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Sequential Organocatalytic Synthesis of [1,2,3]Triazolo[1,5-*a*]quinolines

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Abstract. In this work, a one-pot sequential organocatalytic method for the synthesis of fused [1,2,3]triazolo[1,5-*a*]quinolines through successive cyclization and condensation is presented. In this synthetic strategy, the intermolecular [3+2]-cycloaddition occurs between 1,3-dicarbonyl compounds and *o*-carbonyl-substituted phenylazide compounds, for the formation of the 1,2,3-triazole intermediates. Subsequently, an intramolecular condensation reaction generates the fused quinoline ring by the new C-C bond formation, giving the products in yields ranging from moderate to excellent. All the reactions were performed using 20 mol% of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as catalyst in the presence of DMSO as solvent at 120 °C for 24 h and tolerate a range of 1,3-dicarbonyl compounds, such as *β*-keto esters and 1,3-diketones, and o-formyl, *o*-acetyl or *o*-benzoyl substituted phenylazide compounds.

Keywords: Organocatalysis, quinolines, 1,2,3-triazoles.

Introduction

Heterocycles represent the most general structural units in several natural and synthetic bioactive compounds.[1] In particular, *N*-heterocycles are unquestionably important since over 60% of the FDA-approved drugs contain nitrogen heterocycles.[2] In this sense, 1,2,3-triazoles have attracted significant interest from synthetic organic chemists in developing new compounds, due to their extensive application in drug discovery.[3] Efficient methods to access densely functionalized 1,2,3-triazoles included the organocatalyzed [3+2] cycloaddition reactions[4] via the generation of enamines, also known as Ramachary-Bressy-Wang organocatalytic azide-ketone [3+2]-cycloaddition (OrgAKC),[5] or via enolates,[6] which act as the dipolarophile partner in reactions with organic azides.

Quinolines are a class of synthetic and natural-occurring heterocycles with exciting biological activities.[7] Compounds containing quinolinic core in their structure have attracted considerable interest due to their applications in material science and also due to the wide range of pharmacologic activities, such as antimalarial, antioxidant, anxiolytic, and antitumoral ones.[8] In this context, our group and others have described the synthesis and pharmacological properties of hybrid molecules containing triazoles and quinolines in the structure.[9] As examples, we have prepared compound **A** (QTC-4-MeOBnE), which exerts therapeutic effect through multiple pathways involved in Alzheimer's disease,[9a] and compound **B** (QTCA-1), which presented anticonvulsant, antinociceptive and anti-inflammatory properties,[9b] besides selective cytotoxicity on triple-negative breast cancer cells.[9c] Recently, Upadhyay and coworkers[10] described the synthesis of a similar compound (**C**, Figure 1) that has the potential to act as an antileishmanial agent.

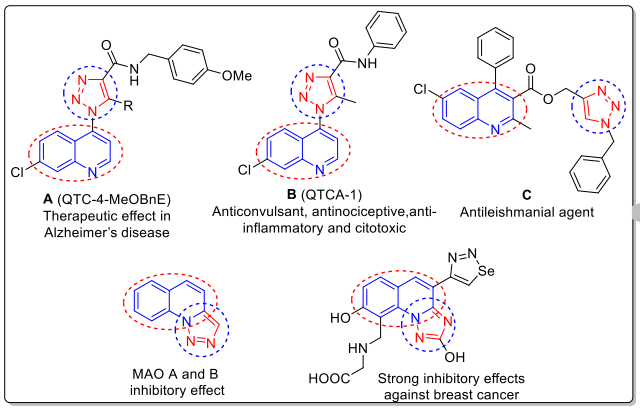

Figure 1 Examples of bioactive hybrid molecules containing triazole and quinoline units.

As demonstrated by several recent reports describing the synthesis of triazole-substituted quinolines,[9,10,11] the combination of the well-known properties of

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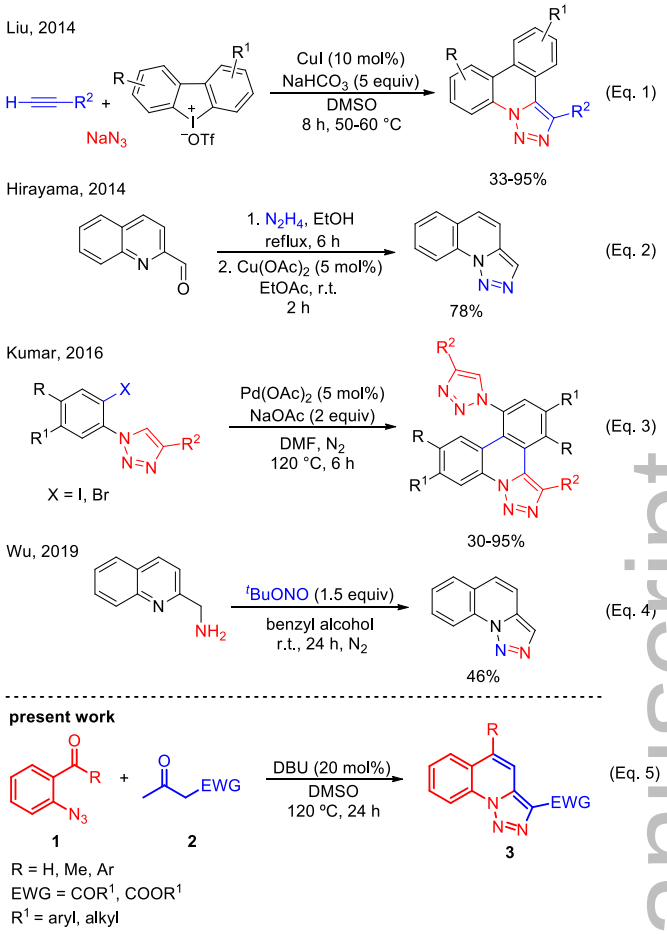
quinolines with those of 1,2,3-triazoles in complex heterocyclic structures, as [1,2,3]triazolo[1,5-*a*]quinolines, has gained significant prominence and remains the need for further studies. In this regard, there are several procedures in the literature for the preparation of these *N*-containing polycycles, mainly involving cyclization reactions.[12] Although most of these methods are very effective, and despite the significant recent advances, some limitations are still present, which includes the use of transition metals, such as Fe,[12c] Cu,[12d-f] or Pd,[12g-i] and require various reaction steps and complex starting materials, which are challenging to prepare and environmentally incompatible.[12j-l]

For instance, in 2014, Liu and coworkers [13] described a three-component cascade reaction of cyclic diaryliodoniums, sodium azide, and terminal alkynes using copper iodide as catalyst. The synthesis of the key cyclic diaryl iodoniums, however, involves 3 steps and harsh reaction conditions (Scheme 1, Eq. 1). In the same year, Hirayama and coworkers[14] reported the synthesis of several [1,2,3]triazolo[1,5-*a*]pyridines and one example of [1,2,3]triazolo[1,5-*a*]quinoline. The used methodology involves a copper(II)-catalyzed oxidative N-N bond formation in the presence of atmospheric oxygen as the terminal oxidant, following by a one-pot hydrazonation (Scheme 1, Eq. 2).

Another study was reported by Kumar, in 2016,[15] in which a palladium-catalyzed domino coupling of 1,4-disubstituted triazoles was carried out *via* the homocondensation with a second molecule, to access different [1,2,3]triazolo[1,5-*f*]phenanthridines (Scheme 1, Eq. 3). More recently, Wu et al.[16] have prepared [1,2,3]triazolo[1,5-*a*]pyridines starting from pyridin-2-ylmethanamines, through an oxidative catalyst-free N-N coupling strategy. In this report, only one [1,2,3]triazolo[1,5-*a*]quinoline was obtained (Scheme 1, Eq. 4).

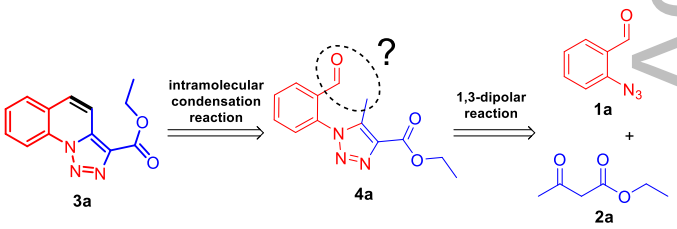
Despite the significant advances toward the synthesis of quinoline-triazole hybrids, the development of more efficient catalytic processes remains an important challenge in synthetic organic chemistry. With the aim to contribute to overcome the current limitations, we describe herein the organocatalytic synthesis of several fused [1,2,3]triazolo[1,5-*a*]quinolines **3**, substituted with ketones or carboxylate groups, through of a simple and efficient approach involving o-formyl, o acetyl or o-benzoyl substituted phenylazides **1** and carbonyl compounds **2**, using DBU (20 mol%) as a catalyst (Scheme 1, Eq. 5).



Scheme 1. Examples of synthesis of [1,2,3]-triazolo[1,5-*a*]quinolines

Results and Discussion

Initially, we wondered whether 2-azidobenzaldehyde **1a** and ethyl acetoacetate **2a** could be used as substrates for the synthesis of fused [1,2,3]triazolo[1,5-*a*]quinoline **3a**, through a cascade formation of 1,2,3-triazole **4a** and intramolecular condensation reaction, as shown in Scheme 2. The C(sp^3)-H functionalization of 2-methyl azaarenes is an excellent strategy for the synthesis of new heterocyclic entities,[17] however this type of reaction in methyl 1,2,3-triazoles is rare.[18]



Scheme 2. General proposal.

With this strategy in mind, and based in the procedure already described by Ramachary and coworkers in 2014,[6c] to prepare 1,2,3-triazoles *via* enolate using DBU a catalyst, we reacted 2-azidobenzaldehyde **1a** and ethyl acetoacetate **2a** in the presence of DBU (10

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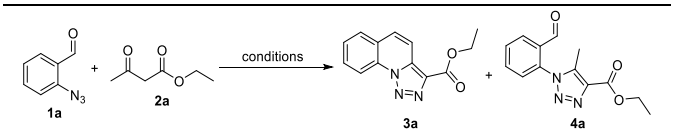
mol%) as a catalyst and DMSO as the solvent. After 24 h at room temperature, the only product observed was the intermediate **4a**, obtained in 82% yield, without the formation of desired product **3a** (Table 1, entry 1).

Focused on obtaining the ethyl[1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate **3a**, we evaluated the influence of temperature, catalyst, and solvent in the reaction. To our delight, when the temperature was raised to 70 ºC, the desired product **3a** was obtained in 46% yield, as a mixture with the intermediate **4a**, which was isolated in 30% yield (Table 1, entry 2).

Table 1. Optimization studies to prepare compound **3a**.[a]



Entry	Catalyst (mol%)	Solvent	Temperature (°C)	Yield (%)[b]	
				3a	**4a**
1	DBU (10)	DMSO	25	-	82
2	DBU (10)	DMSO	70	46	30
3	-	DMSO	70	-	traces
4	Et_2NH (10)	DMSO	70	-	80
5	Et_3N (10)	DMSO	70	traces	67
6	DABCO (10)	DMSO	70	14	60
7	DMAP (10)	DMSO	70	9	64
8	*N*,*N*-dimethyl aniline (10)	DMSO	70	-	28
9	K_2CO_3 (10)	DMSO	70	traces	58
10	Cs_2CO_3 (10)	DMSO	70	6	49
11	KO^{t}Bu (10)	DMSO	70	16	53
12	KOH (10)	DMSO	70	34	50
13	DBU (20)	DMSO	70	53	22
14	DBU (20)	DMSO	100	77	9
15	**DBU (20)**	**DMSO**	**120**	**92 (86)**[c]	**traces**
16	DBU (10)	DMSO	120	62	27
17	KOH (20)	DMSO	120	63	16
18	DBU (20)	toluene	111	-	15
19	DBU (20)	DMF	120	47	19
20	DBU (20)	MeCN	82	17	49
21	DBU (20)	ethyleneglycol	120	-	traces
22[d]	DBU (20)	DMSO	120	65	23
23[e]	DBU (20)	DMSO	120	85	traces

[a] Reactions were carried out using 2-azidobenzaldehyde **1a** (0.25 mmol) and ethyl acetoacetate **2a** (0.25 mmol) in 0.25 mL of solvent under air atmosphere for 24 h. The reaction progress was followed by TLC. [b] Yields are given for isolated products. [c] Yield in parentheses correspond to reactions performed on a 2.5 mmol scale. [d] Reaction performed under microwave irradiation at 120 °C for 1 h. [e] Reaction performed under N_2 atmosphere.

The complete structural characterization of the compound **3a** was achieved by 1D and 2D-NMR techniques, such as COSY, HSQC, and HMBC. After analyzing the NMR spectra, it was possible to discriminate and attribute all the hydrogen and carbon peaks. These results are described in the Supporting Information (Table S1).

In the absence of the catalyst, only trace amounts of the product **4a** were observed by TLC, and in this case, the starting materials were recovered (Table 1, entry 3). Notably, when the reaction was carried out using diethylamine (10 mol%) as the catalyst, only the 1,2,3-triazole intermediate **4a** was obtained in 80% yield (Table 1, entry 4). In an attempt to examine the role of the nature of the base (catalyst), different tertiary amines, such as Et_3N, DABCO, DMAP, *N*,*N*-dimethylaniline, and other conventional bases as K_2CO_3, Cs_2CO_3, ^{t}BuOK, and KOH were tested as catalysts. However, none of them proved to be a catalyst as efficient as DBU, and in all these cases, the triazole **4a** was preferably obtained (Table 1, entries 5-12 *vs*. entry 2). The increase of the load of DBU from 10 to 20 mol% caused a small increment in the yield of **3a** (53%) (Table 1, entry 13 *vs*. entry 2). Gratifyingly, good results were obtained when the reactions were performed at 100 ºC and 120 ºC, with the desired product **3a** being isolated in 77% and 92% yield, respectively (Table 1, entries 14 and 15). Once the ideal temperature of the reaction was determined as 120 ºC, we carried out one experiment decreasing the amount of DBU from 20 to 10 mol%. However, the reaction was incomplete, and the desired product **3a** was obtained in 62% yield (Table 1, entry 16 *vs.* entry 15). The desired product **3a** was obtained in 63% yield when the reaction was carried out using 20 mol% of KOH as a catalyst, proving that DBU was the best catalyst for this methodology (Table 1, entry 17 *vs*. entry 15).

Further screening of solvents, such as toluene, MeCN, DMF, and ethylene glycol, showed that the reaction conducted in DMSO gave a better result (Table 1, entry 15 *vs.* entries 18-21). Furthermore, the use of focused microwave irradiation was evaluated as an alternative energy source, afforded the compound **3a** in 65% yield after 1 h (Table 1, entry 22). Finally, one experiment was conducted under a N_2 atmosphere, giving product **3a** in 85% yield (Table 1, entry 23).

Scope of the Reaction

With the best conditions in hand, we tested the generality and limitations of our methodology, reacting 2-azidobenzaldehyde **1a** with different substituted *β*-keto esters **2a-f** and 1,3-diketones **2g-l** (Scheme 3). When the ethyl group of the *β*-keto ester **2a** was changed for *tert*-butyl (**2b**) or isopentyl group (**2c**), a significant decrease in the yield was observed, and the respective [1,2,3]triazolo[1,5-*a*]quinolines **3b** and **3c** were obtained in 66% and 75% yield. Other alkoxyl groups were also evaluated, such as 2-phenethyl (**2d**), benzyl (**2e**), and prop-2-yn-1-yl (**2f**), giving the desired products **3d-f** in 48%, 51%, and 30% yield, respectively.

The reaction of 2-azidobenzaldehyde **1a** with pentane-2,4-dione **2g** and with 1-phenylbutane-1,3-dione **2h** furnished the corresponding [1,2,3]triazolo[1,5-*a*]quinolines **3g** and **3h**, substituted with ketone groups, in 71% and 68% yield,

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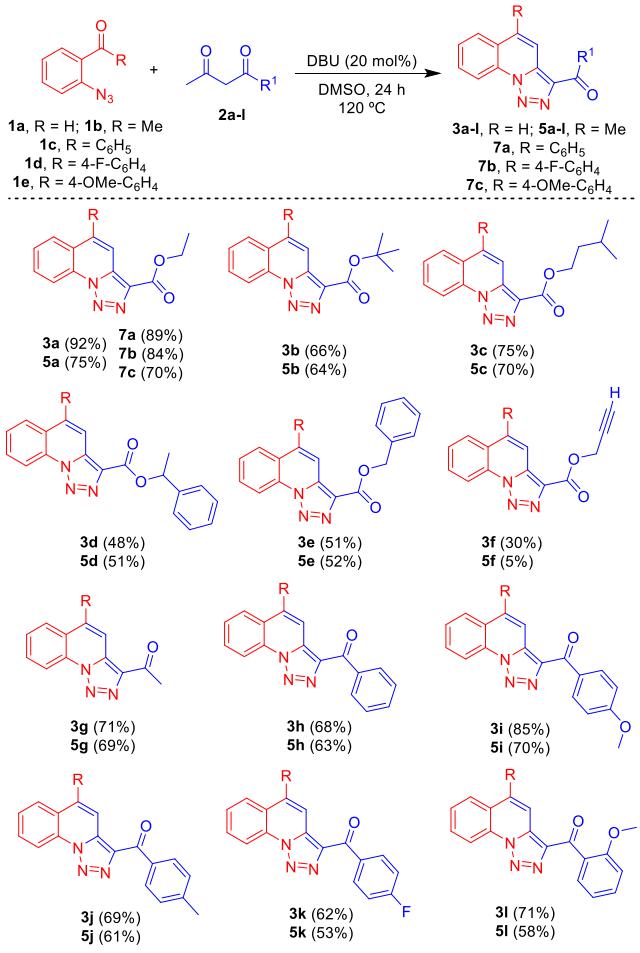
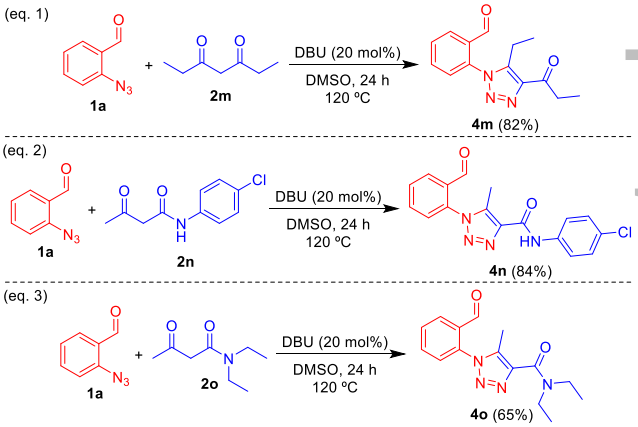
respectively. When the reaction of **1a** was carried out with a range of 1-arylbutane-1,3-diones **2i-l** bearing both electron-donating groups (EDG) or electron-withdrawing groups (EWG), the desired [1,2,3]triazolo[1,5-*a*]quinolines **3i-l** were obtained in moderate to good yields. Interesting, the electron-rich 1-(4-methoxy-phenyl)butane-1,3-dione **2i** was a suitable substrate for the reaction, affording the desired product **3i** in a very good 85% yield, while 1-arylbutane-1,3-diones **2h** and **2j-l** afforded the respective products in moderate yields (Scheme 3). These results suggest that the electron-donating methoxy group could facilitate the intramolecular condensation step (see Scheme 6, the mechanism proposal). When 1-(2-methoxy-phenylbutane)-1,3-dione **2l** was used as the substrate, the desired product **3l** was obtained in 71% yield, despite the steric hindrance caused by the *ortho*-substitution.



Scheme 3. Generality in the synthesis of [1,2,3]triazolo[1,5-*a*]quinolines. Reactions were carried out using azides **1a-b** (0.25 mmol), the carbonyl compound **2a-l** (0.25 mmol), DBU (20 mol%), in DMSO (0.25 mL) at 120 °C under air atmosphere. The reaction progress was followed by TLC, and the yields are given for isolated products.

The strategy above was successfully extended to the reaction of 2'-azidoacetophenone **1b** with different substituted *β*-keto esters and 1,3-diketones. For instance, the reaction of **1b** with ethyl acetoacetate **2a** under the optimal conditions afforded the respective fused triazole **5a** in 75% yield, together with the triazole intermediate **6a** (ethyl 1-(2-acetylphenyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxylate), which was isolated in 16% yield. In addition, we investigate the substrate scope with respect to other *β*-keto esters **2b-f** and 1,3-diketones **2g-l**. The desired products **5** were obtained generally in lower yields compared to the reactions using 2-azidobenzaldehyde **1a** as a starting material (Scheme 3). These results could be attributed, at least in part, to the steric hindrance due to the methyl group in 2-azidoacetophenone **1b**, when compared to the aldehyde **1a**. Interesting, the reaction involving **1b** and the aryl 1,3-diketones **2h-l** was less sensitive to electronic effects in the pendant aromatic ring if compared with the reaction using aldehyde **1a**, even if the fused triazole *p*-methoxy-substituted **5i** was obtained in a slightly higher yield (70%).

Following, we examined the suitableness of our protocol in the reaction of 2-azidobenzophenones **1c-e** with ethyl acetoacetate **2a**. The expected fused triazoles **7a-c** were obtained in good to very good yields under the optimal reaction conditions. For instance, product **7a**, derived from 2-azidobenzophenone **1c**, was obtained in 89% yield, while the *para*-substituted benzophenones **1d** and **1e** reacted with **2a** to afford the respective products **7b** and **7c** in 84% and 70% yield, respectively (Scheme 3). While the presence of the electron-withdrawing fluoro group did not influence the reactivity of substrate **1d**, the electron-donating one methoxy caused a decrease in the reactivity of **1c**, probably due to the decrease in the electrophilicity of the carbonyl group (Scheme 3, compound **7b** *vs.* **7c**).



Scheme 4 - Reactivity of different 1,3-dicarbonyl compounds.

The reactivity of different 1,3-dicarbonyl compounds with 2-azidobenzaldehyde **1a** was then examined. Thus, the reaction of 3,5-heptanedione **2m** with **1a**, under our conditions, gave the 1,2,3-triazole **4m** exclusively as the product of the intermolecular [3+2] cycloaddition reaction, in 82% yield (Scheme 4, eq. 1). A similar result was obtained when *N*-(4-chlorophenyl)-3-oxobutanamide **2n** was used as the substrate in the reaction with **1a**, and product **4n** was isolated in 84% yield, with the expected fused triazole **3n** being observed in trace amounts (Scheme 4, eq. 2). To verify if the free N-H in the amide **2n** was

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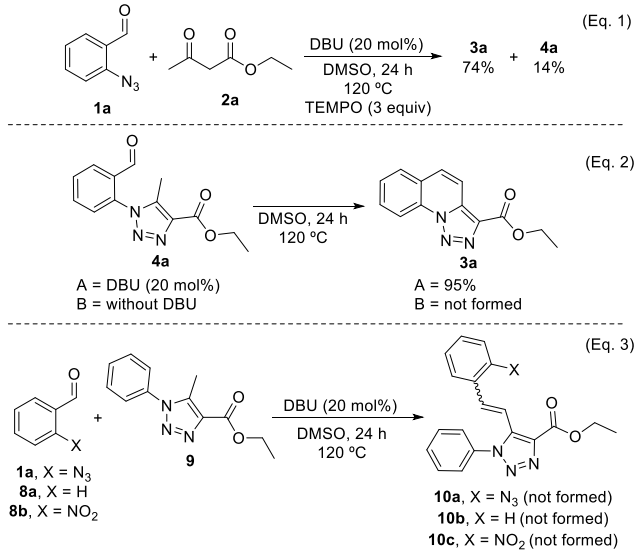
preventing the cyclization step, *N*,*N*-diethyl-3-oxobutanamide **2o** was used as starting material. However, the desired [1,2,3]triazolo[1,5-*a*]quinoline **3o** was not observed, and the 1,2,3-triazole **4o** was the only product, isolated in 65% yield (Scheme 4, eq. 3). These results prove that the intramolecular condensation reaction cannot be extended to amides.

Mechanism Discussion

In order to collect data to subsidize a plausible mechanism for the reaction, some control experiments were conducted. Initially, the reaction between 2-azidobenzaldehyde **1a** and ethyl acetoacetate **2a** under the standard conditions was performed in the presence of TEMPO (3 equiv.). The products **3a** and **4a** were obtained in 74% and 14% yield, respectively. This outcome indicates that the reaction does not occur via a radical pathway (Scheme 5, Eq. 1). In order to confirm the hypothesis that the 1,2,3-triazole **4a** is the intermediate of the reaction, **4a** was used as starting material under the standard conditions, giving the product **3a** in 95% yield after 24 h (Scheme 5, Eq. 2A). Further, we observed that the cyclization did not occur in the absence of DBU, with **4a** remaining unreacted, proving the importance of DBU in the intramolecular condensation step (Scheme 5, Eq. 2B).



Scheme 5 - Control experiments.

Finally, in order to verify the acidity of the methyl proton bonded at the 5-position of triazole **4**, we performed one reaction between 1,2,3-triazole **9** and the corresponding aldehydes 2-azidobenzaldehyde **1a**, benzaldehyde **8a** or 2-nitrobenzaldehyde **8b**, under the standard conditions (Scheme 5, Eq. 3). The condensation products **10a**, **10b** or **10c** were not obtained and the starting materials were recovered. These results indicates that the formation of the thermodynamically stable [1,2,3]triazolo[1,5-*a*]quinoline **3** aromatic system is essential for the accomplishment of the second cyclization step.

Considering the results obtained in the control experiments and the data in the literature on the synthesis of 1,2,3-triazoles using DBU as a catalyst,[6] a plausible mechanism for this one-pot sequential organocatalytic synthesis of [1,2,3]triazolo[1,5-*a*]quinoline **3** is presented in Scheme 6. Firstly, the enolate **2'** is formed by the abstraction of one methylene acidic proton from compound **2** by DBU. Then, a [3+2] cycloaddition reaction occurs between enolate **2'** and 2-azidobenzaldehyde **1a**, generating the intermediate triazoline **A**, which subsequently dehydrates, forming the 1,2,3-triazole intermediate **4**. Following, the 1,2,3-triazole intermediate **4** reacts with DBU, which abstracts a proton from the methyl group at the 5-position of triazole **4**, with the electron displacement by the triazole nucleus and the carbonyl, forming the enolate intermediate **B**. Then, the negative charge present in the oxygen migrates, so that the carbon bonded at position 5 of the triazole performs a nucleophilic attack to the pendent *ortho*-carbonyl group, forming the intermediate **C**, which after a dehydration step forms the [1,2,3]triazolo[1,5-*a*]quinoline **3**. We assume that the driving force for this intramolecular condensation reaction is the aromatization in the formation of the fused [1,2,3]triazolo[1,5-*a*]quinoline heterocycle **3**.

Using the NOESY (Nuclear Overhauser Enhancement Spectroscopy) technique, it is possible to calculate the distance between the nearby hydrogens in a molecule,[19] and thus establish the molecular geometry of the compound through studies described by Bell and Saunders in 1970.[20] After the analysis and calculations of compound 4a, the results suggest that the proximity between H-8 methyl hydrogens and aldehydic H-1 is essential to the intramolecular condensation step (Figure 2). Since DBU is a bulky base and the 1,2,3-triazole nucleus is almost perpendicular to the aromatic ring, the methyl group is turned out of the geometric plane, facilitating the proton abstraction from the methyl group and thus carrying out the intramolecular condensation reaction.

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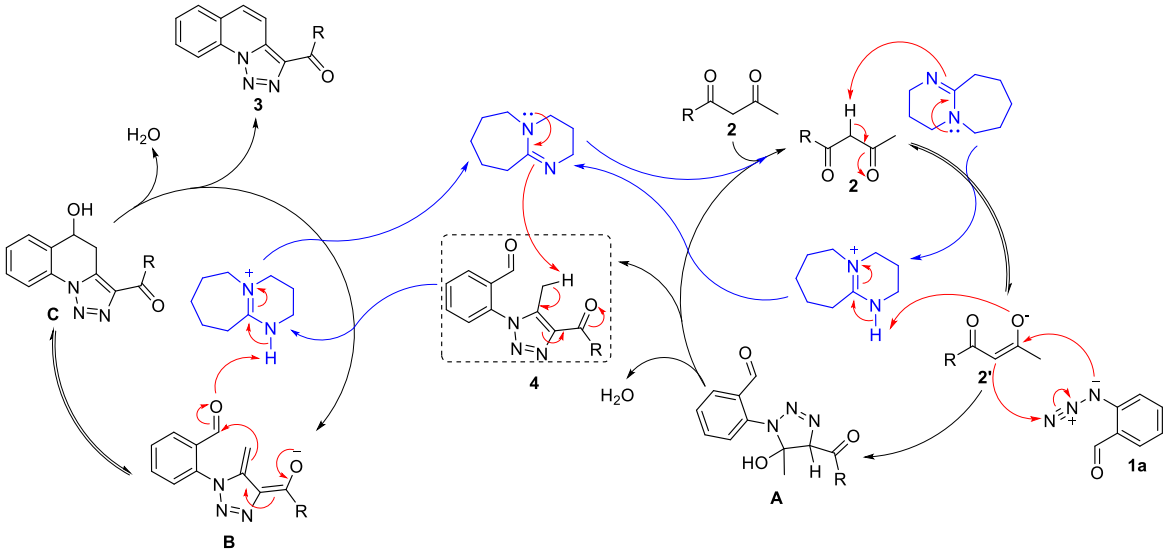

Scheme 6. Proposed mechanism.

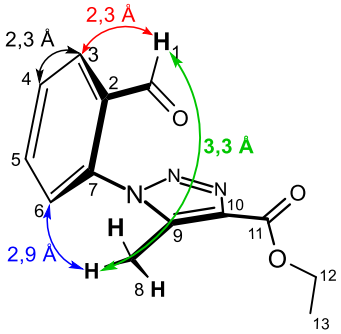

Figure 2. Distance between nearby hydrogens in the compound **4a**.

Conclusion

In summary, we have developed an one-pot sequential organocatalytic method for the synthesis of fused [1,2,3]triazolo[1,5-*a*]quinolines in yields ranging from moderate to excellent. A total of twenty-seven [1,2,3]triazolo[1,5-*a*]quinolines were synthesized by the successive intermolecular [3+2]-cycloaddition between 1,3-dicarbonyl compounds and *o*-carbonyl substituted phenyl azides, followed by an intramolecular condensation reaction of the 1,2,3-triazole intermediates. All the reactions were performed using DBU as a catalyst, and DMSO as solvent at 120 °C for 24 h. This protocol tolerates a range of 1,3-dicarbonyl compounds, such as *β*-keto esters and 1,3-diketones, and *o*-formyl, *o*-acetyl, or *o*-benzoyl-substituted phenylazides.

Experimental Section

Materials and methods

The reactions were monitored by TLC carried out on Merck silica gel (60 F_{254}) by using UV light as visualization agent and the mixture between 5% of vanillin in 10% of H_2SO_4 under heating conditions as developing agents. Merck silica gel (particle size 0.040-0.063 mm) was used to flash chromatography. Hydrogen nuclear magnetic resonance spectra (^{1}H NMR) were obtained on Bruker Avance III HD 400 spectrometer at 400 MHz. The spectra were recorded in $CDCl_3$ solutions. The chemical shifts are reported in ppm, referenced to tetramethylsilane (TMS) as the internal reference. Coupling constants (*J*) are reported in Hertz. Abbreviations to denote the multiplicity of a particular signal are s (singlet), d (doublet), dd (doublet of doublet) t (triplet), q (quartet), quint (quintet) and m (multiplet). Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained on Bruker Avance III HD 400 spectrometer at 100 MHz. The chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$. The high-resolution electrospray ionization mass spectrometry (ESI-QTOF) analysis were performed on a Bruker Daltonics micrOTOF-Q II instrument in positive mode. The samples were solubilized in HPLC-grade acetonitrile and injected into the ESI source by means of a syringe pump at a flow rate of 5.0 µL min^{-1}. The following instrument parameters were applied: capillary and cone voltages were set to +3500 V and -500 V, respectively, with a desolvation temperature of 180 °C. For data acquisition and processing, Compass 1.3 for micrOTOF-Q II software (Bruker daltonics, USA) was used. Low-resolution mass spectra were obtained with a Shimadzu GC-MS-QP2010 mass spectrometer. Melting point (mp) values were measured in a Marte PFD III instrument with a 0.1 °C precision.

General procedure for the synthesis of [1,2,3]triazolo[1,5-*a*]quinolines 3a-l, 5a-I, and 7a-c:
Azide **1a-e** (0.25 mmol), 1,3-dicarbonyl compound **2a-l** (0.25 mmol), DBU (20 mol%, 0.0076 g) and DMSO (0.25 mL) were added to a 5.0 mL glass tube. Then, the reaction mixture was stirred for 24 h at 120 °C under air atmosphere. After this time, the crude product was purified by column chromatography on silica gel with a mixture of hexane/ethyl acetate (5:1) as eluent to afford the desired product (**3a-l**, **5a-l** and **7a-c**). Spectral data for the products prepared are listed below.

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Ethyl [1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (3a): Yield: 0.055 g (92%), white solid, mp: 137 - 139 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.82 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 9.3 Hz, 1H), 7.91 (d, J = 8.4 Hz, 1H), 7.84-7.80 (m, 1H), 7.77 (d, J = 9.3 Hz, 1H), 7.68-7.64 (m, 1H), 4.55 (q, J = 7.1 Hz, 1H), 1.51 (t, J = 7.1 Hz, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 162.0, 134.0, 131.9, 131.7, 131.2, 130.7, 129.1, 128.2, 124.4, 116.9, 115.9, 61.6, 14.9. MS (rel. int., %) *m*/*z*: 241.0 (19.8), 213.0 (1.6), 196.0 (4.1), 169.1 (16.8), 128.2 (100.0), 113.1 (11.6), 101.1 (14,7), 88.1 (3.8). HRMS (ESI-QTOF) calculated mass for $C_{13}H_{12}N_3O_2$ $[M+H]^+$: 242.0924, found: 242.0937.

***tert*-Butyl [1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (3b):** Yield: 0.044 g (66%); yellow solid, mp: 134 - 136 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.83 (d, J = 8.4 Hz, 1H), 8.03 (d, J = 9.3 Hz, 1H), 7.90 (dd, J = 8.0, 1.0 Hz, 1H), 7.83-7.79 (m, 1H), 7.75 (d, J = 9.3 Hz, 1H), 7.68-7.64 (m, 1H), 1.72 (s, 9H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 160.9, 133.3, 132.7, 131.7, 130.8, 130.0, 128.7, 127.8, 124.0, 116.6, 115.9, 82.4, 28.5. MS (rel. int., %) *m*/*z*: 269.1 (6.4), 213.1 (13.1); 196.0 (6.5), 185.1 (8.9), 169.1 (7.9), 156.1 (6.4), 140.1 (33.3), 129.1 (100.0), 113.1 (18.5), 102.1 (15.6). HRMS (ESI-QTOF) calculated mass for $C_{15}H_{16}N_3O_2$ $[M+H]^+$: 270.1237, found: 270.1241.

Isopentyl [1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (3c): Yield: 0.053 g (75%); yellow solid, mp: 139 - 141 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.86 (d, J = 8.3 Hz, 1H), 8.09 (d, J = 9.2 Hz, 1H), 7.93 (d, J = 7.8 Hz, 1H), 7.86 – 7.79 (m, 2H), 7.70-7.67 (m, 1H), 4.52 (t, J = 6.7 Hz, 2H), 1.90 - 176 (m, 3H), 1.01 (d, J = 6.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.8, 133.7, 131.8, 131.5, 131.0, 130.4, 128.8, 127.9, 124.1, 116.7, 115.7, 64.0, 37.6, 25.3, 22.7. MS (rel. int., %) *m*/*z*: 212.0 (4.9), 169.1 (27.9), 157.1 (10.5), 140.2 (32.3), 128.1 (100.0), 102.1 (12.2), 88.1 (31.6). HRMS (ESI-QTOF) calculated mass for $C_{16}H_{18}N_3O_2$ $[M+H]^+$: 284.1394, found: 284.1395.

1-Phenylethyl [1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (3d): Yield: 0.038 g (48%); gray solid, mp: 129 - 131 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.76 (d, J = 8.4 Hz, 1H), 7.97 (d, J = 9.3 Hz, 1H), 7.82 (d, J = 7.9 Hz, 1H), 7.76-7.72 (m, 1H), 7.68 (d, J = 9.3 Hz, 1H), 7.60-7.52 (m, 1H), 7.46 (d, J = 7.4 Hz, 2H), 7.32-7.29 (m, 2H), 7.25-7.21 (m, 1H), 6.21 (q, J = 6.6 Hz, 1H), 1.71 (d, J = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.0, 141.6, 133.8, 131.7, 131.5, 131.0, 130.4, 128.8, 128.7, 128.2, 127.9, 126.4, 124.1, 116.7, 115.7, 73.5, 22.6. MS (rel. int., %) *m*/*z*: 317.1 (2.8), 244.1 (4.8), 213.0 (3.5), 197.0 (6.7), 156.1 (9.4), 128.1 (31.9), 105.1 (100.0). HRMS (ESI-QTOF) calculated mass for $C_{19}H_{16}N_3O_2$ $[M+H]^+$: 318.1237, found: 318.1237.

Benzyl [1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (3e): Yield: 0.038 g (51%); yellowish solid, mp: 132 - 134 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.75 (d, J = 8.4 Hz, 1H), 7.95 (d, J = 9.3 Hz, 1H), 7.82 (d, J = 7.9 Hz, 1H), 7.76-7.72 (m, 1H), 7.68 (d, J = 9.3 Hz, 1H), 7.60-7.56 (m, 1H), 7.46 (d, J = 7.2 Hz, 2H), 7.34 – 7.25 (m, 3H), 5.44 (s, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.5, 135.9, 133.8, 131.7, 131.2, 131.0, 130.6, 128.8, 128.8, 128.6, 128.5, 127.9, 124.1, 116.7, 115.6, 66.9. MS (rel. int., %) *m*/*z*: 303.2 (5.8), 274.1 (1.2), 197.1 (7.7), 156.1 (21.0), 128.2 (96.8), 91.2 (100.0).HRMS (ESI-QTOF) calculated mass for $C_{18}H_{14}N_3O_2$ $[M+H]^+$: 304.1081, found: 304.1087.

Prop-2-yn-1-yl [1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (3f): Yield: 0.019 g (30%); yellowish solid, mp: 165 - 167 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.85 (d, J = 8.4 Hz, 1H), 8.10 (d, J = 11.0 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.87 – 7.82 (m, 2H), 7.72-7.68 (m, 1H), 5.08 (d, J = 2.4 Hz, 2H), 2.58 (t, J = 2.4 Hz, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 160.8, 134.0, 131.7, 131.2, 130.9, 130.6, 128.9, 128.0, 124.1, 116.7, 115.5, 77.6, 75.6, 52.6. MS (rel. int., %) *m*/*z*: 251.0 (17.1), 222.0 (32.0), 194.0 (22.9), 166.1 (28.6), 140.1 (33.7), 128.1 (100.0), 101.1 (26.7), 88.1 (10.4). HRMS (ESI-QTOF) calculated mass for $C_{14}H_{10}N_3O_2$ $[M+H]^+$: 252.0768, found: 252.0765.

1-([1,2,3]Triazolo[1,5-*a*]quinolin-3-yl)ethan-1-one (3g): Yield: 0.037 g (71%); white solid, mp 160 - 162 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.85 (d, J = 8.4 Hz, 1H), 8.23 (d, J = 9.2 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.88 – 7.82 (m, 2H), 7.71 – 7.67 (m, 1H), 2.86 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 193.9, 139.0, 132.3, 131.5, 131.2, 131.1, 128.8, 127.9, 124.4, 116.7, 116.3, 27.6. MS (rel. int., %) *m*/*z*: 211.1 (12.8), 183.1 (25.7), 154.1 (100.0), 140.1 (14.2), 128.1 (22.1), 113.1 (10.7), 88.1 (5.1). HRMS (ESI-QTOF) calculated mass for $C_{12}H_9N_3ONa$ $[M+H]^+$: 234.0638, found: 234.0631.

[1,2,3]Triazolo[1,5-*a*]quinolin-3-yl(phenyl)methanone (3h): Yield.: 0.047 g (68%); yellowish solid, mp: 150 152 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.82 (d, J = 8.4 Hz, 1H), 8.54 (d, J = 7.5 Hz, 2H), 8.34 (d, J = 9.2 Hz 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.83 – 7.79 (m, 2H), 7.66-7.61 (q, m, 2H), 7.57-7.53 (q, m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 186.6, 138.7, 137.4, 134.6, 132.9, 131.4, 131.1, 131.0, 130.7, 128.7, 128.4, 127.9, 124.5, 116.7, 116.6. MS (rel. int., %) *m*/*z*: 273.0 (6.7), 245.0 (45.5), 217.0 (100.0), 163.1 (2.6), 140.1 (5.7), 113.1 (8.3), 88.0 (5.1). HRMS (ESI-QTOF) calculated mass for $C_{17}H_{12}N_3O$ $[M+H]^+$: 274.0975, found: 274.0971.

[1,2,3]Triazolo[1,5-*a*]quinolin-3-yl(4-methoxyphenyl)methanone (3i): Yield: 0.064 g (85%); white solid, mp: 170 - 172 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.83 (d, J = 8.4 Hz, 1H), 8.63 (d, J = 8.9 Hz, 2H), 8.34 (d, J = 9.3 Hz, 1H), 7.89 (d, J = 7.9 Hz, 1H), 7.83-7.79 (m, 2H), 7.66-7.62 (m, 1H), 7.03 (d, J = 8.9 Hz, 2H), 3.91 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 185.0, 163.6, 139.0, 134.6, 133.2, 131.4, 130.9, 130.8, 130.3, 128.7, 127.8, 124.5, 116.9, 116.5, 113.7, 55.6. MS (rel. int., %) *m*/*z*: 303.0 (4.4), 275.0 (71.1), 247.0 (19.2), 232.0 (79.8), 216.0 (7.2), 204.0 (100.0), 176.0 (11.9), 128.0 (10.1), 101.0 (11.6), 88.0 (9.4). HRMS (ESI-QTOF) calculated mass for $C_{20}H_{18}N_3O_3$ $[M+H]^+$: 304.1086, found: 304.1091.

[1,2,3]Triazolo[1,5-*a*]quinolin-3-yl(4-methylphenyl)methanone (3j): Yield: 0.050 g (69%); yellowish solid, mp: 168 - 170 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.84 (d, J = 8.4 Hz, 1H), 8.47 (d, J = 8.2 Hz, 2H), 8.35 (d, J = 9.3 Hz, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.84-7.81 (m, 2H), 7.67-7.63 (m, 1H), 7.35 (d, J = 8.0 Hz,

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2H), 2.46 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 186.3, 143.9, 139.0, 134.9, 134.6, 131.5, 130.9, 130.9, 129.2, 128.7, 127.9, 124.5, 116.8, 116.6, 21.9. MS (rel. int., %) *m*/*z*: 287.0 (4.1), 259.0 (45.7), 230.0 (100.0), 216.0 (19.9), 202.0 (9.6), 189.0 (4.5), 140.0 (5.2), 114.1 (11.1). HRMS (ESI-QTOF) calculated mass for $C_{18}H_{14}N_3O$ $[M+H]^+$: 288.1131, found: 288.1135.

[1,2,3]Triazolo[1,5-*a*]quinolin-3-yl(4-fluorophenyl)methanone (3k): Yield: 0.045 g (62%); white solid, mp: 205 - 207 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.88 (d, *J* = 8.4 Hz, 1H), 8.67 – 8.63 (m, 2H), 8.38 (d, *J* = 9.3 Hz, 1H), 7.96 (d, *J* = 7.9 Hz, 1H), 7.90 – 7.85 (m, 2H), 7.73 – 7.69 (m, 1H), 7.27 – 7.21 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 185.0, 165.9 (d, *J* = 254.6 Hz), 138.7, 134.8, 133.8 (d, *J* = 3.0 Hz), 133.5 (d, *J* = 9.2 Hz), 131.5, 131.3, 131.2, 128.8, 128.0, 124.6, 116.8, 116.7, 115.6 (d, *J* = 21.7 Hz). MS (rel. int., %) *m*/*z*: 291.0 (5.1), 263.0 (51.1), 235.0 (100.0), 214.0 (12.8), 207.0 (21.3), 175.0 (5.2), 149.1 (17.8), 138.1 (10.1), 123.0 (38.6), 111.1 (22.1), 98.1 (16.8), 88.0 (23.6). HRMS (ESI-QTOF) calculated mass for $C_{17}H_{11}FN_3O$ $[M+H]^+$: 292.0881, found: 292.0872.

[1,2,3]Triazolo[1,5-*a*]quinolin-3-yl(2-methoxyphenyl)methanone (3l): Yield: 0.054 g (71%); yellow solid, mp: 131 - 133 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.80 (d, *J* = 8.4 Hz, 1H), 8.28 (d, *J* = 9.2 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.83 – 7.78 (m, 2H), 7.70 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.66 – 7.62 (m, 1H), 7.53 – 7.49 (m, 1H), 7.11 – 7.05 (m, 2H), 3.82 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 189.1, 158.0, 139.2, 133.4, 132.6, 131.4, 131.0, 130.9, 130.4, 128.7, 127.7, 124.4, 120.4, 116.5, 116.4, 111.9, 55.9. MS (rel. int., %) *m*/*z*: 303.0 (7.2), 260.0 (82.3), 244.4 (100.0), 230.0 (20.5), 218.0 (29.8), 204.0 (20.6), 176.0 (10.0), 129.0 (77.8), 119.0 (11.9), 108.5 (13.8), 101.0 (23.3), 91.0 (43.7). HRMS (ESI-QTOF) calculated mass for $C_{18}H_{14}N_3O_2$ $[M+H]^+$: 304.1081, found: 304.1081.

Ethyl 5-methyl-[1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (5a): Yield: 0.047 g (75%); yellow solid, mp: 131 - 133 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.87 (d, *J* = 8.3 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.93 (s, 1H), 7.84-7.81 (m, 1H), 7.72-7.68 (m, 1H), 4.55 (q, *J* = 7.1 Hz, 2H), 2.72 (s, 3H), 1.51 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.9, 138.4, 133.6, 131.4, 130.6, 130.6, 127.7, 125.6, 124.5, 117.0, 114.7, 61.3, 19.7, 14.6. MS (rel. int., %) *m*/*z*: 255.0 (20.0), 227.0 (2.0), 183.0 (23.0), 170.0 (23.6), 142.1 (100.0), 115.1 (31.0). HRMS (ESI-QTOF) calculated mass for $C_{14}H_{14}N_3O_2$ $[M+H]^+$: 256.1081, found: 256.1082.

***t*ert-Butyl 5-methyl-[1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (5b):** Yield: 0.045 g (64%), pink solid, mp: 140 - 142 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.88 (d, *J* = 8.3 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.91 (s, 1H), 7.84-7.81 (m, 1H), 7.72-7.68 (m, 1H), 2.71 (s, 3H), 1.71 (s, 9H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.3, 138.0, 133.3, 131.8, 131.5, 130.6, 127.6, 125.6, 124.5, 117.0, 115.0, 82.4, 28.6, 19.7. MS (rel. int., %) *m*/*z*: 283.1 (9.1), 227.0 (4.9), 210.0 (8.1), 154.1 (23.4), 143.1 (100.0), 115.1 (14.1), 85.1 (4.9). HRMS (ESI-QTOF) calculated mass for $C_{16}H_{18}N_3O_2$ $[M+H]^+$: 284.1394, found: 284.1384.

Isopentyl 5-methyl-[1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (5c): Yield: 0.052 g (70%); pink solid, mp: 144 - 146 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.89 (d, *J* = 8.3 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.94 (s, 1H), 7.86-7.82 (m, 1H), 7.73-7.69 (m, 1H), 4.51 (t, *J* = 6.9 Hz, 2H), 2.73 (s, 3H), 1.91-1.76 (m, 3H), 1.01 (d, *J* = 6.4 Hz, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 162.0, 138.4, 133.6, 131.5, 130.7, 130. 7, 127.8, 125.6, 124.5, 117.0, 114.7, 63.9, 37.6, 25.3, 22.7, 19.8. MS (rel. int., %) *m*/*z*: 297.1 (14.9), 183.0 (41.9), 170.1 (30.6), 154.1 (23.6), 142.1 (100.0), 127.1 (22.1),115.1 (25.0). HRMS (ESI-QTOF) calculated mass for $C_{17}H_{20}N_3O_2$ $[M+H]^+$: 298.1550, found: 298.1545.

1-Phenylethyl 5-methyl-[1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (5d): Yield: 0.042 g (51%); pink solid, mp: 163 - 165 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.88 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.92 (s, 1H), 7.85-7.81 (m, 1H), 7.72-7.68 (m, 1H), 7.55 (d, *J* = 7.3 Hz, 2H), 7.40-7.37 (m, 2H), 7.33-7.29 (m, 1H), 6.27 (q, *J* = 6.6 Hz, 1H), 2.70 (s, 3H), 1.79 (d, *J* = 6.6 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.3, 141.8, 138.4, 133.7, 131.5, 130.7, 130.6, 128.7, 128.1, 127.7, 126.4, 125.6, 124.5, 117.0, 114.8, 73.4, 22.7, 19.8. MS (rel. int., %) *m*/*z*: 331.1 (1.4), 183.1 (3.0), 154.1 (6.1), 142.1 (37.2), 16.1 (11.3), 105.1 (100.0), 88.0 (7.4). HRMS (ESI-QTOF) calculated mass for $C_{20}H_{18}N_3O_2$ $[M+H]^+$: 332.1394, found: 332.1389.

Benzyl 5-methyl-[1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (5e): Yield: 0.041 g (52%); pink solid, mp: 141 - 143 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.87 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.91 (s, 1H), 7.85-7.81 (m, 1H), 7.72-7.68 (m, 1H), 7.55 (d, *J* = 7.1 Hz, 2H), 7.42 – 7.35 (m, 3H), 5.52 (s, 2H), 2.70 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.7, 138.6, 136.0, 133.7, 131.4, 130.7, 130.3, 128.8, 128.6, 128.5, 127.8, 125.6, 124.5, 117.0, 114.7, 66.8, 19.7. MS (rel. int., %) *m*/*z*: 317.0 (8.5), 288.1 (1.8), 170.0 (16.6), 142.1 (100.0), 115.1 (18.2), 91.1 (86.4). HRMS (ESI-QTOF) calculated mass for $C_{19}H_{16}N_3O_2$ $[M+H]^+$: 318.1237, found: 318.1243.

1-(5-Methyl-[1,2,3]triazolo[1,5-*a*]quinolin-3-yl)ethan-1-one (5g): Yield: 0.039 g (69%); Orange solid, mp: 147 - 149 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.73 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 1.0 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.79-7.75 (m, 1H), 7.66-7.62 (m, 1H), 2.82 (s, 3H), 2.65 (d, *J* = 1.0 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 193.6, 139.2, 138.2, 131.8, 130.9, 130.5, 127.5, 125.3, 124.4, 116.6, 115.0, 27.4, 19.4. MS (rel. int., %) *m*/*z*: 225.0 (15.9), 197.1 (31.6), 168.1 (100.0), 154.1 (12.8), 143.1 (17.2), 115.1 (12.7), 102.1 (3.9). HRMS (ESI-QTOF) calculated mass for $C_{13}H_{12}N_3O$ $[M+H]^+$: 226.0975, found: 226.0979.

(5-Methyl-[1,2,3]triazolo[1,5-*a*]quinolin-3-yl)(phenyl)methanone (5h): Yield: 0.045 g (63%); yellow solid, mp: 156 - 158 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.79 (d, *J* = 8.3 Hz, 1H), 8.53 (d, *J* = 7.3 Hz, 2H), 8.14 (s, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.79-7.75 (m, 1H), 7.64 – 7.59 (m, 2H), 7.56 – 7.52 (m, 2H), 2.67 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 186.5, 139.3, 138.0, 137.5, 134.3, 132.8, 130.9, 130.7, 130.6, 128.3,

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127.6, 125.4, 124.6, 116.7, 115.7, 19.6. MS (rel. int., %) *m/z*: 287.1 (5.1), 259.1 (35.2), 230.0 (100.0), 216.0 (28.5), 189.0 (5.2), 165.1 (4.1),140.2 (9.3), 116.1 (20.5), 102.1 (8.4), 88.1 (14.1). HRMS (ESI-QTOF) calculated mass for $C_{18}H_{14}N_3O$ $[M+H]^+$: 288.1131, found: 288.1134.

(4-Methoxyphenyl)(5-methyl-[1,2,3]triazolo[1,5-*a*]quinolin-3-yl)methanone (5i): Yield: 0.056 g (70%); white solid, mp: 153 - 155 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.80 (d, *J* = 8.3 Hz, 1H), 8.62 (d, *J* = 8.9 Hz, 2H), 8.15 (s, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.79-7.75 (m, 1H), 7.65-7.61 (m, 1H), 7.02 (d, *J* = 8.9 Hz, 2H), 3.90 (s, 3H), 2.68 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 184.9, 163.5, 138.9, 138.3, 134.3, 133.1, 131.0, 130.5, 130.4, 127.6, 125.4, 124.7, 116.7, 115.9, 113.6, 55.5, 19.6. MS (rel. int., %) *m/z*: 317.0 (5.0), 289.0 (79.9), 261.0 (21.3), 246.0 (100.0), 218.0 (65.1), 203.0 (18.2), 189.0 (4.8), 140.0 (4.4), 115.0 (13.4). HRMS (ESI-QTOF) calculated mass for $C_{19}H_{16}N_3O_2$ $[M+H]^+$: 318.1237, found: 318.1235.

(5-Methyl-[1,2,3]triazolo[1,5-*a*]quinolin-3-yl)(4-methylphenyl)methanone (5j): Yield: 0.046 g (61%); yellowish solid, mp: 166 - 168 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.82 (d, *J* = 8.3 Hz, 1H), 8.47 (d, *J* = 8.1 Hz, 2H), 8.17 (s, 1H), 7.94 (d, *J* = 8.1 Hz, 1H), 7.81 – 7.77 (m, 1H), 7.66 – 7.62 (m, 1H), 7.34 (d, *J* = 8.0 Hz, 2H), 2.69 (s, 3H), 2.45 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 186.2, 143.6, 139.1, 138.2, 135.0, 134.3, 131.1, 130.9, 130.6, 129.1, 127.6, 125.4, 124.7, 116.8, 115.8, 21.8, 19.6. MS (rel. int., %) *m/z*: 301.0 (5.8), 281.0 (6.7), 273.0 (54.6), 244.0 (100.0), 230.0 (50.3), 151.0 (29.0), 135.1 (33.4), 121.1 (39.7), 109.0 (42.3), 96.1 (52.0), 83.1 (95.9). HRMS (ESI-QTOF) calculated mass for $C_{19}H_{16}N_3O$ $[M+H]^+$: 302.1288, found: 302.1286.

(4-Fluorophenyl)(5-methyl-[1,2,3]triazolo[1,5-*a*]quinolin-3-yl)methanone (5k): Yield: 0.040 g (53%); white solid, mp: 155 - 158 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.83 (d, *J* = 8.3 Hz, 1H), 8.65 – 8.61 (m, 2H), 8.17 (s, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.84 – 7.80 (m, 1H), 7.70 – 7.66 (m, 1H), 7.23 – 7.19 (m, 2H), 2.71 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 184.8, 165.8 (d, *J* = 254.5 Hz), 139.5, 137.9, 134.4, 133.8 (d, *J* = 2.9 Hz), 133.4 (d, *J* = 9.2 Hz), 131.1, 130.7, 127.8, 125.5, 124.8, 116.8, 115.7, 115.5 (d, *J* = 21.6 Hz), 19.7. MS (rel. int., %) *m/z*: 305.0 (6.3), 276.9 (41.4), 248.0 (100.0), 233.9 (27.7), 211.8 (10.5), 140.0 (11.9), 116.0 (60.4), 88.0 (33.6). HRMS (ESI-QTOF) calculated mass for $C_{18}H_{13}FN_3O$ $[M+H]^+$: 306.1037, found: 306.1035.

(2-Methoxyphenyl)(5-methyl-[1,2,3]triazolo[1,5-*a*]quinolin-3-yl)methanone (5l): Yield: 0.046 g (58%); orange solid, mp: 170 - 172 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.83 (d, *J* = 8.3 Hz, 1H), 8.16 (s, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.82 – 7.78 (m, 1H), 7.70 – 7.65 (m, 2H), 7.52 – 7.48 (m, 1H), 7.11 – 7.05 (m, 2H), 3.83 (s, 3H), 2.71 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 189.2, 158.0, 139.3, 138.6, 133.3, 132.4, 131.2, 130.6, 130.4, 128.9, 127.6, 125.5, 124.7, 120.4, 116.8, 115.6, 111.9, 55.9, 19.6. MS (rel. int., %) *m/z*: 317.0 (8.0), 274.0 (77.6), 258.0 (100.0), 230.0 (30.1), 217.0 (25.5), 143.0 (68.3), 115.0 (46.6), 91.0 (29.5). HRMS (ESI-QTOF) calculated mass for $C_{19}H_{16}N_3O_2$ $[M+H]^+$: 318.1237, found: 318.1238.

Ethyl 1-(2-acetylphenyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxylate (6a): Yield: 0.011 g (16%); reddish oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.90 – 7.88 (m, 1H), 7.73 – 7.68 (m, 2H), 7.38-7.36 (m, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 2.47 (s, 3H), 2.32 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 198.0, 161.8, 140.9, 136.8, 136.4, 132.9, 132.6, 131.1, 129.7, 128.5, 61.2, 29.0, 14.4, 9.7. MS (rel. int., %) *m/z*: 273.1 (26.0), 228.0 (20.9), 172.1 (58.8), 157.1 (100.0), 144.1 (68.9), 130.1 (57.5), 91.1 (94.3). HRMS (ESI-QTOF) calculated mass for $C_{14}H_{16}N_3O_3$ $[M+H]^+$: 274.1186, found: 274.1194.

Ethyl 5-phenyl-[1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (7a): Yield: 0.071 g (89%); white solid, mp: 178 - 180 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.95 (d, *J* = 8.4 Hz, 1H), 8.05 (s, 1H), 7.90 – 7.83 (m, 2H), 7.64 – 7.60 (m, 1H), 7.57 – 7.50 (m, 5H), 4.54 (q, *J* = 7.1 Hz, 2H), 1.49 (t, *J* = 7.1 Hz, 3H).^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) =. 161.8, 143.2, 137.4, 133.3, 131.8, 131.6, 130.9, 129.6, 129.0, 128.9, 127.9, 127.7, 123.7, 116.9, 115.3, 61.3, 14.6.MS (rel. int., %) *m/z*: 317.2 (12.5), 289.2 (2.1), 245.2 (27.6), 232.1 (18.9), 217.1 (26.3), 204.1 (100.0) 176.1 (9.5). HRMS (ESI-QTOF) calculated mass for $C_{19}H_{16}N_3O_2$ $[M+H]^+$: 318.1237, found: 318.1240.

Ethyl 5-(4-fluorophenyl)-[1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (7b): Yield: 0.071 g (84%); white solid, mp:189 - 191 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.95 (d, *J* = 8.3 Hz, 1H), 8.02 (s, 1H), 7.88-7.84 (m, 2H), 7.66-7.62 (m, 1H), 7.53-7.50 (m, 2H), 7.28 – 7.24 (m, 2H) 4.54 (q, *J* = 7.1 Hz, 2H), 1.49 (t, *J* = 7.1 Hz, 3H).^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 163.2 (d, *J* = 249.1 Hz), 161.8, 142.1, 133.4 (d, *J* = 3.5 Hz), 133.2, 131.9, 131.4 (d, *J* = 8.3 Hz), 131.0, 127.8, 127.7, 123.7, 117.0, 116.1 (d, *J* = 21.7 Hz), 115.5, 61.4, 14.6.MS (rel. int., %) *m/z*: 335.2 (10.9), 307.2 (1.6), 278.1 (4.7), 263.1 (24.1), 250.1 (18.1), 235.1 (24.0), 222.1 (100.0), 207.1 (8.0), 175.1 (5.1). HRMS (ESI-QTOF) calculated mass for $C_{19}H_{15}FN_3O_2$ $[M+H]^+$: 336.1143, found: 336.1144.

Ethyl 5-(4-methoxyphenyl)-[1,2,3]triazolo[1,5-*a*]quinoline-3-carboxylate (7c): Yield: 0.060 g (70%); white solid, mp:184 - 186 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.95 (d, *J* = 9.1 Hz, 1H), 8.02 (s, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.87-7.83 (m, 1H), 7.65-7.61 (m, 1H), 7.47 (d, *J* = 8.7 Hz, 2H), 7.09 (d, *J* = 8.7 Hz, 2H), 4.54 (q, *J* = 7.1 Hz, 2H), 3.92 (s, 3H), 1.49 (t, *J* = 7.1 Hz, 3H).^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) =.161.9, 160.3, 143.0, 133.5, 131.9, 131.4, 130.9, 130.8, 129.7, 128.0, 127.6, 124.0, 117.0, 115.1, 114.4, 61.3, 55.6, 14.6MS (rel. int., %) *m/z*:. 347.2 (31.9), 319.2 (2.1), 290.2 (29.8), 275.2 (34.5), 262.2 (27.4), 247.1 (67.5), 234.1 (100.0), 2191 (41.1), 204.1 (27.9), 191.1 (20.9). HRMS (ESI-QTOF) calculated mass for $C_{20}H_{18}N_3O_3$ $[M+H]^+$: 348.1343, found: 348.1341.

General procedure for the synthesis of 1,2,3-triazole 4a: 2-azidobenzaldehyde **1a** (0.25 mmol, 0.0368 g), ethyl acetoacetate **2a** (0.25 mmol, 0.0325 g), DBU (10 mol%, 0.0038 g) and DMSO (0.25 mL) were added to a 5.0 mL glass tube. Then, the reaction mixture was stirred for 24 h at room temperature under air atmosphere. After this time, the crude product was purified by column chromatography

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on silica gel with a mixture of hexane/ethyl acetate (3:1) as eluent to afford the desired product (**4a**). Spectral data for the product 4a prepared are listed below.

Ethyl 1-(2-formylphenyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxylate (4a): Yield: 0.053 g (82%); yellowish oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 9.67 (s, 1H), 8.13 (dd, J = 7.5, 1.3 Hz, 1H), 7.87-7.77 (m, 2H), 7.44 (d, *J*=7.5 Hz, 1H), 4.49 (q, *J* = 7.1 Hz, 2H), 2.50 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 187.9 (2C), 140.9, 135.9, 135.0, 132.0, 131.4, 130.8, 128.2, 61.4, 14.5, 9.8. MS (rel. int., %) *m*/*z*: 259.1 (0.6), 231.0 (11.5), 186.0 (12.2), 159.1 (100.0), 143.2 (26.3), 130.1 (99.3), 117.1 (19.3), 103.1 (31.4). HRMS (ESI-QTOF) calculated mass for $C_{13}H_{14}N_3O_3$ $[M+H]^+$: 260.1030, found: 260.1031.

General procedure for the synthesis of 1,2,3-triazoles 4m-o: 2-azidobenzaldehyde **1a** (0.25 mmol, 0.0368 g), 1,3-dicarbonyl compounds **2m-o** (0.25 mmol), DBU (20 mol%, 0.0076 g) and DMSO (0.25 mL) were added to a 5.0 mL glass tube. Then, the reaction mixture was stirred for 24 h at 120 °C under air atmosphere. After this time, the crude product was purified by column chromatography on silica gel with a mixture of hexane/ethyl acetate (2:1) as eluent to afford the desired products (**4m-o**). Spectral data for the products prepared are listed below.

2-(5-Ethyl-4-propionyl-1*H*-1,2,3-triazolyl)benzaldehyde (4m): Yield: 0.053 g (82%); yellowish oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 9.52 (s, 1H), 8.07 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.79 – 7.70 (m, 2H), 7.36 (d, *J* = 7.7 Hz, 1H), 3.20 (q, *J* = 7.4 Hz, 2H), 2.84 (q, *J* = 7.4 Hz, 2H), 1.20 (t, *J* = 7.5 Hz, 3H), 1.00 (t, *J* = 7.5 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 197.1, 187.8, 144.7, 142.6, 136.2, 134.9, 132.2, 131.5, 130.6, 128.1, 33.5, 17.2, 12.8, 7.9. MS (rel. int., %) *m*/*z*: 257.0 (2.5), 228.0 (17.0), 200.0 (47.7), 172.0 (100.0), 158.0 (46.7), 144.1(59.6), 130.1(43.4), 117.1(33.9), 104.1(15.9), 89.1(17.6). HRMS (ESI-QTOF) calculated mass for $C_{14}H_{16}N_3O_2$ $[M+H]^+$: 258.1237, found: 258.1238.

***N*-(4-Chlorophenyl)-1-(2-formylphenyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxamide (4n):** Yield: 0.071 g (84%); yellow solid, mp: 170 - 172 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 9.70 (s, 1H), 9.14 (bs, 1H), 8.13 (d, *J* = 6.8 Hz, 1H), 7.86 – 7.78 (m, 2H), 7.68 (d, *J* = 8.7 Hz, 2H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 8.5 Hz, 2H), 2.55 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 188.0, 159.0, 139.5, 138.3, 136.3, 135.6, 135.0, 131.9, 131.5, 131.1, 129.4, 129.2, 128.1, 121.2, 9.5. MS (rel. int., %) *m*/*z*: 340.0 (50.1), 173.0 (9.9), 158.1 (21.7), 147.1 (100.0), 130.1 (61.2), 119.1 (64.0), 104.1 (38.8). HRMS (ESI-QTOF) calculated mass for $C_{17}H_{14}ClN_4O_2$ $[M+H]^+$: 341.0800, found: 341.0792.

***N*,*N*-Diethyl-1-(2-formylphenyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxamide (4o):** Yield: 0.046 g (65%); yellowish oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 9.65 (s, 1H), 8.14 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.86-7.81 (m, 1H), 7.78-7.74 (m, 1H), 7.43 (d, *J* = 7.8 Hz, 1H), 3.90 (q, *J* = 6.9 Hz, 2H), 3.59 (q, *J* = 7.1 Hz, 2H), 2.45 (s, 3H), 1.37 (t, *J* = 7.0 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 188.0, 161.7, 140.3, 139.5, 136.6, 134.9, 131.9, 131.0, 130.2, 127.8, 43.6, 40.9, 14.8, 12.9, 9.9. MS (rel. int., %) *m*/*z*: 286.05 (0.33), 215.05 (93.75), 187.00 (23.55), 158.05 (27.13), 146.10 (100.00), 130.10 (46.72), 118.10 (12.08), 105.05 (16.77), 91.10 (14.58). HRMS (ESI-QTOF) calculated mass for $C_{15}H_{19}N_4O_2$ $[M+H]^+$: 287.1503, found: 287.1509.

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References

[1] a) G. Brahmachari, (Ed.) Green Synthetic Approaches for Biologically Relevant Heterocycles, Amsterdam, Netherlands: Elsevier, 2014; b) P. N. Kalaria, S. C. Karad, D. K. Raval, *Eur. J. Med. Chem*., **2018**, *158*, 917; c) K. Passador, S. Thorimbert, C. Botuha, *Synthesis*, **2019**, *51*, 384 d) I. Muthukrishnan, V. Sridharan, J. C. Menéndez, *Chem. Rev.*, **2019**, *119*, 5057; e) A. C. Ruberte, C. Sanmartin, C. Aydillo, A. K. Sharma, D. Plano, *J. Med. Chem.*, **2020**, *63*, 1473; f) D. J. Newman, G. M. Cragg, *J. Nat. Prod.*, **2020**, *83*, 770; g) G. Grover, R. Nath, R. Bhatia, M. J. Akhtar, *Bioorgan. Med. Chem*., **2020**, *28*, DOI https://doi.org/10.1016/j.bmc.2020.115585.

[2] E. Vitaku, D. T. Smith, J. T. Njardarson, *J. Med. Chem.*, **2014**, *57*, 10257.

[3] a) R. M. Acheson, In *An introduction to the chemistry of heterocicle compounds*, John Wiley & Sons: Canada, 1977; b) K. Bozorov, J. Zhao, H. A. Aisa, *Bioorg & Med. Chem.*, **2019**, *27*, 3511; c) D. Dheer, V. Singh, R. Shankar, *Bioorg. Chem.*, **2017**, *71*, 30; d) B. Zhang, *Eur. J. Med. Chem.*, **2019**, *168*, 357; e) K. Lal, P. Yadav, *Anti-cancer Agent. Me.* **2018**, *18*, 21; f) L. S. M. Forezi, M. F. C. Cardoso, D. T. G. Gonzaga, F. C. Silva, V. F. Ferreira, *Curr. Top. Med. Chem.*, **2018**, *18*, 1428; g) S. G. Agalave, S. R. Maujan, V. S. Pore, *Chem. Asian J.*, **2011**, *6*, 2696.

[4] a) D. W. C. MacMillan, *Nature*, **2008**, *455*, 304; b) J. John, J. Thomas, W. Dehaen, *Chem. Commun.*, **2015**, *51*, 10797; c) K. Anebouselvy and D. B. Ramachary, *Synthesis of Substituted 1,2,3-Triazoles through Organocatalysis. In Click Reactions in Organic Synthesis*, S. Chandrasekaran (Ed.), Wiley-VCH, 2016; d) B. Gopalan and K. K. Balasubramanian, *Applications of Click Chemistry in Drug Discovery and Development. In Click Reactions in Organic Synthesis*, Chandrasekaran (Ed.), Wiley-VCH, 2016; e) C. C. Chrovian, A. Soyode-Johnson, A. A. Peterson, C. F. Gelin, X. Deng, C. A. Dvorak, N. I. Carruthers, B. Lord, I. Fraser, L. Aluisio, K. J. Coe, B. Scott, T. Koudriakova, F. Schoetens, K. Sepassi, D. J. Gallacher, A. Bhattacharya, M. A. Letavic, *J. Med. Chem.* **2018**, *61*, 207; f) G. S. Reddy, K. Anebouselvy, D. Ramachary, *Chem. Asian J.*, DOI: 10.1002/asia.202000731.

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[5] a) D. B. Ramachary, K. Ramakumar, V. V. Narayana, *Chem. Eur. J.*, **2008**, *14*, 9143; b) L. J. T. Danence, Y. Gao, M. Li, Y. Huang, J. Wang, *Chem. Eur. J.*, **2011**, *17*, 3584; c) M. Belkheira, D. E. Abed, J.-M. Pons, C. Bressy, *Chem. Eur. J.*, **2011**, *17*, 12917; d) L. Wang, S. Peng, L. J. T. Danence, Y. Gao, J. Wang, *Chem. Eur. J*., **2012**, *18*, 6088; e) D. K. J. Yeung, T. Gao, J. Huang, S. Sun, H. Guo, J. Wang, *Green Chem*., **2013**, *15*, 2384; f) D. B. Ramachary, A. B. Shashank, *Chem. Eur. J*., **2013**, *19*, 13175; g) W. Li, Z. Du, J. Huang, Q. Jia, K. Zhang, J. Wang, *Green Chem.*, **2014**, *16*, 3003; h) M. T. Saraiva, G. P. Costa, N. Seus, R. F. Schumacher, G. Perin, M. W. Paixão, R. Luque, D. Alves, *Org. Lett.*, **2015**, *17*, 6206; i) N. Seus, B. Goldani, E. J. Lenardão, L. Savegnago, M. W. Paixão, D. Alves, *Eur. J. Org. Chem.*, **2014**, *5*, 1059; j) G. P. Costa, N. Seus, J. A. Roehrs, R. G. Jacob, R. F. Schumacher, T. Barcellos, R. Luque, D. Alves, *Beilstein J. Org. Chem.*, **2017**, *13*, 694; k) N. Seus, L. C. Gonçalves, A. M. Deobald, L. Savegnago, D. Alves, M. W. Paixão, *Tetrahedron*, **2012**, *68*, 10456; l) L. F. B. Duarte, N. M. Nascimento, G. Perin, R. Luque, D. Alves, R. F. Schumacher, *ChemistrySelect*, **2017**, *2*, 6645; m) D. Alves, B. Goldani, E. J. Lenardão, G. Perin, R. F. Schumacher, M. W. Paixão, *Chem. Rec.*, **2018**, *18*, 527.

[6] a) A. Ali, A. G. Corrêa, D. Alves, J. Zukerman-Schpector, B. Westermann, M. A. B. Ferreira, M. W. Paixão, *Chem. Commun.*, **2014**, *50*, 11926; b) A. B. Shashank, S. Karthik, R. Madhavachary, D. B. Ramachary, *Chem. Eur. J.*, **2014**, *20*, 16877; c) D. B. Ramachary, A. B. Shashank, S. Karthik, *Angew. Chem.*, **2014**, *126*, 10588. d) D. B. Ramachary, A. B. Shashank, S. Karthik, *Angew. Chem. Int. Ed.*, **2014**, *53*, 10420; e) D. B. Ramachary, P. M. Krishna, J. Gujral, G. S. Reddy, *Chem. Eur. J.*, **2015**, *21*, 16775; f) P. M. Krishna, D. B. Ramachary, S. Peesapati, *RSC Adv.*, **2015**, *5*, 62062; g) D. B. Ramachary, G. S. Reddy, S. Peraka, J. Gujral, *ChemCatChem.*, **2017**, *9*, 263; h) D. B. Ramachary, J. Gujral, S. Peraka, G. S. Reddy, *Eur. J. Org. Chem*. **2017**, 459; i) G. Reddy, D. B. Ramachary, *Org. Chem. Front.*, **2019**, *6*, 3620; j) G. S. Reddy, A. S. Kumara, D. B. Ramachary, *Org. Biomol. Chem.*, **2020**, *18*, 4470; k) H. Choi, H. J. Shirley, P. A. Hume, M. A. Brimble, D. P. Furkert, *Angew. Chem. Int. Ed.*, **2017**, *56*, 7420; l) D. González-Calderón, A. Fuentes-Benítes, E. Díaz-Torres, C. A. González-González, C. González-Romero, *Eur. J. Org. Chem.*, **2016**, 668.

[7] a) A. R. Katritzky, A. F. Pozharskii, In *Handbook of Heterocyclic Chemistry*, Pergamon, Oxford, 2000; b) T. Eicher, S. Hauptmann, *The Chemistry of Heterocycles*, Wiley, VCH, 2003; c) S. Kumar, S. Bawa, H. Gupta, *Mini-Rev. Med. Chem.*, **2009**, *9*, 1648; d) X. Nqoro, N. Tobeka, B. A. Aderibigbe, *Molecules*, **2017**, *22*, 2268; e) X.-M. Chu, C. Wang, W. Liu, L.-L. Liang, K.-K. Gong, C.-Y. Zhao, K.-L. Sun, *Eur. J. Med. Chem.*, **2019**, *161*, 101; f) L. M. Nainwal, S. Tasneem, W. Akhtar, G. Verma, M. F. Khan, S. Parvez, M. Shaquiquzzaman, M. Akhter, M. M. Alam, *Eur. J. Med. Chem.*, **2019**, *164*, 121.

[8] a) L. Savegnago, A. I. Vieira, N. Seus, B. S. Goldani, M. R. Castro, E. J. Lenardão, D. Alves, *Tetrahedron Lett.*, **2013**, *54*, 40; b) S. M. Prajapati, K. D. Patel, R. H. Vekariya, S. N. Panchal, H. D. Patel, *RSC Adv.*, **2014**, *4*, 24463; c) A. S. Reis, M. Pinz, L. F. B. Duarte, J. A. Roehrs, D. Alves, C. Luchese, E. A. Wilhelm, *J. of Psychiat. Res.*, **2017**, *84*, 191.

[9] a) M. G. Fronza, R. Baldinotti, M. C. Martins, B. Goldani, B. T. Dalberto, F. S. Kremer, K. Begnini, L. S. Pinto, E. J. Lenardão, F. K. Seixas, T. Collares, D. Alves, L. Savegnago, *Sci. Rep.*, **2019**, *9*, 1; b) E. A. Wilhelm, N. C. Machado, A. B. Pedroso, B. S. Goldani, N. Seus, S. Moura, L. Savegnago, R. G. Jacob, D. Alves, *RSC Adv.*, **2014**, *4*, 41437; c) K. R. Begnini, W. R. Duarte, L. P. da Silva, J. H. Bussa, B. S. Goldani, M. Fronza, N. V. Segatto, D. Alves, L. Savegnago, F. K. Seixas, T. Collares, *Biomed. Pharmacother*., **2017**, *91*, 510. d) M. Kai, A. Noda, H. Noda, S. Goto, *Chem. Pharm. Bull.*, **1988**, *36*, 3604; e) F. A. Bassyouni, S. M. Abu-Baker, K. Mahmoud, M. Moharam, S. S. El-Nakkady, M. A. Rehim, *RSC Adv.*, **2014**, *4*, 24131.

[10] A. Upadhyay, P. Kushwaha, S. Gupta, R. P. Dodda, K. Ramalingam, R. Kant, N. Goyal, K. V. Sashidhara, *Eur. J. Med. Chem.*, **2018**, *154*, 172.

[11] a) J. Zhang, S. Wang, Y. Ba, Z. Xu, *Eur. J. Med. Chem.*, **2019**, *174*, 1; b) K. Oukoloff, B. Lucero, K. R. Francisco, K. R. Brunden, C. Ballatore, *Eur. J. Med. Chem.*, **2019**, *165*, 332; c) V. V. Kouznetsov, L. Y. Vargas-Mendez, F. I. Zubkov, *Mini-Rev. Org. Chem.*, **2016**, *13*, 488.

[12] a) E. A. Shafran, V. A. Bakulev, Y. A. Rozin, Y. M. Shafran, *Chem. Heterocycl. Compd.*, **2008**, *44*, 1040; b) P. Xu, H.-C. Xu, *ChemElectroChem.*, **2019**, *6*, 4177; c) D. Gangaprasad, J. Paul Raj, K. Karthikeyan, R. Rengasamy, J. Elangovan, *Adv. Synth. Catal.*, **2018**, *360*, 4485; d) K. Pericherla, A. Jha, B. Khungar, A. Kumar, *Org. lett.*, **2013**, *15*, 4304; e) K. Li, J. Chen, J. Li, Y. Chen, J. Qu, X. Guo, C. Chen, B. Chen, *Eur. J. Org. Chem.*, **2013**, 6246; f) G. Jiang, Y. Lin, M. Cai, H. Zhao, *Synthesis*, **2019**, *51*, 4487, g) K. Upadhyaya, A. Ajay, R. Mahar, R. Pandey, B. Kumar, S. K. Shukla, R. P. Tripathi, *Tetrahedron*, **2013**, *69*, 8547; h) Z. Wang, B. Li, X. Zhang, X. Fan, *J. Org. Chem.*, **2016**, *81*, 6357; i) J. Wang, J. Yang, X. Fu, G. Qin, T. Xiao, Y. Jiang, *Synlett*, **2019**, *30*, 1452; j) L. D. Caspers, P. Finkbeiner, B. J. Nachtsheim, *Chem. Eur. J.*, **2017**, *23*, 2748; k) N. T. Pokhodyloa, M. D. Obushaka, *Russ. J. Org. Chem.*, **2019**, *55*, 1241; l) J. Yang, Y. Ren, J. Wang, T. Li, T. Xiao, Y. Jiang, *ChemistrySelect*, **2019**, *4*, 6272.

[13] Z. Liu, D. Zhu, B. Luo, N. Zhang, Q. Liu, Y. Hu, R. Pi, P. Huang, S. Wen, *Org. Lett.*, **2014**, *16*, 5600.

[14] B. T. Hirayama, S. Ueda, T. Okada, N. Tsurue, K. Okuda, H. Nagasawa, *Chem. Eur. J.*, **2014**, *20*, 4156.

[15] A. Kumar, S. S. Shinde, D. K. Tiwari, B. Sridhar, P. R. Likhar, *RSC Adv.*, **2016**, *6*, 43638.

[16] Y.-M. Cai, X. Zhang, C. An, Y.-F. Yang, W. Liu, W.-X. Gao, X.-B. Huang, Y.-B. Zhou, M.-C. Liu, H.-Y. Wu, *Org. Chem. Front.*, **2019**, *6*, 1481.

[17] D. S. Latha, S. Yaragorla, *Eur. J. Org. Chem.*, **2020**, 2155.

[18] Y. Shafran, Y. Rozin, T. Beryozkina, S. Zhidovinov, O. Eltsov, J. Subbotina, J. Leban, R. Novikova, V. Bakulev, *Org. Biomol. Chem.*, **2012**, *10*, 5795.

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10.1002/adsc.202000887

[19] a) S. Boros, Z. Gáspári, G. Batta, *Ann. Rep. NMR Spectro.*, **2018**, *94*, 1, DOI: https://doi.org/10.1016/bs.arnmr.2017.12.002; b) C. P. Butts, C. R. Jones, E. C. towers, J. L. Flynn, L. Appleby, N. J. Barron, *Org. Biomol. Chem.*, **2011**, *9*, 177; c) M. P. Williamson, *Ann. Rep. NMR Spectro.*, **2009**, *65*, 77, DOI: 10.1016/S0066-4103(08)00203-2.

[20] R. A. Bell, J. K. Saunders, *Can. J. Chem.*, **1970**, *48*, 1114.

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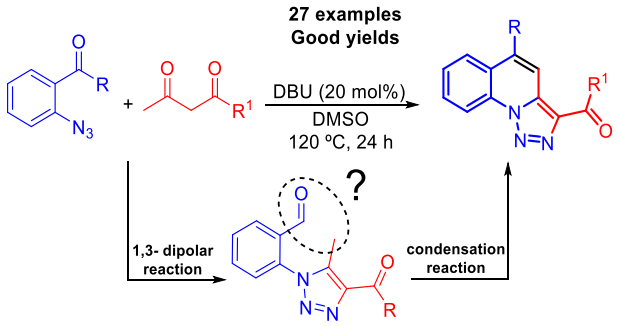

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