An Efficient One-Pot Strategy for the Synthesis of Triazole-Fused 1,4-Benzodiazepinones from N-Substituted 2-Azidobenzamides

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Abstract: A catalyst-free, one-pot strategy for the synthesis of 1,2,3-triazole-fused 1,4-benzodiazepinone derivatives from N-substituted 2-azidobenzamides and propargyl bromide, in the presence of a base, is reported. The products are formed in good to excellent yields via N-alkylation followed by a 1,3-dipolar cycloaddition.

Key words: fused triazole, azide–alkyne cycloaddition, 1,4-benzodiazepinones, N-substituted 2-azidobenzamides, catalyst-free

The benzodiazepine core is considered to be a privileged structure in medicinal chemistry, and has attracted considerable attention as a ligand for various bioreceptors.[1] 1,4-Benzodiazepines play important roles as anti-anxiety and antihistaminic agents.[2] Benzodiazepines with fused 1,2,3-triazole and tetrazole rings have also gained popularity due to their potent biological activity.[3] Tricyclic fused benzodiazepines such as flumazenil (**1**),[4] diazepinone (**2**)[5] and estazolam (**3**)[6] have achieved clinical success in the treatment of central nervous system disorders (Figure 1). ^{18}F-Labelled compound **1** is a useful ligand for positron emission tomography.[7] Furthermore, the tetracyclic benzodiazepine, bretazanil (**4**), has shown activity in the treatment of central nervous system disorders and against neurodegenerative diseases.[8]

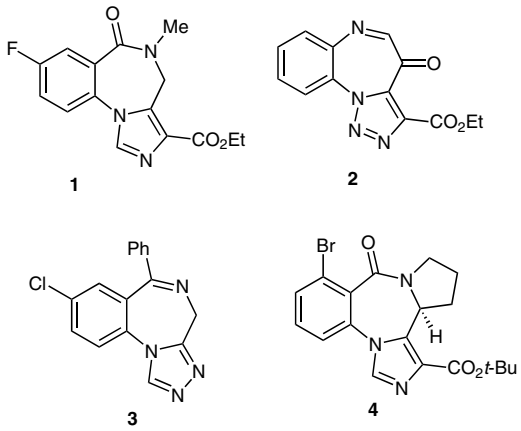

Figure 1 Examples of biologically active fused benzodiazepinones

As a result, considerable interest has been generated in the development of new and more efficient synthetic routes to a diverse range of 1,2,3-triazole-fused pharmacophores.[9] Many research groups have employed the Huisgen 1,3-dipolar cycloaddition of azides with alkynes[10] for the synthesis of bicyclic, polycyclic and triazole-fused nitrogen-containing heterocycles.[11] Various approaches toward the preparation of 1,4-benzodiazepine derivatives have also been reported.[12] Akritopoulou-Zanze et al.[13] have reported a two-step synthesis of fused triazole derivatives via alkyne–azide cycloadditions of substrates obtained from Ugi reactions of isocyanides and *o*-azidobenzaldehyde. Hemming and co-workers[14] reported the synthesis of triazolobenzodiazepines and pyrrolobenzodiazepines using an intramolecular 1,3-dipolar cycloaddition in a multistep process. Furthermore, Chowdhury[15] has described an approach for the synthesis of 1,2,3-triazolo[1,5-*a*][1,4]benzodiazepin-6-ones and 1,2,3-triazolo[1,5-*a*][1,5]benzodiazocin-7-ones through Sonogashira coupling of an aryl iodide with 2-amino-*N*-methyl-*N*-(prop-2-ynyl)benzamide or its homologue, followed by in situ diazotization, azidation and cycloaddition reactions. The Lemrova[16] group have reported a solid-phase synthesis of 1,2,3,4-tetrahydrobenzo[*e*][1,4]diazepin-5-ones using polystyrene resin. A domino approach for the synthesis of polyfunctionalized and tricyclic fused dibenzo[*b*,*e*][1,4]diazepin-1-one and pyrrole derivatives was reported by Jiang and co-workers.[17] Finally, Van der Eycken[18] has synthesized triazolo[1,5-*a*][1,4]benzodiazepinones by employing a post-Ugi copper-catalyzed tandem azide–alkyne cycloaddition and Ullmann coupling strategy. They used *o*-bromobenzaldehyde, an amine, an isocyanide, and propiolic acid derivatives for the synthesis of the Ugi-product. However, the majority of these protocols require the use of very expensive reagents or ligands. In continuation of our efforts to synthesize potentially bioactive heterocycles,[19] we planned to develop a simple protocol for the preparation of triazole-fused 1,4-benzodiazepinones by employing a 1,3-dipolar cycloaddition reaction. The results of this study are reported herein.

The starting materials, N-substituted 2-azidobenzamides **6a**–**g**, were prepared from 2-azidobenzoic acid (**5**), which was converted into the corresponding benzoyl chloride derivative by treatment with thionyl chloride. This was followed by reaction with the appropriate amine under phase-transfer catalysis conditions, using tetrabutylammonium hydrogen sulfate (TBAHS) as the catalyst and potassium carbonate as the base, to afford benzamides **6a**–**g** in 80–90% yields (Scheme 1).

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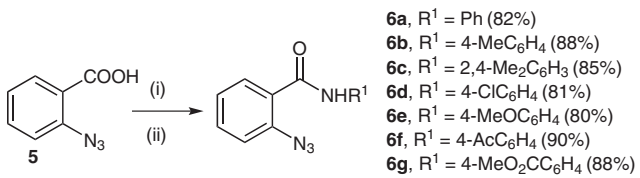


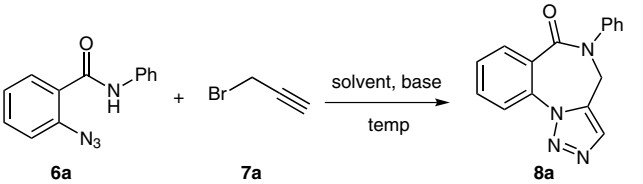
Scheme 1 Preparation of 2-azidobenzamides **6a**–**g**. *Reagents and conditions*: (i) **5**, $SOCl_2$, DMF, reflux, 2 h; (ii) R^1NH_2, TBAHS (cat.), CH_2Cl_2, K_2CO_3 (aq), r.t., 4 h.

Compound **6a** was selected as a model substrate to optimize the reaction conditions. The reaction at room temperature between azidobenzamide **6a** and propargyl bromide (**7a**) in *N*,*N*-dimethylformamide, using potassium carbonate as the base, did not afford the desired cyclized product **8a** (Table 1, entry 1). However, on heating the reaction mixture to 70 °C, product **8a** was obtained in a very satisfactory 89% yield within five hours (Table 1, entry 2). The reaction using copper(I) iodide as a catalyst gave a similar yield (85%) of the product (Table 1, entry 3). Using other bases such as cesium carbonate (Cs_2CO_3), triethylamine or sodium carbonate did not lead to any improvement in the yield of the cyclized product (Table 1, entries 4–6). No reaction occurred in the absence of a base (Table 1, entry 7). The use of other solvents including dimethyl sulfoxide (DMSO), *N*,*N*-dimethylacetamide (DMA), 1,4-dioxane, acetonitrile, toluene and acetone resulted in no improvement in the yield of the cyclized product (Table 1, entries 8–13); *N*,*N*-dimethylacetamide and acetonitrile afforded the desired product in moderate 72% and 50% yields, respectively. Thus, *N*,*N*-dimethylformamide proved to be the best solvent for this cycloaddition.

From these control experiments, the optimized conditions were established as follows: reaction of the N-substituted-2-azidobenzamide (1 equiv) with the alkyne (1.5 equiv) and K_2CO_3 (1.5 equiv) in DMF at 70 °C for five–six hours. These conditions were then applied in the reactions of substrates **6b**–**f** and the results are summarized in Table 2.

Two mechanistic paths (A or B) can be considered for the formation of products **8**. Path A involves N-alkylation of the amide moiety by nucleophilic attack of the benzamide **6** on the propargyl bromide **7**, in the presence of the base, to form intermediate **9**. This subsequently undergoes intramolecular azide–alkyne cycloaddition to yield the triazole-fused 1,4-benzodiazepinone **8**. The alternative mechanism, path B, takes place through initial formation of the bromomethyl-1,2,3-triazole intermediate **11** via an intermolecular azide–alkyne cycloaddition of propargyl bromide with the azide group of benzamide **6**, followed by intramolecular coupling of the bromomethyl group of the triazole with the amide moiety to give product **8**. As it is well known that the reaction is both rapid and exclusively 1,4-directing, it is more likely that the process follows path A rather than path B. If the reaction had followed path B, it would have been expected to afford some di- and oligomerized by-products, along with the desired product, via formation of the intermediate 1,5-regioisomer **10** (Scheme 2).

Table 1 Optimization of the Intramolecular Azide–Alkyne [3+2] Cycloaddition[a]



6a 7a 8a

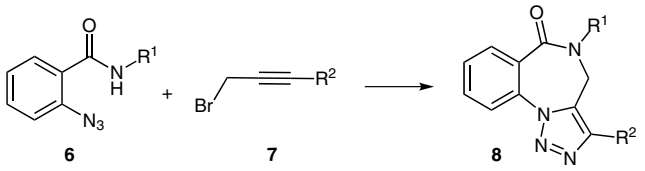
Entry	Solvent	Base	Temp (°C)	Time (h)	Yield (%)[b]
1	DMF	K_2CO_3	r.t.	12	0
2	**DMF**	**K_2CO_3**	**70 °C**	**5**	**89**
3[c]	DMF	K_2CO_3	70 °C	5	85
4	DMF	Cs_2CO_3	70 °C	5	82
5[d]	DMF	Et_3N	70 °C	7	80
6	DMF	Na_2CO_3	70 °C	5	74
7	DMF	–	70 °C	7	0
8	DMSO	K_2CO_3	70 °C	5	<50
9	DMA	K_2CO_3	70 °C	5	72
10	1,4-dioxane	K_2CO_3	70 °C	5	43
11	MeCN	K_2CO_3	70 °C	5	50
12	toluene	K_2CO_3	70 °C	5	30
13	acetone	K_2CO_3	reflux	5	36

[a] All reactions were carried out using **6a** (1 equiv), **7a** (1.5 equiv) and base (1.5 equiv).
[b] Yield of isolated product.
[c] CuI (10 mol%) was used as the catalyst.
[d] Et_3N (3 equiv) was used as the base.

In conclusion, we have developed a simple, one-pot approach for the synthesis of 1,2,3-triazole-fused 1,4-benzodiazepinone derivatives with potential biological activity via intramolecular Huisgen 1,3-dipolar cycloadditions. The protocol is mild and catalyst-free, occurs at ambient temperature, and the products are simple to isolate in high yields.

Silica gel [Rankem (India), 60–120 and 230–400 mesh] was used for column chromatography. Silica gel G [CDH (India), silica gel GF-254] was used for TLC. Petroleum ether (PE) refers to the fraction boiling between 60–80 °C. Melting points were determined in open capillary tubes using a metal bath apparatus from Sunbeam (India) and are uncorrected. IR spectra were recorded on a Perkin-Elmer L 120-000A spectrometer. ^1H and ^{13}C NMR spectra were recorded on Bruker DPX 400 and 300 spectrometers in $CDCl_3$ with TMS as the internal standard. Mass spectrometry was accomplished using a Q-TOF Micro™ instrument at the Indian Institute of Chemical Biology (Kolkata). HRMS were recorded on a Q-TOF Micro YA263 instrument at the Indian Association for the Cultivation of Science (Kolkata). CHN analyses were recorded on a Perkin-Elmer 2400 series II CHN analyzer at the University of Kalyani.

Table 2 Azide–Alkyne [3+2] Cycloaddition Reactions with Various Substrates[a]



6 **7** **8**

Entry	2-Azidobenzamide	Alkyne	Time (h)	Product	Yield (%)[b]
1	**6a** ($R^1 = C_6H_5$)	**7a** (R^2 = H)	5	**8a**	89
2	**6a** ($R^1 = C_6H_5$)	**7b** (R^2 = Me)	6	**8b**	82
3	**6b** (R^1 = 4-MeC_6H_4)	**7a** (R^2 = H)	5	**8c**	86
4	**6c** (R^1 = 2,4-$Me_2C_6H_3$)	**7a** (R^2 = H)	6	**8d**	83
5	**6d** (R^1 = 4-ClC_6H_4)	**7a** (R^2 = H)	5	**8e**	94
6	**6e** (R^1 = 4-MeOC_6H_4)	**7a** (R^2 = H)	5	**8f**	90
7	**6f** (R^1 = 4-MeCOC_6H_4)	**7a** (R^2 = H)	5	**8g**	95
8	**6g** (R^1 = 4-Me$CO_2C_6H_4$)	**7a** (R^2 = H)	5	**8h**	91

[a] Reaction conditions: 2-azidobenzamide **6** (1 equiv), alkyne **7** (1.5 equiv), K_2CO_3 (1.5 equiv), DMF, 70 °C.
[b] Yield of isolated product.

2-Azidobenzoic Acid (5)

2-Aminobenzoic acid (10 g, 72.99 mmol) was added to a beaker containing H_2O (45 mL) and concd H_2SO_4 (15 mL), and cooled to 0 °C. A soln of $NaNO_2$ (6 g, 87.58 mmol) in H_2O (30 mL) was added dropwise at 0 °C over 30 min. Next, an ice-cold soln of NaN_3 (5.7 g, 87.58 mmol) in H_2O (30 mL) was added with stirring and the mixture was heated at 80 °C over a period of 30 min. After cooling, the resulting precipitate was collected, washed with cold H_2O (10 mL) and dried under reduced pressure to afford 2-azidobenzoic acid (**5**) (7.37 g, 45.21 mmol, 62%). The peaks at 2109 and 2137 cm^{-1} in the IR spectrum confirmed the presence of the azide group.

2-Azido-*N*-phenylbenzamide (6a); Typical Procedure

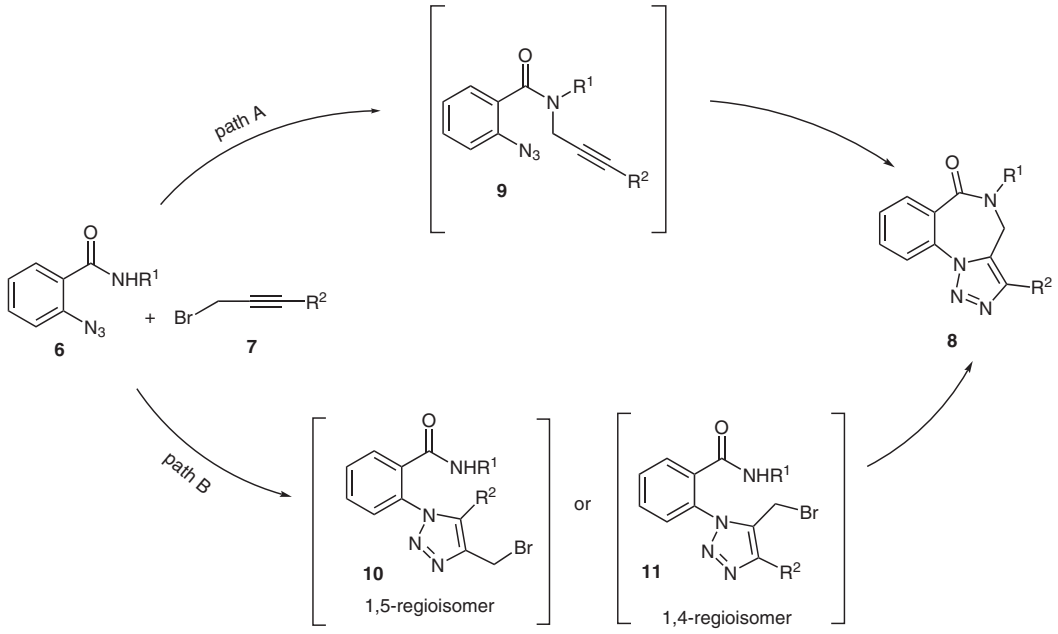
2-Azidobenzoic acid (**5**) (500 mg, 3.07 mmol) was added to a round-bottomed flask and treated with $SOCl_2$ (2 mL) and DMF (1 drop). The resulting mixture was heated at reflux temperature for 2 h and then evaporated under reduced pressure to yield the corresponding 2-azidobenzoyl chloride. To a stirred soln of the 2-azidobenzoyl chloride in CH_2Cl_2 (20 mL) was added a mixture of aniline (428 mg, 4.60 mmol) and TBAHS (78 mg, 5 mol%) in CH_2Cl_2 (20 mL). A soln of K_2CO_3 (635 mg, 4.60 mmol) in H_2O (10 mL) was added dropwise and the mixture was stirred vigorously for 4 h. After completion of the reaction (monitored by TLC), the organic layer was separated and washed with H_2O (2 × 20 mL) and brine (20 mL), dried over anhyd Na_2SO_4 and filtered. The filtrate was concentrated and the crude residue purified by column chromatography over silica gel (PE–EtOAc, 1:9) to give compound **6a** (598 mg, 2.512 mmol, 82%) as a white solid.

Mp 102–104 °C; R_f = 0.50 (15% EtOAc–PE).

IR (KBr): 3288, 2134, 2098, 1651, 1325, 1302, 754 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.14–7.30 (m, 3 H, ArH), 7.37 (t, *J* = 8.0 Hz, 2 H, ArH), 7.46–7.57 (m, 1 H, ArH), 7.67 (d, *J* = 7.2 Hz, 2 H, ArH), 8.23 (d, *J* = 8.0 Hz, 1 H, ArH), 9.28 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 118.5, 120.6, 124.6, 125.5, 129.1, 132.6, 132.8, 136.9, 138.0, 162.6.



Scheme 2 Mechanistic rationalization for the formation of compounds **8**

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{11}N_4O$: 239.0933; found: 239.0878.

2-Azido-*N*-*p*-tolylbenzamide (6b)
Starting from 2-azidobenzoic acid (**5**) (500 mg, 3.07 mmol) and *p*-toluidine (492 mg, 4.60 mmol), compound **6b** was isolated as a white solid (680 mg, 2.69 mmol, 88%).

Mp 82–84 °C; R_f = 0.52 (15% EtOAc–PE).

IR (KBr): 3332, 2138, 2105, 1644, 1327, 811, 746 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.47 (s, 3 H, CH_3), 7.31 (d, *J* = 8.4 Hz, 2 H, ArH), 7.37–7.44 (m, 2 H, ArH), 7.69 (d, *J* = 8.4 Hz, 3 H, ArH), 8.38 (dd, *J* = 8.4, 1.6 Hz, 1 H, ArH), 9.38 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 118.5, 120.5, 125.3, 125.4, 129.5, 132.3, 132.6, 134.2, 135.4, 136.8, 162.6.

MS (ESI): *m*/*z* = 253 (100%) [M + H]$^+$.

Anal. Calcd for $C_{14}H_{12}N_4O$: C, 66.65; H, 4.79; N, 22.21. Found: C, 66.72; H, 4.61; N, 22.35.

2-Azido-*N*-(2,4-dimethylphenyl)benzamide (6c)
Starting from 2-azidobenzoic acid (**5**) (500 mg, 3.07 mmol) and 2,4-dimethylaniline (556 mg, 4.60 mmol), compound **6c** was isolated as a gray solid (693 mg, 2.60 mmol, 85%).

Mp 134–136 °C; R_f = 0.48 (15% EtOAc–PE).

IR (KBr): 3223, 2133, 2094, 1642, 1299, 754 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.32 (s, 3 H, CH_3), 2.35 (s, 3 H, CH_3), 7.05 (d, *J* = 8.0 Hz, 2 H, ArH), 7.25–7.32 (m, 2 H, ArH), 7.55 (t, *J* = 8.0 Hz, 1 H, ArH), 7.90 (d, *J* = 8.0 Hz, 1 H, ArH), 8.29 (d, *J* = 8.0 Hz, 1 H, ArH), 9.15 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.2, 20.9, 118.4, 123.1, 125.5, 127.3, 131.1, 132.7, 132.8, 134.8, 162.4.

MS (ESI): *m*/*z* = 267 (100%) [M + H]$^+$.

Anal. Calcd for $C_{15}H_{14}N_4O$: C, 67.65; H, 5.30; N, 21.04. Found: C, 67.81; H, 5.43; N, 20.97.

2-Azido-*N*-(4-chlorophenyl)benzamide (6d)
Starting from 2-azidobenzoic acid (**5**) (500 mg, 3.07 mmol) and 4-chloroaniline (586 mg, 4.60 mmol), compound **6d** was isolated as a white solid (676 mg, 2.48 mmol, 81%).

Mp 150–152 °C; R_f = 0.51 (15% EtOAc–PE).

IR (KBr): 3310, 2125, 2090, 1650, 1286, 820, 756 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27–7.29 (m, 2 H, ArH), 7.34 (d, *J* = 8.4 Hz, 2 H, ArH), 7.57 (t, *J* = 7.6 Hz, 1 H, ArH), 7.65 (d, *J* = 8.8 Hz, 2 H, ArH), 8.34 (d, *J* = 7.6 Hz, 1 H, ArH), 9.34 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 118.5, 121.8, 124.8, 125.4, 129.0, 129.1, 129.5, 132.5, 133.0, 136.5, 136.9, 162.7.

MS (ESI): *m*/*z* = 273 (100%) [^{35}Cl, M + H]$^+$, 275 (32%) [^{37}Cl, M + H]$^+$.

Anal. Calcd for $C_{13}H_9ClN_4O$: C, 57.26; H, 3.33; N, 20.55. Found: C, 57.33; H, 3.19; N, 20.68.

2-Azido-*N*-(4-methoxyphenyl)benzamide (6e)
Starting from 2-azidobenzoic acid (**5**) (500 mg, 3.07 mmol) and 4-methoxyaniline (566 mg, 4.60 mmol), compound **6e** was isolated as a gray solid (658 mg, 2.45 mmol, 80%).

Mp 130–132 °C; R_f = 0.50 (15% EtOAc–PE).

IR (KBr): 3343, 2140, 2104, 1637, 1248, 1029, 822 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, OCH_3), 6.90 (d, *J* = 8.8 Hz, 2 H, ArH), 7.23–7.28 (m, 2 H, ArH), 7.53 (t, *J* = 8.0 Hz, 1 H, ArH), 7.57 (d, *J* = 8.8 Hz, 2 H, ArH), 8.22 (d, *J* = 8.0 Hz, 1 H, ArH), 9.18 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.5, 114.2, 118.4, 122.3, 125.3, 125.4, 131.1, 132.5, 132.6, 136.8, 156.7, 162.4.

MS (ESI): *m*/*z* = 269 (100%) [M + H]$^+$.

Anal. Calcd for $C_{14}H_{12}N_4O_2$: C, 62.68; H, 4.51; N, 20.88. Found: C, 62.82; H, 4.54; N, 20.97.

***N*-(4-Acetylphenyl)-2-azidobenzamide (6f)**
Starting from 2-azidobenzoic acid (**5**) (500 mg, 3.07 mmol) and 1-(4-aminophenyl)ethanone (621 mg, 4.60 mmol), compound **6f** was isolated as a light yellow solid (773 mg, 2.76 mmol, 90%).

Mp 153–155 °C; R_f = 0.47 (15% EtOAc–PE).

IR (KBr): 3330, 2134, 2105, 1671, 1651, 1274, 754 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.61 (s, 3 H, $COCH_3$), 7.29 (d, *J* = 8.0 Hz, 1 H, ArH), 7.33 (t, *J* = 8.0 Hz, 1 H, ArH), 7.60 (t, *J* = 8.0 Hz, 1 H, ArH), 7.81 (d, *J* = 8.0 Hz, 2 H, ArH), 8.00 (d, *J* = 8.0 Hz, 2 H, ArH), 8.28 (d, *J* = 8.0 Hz, 1 H, ArH), 9.62 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.5, 118.5, 119.7, 124.6, 125.6, 129.8, 132.7, 133.1, 133.3, 137.0, 142.3, 162.8, 197.0.

MS (ESI): *m*/*z* = 281 (100%) [M + H]$^+$.

Anal. Calcd for $C_{15}H_{12}N_4O_2$: C, 64.28; H, 4.32; N, 19.99. Found: C, 64.41; H, 4.27; N, 20.09.

Methyl 4-(2-Azidobenzamido)benzoate (6g)
Starting from 2-azidobenzoic acid (**5**) (500 mg, 3.07 mmol) and methyl 4-aminobenzoate (695 mg, 4.60 mmol), compound **6g** was isolated as a white solid (799 mg, 2.70 mmol, 88%).

Mp 138–140 °C; R_f = 0.46 (15% EtOAc–PE).

IR (KBr): 3310, 2138, 1708, 1668, 1277, 751 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.92 (s, 3 H, $COOCH_3$), 7.28 (d, *J* = 8.0 Hz, 1 H, ArH), 7.32 (t, *J* = 8.0 Hz, 1 H, ArH), 7.59 (t, *J* = 8.0 Hz, 1 H, ArH), 7.78 (d, *J* = 8.4 Hz, 2 H, ArH), 8.06 (d, *J* = 8.4 Hz, 2 H, ArH), 8.26 (d, *J* = 8.0 Hz, 1 H, ArH), 9.57 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.0, 118.5, 119.6, 124.7, 125.6, 125.9, 130.9, 132.8, 133.2, 136.9, 142.1, 162.7, 166.6.

MS (ESI): *m*/*z* = 297 (100%) [M + H]$^+$.

Anal. Calcd for $C_{15}H_{12}N_4O_3$: C, 60.81; H, 4.08; N, 18.91. Found: C, 60.78; H, 4.01; N, 19.09.

5-Phenyl-4*H*-benzo[*f*][1,2,3]triazolo[1,5-*a*][1,4]diazepin-6(5*H*)-one (8a); Typical Procedure
Benzamide **6a** (100 mg, 0.42 mmol) was dissolved in DMF (5 mL) in a sealable tube and then treated with alkyne **7a** (0.06 mL, 0.63 mmol). K_2CO_3 (87 mg, 0.63 mmol) was added, the tube was stoppered, and the mixture was stirred at 70 °C for 5 h. After completion of the reaction (monitored by TLC), the mixture was allowed to cool and H_2O (10 mL) was added. The mixture was extracted with EtOAc (3 × 20 mL) and the combined organic layer washed with H_2O (4 × 10 mL), dried (Na_2SO_4), filtered and concentrated. The crude residue was purified by column chromatography over silica gel (PE–EtOAc, 4:1) to afford product **8a** as a white solid (103 mg, 0.373 mmol, 89%).

Mp 98–100 °C; R_f = 0.48 (30% EtOAc–PE).

IR (KBr): 1645, 1492, 1399, 757, 698 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.84 (s, 2 H, NCH_2), 7.21–7.46 (m, 5 H, ArH), 7.62 (t, *J* = 7.6 Hz, 1 H, ArH), 7.74–7.77 (m, 2 H, ArH, one singlet is overlapped), 8.06 (d, *J* = 8.0 Hz, 1 H, ArH), 8.11 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.3, 120.1, 122.6, 126.2, 127.1, 127.8, 128.8, 129.2, 130.7, 132.7, 133.2, 134.6, 143.5, 165.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{13}N_4O$: 277.1089; found 277.1101.

3-Methyl-5-phenyl-4*H*-benzo[*f*][1,2,3]triazolo[1,5-*a*][1,4]diazepin-6(5*H*)-one (8b)
Starting from compound **6a** (100 mg, 0.42 mmol) and alkyne **7b** (0.07 mL, 0.63 mmol), compound **8b** was isolated as a white solid (100 mg, 0.34 mmol, 82%).

Mp 100–102 °C; R_f = 0.50 (30% EtOAc–PE).

IR (KBr): 1642, 1491, 1407, 755 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 4.75 (s, 2 H, NCH_2), 7.23–7.25 (m, 2 H, ArH), 7.35 (t, *J* = 7.2 Hz, 1 H, ArH), 7.45 (t, *J* = 7.2 Hz, 2 H, ArH), 7.59 (t, *J* = 7.6 Hz, 1 H, ArH), 7.73 (t, *J* = 7.6 Hz, 1 H, ArH), 8.04 (d, *J* = 8.4 Hz, 1 H, ArH), 8.15 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.1, 43.1, 122.4, 126.2, 127.2, 127.8, 129.0, 129.6, 131.6, 132.6, 133.1, 133.2, 139.2, 142.7, 166.1.

MS (ESI): *m*/*z* = 291 (100%) $[M + H]^+$.

Anal. Calcd for $C_{17}H_{14}N_4O$: C, 70.33; H, 4.86; N, 19.30. Found: C, 70.45; H, 4.92; N, 19.41.

5-*p*-Tolyl-4*H*-benzo[*f*][1,2,3]triazolo[1,5-*a*][1,4]diazepin-6(5*H*)-one (8c)
Starting from compound **6b** (100 mg, 0.397 mmol) and alkyne **7a** (0.06 mL, 0.595 mmol), compound **8c** was isolated as a white solid (99 mg, 0.341 mmol, 86%).

Mp 162–164 °C; R_f = 0.51 (30% EtOAc–PE).

IR (KBr): 1659, 1398, 1332, 759 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 4.82 (s, 2 H, NCH_2), 7.13 (d, *J* = 7.6 Hz, 2 H, ArH), 7.24 (d, *J* = 8.0 Hz, 2 H, ArH), 7.62 (t, *J* = 7.6 Hz, 1 H, ArH), 7.74 (s, 1 H, ArH), 7.76 (d, *J* = 7.6 Hz, 1 H, ArH), 8.06 (d, *J* = 8.0 Hz, 1 H, ArH), 8.16 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.1, 43.4, 122.6, 126.0, 127.7, 129.2, 130.2, 130.6, 132.7, 132.8, 133.1, 134.9, 137.9, 140.1, 166.0.

MS (ESI): *m*/*z* = 291 (100%) $[M + H]^+$.

Anal. Calcd for $C_{17}H_{14}N_4O$: C, 70.33; H, 4.86; N, 19.30. Found: C, 70.49; H, 4.94; N, 19.27.

5-(2,4-Dimethylphenyl)-4*H*-benzo[*f*][1,2,3]triazolo[1,5-*a*][1,4]diazepin-6(5*H*)-one (8d)
Starting from compound **6c** (100 mg, 0.376 mmol) and alkyne **7a** (0.06 mL, 0.564 mmol), compound **8d** was isolated as a white solid (95 mg, 0.31 mmol, 83%).

Mp 130–132 °C; R_f = 0.48 (30% EtOAc–PE).

IR (KBr): 1660, 1489, 1396, 1333, 757 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.04 (s, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 4.75 (s, 2 H, NCH_2), 6.98 (s, 1 H, ArH), 7.12 (d, *J* = 8.4 Hz, 2 H, ArH), 7.691 (td, *J* = 8.0, 1.2 Hz, 1 H, ArH), 7.694 (s, 1 H, ArH), 7.78 (td, *J* = 8.0, 1.2 Hz, 1 H, ArH), 8.06 (d, *J* = 8.2 Hz, 1 H, ArH), 8.17 (d, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9, 21.1, 43.2, 122.7, 126.5, 127.3, 128.2, 129.2, 130.6, 132.0, 132.6, 133.2, 134.9, 138.9, 139.5, 165.6.

MS (ESI): *m*/*z* = 305 (100%) $[M + H]^+$.

Anal. Calcd for $C_{18}H_{16}N_4O$: C, 71.04; H, 5.30; N, 18.41. Found: C, 71.22; H, 5.38; N, 18.52.

5-(4-Chlorophenyl)-4*H*-benzo[*f*][1,2,3]triazolo[1,5-*a*][1,4]diazepin-6(5*H*)-one (8e)
Starting from compound **6d** (100 mg, 0.367 mmol) and alkyne **7a** (0.05 mL, 0.551 mmol), compound **8e** was isolated as a white solid (107 mg, 0.345 mmol, 94%).

Mp 94–96 °C; R_f = 0.49 (30% EtOAc–PE).

IR (KBr): 1647, 1492, 1408, 754 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.82 (s, 2 H, NCH_2), 7.20 (d, *J* = 8.8 Hz, 2 H, ArH), 7.40 (d, *J* = 8.2 Hz, 2 H, ArH), 7.61 (t, *J* = 8.0 Hz, 1 H, ArH), 7.75 (d, *J* = 7.6 Hz, 1 H, ArH), 7.79 (s, 1 H, ArH), 8.05 (d, *J* = 8.2 Hz, 1 H, ArH), 8.12 (d, *J* = 8.2 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.2, 122.7, 127.2, 127.6, 129.3, 129.8, 130.7, 132.7, 133.4, 133.5, 134.4, 140.9, 165.9.

MS (ESI): *m*/*z* = 311 (100%) $[^{35}Cl, M + H]^+$, 313 (32%) $[^{37}Cl, M + H]^+$.

Anal. Calcd for $C_{16}H_{11}ClN_4O$: C, 61.84; H, 3.57; N, 18.03. Found: C, 61.96; H, 3.66; N, 17.98.

5-(4-Methoxyphenyl)-4*H*-benzo[*f*][1,2,3]triazolo[1,5-*a*][1,4]diazepin-6(5*H*)-one (8f)
Starting from compound **6e** (100 mg, 0.373 mmol) and alkyne **7a** (0.05 mL, 0.560 mmol), compound **8f** was isolated as a white solid (103 mg, 0.336 mmol, 90%).

Mp 162–164 °C; R_f = 0.45 (30% EtOAc–PE).

IR (KBr): 1654, 1509, 1402, 1257, 756 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 3.83 (s, 3 H, OCH_3), 4.80 (s, 2 H, NCH_2), 6.94 (d, *J* = 9.2 Hz, 2 H, ArH), 7.15 (d, *J* = 9.2 Hz, 2 H, ArH), 7.63 (t, *J* = 8.8 Hz, 1 H, ArH), 7.73–7.79 (m, 2 H, ArH one singlet is overlapped), 8.06 (d, *J* = 8.8 Hz, 1 H, ArH), 8.17 (d, *J* = 8.8 Hz, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 43.6, 55.6, 114.8, 122.6, 127.4, 129.2, 130.6, 132.6, 132.7, 133.1, 134.7, 135.4, 140.1, 158.9, 166.2.

MS (ESI): *m*/*z* = 307 (100%) $[M + H]^+$.

Anal. Calcd for $C_{17}H_{14}N_4O_2$: C, 66.66; H, 4.61; N, 18.29. Found: C, 66.81; H, 4.75; N, 18.32.

5-(4-Acetylphenyl)-4*H*-benzo[*f*][1,2,3]triazolo[1,5-*a*][1,4]diazepin-6(5*H*)-one (8g)
Starting from compound **6f** (100 mg, 0.357 mmol) and alkyne **7a** (0.05 mL, 0.535 mmol), compound **8g** was isolated as a white solid (108 mg, 0.339 mmol, 95%).

Mp 178–180 °C; R_f = 0.46 (30% EtOAc–PE).

IR (KBr): 1686, 1666, 1600, 1380, 1270, 752 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.62 (s, 3 H, $COCH_3$), 4.90 (s, 2 H, NCH_2, ArH), 7.41 (d, *J* = 8.2 Hz, 2 H, ArH), 7.64 (t, *J* = 8.0 Hz, 1 H, ArH), 7.77 (s, 1 H, ArH), 7.79 (d, *J* = 7.6 Hz, 1 H, ArH), 8.03 (dd, *J* = 8.7, 0.8 Hz, 2 H, ArH), 8.07 (d, *J* = 8.4 Hz, 1 H, ArH), 8.18 (dd, *J* = 8.4, 0.8 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.7, 43.0, 122.7, 126.0, 126.8, 129.3, 129.7, 130.8, 132.6, 132.7, 133.5, 134.2, 136.0, 146.3, 165.8, 196.9.

MS (ESI): *m*/*z* = 319 (100%) $[M + H]^+$.

Anal. Calcd for $C_{18}H_{14}N_4O_2$: C, 67.91; H, 4.43; N, 17.60. Found: C, 68.01; H, 4.52; N, 17.67.

Methyl 4-{6-Oxo-4*H*-benzo[*f*][1,2,3]triazolo[1,5-*a*][1,4]diazepin-5(6*H*)-yl}benzoate (8h)
Starting from compound **6g** (100 mg, 0.337 mmol) and alkyne **7a** (0.05 mL, 0.506 mmol), compound **8h** was isolated as a white solid (103 mg, 0.308 mmol, 91%).

Mp 122–124 °C; R_f = 0.45 (30% EtOAc–PE).

IR (KBr): 1719, 1647, 1604, 1385, 1284, 754 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.94 (s, 3 H, $COOCH_3$), 4.89 (s, 2 H, NCH_2), 7.38 (dd, *J* = 8.4, 1.6 Hz, 2 H, ArH), 7.64 (t, *J* = 7.6 Hz, 1 H, ArH), 7.79 (td, *J* = 7.6, 1.2 Hz, 2 H, ArH), 8.08–8.18 (m, 4 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.1, 52.4, 122.8, 125.9, 127.1, 129.3, 129.4, 130.8, 131.0, 132.7, 132.8, 133.7, 134.2, 146.2, 165.8, 166.1.

MS (ESI): m/z = 335 (100%) $[M + H]^+$.

Anal. Calcd for $C_{18}H_{14}N_4O_3$: C, 64.66; H, 4.22; N, 16.76. Found: C, 64.54; H, 4.17; N, 16.88.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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