 °C, yield 81%. IR (neat): $\tilde{\nu}$ = 3134, 1639, 1583, 1514, 1302, 1213 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.14 (s, 1 H), 8.07 (d, J = 7.7 Hz, 1 H), 7.91 (dd, J = 2.4, 1.4 Hz, 1 H), 7.31–7.44 (m, 6 H), 7.16 (dd, J = 8.2, 2.5 Hz, 1 H), 5.60 (s, 2 H), 3.87 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 185.3, 159.5, 137.7, 133.6, 129.4, 129.3, 129.1, 128.4, 123.4, 120.1, 114.4, 55.4, 54.5 ppm. HRMS (DCI/CH_4): calcd. for $C_{17}H_{16}N_3O_2$ 294.1243; found 294.1252.

(1-Benzyl-1*H*-1,2,3-triazol-4-yl)(3-nitrophenyl)methanone (2n): White powder, m.p. 146.4 °C, yield 72%. IR (neat): $\tilde{\nu}$ = 3131, 2923, 1652, 1526, 1343, 1226 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 9.28 (s, 1 H), 8.85 (d, J = 7.8 Hz, 1 H), 8.46 (d, J = 8.2 Hz, 1 H), 7.72 (t, J = 8.0 Hz, 1 H), 7.42 (m, 3 H), 7.36 (m, 2 H), 5.64 (s, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 183.1, 148.2, 147.6, 129.6, 129.44, 129.36, 128.7, 128.5, 127.4, 125.6, 54.6 ppm. HRMS (DCI/CH_4): calcd. for $C_{16}H_{13}N_4O_3$ 309.0988; found 309.0981.

(1-Benzyl-5-iodo-1*H*-1,2,3-triazol-4-yl)(phenyl)methanone (2p): Colorless crystal (crystallization: AcOEt/heptane), m.p. 114.6 °C, yield 8%. ^1H NMR ($CDCl_3$): δ = 8.33 (d, J = 7.1 Hz, 4 H), 7.61 (t, J = 7.3 Hz, 2 H), 7.51 (t, J = 7.4 Hz, 4 H), 7.36 (m, 10 H), 5.72 (s, 4

H) ppm. ^{3}C NMR ($CDCl_3$): δ = 185.5, 136.6, 133.6, 133.3, 130.7, 129.0, 128.8, 128.3, 128.0, 54.2 ppm. HRMS (DCI/CH_4): calcd. for $C_{32}H_{25}N_6O_2$ 525.2039; found 525.2059.

Supporting Information (see footnote on the first page of this article): Analytical data for **1l**, **1m**, and **1n**, X-ray structure determination of **2p**, and ^{1}H and ^{13}C NMR spectra.

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[21] CCDC-915771 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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