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Regioselective Approach to 5-Carboxy-1,2,3-triazoles Based on Palladium-Catalyzed Carbonylation

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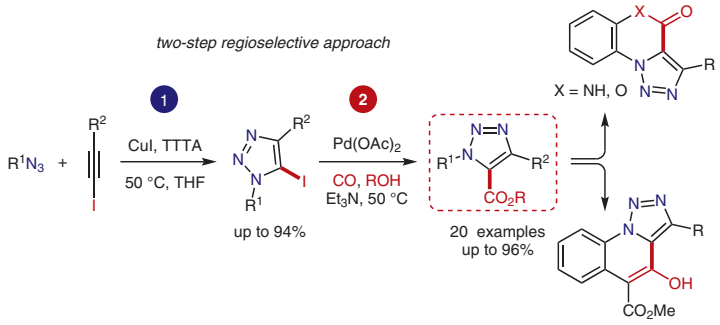

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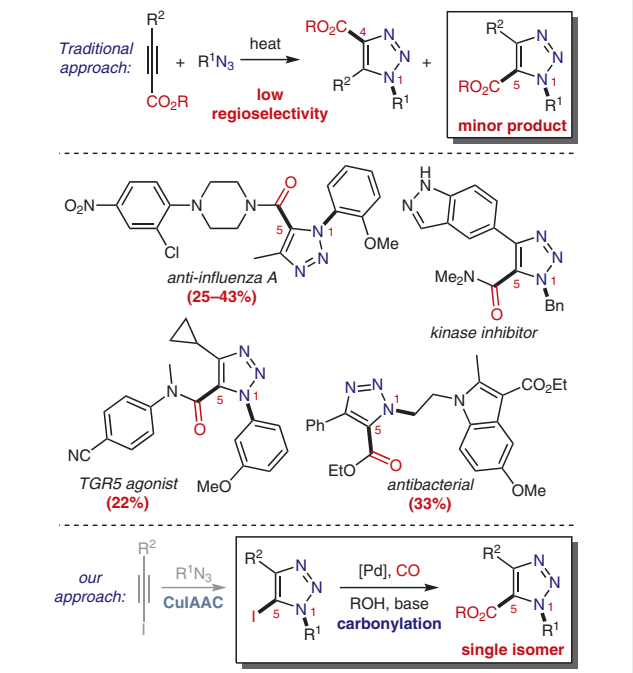
Abstract A regioselective two-step approach to 5-carboxy-1,2,3-triazoles based on palladium-catalyzed carbonylation has been developed. The protocol utilizes readily available 5-iodotriazoles as starting materials. The obtained products were used in the syntheses of fused heterocycles as well as derivatization of the steroidal hormone cortexolone.

Key words 1,2,3-triazole, carbonylation, catalysis, palladium, copper

Various compounds containing the 1,2,3-triazole moiety are of importance in coordination and supramolecular chemistry and polymer and materials sciences.[1] This type of nitrogen heterocycle has also been shown to be a pharmacophore, and is now intensively studied in medicinal chemistry.[2] In particular, some 5-carboxy-1,2,3-triazoles have been shown to be kinase inhibitors, PPARα/γ and TGR5 agonists, and also exhibit antiviral and antibacterial effects.[3]

So far, the major synthetic route to 5-carboxy-1,2,3-triazoles has been thermal 1,3-dipolar cycloaddition of organic azides to propiolic acid derivatives (Scheme 1). This method suffers from rather harsh conditions, low to moderate yields, and low regioselectivity.[3,4] In the absence of bulky R groups both in the ester and azide, the major product of this reaction is the undesired 4-carboxytriazole isomer. Nevertheless, this approach has traditionally been used as a preparative method to access various biologically active 5-carboxytriazoles. For instance, the yields of the desired regioisomers at the cycloaddition step in the syntheses of a number of triazole-based drugs are in the range of 22–43% and, in some cases, even less than 10%. Moreover, separation of the regioisomeric adducts is problematic and can be achieved only by tedious column chromatography or preparative HPLC.



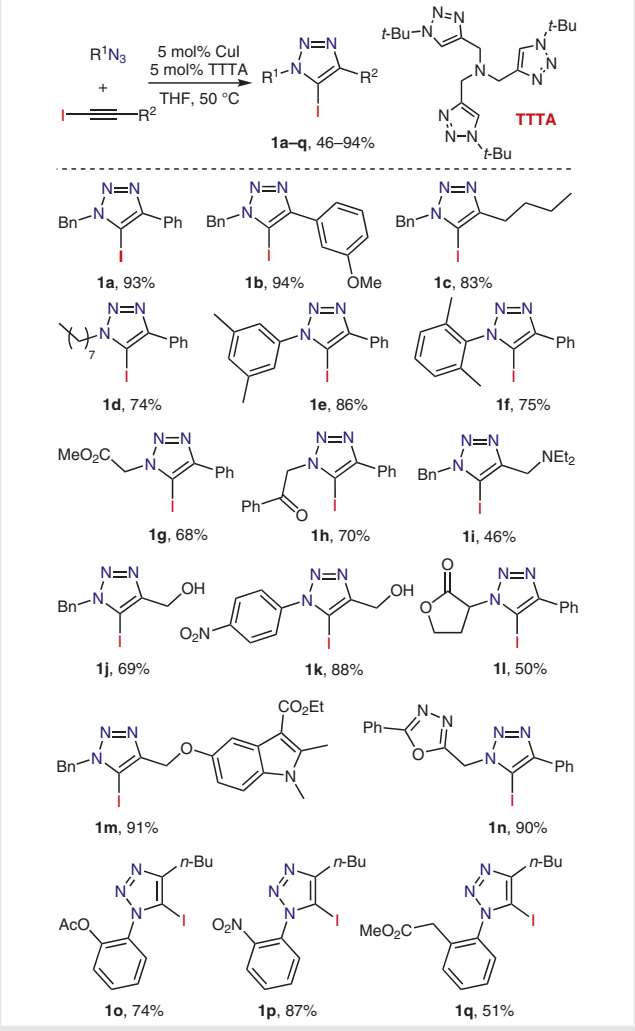
Scheme 1 Synthetic routes to biologically active 5-carboxy-1,2,3-triazoles (yields at cycloaddition step are presented in parentheses)

Since 5-iodo-1,2,3-triazoles are readily accessible via Cu(I) catalysis,[5] the subsequent carbonylation reaction could become a new regioselective approach to 5-carboxy-1,2,3-triazoles. To the best of our knowledge, there have been no reports on the carbonylation of 5-iodo-1,2,3-triazoles, although these substrates have been successfully

involved in a number of Pd-catalyzed transformations,[6] such as Suzuki, Stille, and Sonogashira cross-couplings and the Heck reaction.

Nevertheless, Pd-catalyzed carbonylation of vinyl, aryl, or hetaryl halides is a powerful methodology, which can be used as a straightforward, efficient, and convenient route to various derivatives of carboxylic acids.[7] Herein, we report a regioselective approach to 5-carboxy-1,2,3-triazoles based on Cu-catalyzed synthesis of 5-iodo-1,2,3-triazoles followed by Pd-catalyzed carbonylation.

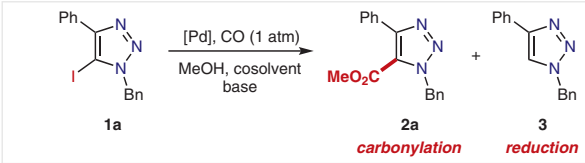
A number of 5-iodo-1,2,3-triazoles **1a–q** were prepared according to a slightly modified reported procedure[5a] from azides and 1-iodoalkynes in the presence of 5 mol% CuI and 5 mol% of the auxiliary ligand tris[(1-*tert*-butyl-1H-1,2,3-triazolyl)methyl]amine (TTTA) in THF at 50 °C (Scheme 2).



Scheme 2 Preparation of 5-iodo-1,2,3-triazoles

High yields of up to 94% were observed for both aliphatic and aromatic R substituents (**1a–f**), including some bulky ones (**1e** and **1f**), although only 20% conversion was reached in the reaction of *tert*-butyl azide and (iodoethynyl)-benzene. The protocol tolerates the presence of various functional groups, such as hydroxyl (**1j**, **1k**), ester (**1g**, **1l**, **1m**, **1q**), ketone (**1h**), tertiary amine (**1i**), and nitro (**1k**, **1p**); however, the presence of free phenol inhibited the reaction. Preliminary acylation of the OH group allowed us to achieve a good yield of iodotriazole **1o** (74%). Excellent yields (90–91%) were achieved for compounds bearing an additional heterocyclic moiety, such as indole (**1m**) and 1,3,4-oxadiazole (**1n**) (Scheme 2).

Iodotriazole **1a** was chosen as a model substrate for Pd-catalyzed methoxycarbonylation (Scheme 3). The formation of target methyl ester **2a** was accompanied by undesirable reduction of the starting iodotriazole **1a** affording **3** as a byproduct (Table 1, entry 1). To find appropriate reaction conditions providing sufficient efficiency and selectivity, we have optimized a number of parameters, such as catalyst, base, and solvent.



Scheme 3 Model reaction for Pd-catalyzed carbonylation of 5-iodo-1,2,3-triazoles

Table 1 Ligand and Solvent Effect on Methoxycarbonylation of **1a**[a]

Entry	Catalyst	Additive	Solvent	Yield (%)[b]	
				2a	**3**
1	$Pd(OAc)_2$	–	THF–MeOH (1:1)	23	4
2	$Pd(PPh_3)_4$	–	THF–MeOH (1:1)	21	6
3	$Pd(PPh_3)_2Cl_2$	–	THF–MeOH (1:1)	10	14
4	$Pd(dppf)Cl_2$[c]	–	THF–MeOH (1:1)	6	7
5	$Pd(dppb)Cl_2$[c]	–	THF–MeOH (1:1)	0	19
6	$Pd(OAc)_2$	40% PVI[c]	THF–MeOH (1:1)	0	2
7	$Pd(OAc)_2$	40% PVP[c]	THF–MeOH (1:1)	40	2
8	$Pd(OAc)_2$	–	MeCN–MeOH (1:1)	35	7
9	$Pd(OAc)_2$	–	DMF–MeOH (1:1)	35	5
10	$Pd(OAc)_2$	–	MeOH	63	5
11	$Pd(OAc)_2$	40% PVP[c]	MeOH	51	1

[a] Reaction conditions: **1a** (0.1 mmol), cat. (5 mol%), Et_3N (20 equiv), solvent (0.1 M solution), CO (1 atm), r.t., 17 h.
[b] Yield determined by ^1H NMR.
[c] dppf = 1,1′-bis(diphenylphosphino)ferrocene; dppb = 1,4-bis(diphenylphosphino)butane; PVI = polyvinylimidazole; PVP = polyvinylpyrrolidone.

Screening of Pd catalysts under 1 atm of CO at ambient temperature (Table 1) in a MeOH–THF mixture has shown that $Pd(OAc)_2$ and $Pd(PPh_3)_4$ were the most efficient. Other phosphine complexes such as $Pd(dppb)Cl_2$ and $Pd(dppf)Cl_2$, which are known to produce highly active catalysts in the carbonylation of hetaryl chlorides,[8] gave lower yields and selectivity in comparison with $Pd(OAc)_2$ and $Pd(PPh_3)_4$ (cf. entries 1, 2 and 4, 5).

During the initial stage of the reaction we observed rapid formation of Pd black. In order to prevent aggregation of Pd nanoparticles, believed to play a crucial role in phosphine-free catalysis,[9] several soluble polymers capable of retarding the Ostwald ripening were examined. While the reaction was inhibited by polyvinylimidazole, the yield of **2a** was enhanced by addition of polyvinylpyrrolidone (PVP) (entries 6 and 7). The change of THF for other cosolvents, such as MeCN and DMF, slightly increased the yield of **2a** (entries 8 and 9), but the best results were obtained in neat MeOH (entry 10). It should be noted that the beneficial effect of PVP was reversed when the THF–MeOH solvent mixture was changed to MeOH (entry 1 vs 7 and entry 10 vs 11).

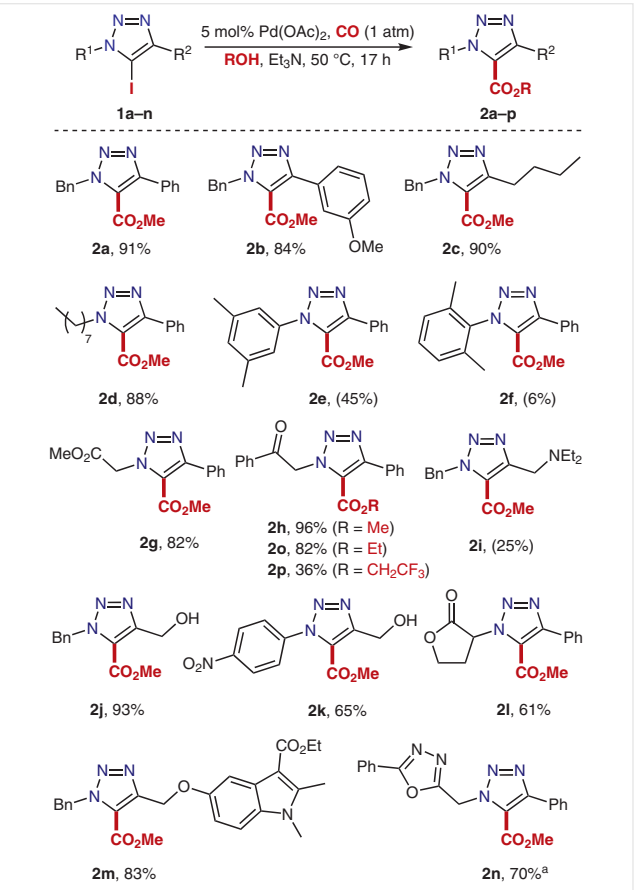
Triethylamine was found to be the best base for the reaction (Table 2). Interestingly, the use of a large excess of base (20 equiv instead of 5) increased the yield of **2a** from 49 to 63% (entries 1 and 2). A complete conversion of **1a** and high yield of **2a** were achieved by raising the temperature to 50 °C (entry 7). Thus, it was established that Pd-catalyzed alkoxycarbonylation of 5-iodo-1,2,3-triazoles could be carried out efficiently under very mild conditions, employing only 1 atm of CO at 50 °C in the presence of 5 mol% $Pd(OAc)_2$ and Et_3N in MeOH.

Table 2 Effect of Base and Temperature[a]

Entry	Base	Temp	Yield (%)[b]	
			2a	**3**
1	Et_3N (5 equiv)	r.t.	49	1
2	Et_3N (20 equiv)	r.t.	63	5
3	DIPEA (20 equiv)	r.t.	60	3
4	DABCO (20 equiv)	r.t.	35	6
5	DMAP (20 equiv)	r.t.	0	0
6[c]	K_2CO_3 (2 equiv)	r.t.	8	54
7	Et_3N (20 equiv)	50 °C	94	6

[a] Reaction conditions: **1a** (0.1 mmol), $Pd(OAc)_2$ (5 mol%), base, MeOH (2 mL), CO (1 atm), 17 h.
[b] Yield determined by ^1H NMR.
[c] MeCN–MeOH (1:1) mixture used as solvent.

With the optimized conditions for carbonylation in hand, we investigated the scope of the protocol employing 5-iodotriazoles **1a–n** (Scheme 4). In most cases, the developed procedure was quite efficient and the target methyl 1,2,3-triazole-5-carboxylates **2** were obtained in good yields (up to 96%). Substrates with both aliphatic and aromatic substituents afforded the corresponding products **2a–d** in high yields (84–91%). However, the carbonylation proved to be rather sensitive to steric hindrance. 1,4-Diaryl-5-iodotriazoles were much less reactive and gave incomplete conversions of **1** with significant amounts of reduction byproducts (40–50%). For instance, the yield of ester **2e** bearing the 3,5-dimethylphenyl group was only 45%. Moreover, in the case of the even more sterically demanding 2,6-dimethylphenyl substituent, only trace amounts of product **2f** were observed (6%).



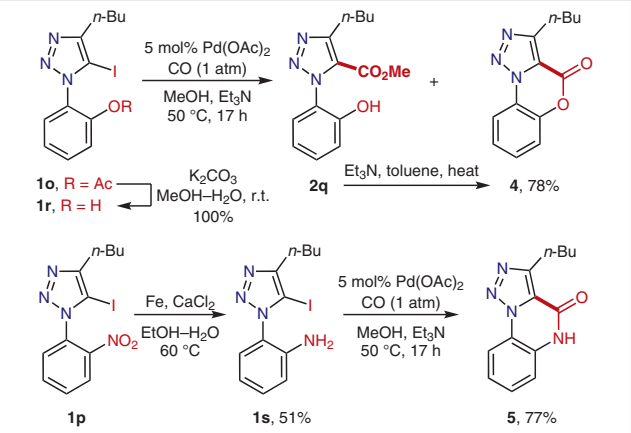
Scheme 4 Pd-catalyzed alkoxycarbonylation of 5-iodo-1,2,3-triazoles **1** (yields determined by ^1H NMR are presented in parentheses). [a] MeOH–DMF (4:1) as solvent.

Various functional groups, such as ester (**2g**, **2l**), ketone (**2h**), hydroxyl (**2j**, **2k**), and nitro (**2k**), were tolerated by the developed carbonylation protocol, and the corresponding products were isolated in good to excellent yields (61–96%) (Scheme 4). The combination of steric hindrance and competing cleavage of γ-butyrolactone moiety by methanol led to a somewhat diminished yield of **2l** (61%). High yields were achieved for heterocyclic derivatives **2m** (83%) and **2n** (70%). The poor yield (25%) for **2i** bearing a tertiary amine

substituent is likely to be associated with the involvement of amine in intramolecular coordination with the Pd center, hindering the binding of a CO molecule.

Carbonylation of iodotriazole **1h** in other alcohols allowed the formation of ethyl and trifluoroethyl esters **2o** and **2p** (Scheme 4). High yields were achieved by carrying out the reaction in MeOH and EtOH (96 and 82%, respectively). The use of the much less nucleophilic CF_3CH_2OH led to the predominant formation of deiodinated triazole. Therefore, the corresponding ester **2p** was obtained in rather low yield (36%).

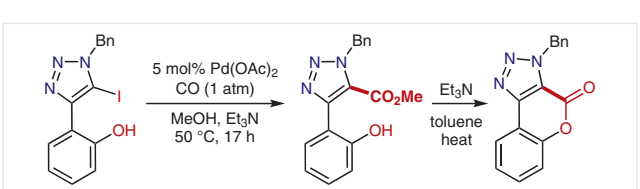
The introduction of the ester moiety to the 1,2,3-triazole ring can be used to obtain substrates that serve as valuable precursors of various fused heterocyclic systems. For instance, Pd-catalyzed carbonylation of **1o**, bearing the easily cleavable phenyl ester moiety, as well as its deacetylated analog **1r** led to an approximately equimolar mixture of methyl ester **2q** and lactone **4** (Scheme 5). Complete cyclization to **4** was achieved by heating the crude mixture in refluxing toluene in the presence of Et_3N. Similarly, reduction of the nitro group[10] in **1p** and the subsequent carbonylation of aniline **1s** furnished lactam **5** in high yield (77%) (Scheme 5).



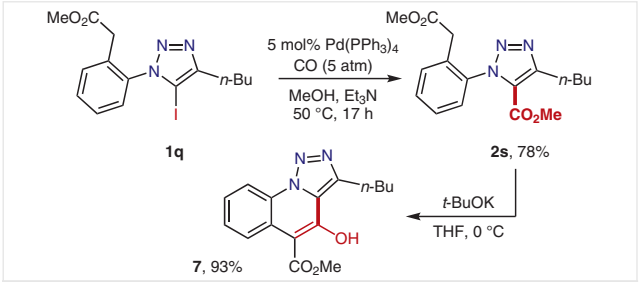
Scheme 5 Routes to triazole-fused benzoxazinone **4** and quinoxalinone **5**

A similar approach was utilized for the preparation of fused heterocycle **6** comprising 1,2,3-triazole and coumarin (Scheme 6). Iodotriazole **1t** was prepared from **1a** by Pd-catalyzed acetoxylation followed by hydrolysis according to a previously reported procedure.[11] In contrast to the carbonylation of **1o** and **1r** (Scheme 5), the same reaction in the case of **1t** afforded methyl ester **2r** with only trace amounts of cyclized product **6**. Nevertheless, complete lactonization was achieved after heating **2r** in refluxing toluene for several hours, furnishing **6** in excellent yield (92%).

Iodotriazole **1q** bearing an enolizable ester group in the *ortho* position was found to be rather unreactive in Pd-catalyzed carbonylation, and the use of the standard reaction conditions was complicated by low conversion (less than 50%) and deiodination. Surprisingly, increasing the CO pressure led to a sharp decrease in the yield of **2s**, which is probably attributed to the accelerated reduction of the precatalyst and aggregation of the formed Pd(0) complexes to give catalytically inactive Pd black. Gratifyingly, the yield of the desired diester **2s** was improved to 78% by carrying out the reaction under an increased pressure of CO (5 atm) in the presence of 5 mol% $Pd(PPh_3)_4$ as the catalyst (Scheme 7). The subsequent Dieckmann condensation of **2s** was performed by addition of potassium *tert*-butoxide, smoothly affording [1,2,3]triazolo[1,5-*a*]quinoline **7** in excellent yield (93%).



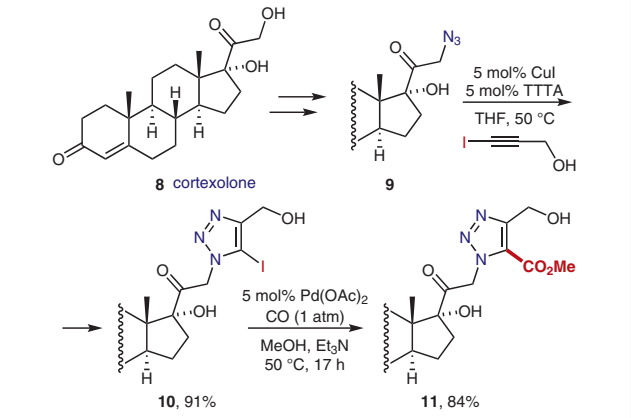
Scheme 6 Synthesis of triazolocoumarin **6**



Scheme 7 Synthesis of [1,2,3]triazolo[1,5-*a*]quinoline **7**

To demonstrate the applicability of our protocol for the derivatization of complex natural products, we followed a previously reported procedure[12] to introduce an azido group to cortexolone **8**, an important steroidal hormone (Scheme 8). Azide **9** was subsequently transformed into iodotriazole **10** and the corresponding methyl ester **11**, in high yields for both steps (91 and 84%, respectively).

In conclusion, we have developed a regioselective approach to 5-carboxy-1,2,3-triazoles based on Cu-catalyzed synthesis of 5-iodo-1,2,3-triazoles and subsequent Pd-catalyzed carbonylation. We have shown that alkoxycarbonylation of iodotriazoles can be performed efficiently under mild conditions (1 atm CO, 50 °C) employing a simple palladium catalyst $Pd(OAc)_2$. The method featured very good functional group tolerance, furnishing the target compounds in high yields (up to 96%). The obtained 5-carboxy-1,2,3-triazoles were shown to be valuable precursors in the preparation of diverse fused heterocyclic scaffolds combining 1,2,3-triazole with benzoxazinone, quinoxalinone, quinoline, and coumarin. Synthetic utility of the protocol was also demonstrated in derivatization of the steroidal hormone cortexolone.



Scheme 8 Modification of cortexolone

NMR spectra were recorded on Bruker Avance 400, Agilent 400MR (^{1}H, 400 MHz; ^{13}C, 100.6 MHz; ^{19}F, 376 MHz) and Bruker Avance 600 (^{1}H, 600 MHz; ^{13}C, 150 MHz) spectrometers at ambient temperature. Chemical shifts in ppm are referenced to hexamethyldisiloxane (δ = 0.05 ppm) or tetramethylsilane (δ = 0 ppm) in the ^{1}H NMR spectra and to the solvent signal in the ^{13}C NMR spectra. MALDI-TOF spectra were recorded with a Bruker Daltonics UltraFlex instrument in a dithranol matrix using PEG 400 or PEG 600 as the internal standard. ESI-TOF spectra were recorded with a Thermo Scientific Orbitrap Elite instrument. Elemental analyses were performed with an Elementar Vario MICRO cube apparatus. Column chromatography was carried out on Macherey–Nagel silica gel 60 (0.040–0.063 mm).

Palladium-Catalyzed Carbonylation of 5-Iodo-1*H*-1,2,3-triazoles 1; General Procedure

In a flask, equipped with a condenser, the appropriate 5-iodo-1*H*-1,2,3-triazole **1** (0.25 mmol), $Pd(OAc)_2$ (2.8 mg, 12.5 µmol, 5 mol%), and Et_3N (0.70 mL, 5 mmol, 20 equiv) were mixed under a CO atmosphere in the appropriate alcohol (MeOH, EtOH, or CF_3CH_2OH) as a solvent (5 mL). The reaction mixture was stirred at 50 °C for 17 h, then diluted with CH_2Cl_2 (25 mL), washed with 10% aq HCl (25 mL) and H_2O (25 mL). The organic layer was dried with anhydrous Na_2SO_4, and the solvents were evaporated in vacuo. The residue was purified by column chromatography.

Methyl 1-Benzyl-4-phenyl-1*H*-1,2,3-triazole-5-carboxylate (2a)

Prepared from **1a** (0.25 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, hexanes–EtOAc, 4:1). Spectral data are in accordance with the literature.[13]

Yellowish oil; yield: 66.8 mg (91%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71–7.66 [m, 2 H, 2,6-CH(4-Ph)], 7.43–7.36 [m, 3 H, CH(Ph)], 7.34–7.25 [m, 5 H, CH(Ph)], 5.90 (s, 2 H, CH_2), 3.73 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 159.5 (C=O), 150.5 [4-C(triazole)], 135.1 [1-C(1-CH_2*Ph*)], 130.2 [1-C(4-Ph)], 129.2 [2 C, CH(Ph)], 128.9 [4-CH(Ph)], 128.7 [2 C, CH(Ph)], 128.3 [4-CH(Ph)], 128.0 [2 C, CH(Ph)], 127.8 [2 C, CH(Ph)], 123.7 [5-C(triazole)], 54.2 (CH_2), 52.2 (CH_3).

HRMS (MALDI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{16}N_3O_2$: 294.1237; found: 294.1247.

Methyl 1-Benzyl-4-(3-methoxyphenyl)-1*H*-1,2,3-triazole-5-carboxylate (2b)

Prepared from **1b** (0.25 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, hexanes–EtOAc, 4:1).

Yellowish oil; yield: 67.8 mg (84%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 8 H, 5 H Ph + 3 H Ar), 6.94 [ddd, *J* = 7.8, 2.7, 1.3 Hz, 1 H, 4-CH(Ar)], 5.89 (s, 2 H, CH_2), 3.80 (s, 3 H, CH_3), 3.75 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 159.5 [C=O or 3-C(Ar)], 159.2 [C=O or 3-C(Ar)], 150.2 [4-C(triazole)], 135.0 [1-C(Ph)], 131.3 [1-C(Ar)], 129.0 [5-CH(Ar)], 128.7 [2 C, CH(Ph)], 128.3 [4-CH(Ph)], 127.8 [2 C, CH(Ph)], 123.8 [5-C(triazole)], 121.7 [6-CH(Ar)], 115.1 [2- or 4-CH(Ar)], 114.3 [2- or 4-CH(Ar)], 55.3 (*C*H$_3$OAr), 54.2 (CH_2), 52.3 (CO_2CH_3).

HRMS (MALDI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{17}N_3NaO_3$: 346.1162; found: 346.1166.

Anal. Calcd for $C_{18}H_{17}N_3O_3$: C, 66.86; H, 5.30; N, 13.00. Found: C, 66.69; H, 5.28; N, 12.89.

Methyl 1-Benzyl-4-butyl-1*H*-1,2,3-triazole-5-carboxylate (2c)

Prepared from **1c** (0.25 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, hexanes–EtOAc, 4:1).

Yellowish oil; yield: 61.3 mg (90%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.21 (m, 5 H, Ph), 5.84 (s, 2 H, CH_2N), 3.85 (s, 3 H, CH_3O), 2.92–2.87 (m, 2 H, *C*H$_2$Pr), 1.67 (m, 2 H, *C*H$_2$Et), 1.37 (sext, *J* = 7.3 Hz, 2 H, *C*H$_2$CH$_3$), 0.91 (t, *J* = 7.3 Hz, 3 H, CH$_2$*C*H$_3$).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 159.5 (C=O), 152.9 [4-C(triazole)], 135.3 [1-C(Ph)], 128.6 [2 C, CH(Ph)], 128.1 [4-CH(Ph)], 127.7 [2 C, CH(Ph)], 123.6 [5-C(triazole)], 53.8 (CH_2N), 52.0 (CH_3O), 31.2 (*C*H$_2$Pr), 26.1 (*C*H$_2$Et), 22.4 (*C*H$_2$CH$_3$), 13.7 (CH$_2$*C*H$_3$).

HRMS (MALDI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{20}N_3O_2$: 274.1550; found: 274.1559.

Anal. Calcd for $C_{15}H_{19}N_3O_2$: C, 65.91; H, 7.01; N, 15.37. Found: C, 65.90; H, 7.08; N, 15.03.

Methyl 1-Octyl-4-phenyl-1*H*-1,2,3-triazole-5-carboxylate (2d)

Prepared from **1d** (0.25 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, CH_2Cl_2).

Yellowish oil; yield: 69.6 mg (88%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72–7.65 [m, 2 H, 2,6-CH(Ph)], 7.46–7.36 [m, 3 H, 3,4,5-CH(Ph)], 4.69 (t, *J* = 7.3 Hz, 2 H, CH_2N), 3.82 (s, 3 H, CH_3O), 1.91 (quin, *J* = 7.3 Hz, 2 H, *C*H$_2$CH$_2$N), 1.43–1.17 (m, 10 H), 0.86 (t, *J* = 7.0 Hz, 3 H, CH$_2$*C*H$_3$).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 159.7 (C=O), 150.2 [4-C(triazole)], 130.4 [1-C(Ph)], 129.2 [2 C, CH(Ph)], 128.8 [4-CH(Ph)], 128.0 [2 C, CH(Ph)], 123.7 [5-C(triazole)], 52.2 (CH_3O), 51.1 (CH_2N), 31.6, 30.3, 29.0, 28.9, 26.4, 22.5, 14.0 (CH$_2$*C*H$_3$).

HRMS (MALDI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{26}N_3O_2$: 316.2020; found: 316.2023.

Anal. Calcd for $C_{18}H_{25}N_3O_2$: C, 68.54; H, 8.01; N, 13.32. Found: C, 68.66; H, 8.01; N, 13.20.

Methyl 1-(2-Methoxy-2-oxoethyl)-4-phenyl-1*H*-1,2,3-triazole-5-carboxylate (2g)

Prepared from **1g** (0.25 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, hexanes–EtOAc, 4:1).

Yellowish oil; yield: 56.6 mg (82%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77–7.72 [m, 2 H, 2,6-CH(Ph)], 7.46–7.39 [m, 3 H, 3,4,5-CH(Ph)], 5.49 (s, 2 H, CH_2), 3.81 (s, 3 H, CH_3), 3.79 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 166.8 (CH_2CO_2Me), 159.5 (CCO_2Me), 150.2 [4-C(triazole)], 129.8 [1-C(Ph)], 129.4 [2 C, CH(Ph)], 129.1 [4-CH(Ph)], 128.0 [2 C, CH(Ph)], 124.3 [5-C(triazole)], 52.9, 52.4, 52.0.

HRMS (MALDI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{13}N_3NaO_3$: 298.0798; found: 298.0811.

Anal. Calcd for $C_{13}H_{13}N_3O_4$: C, 56.72; H, 4.76; N, 15.27. Found: C, 56.76; H, 4.86; N, 15.09.

Methyl 1-(2-Oxo-2-phenylethyl)-4-phenyl-1*H*-1,2,3-triazole-5-carboxylate (2h)

Prepared from **1h** (0.25 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, CH_2Cl_2–MeOH, 100:1).

Yellow oil; yield: 77.0 mg (96%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03–7.97 [m, 2 H, 2,6-CH(Bz)], 7.80–7.75 [m, 2 H, 2,6-CH(4-Ph)], 7.68–7.62 [m, 1 H, 4-CH(Bz)], 7.56–7.50 [m, 2 H, 3,5-CH(Bz)], 7.47–7.39 [m, 3 H, 3,4,5-CH(Ph)], 6.20 (s, 2 H, CH_2), 3.72 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 190.2 [C=O(ketone)], 159.6 [C=O(ester)], 150.1 [4-C(triazole)], 134.3 [4-CH(Bz)], 134.1 [1-C(Bz)], 130.1 [1-C(4-Ph)], 129.5 [2 C, CH(Ph)], 129.1 [2 C, CH(Ph)], 129.0 [4-CH(4-Ph)], 128.0 [4 C, CH(Ph)], 124.8 [5-C(triazole)], 57.0 (CH_2), 52.3 (CH_3).

HRMS (MALDI-TOF): *m*/*z* [M + K]$^+$ calcd for $C_{18}H_{15}KN_3O_3$: 360.0745; found: 360.0752.

Methyl 1-Benzyl-4-(hydroxymethyl)-1*H*-1,2,3-triazole-5-carboxylate (2j)

Prepared from **1j** (0.25 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, CH_2Cl_2–MeOH, 30:1).

Yellow oil; yield: 57.3 mg (93%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.23 (m, 5 H, Ph), 5.85 (s, 2 H, CH_2N), 4.90 (s, 2 H, CH_2OH), 3.89 (s, 3 H, CH_3), 3.29 (br s, 1 H, OH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 158.9 (C=O), 151.5 [4-C(triazole)], 134.8 [1-C(Ph)], 128.7 [2 C, CH(Ph)], 128.3 [4-CH(Ph)], 127.8 [2 C, CH(Ph)], 124.1 [5-C(triazole)], 56.7 (CH_2O), 54.0 (CH_2N), 52.6 (CH_3).

HRMS (MALDI-TOF): *m*/*z* [M + K]$^+$ calcd for $C_{12}H_{13}KN_3O_3$: 286.0588; found: 286.0590.

Anal. Calcd for $C_{12}H_{13}N_3O_3$: C, 58.29; H, 5.30; N, 17.00. Found: C, 58.47; H, 5.58; N, 16.63.

Methyl 4-(Hydroxymethyl)-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-5-carboxylate (2k)

Prepared from **1k** (0.25 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, CH_2Cl_2–MeOH, 30:1).

Off-white solid; yield: 45.3 mg (65%); mp 150–151 °C.

^{1}H NMR (400 MHz, DMSO-d_6–CCl_4): δ = 8.42–8.36 [m, 2 H, 3,5-CH(Ar)], 7.87–7.82 [m, 2 H, 2,6-CH(Ar)], 5.08 (br s, 1 H, OH), 4.76 (s, 2 H, CH_2), 3.83 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, DMSO-d_6–CCl_4): δ = 157.8 (C=O), 151.1 [4-C(triazole)], 147.6 [4-C(Ar)], 141.2 [1-C(Ar)], 126.7 [2 C, CH(Ar)], 125.7 [2 C, CH(Ar)], 123.9 [5-C(triazole)], 54.4 (CH_2), 52.3 (CH_3).

HRMS (MALDI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{11}N_4O_5$: 279.0724; found: 279.0720.

Methyl 1-(2-Oxotetrahydrofuran-3-yl)-4-phenyl-1*H*-1,2,3-triazole-5-carboxylate (2l)

Prepared from **1l** (0.25 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, hexanes–EtOAc, 1:1).

Yellowish oil; yield: 43.6 mg (61%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71–7.65 [m, 2 H, 2,6-CH(Ph)], 7.46–7.40 [m, 3 H, 3,4,5-CH(Ph)], 6.17 (dd, *J* = 10.2, 9.3 Hz, 1 H, CHN), 4.71 (td, *J* = 9.3, 2.6 Hz, 1 H, CH_2O), 4.50 (td, *J* = 9.3, 7.0 Hz, 1 H, CH_2O), 3.82 (s, 3 H, CH_3), 3.13 (dq, *J* = 12.7, 9.3 Hz, 1 H, CH_2CH), 2.92 (dddd, *J* = 12.7, 10.2, 7.0, 2.6 Hz, 1 H, CH_2CH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 170.8 ($CHCO_2$), 159.7 (CO_2Me), 150.5 [4-C(triazole)], 129.7 [1-C(Ph)], 129.4 [2 C, CH(Ph)], 129.2 [4-CH(Ph)], 128.1 [2 C, CH(Ph)], 124.1 [5-C(triazole)], 66.0 (CH_2O), 58.3 (CHN), 52.7 (CH_3), 28.6 (CH_2CH).

HRMS (MALDI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{13}N_3NaO_4$: 310.0798; found: 310.0802.

Anal. Calcd for $C_{14}H_{13}N_3O_4$: C, 58.53; H, 4.56; N, 14.63. Found: C, 58.35; H, 4.55; N, 14.32.

Ethyl 5-{[1-Benzyl-5-(methoxycarbonyl)-1*H*-1,2,3-triazol-4-yl]methoxy}-1,2-dimethyl-1*H*-indole-3-carboxylate (2m)

Prepared from **1m** (0.15 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, CH_2Cl_2–MeOH, 50:1).

Off-white solid; yield: 66.1 mg (83%); mp 99–101 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 [d, *J* = 2.5 Hz, 1 H, 4-CH(indole)], 7.34–7.25 (m, 5 H, Ph), 7.13 [d, *J* = 8.8 Hz, 1 H, 7-CH(indole)], 6.91 [dd, *J* = 8.8, 2.5 Hz, 1 H, 6-CH(indole)], 5.89 (s, 2 H, $PhCH_2$), 5.15 [s, 2 H, CH_2C(triazole)], 5.36 [s, 2 H, CH_2C(triazole)], 4.36 (q, *J* = 7.1 Hz, 2 H, CH_2CH_3), 3.82 (s, 3 H, OCH_3), 3.60 (s, 3 H, NCH_3), 2.70 (s, 3 H, 2-CH_3), 1.41 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 166.0 (CO_2Et), 158.8 (CO_2Me), 154.5 [5-C(indole)], 147.3 [4-C(triazole)], 145.4 [2-C(indole)], 134.8 [1-C(Ph)], 131.9 [7a-C(indole)], 128.7 [2 C, CH(Ph)], 128.3 [4-CH(Ph)], 128.0 [2 C, CH(Ph)], 127.2 [3a-C(indole)], 125.6 [5-C(triazole)], 112.5 [6- or 7-CH(indole)], 109.6 [6- or 7-CH(indole)], 105.6 [4-CH(indole)], 103.6 [3-C(indole)], 62.6 [CH_2C(triazole)], 59.2 (CH_2CH_3), 53.8 ($PhCH_2$), 52.5 (OCH_3), 29.6 (NCH_3), 14.6 (2-CH_3), 11.9 (CH_2CH_3).

HRMS (MALDI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{27}N_4O_5$: 463.1976; found: 463.1991.

Anal. Calcd for $C_{25}H_{26}N_4O_5$: C, 64.92; H, 5.67; N, 12.11. Found: C, 65.13; H, 5.88; N, 11.86.

Methyl 4-Phenyl-1-[(5-phenyl-1,3,4-oxadiazol-2-yl)methyl]-1*H*-1,2,3-triazole-5-carboxylate (2n)

Prepared from **1n** (0.2 mmol) according to the general procedure for carbonylation using MeOH–DMF (4:1) mixture as a solvent to increase the substrate solubility; purification by column chromatography (silica gel, hexanes–EtOAc, 4:1).

White solid; yield 50.5 mg (70%); mp 96–98 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02–7.97 [m, 2 H, 2,6-CH(5-Ph)], 7.79–7.73 [m, 2 H, 2,6-CH(4-Ph)], 7.55–7.41 [m, 6 H, CH(Ph)], 6.25 (s, 2 H, CH_2), 3.86 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 165.7 [5-C(oxadiazole)], 160.3 [2-C(oxadiazole) or C=O], 159.2 [2-C(oxadiazole) or C=O], 150.7 [4-C(triazole)], 132.1 [4-CH(5-Ph)], 129.5 [1-C(4-Ph)], 129.4 [2 C, CH(Ph)], 129.3 [4-CH(4-Ph)], 129.1 [2 C, CH(Ph)], 128.1 [2 C, CH(Ph)], 127.0 [2 C, CH(Ph)], 124.3 [5-C(triazole)], 123.2 [1-C(5-Ph)], 52.7 (CH_3), 45.5 (CH_2).

HRMS (MALDI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{16}N_5O_3$: 362.1248; found: 362.1247.

Ethyl 1-(2-Oxo-2-phenylethyl)-4-phenyl-1*H*-1,2,3-triazole-5-carboxylate (2o)

Prepared from **1h** (0.15 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, hexanes–EtOAc, 4:1).

White solid; yield: 41.0 mg (82%); mp 101–103 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01–7.97 [m, 2 H, 2,6-CH(Bz)], 7.80–7.75 [m, 2 H, 2,6-CH(4-Ph)], 7.66–7.61 [m, 1 H, 4-CH(Bz)], 7.55–7.49 [m, 2 H, 3,5-CH(Bz)], 7.45–7.37 [m, 3 H, 3,4,5-CH(Ph)], 6.19 (s, 2 H, CH_2N), 4.19 (q, *J* = 7.1 Hz, 2 H, CH_2O), 1.12 (t, *J* = 7.1 Hz, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 190.2 [C=O(ketone)], 159.2 [C=O(ester)], 150.2 [4-C(triazole)], 134.3 [4-CH(Bz)], 134.2 [1-C(Bz)], 130.2 [1-C(4-Ph)], 129.6 [2 C, CH(Ph)], 129.1 [2 C, CH(Ph)], 129.0 [4-CH(4-Ph)], 128.0 [2 C, CH(Ph)], 127.9 [2 C, CH(Ph)], 125.2 [5-C(triazole)], 61.9 (CH_2O), 57.0 (CH_2N), 13.6 (CH_3).

HRMS (MALDI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{18}N_3O_3$: 336.1343; found: 336.1341.

Anal. Calcd for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53. Found: C, 68.39; H, 5.37; N, 12.45.

2,2,2-Trifluoroethyl 1-(2-Oxo-2-phenylethyl)-4-phenyl-1*H*-1,2,3-triazole-5-carboxylate (2p)

Prepared from **1h** (0.2 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, hexanes–EtOAc, 4:1).

Off-white solid; yield: 27.9 mg (36%); mp 85–87 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03–7.98 [m, 2 H, 2,6-CH(Bz)], 7.78–7.72 [m, 2 H, 2,6-CH(4-Ph)], 7.71–7.65 [m, 1 H, 4-CH(Bz)], 7.58–7.52 [m, 2 H, 3,5-CH(Bz)], 7.48–7.42 [m, 3 H, 3,4,5-CH(Ph)], 6.22 (s, 2 H, CH_2N), 4.50 (q, J_{HF} = 8.2 Hz, 2 H, CH_2O).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 189.9 [C=O(ketone)], 157.6 [C=O(ester)], 151.3 [4-C(triazole)], 134.6 [4-CH(Bz)], 133.9 [1-C(Bz)], 129.6 [2 C, CH(Ph)], 129.5 [1-C(4-Ph)], 129.4 [4-CH(4-Ph)], 129.1 [2 C, CH(Ph)], 128.1 [2 C, CH(Ph)], 128.0 [2 C, CH(Ph)], 123.7 [5-C(triazole)], 122.3 (q, J_{CF} = 277.5 Hz, CF_3), 60.9 (q, J_{CF} = 37.4 Hz, CH_2O), 57.2 (CH_2N).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –73.1 (t, J_{HF} = 8.2 Hz, 3 F).

HRMS (MALDI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{15}F_3N_3O_3$: 390.1060; found: 390.1073.

Anal. Calcd for $C_{19}H_{14}F_3N_3O_3$: C, 58.62; H, 3.62; N, 10.79. Found: C, 58.65; H, 3.80; N, 10.47.

Methyl 1-Benzyl-4-(2-hydroxyphenyl)-1*H*-1,2,3-triazole-5-carboxylate (2r)

Prepared from **1t** (0.25 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, CH_2Cl_2 CH_2Cl_2–MeOH, 100:1).

White solid; yield: 54.0 mg (70%); mp 154–156 °C.

^{1}H NMR (400 MHz, $CDCl_3$–CD_3OD): δ = 7.57 [d, *J* = 7.6 Hz, 1 H, 6-CH(Ar)], 7.38–7.20 [m, 6 H, 5 H Ph + 1 H 4-CH(Ar)], 6.99–6.89 [m, 2 H, 3,5-CH(Ar)], 5.89 (s, 2 H, CH_2), 3.77 (s, 3 H, CH_3), 3.74 (br s, 1 H, OH).

^{13}C NMR (100.6 MHz, $CDCl_3$–CD_3OD): δ = 159.8 (CO_2), 155.0 [4-C(triazole) or 2-C(Ar)], 147.2 [4-C(triazole) or 2-C(Ar)], 134.4 [1-C(Ph)], 130.5 [4- or 6-CH(Ar)], 129.6 [4- or 6-CH(Ar)], 128.6 [2 C, CH(Ph)], 128.3 [4-CH(Ph)], 127.6 [2 C, CH(Ph)], 124.9 [5-C(triazole)], 119.3 [3- or 5-CH(Ar)], 116.2 [3- or 5-CH(Ar)], 115.4 [1-C(Ar)], 54.0 (CH_2), 52.3 (OCH_3).

HRMS (MALDI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{16}N_3O_3$: 310.1186; found: 310.1179.

Methyl 4-Butyl-1-[2-(2-methoxy-2-oxoethyl)phenyl]-1*H*-1,2,3-triazole-5-carboxylate (2s)

Carbonylation of **1q** was performed in a 25 mL capacity glass low pressure reactor RLP25ML (www.openscience.ru) equipped with gas feeding system, magnetic stirrer and manometer. In a pressure vessel, **1q** (0.5 mmol), $Pd(PPh_3)_4$ (29.0 mg, 25 μmol, 5 mol%), and Et_3N (1.40 mL, 10 mmol, 20 equiv) were mixed in MeOH (5 mL). The reaction mixture was stirred under a CO atmosphere (5 atm) at 50 °C for 18 h, then diluted with CH_2Cl_2 (25 mL) and washed with 10% aq HCl (25 mL) and H_2O (25 mL). The organic layer was dried with anhydrous Na_2SO_4, and the solvents were evaporated in vacuo. The residue was purified by column chromatography (silica gel, hexanes–EtOAc, 4:1).

Brown oil; yield: 129.4 mg (78%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.47 [m, 2 H, CH(Ar)], 7.46–7.40 [m, 1 H, 4- or 5-CH(Ar)], 7.29 [d, *J* = 7.8 Hz, 1 H, 3- or 6-CH(Ar)], 3.73 [s, 3 H, C(triazole)CO_2CH_3], 3.55 (s, 3 H, $CH_2CO_2CH_3$), 3.35 (s, 2 H, CH_2CO_2), 3.03 (t, *J* = 7.7 Hz, 2 H, CH_2Pr), 1.84–1.75 (m, 2 H, CH_2Et), 1.45 (sext, *J* = 7.4 Hz, 2 H, CH_2Me), 0.98 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 170.1 (CH_2CO_2Me), 158.7 [C(triazole)CO_2Me], 152.1 [4-C(triazole)], 136.5 [1-C(Ar)], 131.2 [2-C(Ar)], 131.1 [CH(Ar)], 130.3 [CH(Ar)], 127.7 [CH(Ar)], 127.5 [CH(Ar)], 126.3 [5-C(triazole)], 52.0 (CH_3O), 51.9 (CH_3O), 36.5 (CH_2CO_2), 31.1 (CH_2Pr), 25.7 (CH_2Et), 22.2 (CH_2Me), 13.7 (CH_2CH_3).

HRMS (MALDI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{22}N_3O_4$: 332.1605; found: 332.1615.

3-Butyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]benzoxazin-4-one (4)

In a flask, equipped with a condenser, **1o** (0.25 mmol), $Pd(OAc)_2$ (2.8 mg, 12.5 μmol, 5 mol%), and Et_3N (0.70 mL, 5 mmol, 20 equiv) were mixed under a CO atmosphere in MeOH (5 mL). The reaction mixture was stirred at 50 °C for 17 h, then diluted with CH_2Cl_2 (25 mL), and washed with 10% aq HCl (25 mL) and H_2O (25 mL). The organic layer was dried with anhydrous Na_2SO_4, and the solvents were evaporated in vacuo. The residue was dissolved in a mixture of toluene (3 mL)

and Et_3N (0.1 mL) and refluxed for 1 h. The solvents were evaporated in vacuo and the residue was purified by column chromatography (silica gel, CH_2Cl_2).

White solid; yield: 47.5 mg (78%); mp 130–131 °C.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.31 [dd, *J* = 8.0, 1.4 Hz, 1 H, 9-CH(Ar)], 7.52 [ddd, *J* = 8.6, 7.0, 1.4 Hz, 1 H, 7-CH(Ar)], 7.47–7.41 [m, 2 H, 6,8-CH(Ar)], 3.13 (t, *J* = 7.6 Hz, 2 H, CH_2Pr), 1.85–1.76 (m, 2 H, CH_2Et), 1.43 (sext, *J* = 7.4 Hz, 2 H, CH_2Me), 0.95 (t, *J* = 7.4 Hz, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 153.7 [3- or 4-C], 152.3 [3- or 4-C], 142.8 [5a-C], 129.8 [CH(Ar)], 125.8 [CH(Ar)], 121.2 [3a- or 9a-C], 118.2 [3a- or 9a-C], 117.9 [CH(Ar)], 116.2 [CH(Ar)], 30.9 (*C*H_2Pr), 25.3 (*C*H_2Et), 22.2 (*C*H_2Me), 13.7 (CH_3).

HRMS (MALDI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{14}N_3O_2$: 244.1081; found: 244.1087.

Anal. Calcd for $C_{13}H_{13}N_3O_2$: C, 64.19; H, 5.39; N, 17.27. Found: C, 64.32; H, 5.42; N, 16.82.

3-Butyl-[1,2,3]triazolo[1,5-*a*]quinoxalin-4(5*H*)-one (5)

Prepared from **1s** (0.25 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, hexanes–EtOAc, 4:1).

White solid; yield: 46.5 mg (77%); mp 234–235 °C.

^1H NMR (400 MHz, $CDCl_3$–CD_3OD): δ = 8.38 [d, *J* = 8.1 Hz, 1 H, 9-CH(Ar)], 7.51–7.45 [m, 1 H, 7-CH(Ar)], 7.42–7.32 [m, 2 H, 6,8-CH(Ar)], 3.19 (t, *J* = 7.6 Hz, 2 H, CH_2Pr), 1.88–1.78 (m, 2 H, CH_2Et), 1.45 (sext, *J* = 7.4 Hz, 2 H, CH_2Me), 0.97 (t, *J* = 7.4 Hz, 3 H, CH_3), N*H* proton was not assigned.

^{13}C NMR (100.6 MHz, $CDCl_3$–CD_3OD): δ = 155.4 [3- or 4-C], 150.0 [3- or 4-C], 129.0 [CH(Ar)], 128.4 [5a-C], 124.0 [CH(Ar)], 122.8 [3a- or 9a-C], 121.5 [3a- or 9a-C], 116.6 [CH(Ar)], 116.0 [CH(Ar)], 31.2 (*C*H_2Pr), 25.1 (*C*H_2Et), 22.1 (*C*H_2Me), 13.5 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{15}N_4O$: 243.1240; found: 243.1241.

3-Benzylchromeno[3,4-*d*][1,2,3]triazol-4(3*H*)-one (6)

In a flask, equipped with a condenser, **2r** (0.15 mmol) and Et_3N (0.1 mL) were mixed in toluene (3 mL). After reflux of the mixture for 5 h, the solvents were evaporated in vacuo and the residue was purified by column chromatography (silica gel, CH_2Cl_2).

White solid; yield: 38.3 mg (92%); mp 197–198 °C.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.24 [dd, *J* = 7.7, 0.9 Hz, 1 H, 9-CH(Ar)], 7.55–7.50 [m, 3 H, 2 H 2,6-CH(Ph) + 1 H CH(Ar)], 7.45–7.39 [m, 2 H, CH(Ar)], 7.37–7.30 [m, 3 H, CH(Ar)], 6.00 (s, 2 H, CH_2).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 153.0 (quat.), 152.3 (quat.), 148.3 (quat.), 134.1 [1-C(Ph)], 130.7 [CH(Ar)], 129.0 [2 C, CH(Ph)], 128.9 [4-CH(Ph)], 128.7 [2 C, CH(Ph)], 125.4 [CH(Ar)], 123.0 [CH(Ar)], 119.8 [3a- or 9a-C], 117.3 [6-CH], 114.1 [3a- or 9a-C], 53.8 (CH_2).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{12}N_3O_2$: 278.0924; found: 278.0913.

Methyl 3-Butyl-4-hydroxy-[1,2,3]triazolo[1,5-*a*]quinoline-5-carboxylate (7)

In a flask, **2s** (0.231 mmol) was dissolved in THF (3 mL). The solution was cooled in an ice–water bath and *t*-BuOK (31.1 mg, 0.277 mmol, 1.2 equiv) was added under an argon atmosphere. After stirring for 30 min, the reaction mixture was diluted with 10% aq HCl (25 mL) and extracted with CH_2Cl_2 (25 mL). The organic layer was dried with anhydrous Na_2SO_4, the solvents were evaporated in vacuo, and the residue was purified by column chromatography (silica gel, CH_2Cl_2–MeOH, 100:1).

White solid; yield: 64.6 mg (93%); mp 120–122 °C.

^1H NMR (400 MHz, $CDCl_3$): δ = 13.39 (s, 1 H, OH), 8.63–8.59 [m, 1 H, 6- or 9-CH(Ar)], 8.51–8.47 [m, 1 H, 6- or 9-CH(Ar)], 7.49–7.40 [m, 2 H, 7,8-CH(Ar)], 4.10 (s, 3 H, OCH_3), 3.19 (t, *J* = 7.7 Hz, 2 H, CH_2Pr), 1.88–1.79 (m, 2 H, CH_2Et), 1.46 (sext, *J* = 7.4 Hz, 2 H, CH_2Me), 0.98 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 171.9 (CO_2), 158.4 (quat.), 146.2 (quat.), 127.9 (quat.), 127.5 [CH(Ar)], 126.5 [CH(Ar)], 126.2 [CH(Ar)], 123.1 [3a- or 5a-C(Ar)], 121.1 [3a- or 5a-C(Ar)], 116.1 [9-CH(Ar)], 99.0 [5-C(Ar)], 52.9 (OCH_3), 31.9 (*C*H_2Pr), 25.9 (*C*H_2Et), 22.3 (*C*H_2Me), 13.8 (CH_2CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{18}N_3O_3$: 300.1343; found: 300.1343.

Methyl 1-(17-Hydroxy-3,20-dioxopregn-4-en-21-yl)-4-(hydroxymethyl)-1*H*-1,2,3-triazole-5-carboxylate (11)

Prepared from **10** (0.15 mmol) according to the general procedure for carbonylation; purification by column chromatography (silica gel, hexanes–EtOAc, 1:3).

Off-white solid; yield: 61.4 mg (84%); mp 230–231 °C.

^1H NMR (400 MHz, $CDCl_3$–CD_3OD): δ = 6.12 (d, *J* = 18.3 Hz, 1 H, 21-CH_2), 5.73 (br s, 1 H, 4-CH), 5.57 (d, *J* = 18.3 Hz, 1 H, 21-CH_2), 4.89 (s, 2 H, CH_2OH), 3.90 (s, 3 H, OCH_3), 3.49 (br s, 2 H, OH), 2.66–2.58 (m, 1 H), 2.47–2.25 (m, 4 H), 2.07–2.01 (m, 1 H), 1.97 (td, *J* = 12.8, 3.8 Hz, 1 H), 1.89–1.54 (m, 6 H), 1.48 (qd, *J* = 13.1, 3.8 Hz, 1 H), 1.36–1.21 (m, 3 H), 1.19 (s, 3 H, 19-CH_3), 1.15–1.06 (m, 1 H), 1.04–0.98 (m, 1 H), 0.66 (s, 3 H, 18-CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$–CD_3OD): δ = 204.1 [C(20)=O], 200.5 [C(3)=O], 172.4 (5-C), 159.0 (CO_2Me), 150.0 [4-C(triazole)], 125.6 [5-C(triazole)], 123.4 (4-CH), 89.4 (17-COH), 58.0 (21-CH_2 or CH_2OH), 55.7 (21-CH_2 or CH_2OH), 53.0, 52.6, 50.4, 48.2 (quat.), 38.5 (quat.), 35.4, 35.3, 34.4, 33.6, 32.7, 31.8, 29.9, 23.4, 20.6, 17.1, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{36}N_3O_6$: 486.2599; found: 486.2601.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1591896.

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