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Efficient Solid-Phase Synthesis of Highly Functionalized 1,4-Benzodiazepin-5-one Derivatives and Related Compounds by Intramolecular Aza–Wittig Reactions**

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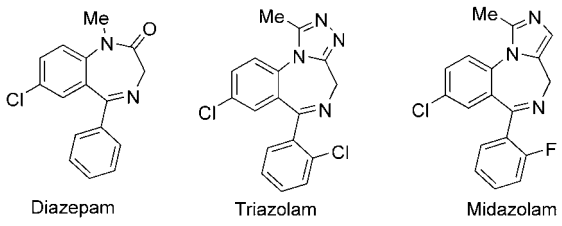
Abstract: Due to their widespread biological activities and favorable pharmacokinetic properties, benzodiazepines were among the first classes of small molecules to be synthesized on solid supports. Since then, there have been numerous reports on the synthesis of similar skeletons. We have employed the T1 triazene linker to yield 1,4-benzodiazepin-5-one. Starting from various substituted triazene resins, cleavage in the presence of an azide donor, such as trimethylsilylazide, gave rise to aryl azides. Intramolecular aza–Wittig reactions produced the appropriately functionalized *N*-heterocycles. By using this route, the natural product deoxyvasicinone and related compounds were prepared.

Keywords: aza–Wittig reaction · benzodiazepines · heterocycles · solid-phase synthesis · traceless linker

Introduction

The discovery of new drugs often begins with the modification of natural products[1] and commonly known privileged structures.[2] One example of this is the modification of the azepine class of drugs. This scaffold is a prototype of a privileged structure and is able to provide ligands for diverse receptors, such as cholecystokinin, gastrin, and central benzodiazepine receptors.[3] Diazepam, triazolam, and midazolam, which contain the benzodiazepine moiety, are well-known anxiolytic,[4] sedative,[5] and anticonvulsant drugs .[6] Benzodiazepines represent an important class of molecules with a broad range of biological activities. Many different types of benzodiazepinones have been synthesized and their pharmacology has been extensively published.[7–9] In addition, the 1,4-benzodiazepin-2,5-dione core is found in a number of natural products.[10,11]



Due to their widespread biological activities and favorable pharmacokinetical properties,[12] benzodiazepines were among the first classes of small molecules to be synthesized on solid supports.[13–15] Since then, there have been numerous reports of synthesis by using similar skeletons. The initial efforts to prepare libraries of this type focused on 1,4-benzodiazepin-2-ones and 1,4-benzodiazepin-2,5-diones;[16] however, there are also examples for the solid-supported synthesis of 2,3-benzodiazepin-4-ones,[17] 1,4-benzodiazepin-2,3-diones,[18] and pyrrolo[2,1-*c*][1,4]benzodiazepines.[19,20]

Substantial progress has been made in the field of heterocyclic synthesis by use of the aza–Wittig methodology. This has been utilized for the synthesis of five-, six-, and seven-membered azaheterocycles. Several successful examples of natural product synthesis, in which this cyclization reaction was the key step, have been published.[21,22]

The use of commercially available polymer-bound triphenylphosphine for Wittig reactions enables the principles of solid-phase synthesis to be combined with the application of polymer-supported reagents.[23–26] The byproduct triphenylphosphine oxide, derived from Wittig reactions in the solution phase, is often difficult to separate from the end-product. Following the use of a polymer-supported Wittig reagent, the triarylphosphine oxide remains attached to the

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[**] The IUPAC Chemset notation is used throughout this paper.

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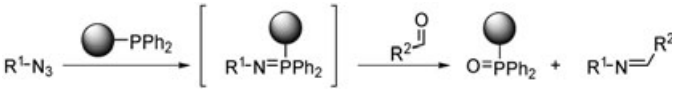
resin, and can be separated only by filtration. After reduction, the triarylphosphine oxide is recycled with trichlorosilane to give the phosphine (Scheme 1).[27] A triphenylphosphine reagent linked to a linear polystyrene has also been synthesized for this purpose.[28]



Scheme 1. Aza–Wittig reaction employing polymer-supported triphenylphosphine.

In this paper, we employed the methodology described above to obtain 1,4-benzodiazepin-5-one derivatives by solid-phase methods, the solution synthesis of which was reported by Eguchi and co-workers[29] In addition, the extension to deoxyvasicinone, one of the secondary metabolites identified in *Isatis tinctoria*, is demonstrated.[30]

Results and Discussion

We chose to focus on the 1,4-benzodiazepin-5-one structure as our first target, because a majority of the biologically active benzodiazepines identified to date fall within this subclass. Recently, we successfully completed a benzotriazinone synthesis by using polymer-bound triazenes that were coupled with different amino acids and amines.[31,32] By using this process, *o*-azidobenzoylamides were prepared by a post-cleavage modification of polymer-bound triazenes.

Triazene carboxylate resins **3**{1–7} were prepared on a multigram scale by diazotation of the anthranilic acids **1**{1–7} (Figure 1) with isoamyl nitrite, and a subsequent coupling to the benzylamine resin **2** (Scheme 2).

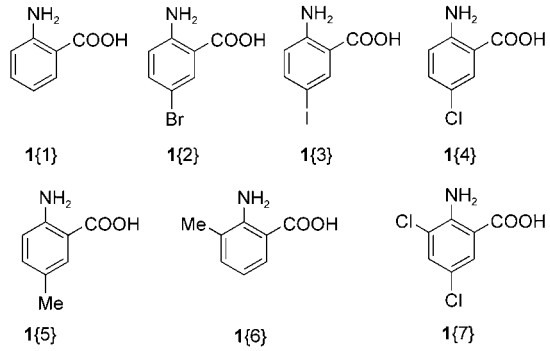
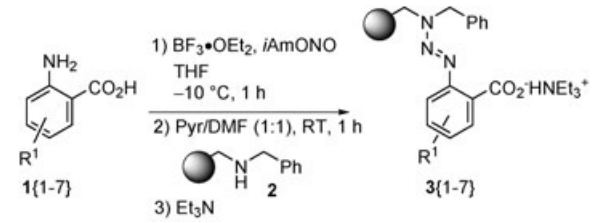
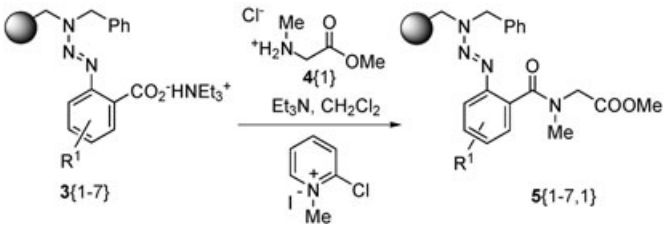


Figure 1. Anthranilic acids **1** used for library production.

The triazene carboxylate resins **3**{1–7} were then coupled with the methyl ester hydrochloride of sarcosine (**4**{1}) by using 2-chloro-1-methylpyridinium iodide as the coupling reagent[33,34] (Scheme 3). Triazene resin cleavage was achieved by applying 5% TFA in dichloromethane at room temperature to obtain the corresponding diazonium salts. These salts

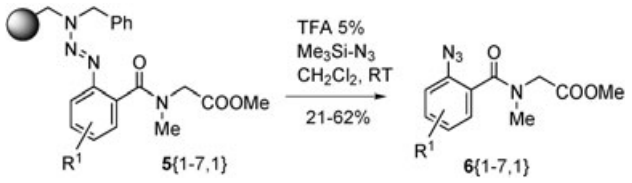


Scheme 2. Synthesis of the triazene resins **3**.



Scheme 3. Amide coupling on solid supports.

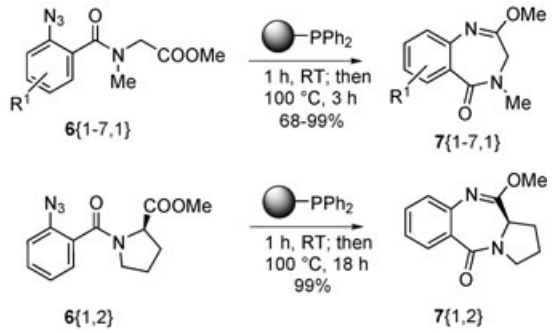
were reacted immediately with the azide transfer reagent trimethylsilyl azide[35] to achieve the aryl azides **6**{1–7,1} in moderate yields (21–62%) (Scheme 4). Azide **6**{1,2} was obtained after the reaction of **3**{1} with the methyl ester hydrochloride of L-proline **4**{2} using the same method.



Scheme 4. Cleavage and azide **6**{1–7,1} formation.

The 1,4-benzodiazepin-5-ones were obtained by cyclization of the azides **6**{1–7,1} and **6**{1,2} with polymer-supported triphenylphosphine, via the corresponding iminophosphoranes, at room temperature in toluene. They were heated at 100 °C in the same solvent without further purification for 3 or 18 h to produce the intramolecular aza–Wittig products **7**{1–7,1} and **7**{1,2}, respectively. The desired benzodiazepines were isolated in 68–99% yield and 68–94% purity without any further purification (Scheme 5). The use of polymer-supported triphenylphosphine provides a more simplified purification procedure, relative to the corresponding solution-phase method. The polymer-supported phosphine oxides were easily removed through filtration.

Secondary amines were synthesized to introduce a variety of products with the 1,4-benzodiazepin-5-one core (Figure 2). Following a reductive amination procedure using $NaBH_4$ as the reducing reagent (see Experimental Section),[36] the methyl esters of three amino acids were combined with four different aromatic aldehydes to give amines **4**{3–8}. With these unpurified six amines **4**{3–8}, the aryl azides **6**{1,3–8} were used for the synthesis of benzodiaze-



Scheme 5. Intramolecular aza–Wittig reaction.

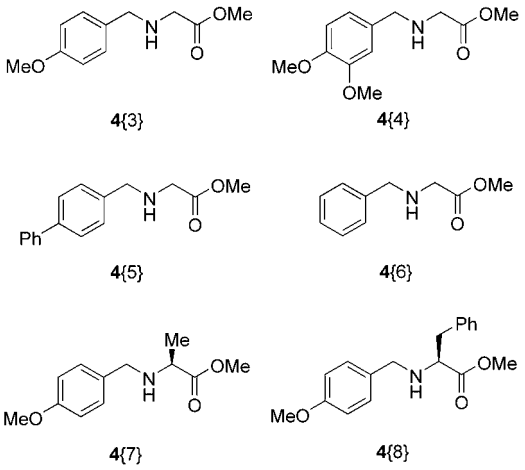
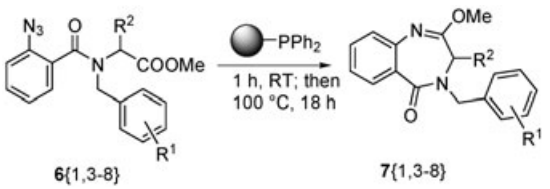


Figure 2. Secondary amines used for library synthesis.

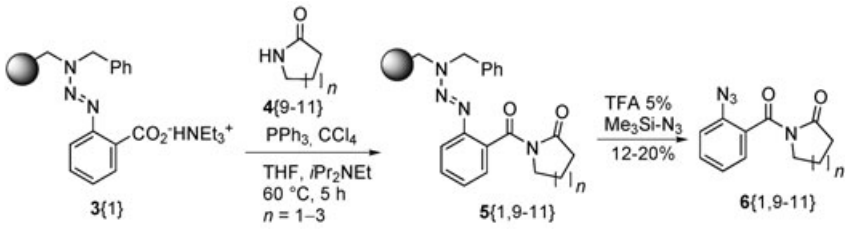
pines, according to the procedure described above. For compounds **7**{1,3–8}, the cyclization by an aza–Wittig reaction requires heating at 100 °C for 18 h (Scheme 6). A reduction of polystyryldiphenylphosphine oxide to polystyryldiphenylphosphine was attempted using trichlorosilane and *N*,*N*-dimethylaniline at 100 °C.[27] This phosphine was later reused for aza–Wittig syntheses without producing a lower yield. After reduction, the resin was washed thoroughly until trichlorosilane had been completely eliminated. In this way, the acid hydrolysis of 1,4-benzodiazepin-5-ones to 1,4-benzodiazepin-2,5-(1*H*)-dione derivatives was avoided.[37]

We also applied this methodology to the synthesis of deoxyvasicinone and a few related compounds. This alkaloid was isolated from *Isatis tinctoria*, and its synthesis by different routes has already been described.[38] Amongst these, a solution procedure published by Eguchi and co-workers employed a domino Staudinger/intramolecular aza–Wittig reaction as the key step.[39] Until now, no solid-phase approach has been reported. Here, we present the synthesis of deoxyvasicinone on solid supports by using the T1 triazene linker to obtain the corresponding azides, and the subsequent solid-phase, intramolecular aza–Wittig reaction.

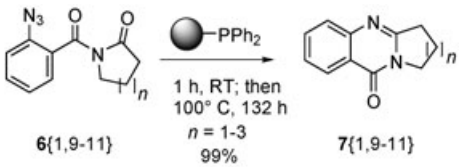


Scheme 6. Intramolecular aza–Wittig reaction.

Amides are less nucleophilic than amines. Therefore, the Mukayama reagent 2-chloro-1-methylpyridinium iodide was not efficient for the coupling of carboxylates to amides. Moreover, the sensitivity of the triazene moiety to traces of acid prevented the conventional transformation of carboxylates into acid chlorides using sulfuryl chlorides, thionyl chorides, or phosphoryl chlorides, due to trace amounts of hydrogen chloride. The reagent combination of aryl phosphines/tetrachloromethane has been reported as an in situ preparation of acyl chlorides.[40] Thus, the treatment of the triazene carboxylate resin **3**{1} with triphenylphosphine and tetrachloromethane generated the acyl chlorides, which reacted in situ with the lactams **4**{9–11} to obtain amides **5**{1,9–11} (Scheme 7). The azides **6**{1,9–11} were then obtained in moderate yields (12–20 %) by cleavage of the corresponding triazene resins **5**{1,9–11} with TFA. Finally, deoxyvasicinone **7**{1,9} ($n=1$) and related heterocycles **7**{1,10} ($n=2$) and **7**{1,11} ($n=3$) were obtained by treatment with triphenylphosphine polystyrene at 100 °C for 132 h (Scheme 8).



Scheme 7. Synthesis of the azides **6**{1,9–11}.



Scheme 8. Synthesis of deoxyvasicinone (**7**{1,9}) and related heterocycles.

Conclusion

We have employed the T1 triazene linker[41] to yield aryl azides that subsequently reacted with triphenylphosphine polystyrene to give the appropriately functionalized *N*-heterocycles. It was proven that the solid-phase aza–Wittig reaction provides an effective method to create a variety of 1,4-benzodiazepin-5-one or quinazoline derivatives. The natural product deoxyvasicinone and related compounds were prepared using this method.

Experimental Section

General: ^{1}H NMR: Bruker DP 300 (300 MHz), Bruker DP 400 (400 MHz); $\delta = 7.19$ ppm for $CHCl_3$. Description of signals: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet, mc = centered multiplet, ca = complex area, dd = doublet of doublet, ddd = doublet of dd, dt = doublet of triplets, dq = doublet of quartets, tt = triplet of triplets. The spectra were analyzed according to first order. All coupling constants are absolute values. Abbreviations for signals: Ar-H = aromatic, Aliph-H = aliphatic. ^{13}C NMR: Bruker DP 300 (75 MHz), Bruker DP 400 (100 MHz); $\delta = 77.00$ ppm for deuterochloroform. IR (infrared spectroscopy): The resins were measured as KBr pellets by using a Bruker IFS88 instrument; ps = polystyrene. MS (mass spectroscopy): EI-HRMS (electronic ionization-high resolution mass spectroscopy) was performed by using Kratos MS 50 (70 eV) and Thermo Quest Finnegan MAT 95 XL (70 eV) instruments. GC (gas chromatography) analytical (achiral stationary-phase): Hewlett–Packard HP 5890 Serie II 12 m × 0.25 mm capillary column HP I (carrier gas N_2). TLC (thin layer chromatography): Silica gel-coated aluminium plates (Merck, silica gel 60, F_{254}). Detection under UV light at 254 nm. Elemental analysis: Elementar Vario EL analyzer at the Mikroanalytisches Labor des Instituts für Organische Chemie der Universität Bonn (Germany). Descriptions without nominated temperature were conducted at room temperature (RT). Solid materials (except resins) were powdered. Chemicals, solvents, reagents, and chemicals were purchased from Aldrich, Fluka, Janssen, and Merck. Merrifield resin (1–2 % cross-linked, 200–400 mesh) was obtained from CalBioChem-NovaBioChem with loading = 1.06 mmol g^{-1}. To obtain the molecular mass of the resin and to calculate the elemental analysis, the following calculation must be performed, in which molar $mass_{sub}$ is the molecular mass of the fragment being substituted (e.g., Cl in the case of Merrifield resin), and molar $mass_{add}$ is the molecular mass of the fragment being added (e.g., HN–CH_2Ph in case of resin **2**):

$$\text{molar mass}_{new} = \frac{1000}{\text{loading}_{old}} - (\text{molar mass}_{sub} - \text{molar mass}_{add})$$

All resins were washed sequentially by using a vacuum reservoir connected to a sintered glass frit. Cleavage was conducted using a glass pipette filled with glass wool. Evaporation of the solvent was achieved by using a rotary vaporizer and/or a high vacuum (ca. 0.1 mbar). All solvents were dried by usual methods and distilled under argon.

General washing procedure: Three times with (methanol, THF, pentane, dichloromethane), once with (methanol, DMF, pentane, THF), and twice with (pentane, dichloromethane, pentane).

General procedure for the synthesis of triazene resin T1 (3):[31] The anthranilic acid derivatives **1** (26.5 mmol, 5 equiv) were dissolved in THF (50 mL) and cooled to −10 °C. $BF_3{\cdot}Et_2O$ (13.2 mL, 53 mmol, 10 equiv) and isoamyl nitrite (7.5 mL, 53 mmol, 10 equiv) were added dropwise under stirring for 5–15 min. The reaction mixture was stirred at −10 °C for 1 h and then diluted with pyridine (25 mL) and DMF (25 mL). Benzylamine resin **2** (5.0 g, 4.5 mmol, 1 equiv) was added and the resulting mixture stirred at RT for 1 h. Resin **3** was filtered off, washed sequentially with pyridine/DMF (1:1), THF/NEt_3 (1:1), MeOH/NEt_3 (1:1), DMF, THF, CH_2Cl_2, methanol, and pentane, and then dried under high vacuum.

Triethylammonium 2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)benzoate 3{1}: IR (KBr): $\tilde{\nu} = 3600$ (w, br, ps), 3061 (s, ps), 3027 (s, ps), 2930 (s, ps), 2847 (s, ps), 1944 (m, ps), 1874 (m, ps), 1804 (m, ps), 1739 (s), 1600 (s, ps), 1493 (s, ps), 1451 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{93}H_{100}N_4O_2$: C 85.55, H 7.71, N 4.28; found: C 84.65, H 8.67, N 4.27; loading: 0.764 mmol g^{-1}.[42]

Triethylammonium 2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)-5-bromobenzoate 3{2}: IR (KBr): $\tilde{\nu} = 3647$ (w, br, ps), 3027 (s, ps), 2912 (s, ps), 2870 (s, ps), 1943 (m, ps), 1871 (m, ps), 1803 (m, ps), 1739 (s), 1601 (s, ps), 1493 (s, ps), 1451 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{103}H_{109}N_4O_2Br$: C 81.75, H 7.25, N 3.66; found: C 83.40, H 7.28, N 2.86; loading: 0.629 mmol g^{-1}.

Triethylammonium 2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)-5-iodobenzoate 3{3}: IR (KBr): $\tilde{\nu} = 3464$ (w, br, ps), 3060 (s, ps), 3026 (s, ps), 2913 (s, ps), 2846 (s, ps), 1944 (m, ps), 1874 (m, ps), 1804 (m, ps), 1743 (s), 1601 (s, ps), 1493 (s, ps), 1451 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{103}H_{109}N_4O_2I$: C 79.31, H 7.03, N 3.55; found: C 81.77, H 7.19, N 2.70; loading: 0.611 mmol g^{-1}.

Triethylammonium 2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)-5-chlorobenzoate 3{4}: IR (KBr): $\tilde{\nu} = 3456$ (w, br, ps), 3026 (s, ps), 2923 (s, ps), 2870 (s, ps), 1943 (m, ps), 1872 (m, ps), 1803 (m, ps), 1741 (s), 1601 (s, ps), 1493 (s, ps), 1452 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{95}H_{101}N_4O_2Cl$: C 83.52, H 7.45, N 4.09; found: C 85.78, H 7.42, N 2.64; loading: 0.555 mmol g^{-1}.

Triethylammonium 2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)-5-methylbenzoate 3{5}: IR (KBr): $\tilde{\nu} = 3465$ (w, br, ps), 3026 (s, ps), 2916 (s, ps), 2850 (s, ps), 1943 (m, ps), 1872 (m, ps), 1803 (m, ps), 1737 (s), 1601 (s, ps), 1493 (s, ps), 1452 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{96}H_{104}N_4O_2$: C 85.74, H 7.71, N 4.15; found: C 87.70, H 7.59, N 2.33; loading: 0.460 mmol g^{-1}.

Triethylammonium 2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)-3-methylbenzoate 3{6}: IR (KBr): $\tilde{\nu} = 3449$ (w, br, ps), 3026 (s, ps), 2924 (s, ps), 2850 (s, ps), 1943 (m, ps), 1871 (m, ps), 1803 (m, ps), 1736 (s), 1602 (s, ps), 1493 (s, ps), 1451 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{107}H_{115}N_4O_2$: C 86.32, H 7.78, N 3.75; found: C 87.71, H 7.42, N 2.02; loading: 0.390 mmol g^{-1}.

Triethylammonium 2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)-3,5-dichlorobenzoate 3{7}: IR (KBr): $\tilde{\nu} = 3450$ (w, br, ps), 3025 (s, ps), 2914 (s, ps), 2850 (s, ps), 1944 (m, ps), 1871 (m, ps), 1802 (m, ps), 1736 (s), 1601 (s, ps), 1493 (s, ps), 1450 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{106}H_{111}N_4O_2Cl_2$: C 82.48, H 7.24, N 3.62; found: C 83.62, H 6.85, N 2.87; loading: 0.631 mmol g^{-1}.

General procedure for amine coupling (5{1–7,1} and 5{1,2}): Resin **3**{1–7} (1 equiv) and 2-chloro-1-methylpyridinium iodide (2 equiv) were suspended in CH_2Cl_2 (80 mL), and then 20 equiv of NEt_3 were added. The corresponding amine **4**{1–2} (3 equiv) was added after 15 min. The resulting mixture was stirred overnight at RT. The resin **5** was filtered off, washed sequentially with THF, Et_2O, MeOH, DMF, THF, CH_2Cl_2, methanol, and pentane, and then dried under high vacuum.

Methyl ester of (2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)benzoylaminomethyl)acetic acid 5{1,1}: IR (KBr): $\tilde{\nu} = 3647$ (w, br, ps), 3467 (s, ps), 3025 (s, ps), 2934 (s, ps), 2800 (s, ps), 1944 (m, ps), 1872 (m, ps), 1804 (m, ps), 1753 (s), 1650 (s), 1601 (s, ps), 1493 (s, ps), 1453 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{115}H_{116}N_4O_3$: C 86.25, H 7.30, N 3.74; found: C 85.49, H 7.71, N 2.62; loading: 0.537 mmol g^{-1}.

Methyl ester of (2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)-5-bromobenzoylaminomethyl)acetic acid 5{2,1}: IR (KBr): $\tilde{\nu} = 3647$ (w, br, ps), 3479 (s, ps), 3024 (s, ps), 2921 (s, ps), 2790 (s, ps), 1944 (m, ps), 1874 (m, ps), 1804 (m, ps), 1753 (s), 1654 (s), 1601 (s, ps), 1492 (s, ps), 1451 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{137}H_{137}N_4O_3Br$: C 83.65, H 7.02, N 2.84; found: C 82.48, H 7.03, N 3.35; loading: 0.772 mmol g^{-1}.

Methyl ester of (2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)-5-iodobenzoylaminomethyl)acetic acid 5{3,1}: IR (KBr): $\tilde{\nu} = 3646$ (w, br, ps), 3465 (s, ps), 3026 (s, ps), 2923 (s, ps), 2849 (s, ps), 1944 (m, ps), 1873 (m, ps), 1803 (m, ps), 1754 (s), 1650 (s), 1602 (s, ps), 1493 (s, ps), 1451 cm^{-1} (s,

ps); elemental analysis calcd (%) for $C_{140}H_{140}N_4O_3I$: C 81.94, H 6.87, N 2.71; found: C 80.70, H 7.29, N 3.17; loading: 0.744 mmol g^{-1}.

Methyl ester of (2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)-5-chlorobenzoylaminomethyl)acetic acid 5{4,1}: IR (KBr): $\tilde{\nu}$ = 3646 (w, br, ps), 3026 (s, ps), 2924 (s, ps), 2800 (s, ps), 1944 (m, ps), 1873 (m, ps), 1804 (m, ps), 1754 (s), 1657 (s), 1601 (s, ps), 1493 (s, ps), 1451 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{153}H_{153}N_4O_3Cl$: C 86.24, H 7.23, N 2.61; found: C 84.23, H 7.22, N 3.15; loading: 0.691 mmol g^{-1}.

Methyl ester of (2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)-5-methylbenzoylaminomethyl)acetic acid 5{5,1}: IR (KBr): $\tilde{\nu}$ = 3650 (w, br, ps), 3465 (s, ps), 3024 (s, ps), 2923 (s, ps), 2850 (s, ps), 1944 (m, ps), 1873 (m, ps), 1803 (m, ps), 1754 (s), 1650 (s), 1601 (s, ps), 1493 (s, ps), 1451 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{183}H_{185}N_4O_3$: C 88.33, H 7.49, N 2.24; found: C 87.70, H 7.59, N 2.33; loading: 0.460 mmol g^{-1}.

Methyl ester of (2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)-3-methylbenzoylaminomethyl)acetic acid 5{6,1}: IR (KBr): $\tilde{\nu}$ = 3648 (w, br, ps), 3444 (s, ps), 3029 (s, ps), 2847 (s, ps), 1944 (m, ps), 1872 (m, ps), 1804 (m, ps), 1755 (s), 1651 (s), 1602 (s, ps), 1495 (s, ps), 1455 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{213}H_{215}N_4O_3$: C 88.86, H 7.52, N 1.94; found: C 87.15, H 7.92, N 2.45; loading: 0.505 mmol g^{-1}.

Methyl ester of (2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)-3,5-dichlorobenzoylaminomethyl)-acetic acid 5{7,1}: IR (KBr): $\tilde{\nu}$ = 3646 (w, br, ps), 3027 (s, ps), 2914 (s, ps), 2850 (s, ps), 1944 (m, ps), 1873 (m, ps), 1804 (m, ps), 1755 (s), 1658 (s), 1602 (s, ps), 1494 (s, ps), 1452 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{137}H_{136}N_4O_3\ Cl_2$: C 84.06, H 7.00, N 2.86; found: C 81.64, H 7.43, N 3.13; loading: 0.700 mmol g^{-1}.

(2-(3-Benzyl-3-polystyrylmethyl-1-triazenyl)benzoyl-L-proline methyl ester 5{1,2}: IR (KBr): $\tilde{\nu}$ = 3647 (w, br, ps), 3464 (s, ps), 3026 (s, ps), 2913 (s, ps), 2847 (s, ps), 1944 (m, ps), 1872 (m, ps), 1803 (m, ps), 1748 (s), 1644 (s), 1601 (s, ps), 1493 (s, ps), 1452 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{156}H_{157}N_4O_3$: C 87.74, H 7.41, N 2.61; found: C 86.41, H 8.13, N 2.67; loading: 0.551 mmol g^{-1}.

General procedure for the generation of azides (6{1–7,1} and 6{1,2}): The corresponding resin **5** was suspended in 5% TFA/CH_2Cl_2 at RT. After 5–10 min, the mixture was filtered and trimethylsilylazide was added. The solvents and the remnants of TFA and trimethylsilylazide were removed by evaporation. The residue was purified by using flash chromatography, eluting with a 3:1 cyclohexane/AcOEt system.

***N*-(2-Azidobenzoyl)-*N*-methylglycine methyl ester 6{1,1}**: R_f: 0.2 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.84 (s, 2.0H; *syn*-NCH_3), 3.08 (s, 1.0H; *anti*-NCH_3), 3.63 (s, 1.0H; *anti*-$COOCH_3$), 3.72 (s, 2.0H; *syn*-$COOCH_3$), 3.80 (m, 0.7H; *anti*-NCH_2), 4.23 (brs, 1.3H; *syn*-NCH_2), 7.50–7.12 ppm (m, 4Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.0 (*anti*-NCH_3), 37.5 (*syn*-NCH_3), 48.5 (*syn*-NCH_2), 52.2 (*syn*-OCH_3), 52.2 (*anti*-OCH_3), 52.4 (*anti*-NCH_2), 118.5, 125.1, 128.3, 130.6 (Ar-C), 127.7 (*anti*-C-2), 127.9 (*syn*-C-2), 136.3 (*anti*-C-1), 136.5 (*syn*-C-1), 169.1 (*anti*-$COOCH_3$), 169.2 ppm (*syn*-$COOCH_3$); EI-HRMS: *m*/*z* calcd for $C_{11}H_{12}N_4O_3$: 248.0909; found: 248.0915; MS (EI): *m*/*z* (%): 248 (12) [M^+], 147 (100); yield: 32%.

***N*-(2-Azido-5-bromobenzoyl)-*N*-methylglycine methyl ester 6{2,1}**: R_f: 0.2 (Cyclohexane/AcOEt 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.85 (s, 2.0H; *syn*-NCH_3), 3.06 (s, 1.0H; *anti*-NCH_3), 3.66 (s, 1.0H; *anti*-$COOCH_3$), 3.72 (s, 2.0H; *syn*-$COOCH_3$), 3.80 (m, 0.7H; *anti*-NCH_2), 4.20 (brs, 1.3H; *syn*-NCH_2), 6.96–7.48 ppm (m, 3Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.1 (*anti*-NCH_3), 37.0 (*syn*-NCH_3), 48.5 (*syn*-NCH_2), 52.2 (*syn*-OCH_3), 52.3 (*anti*-NCH_2), 52.4 (*anti*-OCH_3), 117.9 (*syn*-C-5), 118.0 (*anti*-C-5) 120.1, 131.1, 133.5, (Ar-C), 129.3 (*anti*-C-2), 129.5 (*syn*-C-2), 135.5 (*anti*-C-1), 135.7 (*syn*-C-1), 167.1 (*anti*-CON), 167.4 (*syn*-CON), 168.9 (*anti*-$COOCH_3$), 169.0 ppm (*syn*-$COOCH_3$); EI-HRMS: *m*/*z* calcd for $C_{11}H_{11}N_4O_3Br$: 326.0015; found: 326.0016; MS (EI): *m*/*z* (%): 326/328 (8) [M^+], 224/226 (100); yield: 46%.

***N*-(2-Azido-5-iodobenzoyl)-*N*-methylglycine methyl ester 6{3,1}**: R_f: 0.3 (Cyclohexane/AcOEt 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.85 (s, 2.0H; *syn*-NCH_3), 3.07 (s, 1.0H; *anti*-NCH_3), 3.67 (s, 1.0H; *anti*-$COOCH_3$), 3.72 (s, 2.0H; *syn*-$COOCH_3$), 3.80 (m, 0.7H; *anti*-NCH_2), 4.20 (brs, 1.3H; *syn*-NCH_2), 6.85 (d, J(H3,H4) = 8.3 Hz, 0.3H; *anti*-H-3), 6.88 (d, J(H3,H4) = 8.3 Hz, 0.7H; *syn*-H-3), 7.50 (d, J(H6,H4) = 2.0 Hz, 0.3H; *anti*-H-6), 7.56 (d, J(H6,H4) = 2.0 Hz, 0.7H; *syn*-H-6), 7.63 (dd, 0.3H; *anti*-H-4), 7.65 ppm (dd, 0.7H; *syn*-H-4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.1 (*anti*-NCH_3), 37.5 (*syn*-NCH_3), 48.5 (*syn*-NCH_2), 52.3 (*syn*-OCH_3), 52.4 (*anti*-NCH_2), 52.4 (*anti*-OCH_3), 88.2 (C-5), 120.4, 137.0, 139.4, (Ar-C), 129.6 (*anti*-C-2), 129.8 (*syn*-C-2), 136.3 (*anti*-C-1), 136.4 (*syn*-C-1), 167.0 (*anti*-CON), 167.3 (*syn*-CON), 169.0 (*anti*-$COOCH_3$), 169.0 ppm (*syn*-$COOCH_3$); EI-HRMS: *m*/*z* calcd for $C_{11}H_{11}N_4O_3I$: 373.9876; found: 373.9876; MS (EI): *m*/*z* (%): 374 (12) [M^+], 272 (100); yield: 62%.

***N*-(2-Azido-5-chlorobenzoyl)-*N*-methylglycine methyl ester 6{4,1}**: R_f: 0.2 (Cyclohexane/AcOEt 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.82 (s, 2.0H; *syn*-NCH_3), 3.06 (s, 1.0H; *anti*-NCH_3), 3.65 (s, 1.0H; *anti*-$COOCH_3$), 3.71 (s, 2.0H; *syn*-$COOCH_3$), 3.80 (m, 0.7H; *anti*-NCH_2), 4.21 (brs, 1.3H; *syn*-NCH_2), 7.03 (d, J(H3,H4) = 8.4 Hz, 0.3H; *anti*-H-3), 7.06 (d, J(H3,H4) = 8.4 Hz, 0.7H; *syn*-H-3), 7.18 (d, J(H6,H4) = 2.4 Hz, 0.3H; *anti*-H-6), 7.24 (d, J(H6,H4) = 2.4 Hz, 0.7H; *syn*-H-6), 7.30 (dd, 0.3H; *anti*-H-4), 7.32 ppm (dd, 0.7H; *syn*-H-4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.1 (*anti*-NCH_3), 37.4 (*syn*-NCH_3), 48.5 (*syn*-NCH_2), 52.2 (*syn*-OCH_3), 52.3 (*anti*-NCH_2), 52.4 (*anti*-OCH_3), 119.9, 128.3, 130.7 (Ar-C), 129.0 (*anti*-C-2), 129.2 (*syn*-C-2), 130.59 (*syn*-C-5), 130.61 (*anti*-C-5), 135.0 (*anti*-C-1), 135.1 (*syn*-C-1), 167.3 (*anti*-CON), 167.5 (*syn*-CON), 168.9 (*anti*-$COOCH_3$), 169.0 ppm (*syn*-$COOCH_3$); EI-HRMS: *m*/*z* calcd for $C_{11}H_{11}N_4O_3Cl$: 282.0520; found: 282.0527; MS (EI): *m*/*z* (%): 282/284 (12) [M^+], 180/182 (100); yield: 44%.

***N*-(2-Azido-5-methylbenzoyl)-*N*-methylglycine methyl ester 6{5,1}**: R_f: 0.1 (Cyclohexane/AcOEt 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.22 (s, 1.0H; *anti*-CH_3), 2.26 (s, 2.0H; *syn*-CH_3), 2.48 (s, 2.0H; *syn*-NCH_3), 3.07 (s, 1.0H; *anti*-NCH_3), 3.63 (s, 1.0H; *anti*-$COOCH_3$), 3.71 (s, 2.0H; *syn*-$COOCH_3$), 3.82 (m, 0.7H; *anti*-NCH_2), 4.22 (brs, 1.3H; *syn*-NCH_2), 6.97–7.17 ppm (m, 3Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6 (*syn*-CH_3), 20.6 (*anti*-CH_3), 33.9 (*anti*-NCH_3), 37.5 (*syn*-NCH_3), 48.4 (*syn*-NCH_2), 52.1 (*syn*-OCH_3), 52.2 (*anti*-OCH_3), 52.4 (*anti*-NCH_2), 118.3, 128.7, 131.2 (Ar-C), 127.5 (*anti*-C-2), 127.7 (*syn*-C-2), 133.5 (*anti*-C-5), 133.6 (*syn*-C-5), 135.1 (*syn*-C-1), 135.2 (*anti*-C-1), 169.0 (*anti*-CON), 169.2 (*syn*-CON), 169.2 (*anti*-$COOCH_3$), 169.3 ppm (*syn*-$COOCH_3$); EI-HRMS: *m*/*z* calcd for $C_{12}H_{14}N_4O_3$: 262.1066; found: 262.1067; MS (EI): *m*/*z* (%): 262 (12) [M^+], 161 (100); yield: 25%.

***N*-(2-Azido-3-methylbenzoyl)-*N*-methylglycine methyl ester 6{6,1}**: R_f: 0.3 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.25 (s, 1.0H; *anti*-CH_3), 2.28 (s, 2.0H; *syn*-CH_3), 2.89 (s, 2.0H; *syn*-NCH_3), 3.08 (s, 1.0H; *anti*-NCH_3), 3.65 (s, 1.0H; *anti*-$COOCH_3$), 3.72 (s, 2.0H; *syn*-$COOCH_3$), 3.88 (m, 0.7H; *anti*-NCH_2), 4.25 (brs, 1.3H; *syn*-NCH_2), 6.98–7.14 ppm (m, 3Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9 (*syn*-CH_3), 17.9 (*anti*-CH_3), 33.8 (*anti*-NCH_3), 37.7 (*syn*-NCH_3), 48.4 (*syn*-NCH_2), 52.2 (*syn*-OCH_3), 52.3 (*anti*-OCH_3), 52.6 (*anti*-NCH_2), 125.6, 125.9, 132.1 (Ar-C), 129.3 (*anti*-C-2), 129.8 (*syn*-C-2), 132.4 (*syn*-C-5), 132.4 (*anti*-C-5), 134.3 (*anti*-C-1), 134.4 (*syn*-C-1), 169.0 (*anti*-CON), 169.1 (*syn*-CON), 169.2 (*syn*-$COOCH_3$), 169.2 ppm (*anti*-$COOCH_3$); EI-HRMS: *m*/*z* calcd for $C_{12}H_{14}N_4O_3$: 262.1066; found: 262.1065; MS (EI): *m*/*z* (%): 262 (4), [M^+], 161 (100); yield: 21%.

***N*-(2-Azido-3,5-dichlorobenzoyl)-*N*-methylglycine methyl ester 6{7,1}**: R_f: 0.4 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.87 (s, 2.0H; *syn*-NCH_3), 3.07 (s, 1.0H; *anti*-NCH_3), 3.67 (s, 1.0H; *anti*-$COOCH_3$), 3.72 (s, 2.0H; *syn*-$COOCH_3$), 3.82 (m, 0.7H; *anti*-NCH_2), 4.20 (brs, 1.3H; *syn*-NCH_2), 7.08 (d, J = 2.4 Hz, 0.3H; *anti*-H-4), 7.15 (d, J = 2.4 Hz, 0.7H; *syn*-H-4), 7.32 (d, 0.3H; *anti*-H-6), 7.35 ppm (d, J = 2.4 Hz, 0.7H; *syn*-H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.0 (*anti*-NCH_3), 37.5 (*syn*-NCH_3), 48.5 (*syn*-NCH_2), 52.3 (*anti*-NCH_2), 52.5 (*anti*-OCH_3), 126.5, 131.1, 131.2, 131.5, 132.3 (Ar-C), 129.6 (*anti*-C-2), 129.7 (*syn*-C-2), 166.4 (*anti*-CON), 166.7 (*syn*-CON), 168.7 (*anti*-$COOCH_3$), 168.8 ppm (*syn*-$COOCH_3$); EI-HRMS: *m*/*z* calcd for $C_{11}H_{10}N_4O_3Cl_2$: 316.0130; found: 316.0129; MS (EI): *m*/*z* (%): 316/318 (4) [M^+], 215/217 (100); yield: 27%.

***N*-(2-Azidobenzoyl)-L-proline methyl ester 6{1,2}**: R_f: 0.1 (Cyclohexane/AcOEt 2:1); $[\alpha]^{20}$ = −84.66 ($CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.78–2.30 (m, 4H; CH_2CH_2), 3.21–3.34 (m, 2H; NCH_2), 3.44 (s, 0.75H; *anti*-$COOCH_3$), 3.72 (s, 2.25H; *syn*-$COOCH_3$), 4.12 (dd, J = 2.6, 8.2 Hz, 0.25H; *anti*-NCH), 4.61 (dd, J = 3.9, 8.2 Hz, 0.75H; *syn*-NCH), 7.03–

7.38 ppm (m, 4Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.9 (*anti*-CH_2), 24.7 (*syn*-CH_2), 29.5 (*syn*-CH_2), 31.2 (*anti*-CH_2), 46.3 (*anti*-NCH_2), 48.3 (*syn*-NCH_2), 52.1 (*anti*-OCH_3), 52.2 (*syn*-OCH_3), 58.4 (*syn*-NCH), 60.3 (*anti*-NCH), 118.5, 125.0, 128.2, 130.5 (Ar-C), 128.8 (*anti*-C-2), 129.1 (*syn*-C-2), 136.3 (C-1), 166.9 (*syn*-CON), 167.1 (*anti*-CON), 172.4 ppm ($COOCH_3$); EI-HRMS: *m/z* calcd for $C_{14}H_{15}N_3O_3$: 274.0676; found: 274.1068; MS (EI): *m/z* (%): 274 (8) [M^+], 187 (100); yield: 12%.

General procedure for the synthesis of 1,4-benzodiazepin-5-ones (7{1–7,1} and 7{1,2}): The triphenylphosphine polystyrene (4 equiv) was distended with dry toluene (8 mL) in a glass vial and was sealed under argon. A solution of the corresponding azide **6** (1 equiv) in dry toluene was injected into the suspension. The reaction mixture was shaken at RT for 1 h, and then heated at 100 °C for 3 and 18 h for **6**{1–7,1} and **6**{1,2}, respectively. After cooling, the resin was separated by filtration and washed with dichloromethane. The filtrate was concentrated until dry to give the benzodiazepines **7**{1–7,1} and **7**{1,2}.

3,4-Dihydro-2-methoxy-4-methyl-1,4-benzodiazepin-5(5*H*)-one 7{1,1}: R_f: 0.02 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.20 (s, 3H, NCH_3), 3.67 (s, 2H; CH_2), 3.84 (s, 3H; OCH_3), 6.90–7.87 ppm (m, 4Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.4 (NCH_3), 48.3 (CH_2), 54.4 (OCH_3), 120.5 (C-5a), 124.3, 126.0, 130.7, 131.5 (Ar-C), 144.7 (C-9a), 162.8 ($COCH_3$), 167.8 ppm (CO); MS (EI): *m/z* (%): 204 (8) [M^+], 190 (100); purity: 68% (by GC); yield: 68%.

3,4-Dihydro-2-methoxy-4-methyl-7-bromo-1,4-benzodiazepin-5(5*H*)-one 7{2,1}: R_f: 0.2 (Cyclohexane/AcOEt 4:3); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.14 (s, 3H; NCH_3), 3.67 (s, 2H; CH_2), 3.83 (s, 3H; OCH_3), 6.95 (d, *J*(H9,H8) = 8.4 Hz, 1H; H-9), 7.45 (dd, 1H; H-8), 7.98 ppm (d, *J*(H6,H8) = 2.5 Hz, 1H; H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.5 (NCH_3), 48.3 (CH_2), 54.6 (OCH_3), 117.4 (C-7), 128.0, 133.3, 134.5 (Ar-C), 129.0 (C-5a), 143.8 (C-9a), 163.0 ($COCH_3$), 166.5 ppm (CO); MS (EI): *m/z* (%): 282/284 (100) [M^+]; purity: 83% (by GC); yield: 99%.

3,4-Dihydro-2-methoxy-4-methyl-7-iodo-1,4-benzodiazepin-5(5*H*)-one 7{3,1}: R_f: 0.3 (Cyclohexane/AcOEt 4:3); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.14 (s, 3H; NCH_3), 3.66 (s, 2H; CH_2), 3.83 (s, 3H; OCH_3), 6.82 (d, *J*(H9,H8) = 8.4 Hz, 1H; H-9), 7.64 (dd, 1H; H-8), 8.16 ppm (d, *J*(H6,H8) = 2.0 Hz, 1H; H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.5 (NCH_3), 48.4 (CH_2), 54.6 (OCH_3), 88.1 (C-7), 128.1, 139.3, 140.3 (Ar-C), 129.3 (C-5a), 144.4 (C-9a), 163.1 ($COCH_3$), 166.3 ppm (CO); MS (EI): *m/z* (%): 330 (100) [M^+]; purity: 88% (by GC); yield: 93%.

3,4-Dihydro-2-methoxy-4-methyl-7-chloro-1,4-benzodiazepin-5(5*H*)-one 7{4,1}: R_f: 0.3 (Cyclohexane/AcOEt 4:3); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.14 (s, 3H; NCH_3), 3.67 (s, 2H; CH_2), 3.83 (s, 3H; OCH_3), 7.02 (d, *J*(H9,H8) = 8.4 Hz, 1H; H-9), 7.31 (dd, 1H; H-8), 7.83 ppm (d, *J*(H6,H8) = 2.4 Hz, 1H; H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.4 (NCH_3), 48.3 (CH_2), 54.6 (OCH_3), 127.7, 130.6, 131.6 (Ar-C), 128.7 (C-7), 129.8 (C-5a), 143.3 (C-9a), 163.0 ($COCH_3$), 166.6 ppm (CO); MS (EI): *m/z* (%): 238/240 (90) [M^+], 180/182 (100); purity: 83% (by GC); yield: 99%.

3,4-Dihydro-2-methoxy-4,7-dimethyl-1,4-benzodiazepin-5(5*H*)-one 7{5,1}: R_f: 0.2 (Cyclohexane/AcOEt 4:3); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.29 (s, 3H; CH_3), 3.14 (s, 3H; NCH_3), 3.66 (s, 2H; CH_2), 3.82 (s, 3H; OCH_3), 6.97 (d, *J*(H9,H8) = 8.0 Hz, 1H; H-9), 7.17 (dd, 1H; H-8), 7.66 ppm (d, *J*(H6,H8) = 1.7 Hz, 1H; H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7 (CH_3), 36.3 (NCH_3), 48.4 (CH_2), 54.3 (OCH_3), 126.0, 130.7, 132.5 (Ar-C), 127.1 (C-5a), 134.0 (C-7), 142.4 (C-9a), 162.5 ($COCH_3$), 168.0 ppm (CO); MS (EI): *m/z* (%): 218 (68) [M^+], 160 (100); purity: 72% (by GC); yield: 98%.

3,4-Dihydro-2-methoxy-4,9-methyl-1,4-benzodiazepin-5(5*H*)-one 7{6,1}: R_f: 0.04 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.26 (s, 3H; CH_3), 3.15 (s, 3H; NCH_3), 3.66 (s, 2H; CH_2), 3.85 (s, 3H; OCH_3), 7.02 (t, *J* = 7.5 Hz, 1H; H-7), 7.24 (d, 1H; H-8), 7.69 ppm (d, 1H; H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.4 (CH_3), 36.3 (NCH_3), 48.3 (CH_2), 54.2 (OCH_3), 124.0, 128.4, 132.6 (Ar-C), 127.5 (C-5a), 133.4 (C-7), 143.1 (C-9a), 161.2 ($COCH_3$), 168.2 ppm (CO); MS (EI): *m/z* (%): 218 (100) [M^+]; EI-HRMS: *m/z* calcd for $C_{12}H_{14}N_2O_2$: 218.1055; found: 218.1056; purity: 74% (by GC); yield: 93%.

3,4-Dihydro-2-methoxy-4-methyl-5,9-dichloro-1,4-benzodiazepin-5(5*H*)-one 7{7,1}: R_f: 0.1 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.15 (s, 3H; NCH_3), 3.69 (s, 2H; CH_2), 3.91 (s, 3H; OCH_3), 7.47 (d, *J* = 2.5 Hz, 1H; H-8), 7.75 ppm (d, 1H; H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.6 (NCH_3), 48.4 (CH_2), 55.0 (OCH_3), 128.8, 129.1, 129.6, 129.8, 131.9 (Ar-C), 140.4 (C-9a), 163.0 ($COCH_3$), 165.7 ppm (CO); EI-HRMS: *m/z* calcd for $C_{11}H_{10}N_2O_2Cl_2$: 272.0119; found: 272.0115; MS (EI): *m/z* (%): 272/274 (100), [M^+]; purity: 94% (by GC); yield: 99%.

11-Methoxy-1,2,3,11a-tetrahydro-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepin-5-one 7{1,2}: R_f: 0.1 (Cyclohexane/AcOEt 2:1); $[\alpha]^{20} = +524$ ($CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.93–1.97 (m, 4H; CH_2CH_2), 3.40–3.49 (m, 2H; NCH_2), 3.82 (s, 3H; OCH_3), 3.90–3.92 (m, 1H; NCH), 7.07–7.14 (m, 2Ar-H), 7.37 (t, *J* = 1.6, 7.1 Hz, 1H), 7.92 ppm (dd, *J* = 1.3, 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.9, 26.5 (CH_2CH_2), 46.8 (NCH_2), 54.4 (OCH_3), 54.4 (NCH), 124.1, 126.4, 130.2, 131.5 (Ar-C), 127.4 (C-5a), 144.1 (C-9a), 162.3 ($COCH_3$), 165.7 ppm (CO); EI-HRMS: *m/z* calcd for $C_{13}H_{14}N_2O_2$: 230.1055; found: 230.1057; MS (EI): *m/z* (%): 230 (88) [M^+], 145 (100); purity: 83% (by GC); yield: 99%.

General procedure for the reductive amination (4{3–8}): The methyl ester hydrochlorides of the amino acids (1.5 equiv) were dissolved in MeOH and cooled to 0 °C. Triethylamine (1.5 equiv) was added to this solution, then the reaction mixture was stirred for 10 min and allowed to warm up to room temperature. The aldehydes (1 equiv) were added and the reaction mixtures were stirred for 12 h at room temperature. The solutions were cooled to 0 °C and $NaBH_4$ (2 equiv) was added portionwise to the reaction mixtures over a period of 30 min. After stirring for 2 h at 0 °C and for 1 h at room temperature, the reaction mixtures were acidified with 10% aqueous $NaHSO_4$ and ether was added (25 mL). The phases were then separated. The organic phases were washed with 10% aqueous $NaHSO_4$ and the combined aqueous layers were carefully neutralized with solid sodium carbonate. The latter were extracted with ether (3 × 10 mL). The combined ether layers were dried over sodium sulfate and evaporated to achieve the amines **4**{3–8}.

Methyl ester of (4-methoxybenzylamino)acetic acid 4{3}: R_f: 0.1 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.97 (br s, 1H; N*H*), 3.35 (s, 2H; NCH_2COOMe), 3.64 (s, 3H; OCH_3), 3.70 (s, 2H; $PhCH_2N$), 3.71 (s, 3H; $COOCH_3$), 6.78 (d, *J* = 8.7 Hz, 2H; Ar-H), 7.17 ppm (d, 2H; Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 49.2 (NCH_2COOMe), 51.8 ($COOCH_3$), 52.3 ($PhCH_2N$), 55.2 (OCH_3), 113.9, 129.6, 130.5, 158.9 (Ar-C), 172.6 ppm ($COOCH_3$); EI-HRMS: *m/z* calcd for $C_{11}H_{15}NO_3$: 209.1052; found: 209.1047; MS (EI): *m/z* (%): 209 (4), [M^+], 121 (100); purity: 94% (by GC); yield: 85%.

Methyl ester of (3,4-dimethoxybenzylamino)acetic acid 4{4}: R_f: 0.1 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.77 (br s, 1H; N*H*), 3.34 (s, 2H; NCH_2COOMe), 3.66 (s, 3H; $COOCH_3$), 3.67 (s, 2H; $PhCH_2N$), 3.79 (s, 3H; OCH_3), 3.81 (s, 3H; OCH_3), 6.73–6.83 ppm (m, 3H; Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 49.8 (NCH_2COOMe), 51.7 ($COOCH_3$), 53.1 ($PhCH_2N$), 55.9 (OCH_3), 55.9 (OCH_3), 111.1, 111.5, 120.4, 132.0, 148.3, 149.1 (Ar-C), 172.9 ppm ($COOCH_3$); EI-HRMS: *m/z* calcd for $C_{12}H_{17}NO_4$: 239.1158; found: 239.1159; MS (EI): *m/z* (%): 239 (12) [M^+], 151 (100); purity: 93% (by GC); yield: 33%.

Methyl ester of (4-phenylbenzylamino)acetic acid 4{5}: R_f: 0.1 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.06 (br s, 1H; N*H*), 3.37 (s, 2H; NCH_2COOMe), 3.65 (s, 3H; $COOCH_3$), 3.76 (s, 2H; $PhCH_2N$), 7.22–7.51 ppm (m, 9H; Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 49.9 (NCH_2COOMe), 51.7 ($COOCH_3$), 52.9 ($PhCH_2N$), 127.0, 127.2, 128.7, 128.7, 138.5, 140.2, 140.9 (Ar-C), 172.8 ppm ($COOCH_3$); EI-HRMS: *m/z* calcd for $C_{16}H_{17}NO_2$: 255.1259; found: 255.1256; MS (EI): *m/z* (%): 255 (8) [M^+], 167 (100); purity: 97% (by GC); yield: 64%.

Methyl ester of benzylaminoacetic acid 4{6}: R_f: 0.2 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.34 (br s, 1H; N*H*), 3.35 (s, 2H; NCH_2COOMe), 3.65 (s, 3H; $COOCH_3$), 3.74 (s, 2H; $PhCH_2N$), 7.21–7.36 ppm (m, 5H; Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 49.8 (NCH_2COOMe), 51.7 ($COOCH_3$), 53.2 ($PhCH_2N$), 127.2, 128.3, 128.4, 139.2 (Ar-C), 172.7 ppm ($COOCH_3$); MS (EI): *m/z* (%): 179 (4) [M^+], 91 (100); EI-HRMS: *m/z* calcd for $C_{10}H_{13}NO_2$: 179.0946; found: 179.0946; purity: 53% (by GC), yield: 43%.

Methyl ester of 2-(4-methoxybenzylamino)propionic acid 4{7}: R_f: 0.3 (Cyclohexane/AcOEt 2:1); $[\alpha]^{20} = -2.68$ ($CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.23$ (d, $J = 7.1$ Hz, 3H; CH_3), 2.33 (br s, 1H; NH), 3.31 (c, 1H; CH), 3.64 (s, 3H; OCH_3), 3.64 (s, 2H; PhCH_2N), 3.70 (s, 3H; COOCH_3), 6.76 (d, $J = 8.7$ Hz, 2H; Ar-H), 7.16 ppm (d, 2H; Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 18.96$ (CH_3), 51.2 (PhCH_2N), 51.7 (COOCH_3), 55.2 (CH), 55.7 (OCH_3), 113.8, 129.5, 131.6, 158.8 (Ar-C), 176.0 ppm (COOCH_3); EI-HRMS: m/z calcd for $C_{12}H_{17}NO_3$: 223.12; found: 223.12; MS (EI): m/z (%): 223 (4) [M^+], 121 (100); purity: 97% (by GC); yield: 37%.

Methyl ester of 2-(4-methoxybenzylamino)-3-phenylpropionic acid 4{8}: R_f: 0.2 (Cyclohexane/AcOEt 2:1); $[\alpha]^{20} = -0.07$ ($CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.84$ (br s, 1H; NH), 2.88 (d, $J = 6.9$ Hz, 2H; CHCH_2Ph), 3.45 (t, 1H; CH), 3.52 (s, 3H; OCH_3), 3.52 (s, 2H; PhCH_2N), 3.65 (s, 3H; COOCH_3), 6.69–7.19 ppm (m, 9H; Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 39.5$ (CHCH_2Ph), 51.3 (PhCH_2N), 51.6 (COOCH_3), 61.8 (CH), 55.2 (OCH_3), 113.8, 126.7, 128.4, 129.2, 129.5, 131.1, 137.2, 158.8 (Ar-C), 174.6 ppm (COOCH_3); EI-HRMS: m/z calcd for $C_{18}H_{21}NO_3$: 299.1521; found: 299.1506; MS (EI): m/z (%): 299 (4) [M^+], 121 (100); purity: 98% (by GC); yield: 64%.

General procedure for the amine coupling (5{1,3–8}): Resin **3**{1} (1 equiv) and 2-chloro-1-methylpyridinium iodide (2 equiv) were suspended in 80 mL of CH_2Cl_2, after which NEt_3 (20 equiv) was added. The corresponding amine **4**{3–8} (3 equiv) was added after 15 min. The resulting mixture was stirred overnight at RT. The resin **5**{1,3–8} was filtered off, washed sequentially with THF, Et_2O, MeOH, DMF, THF, CH_2Cl_2, methanol, and pentane, and was dried under high vacuum.

Methyl ester of [(2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)benzoyl)(4-methoxybenzyl)amino]acetic acid 5{1,3}: IR (KBr): $\tilde{\nu} = 3647$ (w, br, ps), 3476 (s, ps), 3026 (s, ps), 2927 (s, ps), 2850 (s, ps), 1945 (m, ps), 1874 (m, ps), 1805 (m, ps), 1754 (s), 1650 (s), 1601 (s, ps), 1493 (s, ps), 1452 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{147}H_{147}N_4O_4$: C 86.83, H 7.28, N 2.74; found: C 84.71, H 6.98, N 3.31; loading: 0.774 mmol g^{-1}.

Methyl ester of [(2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)benzoyl)(3,4-dimethoxybenzyl)amino]acetic acid 5{1,4}: IR (KBr): $\tilde{\nu} = 3647$ (w, br, ps), 3479 (s, ps), 3026 (s, ps), 2927 (s, ps), 2850 (s, ps), 1945 (m, ps), 1873 (m, ps), 1803 (m, ps), 1751 (s), 1651 (s), 1601 (s, ps), 1493 (s, ps), 1454 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{148}H_{149}N_4O_5$: C 86.15, H 7.27, N 2.70; found: C 84.24, H 7.28, N 3.63; loading: 0.898 mmol g^{-1}.

Methyl ester of [(2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)benzoyl)(4-phenylbenzyl)amino]acetic acid 5{1,5}: IR (KBr): $\tilde{\nu} = 3645$ (w, br, ps), 3622 (s, ps), 3025 (s, ps), 2926 (s, ps), 2850 (s, ps), 1944 (m, ps), 1872 (m, ps), 1802 (m, ps), 1748 (s), 1649 (s), 1601 (s, ps), 1493 (s, ps), 1452 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{186}H_{183}N_4O_3$: C 88.58, H 7.31, N 2.21; found: C 86.84, H 7.55, N 2.57; loading: 0.578 mmol g^{-1}.

Methyl ester of [(2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)benzoyl)benzylamino]acetic acid 5{1,6}: IR (KBr): $\tilde{\nu} = 3648$ (w, br, ps), 3026 (s, ps), 2922 (s, ps), 2847 (s, ps), 1944 (m, ps), 1871 (m, ps), 1803 (m, ps), 1753 (s), 1652 (s), 1601 (s, ps), 1493 (s, ps), 1453 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{185}H_{184}N_4O_3$: C 88.48, H 7.38, N 2.22; found: C 85.92, H 6.74, N 2.12; loading: 0.462 mmol g^{-1}.

Methyl ester of 2-[(2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)benzoyl)-(4-methoxybenzyl)amino]propionic acid 5{1,7}: IR (KBr): $\tilde{\nu} = 3652$ (w, br, ps), 3466 (s, ps), 3026 (s, ps), 2928 (s, ps), 2850 (s, ps), 1944 (m, ps), 1873 (m, ps), 1796 (m, ps), 1743 (s), 1642 (s), 1601 (s, ps), 1493 (s, ps), 1453 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{154}H_{153}N_4O_4$: C 87.10, H 7.26, N 2.62; found: C 86.54, H 7.35, N 3.57; loading: 0.923 mmol g^{-1}.

Methyl ester of 2-[(2-(3-benzyl-3-polystyrylmethyl-1-triazenyl)benzoyl)-(4-methoxybenzyl)amino]-3-phenylpropionic acid 5{1,8}: IR (KBr): $\tilde{\nu} =$ 3646 (w, br, ps), 3458 (s, ps), 3026 (s, ps), 2928 (s, ps), 2851 (s, ps), 1944 (m, ps), 1872 (m, ps), 1796 (m, ps), 1741 (s), 1640 (s), 1601 (s, ps), 1493 (s, ps), 1453 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{154}H_{153}N_4O_4$: C 87.10, H 7.26, N 2.62; found: C 85.96, H 7.44, N 3.55; loading: 0.900 mmol g^{-1}.

General procedure for the generation of azides (6{1,3–8}): The resin **5**{1,3–8} was suspended in 5% TFA/CH_2Cl_2 at RT. After 5–10 min, the mixture was filtered, and trimethylsilylazide was added. The solvents and the remnants of TFA and trimethylsilylazide were removed by evaporation. The residue was purified by performing flash chromatography, eluting with a 3:1 cyclohexane/AcOEt system.

Methyl ester of [(2-azidobenzoyl)(4-methoxybenzyl)amino]acetic acid 6{1,3}: R_f: 0.3 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.56$, 3.68, 3.72, 3.74 (8Aliph-H), 4.30 (s, 2H; NCH_2Ph), 6.77–7.39 ppm (m, 8Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 45.1$ (*syn*-NCH_2Ph), 48.1 (*anti*-NCH_2Ph), 48.7 (*anti*-CH_2COOCH_3), 52.1 (*anti*-COOCH_3), 52.2 (*syn*-COOCH_3), 52.8 (*syn*-CH_2COOCH_3), 55.3 (OCH_3), 114.1, 114.2, 118.4, 118.7, 125.1, 125.1, 128.2, 128.2, 129.1, 129.8, 130.6, 130.7, 136.3, 136.8, 159.3, 159.4 (Ar-C), 162.3 (*syn*-COOCH_3), 169.0 (*anti*-COOCH_3), 169.3 (*syn*-NCO), 169.3 ppm (*anti*-NCO); yield: 55%.

Methyl ester of [(2-azidobenzoyl)(3,4-dimethoxybenzyl)amino]acetic acid 6{1,4}: R_f: 0.2 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.56$, 3.68, 3.78, 3.81, 3.83 (11Aliph-H), 4.30 (s, 2H; NCH_2Ph), 6.64–7.38 ppm (m, 7Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 48.4$ (*anti*-CH_2COOCH_3), 48.7 (*syn*-CH_2COOCH_3), 52.1 (*syn*-COOCH_3), 52.2 (*anti*-COOCH_3), 53.2 (NCH_2Ph), 55.8 (*syn*-OCH_3), 55.8 (*anti*-OCH_3), 55.9 (*syn*-OCH_3), 55.9 (*anti*-OCH_3), 110.7, 111,0, 111.2, 111.4, 118.5, 118.7, 120.2, 120.9, 125.1, 125.2, 127.8, 127.8, 127.8, 128.1, 128.2, 128.5, 130.6, 130.7, 136.2, 136.6, 148.7, 148.9, 149.4, 149.4 (Ar-C), 169.0 (*anti*-NCO), 169.3 (*syn*-NCO), 169.3 (*syn*-COOCH_3), 169.4 ppm (*anti*-COOCH_3); MS (FAB): m/z (%): 385 (26) [M^+], 307 (100); yield: 37%.

Methyl ester of [(2-azidobenzoyl)(4-phenylbenzyl)amino]acetic acid 6{1,5}: R_f: 0.5 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.56$, 3.68, 3.71 (5 Aliph-H), 4.41 (s, 2H; NCH_2Ph), 7.07–7.53 ppm (m, 13Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 48.5$ (*anti*-CH_2COOCH_3), 49.07 (*syn*-CH_2COOCH_3), 52.2 (*syn*-COOCH_3), 52.2 (*anti*-COOCH_3), 53.1 (NCH_2Ph), 118.5, 118.7, 125.1, 125.2, 127.0, 127.0, 127.4, 127.5, 127.5, 128.1, 128.2, 128.3, 128.8, 130.7, 130.7, 134.4, 135.0, 136.3, 136.8, 140.4, 140.7, 140.7, 141.0 (Ar-C), 169.1 (*anti*-NCO), 169.3 (*syn*-NCO), 169.4 (*anti*-COOCH_3), 169.5 ppm (*syn*-COOCH_3); yield: 20%.

Methyl ester of [(2-azidobenzoyl)benzylamino]acetic acid 6{1,6}: R_f: 0.3 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.55$ (s, 2H; CH_2COOCH_3), 3.67 (s, 3H; COOCH_3), 4.37 (s, 2H; NCH_2Ph), 7.07–7.32 ppm (m, 9Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 48.7$ (*anti*-CH_2COOCH_3), 48.9 (*syn*-CH_2COOCH_3), 52.1 (*anti*-COOCH_3), 52.1 (*syn*-COOCH_3), 53.3 (NCH_2Ph), 118.4, 118,6, 125.0, 125.1, 126.9, 127.6, 127.7, 127.9, 127.9, 128.2, 128.3, 128.5, 128.7, 128.7, 128.8, 130.6, 130.6, 131.4, 135.4, 135.9, 136.3, 136.8 (Ar-C), 169.0 (*anti*-NCO), 169.2 (*syn*-NCO), 169.3 (*anti*-COOCH_3), 169.4 ppm (*syn*-COOCH_3); yield: 16%.

Methyl ester of 2-[(2-azidobenzoyl)(4-methoxybenzyl)amino]propionic acid 6{1,7}: R_f: 0.3 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.34$ (d, 2H, $J = 7.1$ Hz; CH_3), 3.75 (s, 3H; COOCH_3), 3.76 (s, 3H; OCH_3), 4.30 (NCH_2Ph), 6.78–7.79 ppm (m, 8Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 12.8$ (*syn*-CH$_3$), 14.0 (*anti*-CH$_3$), 39.0 (*syn*-NCH_2Ph), 42.9 (*anti*-NCH_2Ph), 52.2 (*syn*-COOCH_3), 52.2 (*anti*-COOCH_3), 55.2 (OCH$_3$), 57.0 (CH), 113.7, 113,9, 118.5, 125.0, 126.8, 127.6, 127.9, 128.4, 128.9, 130.4, 130.5, 136.2, 136.6, 158.7, 159.2 (Ar-C), 167.8 (*syn*-COOCH_3), 169.4 (*anti*-COOCH_3), 171.6 ppm (NCO); MS (FAB): m/z (%): 369 (28) [M^+], 219 (100); yield: 15%.

Methyl ester of 2-[(2-azidobenzoyl)(4-methoxybenzyl)amino]-3-phenylpropionic acid 6{1,8}: R_f: 0.3 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.69$ (s, 3H; COOCH_3), 3.73 (s, 3H; OCH_3), 6.66–7.34 ppm (m, 13Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 39.0$ (CHCH$_2$), 42.9 (NCH_2Ph), 52.2 (*syn*-COOCH_3), 53.4 (*anti*-COOCH_3), 55.2 (*syn*-OCH$_3$), 55.3 (*anti*-OCH$_3$), 113.8, 118.5, 125.0, 126.7, 127.2, 127.6, 128.0, 128.3, 129.4, 129.8, 129.9, 130.4, 136.2, 159.3 (Ar-C), 167.8 (COOCH_3), 168.7 (*anti*-NCO), 170.4 ppm (*syn*-NCO); yield: 5%.

General procedure for the synthesis of 1,4-benzodiazepin-5-ones (7{1,3–8}): The triphenylphosphine polystyrene (4 equiv) was distended with dry toluene (8 mL) in a glass vial and was sealed under argon. A solution of the azide **6**{1,3–8} (1 equiv) in dry toluene was injected into the suspension. The reaction mixture was shaken at RT for 1 h and then heated at 100 °C for 18 h. After cooling, the resin was separated by filtration and washed with dichloromethane. The filtrate was concentrated until dry to give the benzodiazepines **7**{1,3–8}.

2-Methoxy-4-(4-methoxybenzyl)-3,4-dihydrobenzo[*e*][1,4]diazepin-5-one 7{1,3}: R_f: 0.1 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.68$ (s, 2H, NCH_2), 3.71 (s, 3H, $PhOCH_3$), 3.72 (s, 3H, OCH_3), 4.69 (s, 2H, NCH_2Ph), 6.78–7.96 ppm (m, 8Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 45.8$ (NCH_2), 51.1 (NCH_2Ph), 54.2 (OCH_3), 55.3 ($PhOCH_3$), 114.1, 124.4, 126.1, 128.8, 129.6, 131.0, 131.7, 135.8, 144.9, 159.3 (Ar-C), 163.3 ($COCH_3$), 167.8 ppm (CO); EI-HRMS: *m/z* calcd for $C_{18}H_{18}N_2O_3$: 310.1317; found: 310.1315; MS (EI): *m/z* (%): 310 (24) [M^+], 201 (100); yield: 98%.

4-(3,4-Dimethoxybenzyl)-2-methoxy-3,4-dihydrobenzo[*e*][1,4]diazepin-5-one 7{1,4}: R_f: 0.03 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.60$ (s, 2H; NCH_2), 3.78 (s, 3H; $PhOCH_3$), 3.79 (s, 3H; $PhOCH_3$), 3.68 (s, 3H; OCH_3), 4.60 (s, 2H; NCH_2Ph), 6.73–8.22 ppm (m, 7Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 45.7$ (NCH_2), 51.5 (NCH_2Ph), 54.2 (OCH_3), 55.9 ($PhOCH_3$), 55.9 ($PhOCH_3$), 111.1, 111.4, 120.8, 124.4, 126.2, 129.0, 132.5, 144.9, 148.8, 149.3 (Ar-C), 163.3 ($COCH_3$), 167.9 ppm (CO); EI-HRMS: *m/z* calcd for $C_{19}H_{20}N_2O_4$: 340.1423; found: 340.1426; MS (EI): *m/z* (%): 340 (16) [M^+], 201 (100).

2-Methoxy-4-(4-phenylbenzyl)-3,4-dihydrobenzo[*e*][1,4]diazepin-5-one 7{1,5}: R_f: 0.1 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.64$ (s, 2H; NCH_2), 3.67 (s, 3H; OCH_3), 4.79 (s, 2H; NCH_2Ph), 6.89–7.96 ppm (m, 13Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 46.1$ (NCH_2), 51.5 (NCH_2Ph), 54.2 (OCH_3), 124.5, 126.2, 127.0, 127.4, 128.6, 128.8, 131.0, 131.8, 135.8, 140.7, 145.0 (Ar-C), 163.2 ($COCH_3$), 168.0 ppm (CO).

4-Benzyl-2-methoxy-3,4-dihydrobenzo[*e*][1,4]diazepin-5-one 7{1,6}: R_f: 0.1 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.61$ (s, 2H; NCH_2), 3.67 (s, 3H; OCH_3), 4.76 (s, 2H; NCH_2Ph), 6.86–7.73 ppm (m, 9Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 46.0$ (NCH_2), 51.7 (NCH_2Ph), 54.2 (OCH_3), 1117.6, 124.4, 128.1, 128.5, 128.6, 131.0, 131.5, 136.1, 144.9 (Ar-C), 167.2 ppm (CO).

2-Methoxy-4-(4-methoxybenzyl)-3-methyl-3,4-dihydrobenzo[*e*]-[1,4]diazepin-5-one 7{1,7}: R_f: 0.1 (Cyclohexane/AcOEt 2:1); $[\alpha]^{20} = -3.61$ ($CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.38$ (d, $J = 7.0$ Hz, 3H, CH_3), 3.64 (s, 3H, $PhOCH_3$), 3.72 (s, 3H, OCH_3), 4.45 (c, 1H, CH), 6.65–7.21 ppm (m, 8Ar-H).

3-Benzyl-2-methoxy-4-(4-methoxybenzyl)-3,4-dihydrobenzo[*e*]-[1,4]diazepin-5-one 7{1,8}: R_f: 0.03 (Cyclohexane/AcOEt 2:1); $[\alpha]^{20} = -0.05$ ($CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.51$ (s, 3H; $PhOCH_3$), 3.72 (s, 3H; OCH_3), 6.72–8.03 ppm (m, 13Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 34.5$ (CH_2Ph), 52.9 (NCH_2Ph), 54.0 (OCH_3), 55.2 (CH), 61.3 (PhOMe), 113.9, 120.7, 124.5, 126.9, 128.5, 128.7, 128.8, 129.8, 131.0, 136.1, 139.3, 143.3, 159.2 (Ar-C), 163.2 ($COCH_3$), 166.8 ppm (CO); EI-HRMS: *m/z* calcd for $C_{25}H_{24}N_3O_3$: 400.1787; found: 400.1787; MS (EI): *m/z* (%): 400 (12) [M^+], 201 (100).

General procedure for the coupling via acid chlorides (5{1,9–11}): A mixture of triphenylphosphine (3 equiv), resin **3**{1} (1 equiv), lactams **4**{9–11} (2 equiv), diisopropylethylamine (4 equiv), and carbon tetrachloride (3 equiv) was heated at reflux in THF for 5 h. After cooling, the resin **5**{1,9–11} was filtered off, washed sequentially with THF, Et_2O, MeOH, DMF, THF, CH_2Cl_2, methanol, and pentane, and was dried under high vacuum.

(2-(3-Benzyl-3-polystyrylmethyl-1-triazenyl)benzoylpyrrolidin-2-one 5{1,9}: IR (KBr): $\tilde{\nu} = 3647$ (s, ps), 3620 (w, ps), 3061 (w, br, ps), 2951 (w, br, ps), 1944 (m, ps), 1872 (m, ps), 1800 (m, ps), 1751 (s), 1679 (s), 1601 (s, ps), 1494 (s, ps), 1461 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{181}H_{180}N_4O_2$: C 88.98, H 7.42, N 2.28; found: C 87.34, H 7.86, N 2.46; loading: 0.501 mmol g^{-1}.

(2-(3-Benzyl-3-polystyrylmethyl-1-triazenyl)benzoylpiperidin-2-one 5{1,10}: IR (KBr): $\tilde{\nu} = 3649$ (s, ps), 3621 (w, ps), 3026 (s, ps), 2926 (w, br, ps), 1944 (m, ps), 1872 (m, ps), 1802 (m, ps), 1713 (s), 1679 (s), 1601 (s, ps), 1493 (s, ps), 1452 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{182}H_{182}N_4O_2$: C 88.96, H 7.46, N 2.27; found: C 86.33, H 8.02, N 2.32; loading: 0.462 mmol g^{-1}.

(2-(3-Benzyl-3-polystyrylmethyl-1-triazenyl)benzoylazepan-2-one 5{1,11}: IR (KBr): $\tilde{\nu} = 3645$ (s, ps), 3620 (w, ps), 3026 (s, ps), 2926 (w, br, ps), 1944 (m, ps), 1873 (m, ps), 1802 (m, ps), 1713 (s), 1679 (s), 1601 (s, ps), 1493 (s, ps), 1452 cm^{-1} (s, ps); elemental analysis calcd (%) for $C_{183}H_{184}N_4O_2$: C 88.94, H 7.50, N 2.26; found: C 87.68, H 7.57, N 2.49; loading: 0.512 mmol g^{-1}.

General procedure for the generation of azides (6{1,9–12}): The resin **5**{1,9–12} was suspended in 5% TFA/CH_2Cl_2 at RT. After 5–10 min, the mixture was filtered and trimethylsilylazide was added. The solvents and the remnants of TFA and trimethylsilylazide were removed by evaporation. The residue was purified by performing flash chromatography, eluting with a 3:1 cyclohexane/AcOEt system.

1-(2-Azidobenzoyl)pyrrolidin-2-one 6{1,9}: R_f: 0.4 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.06$ (q, 2H, CH_2), 2.41 (t, $J = 8.2$ Hz, 2H; $COCH_2$), 3.90 (t, $J = 7.0$ Hz, 2H; NCH_2), 7.11 (m, 2Ar-H), 7.21 (d, $J = 7.5$ Hz, 1Ar-H), 7.39 ppm (t, $J = 7.7$ Hz, 1Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 17.4$ (CH_2), 33.0 ($COCH_2$), 45.5 (NCH_2), 118.1, 124.7, 128.3, 131.2, 137.2 (Ar-C), 167.3 (CON), 174.1 ppm ($COCH_2$); EI-HRMS: *m/z* calcd for $C_{11}H_{10}N_4O_2$: 230.0804, found: 230.0802; MS (EI): *m/z* (%): 230 (18) [M^+], 116 (100); yield: 12%.

1-(2-Azidobenzoyl)piperidin-2-one 6{1,10}: R_f: 0.5 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.79$–1.91 (m, 4H; CH_2CH_2), 2.46 (t, $J = 6.4$ Hz, 2H; $COCH_2$), 3.78 (t, $J = 6.2$ Hz, 2H; NCH_2), 7.04 (d, $J = 8.1$ Hz, 1Ar-H), 7.10 (t, $J = 7.5$ Hz, 1Ar-H), 7.26 (d, $J = 7.7$ Hz, 1Ar-H), 7.34 ppm (t, $J = 7.3$ Hz, 1Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 20.8$, 22.5 (CH_2), 34.3 ($COCH_2$), 44.9 (NCH_2), 118.1, 125.0, 128.4, 130.8, 135.9 (Ar-C), 170.2 (CON), 172.8 ppm ($COCH_2$); EI-HRMS: *m/z* calcd for $C_{12}H_{12}N_4O_2$: 244.0906, found: 244.0955; MS (EI): *m/z* (%): 244 (4) [M^+], 117 (100); yield: 17%.

1-(2-Azidobenzoyl)azepan-2-one 6{1,11}: R_f: 0.5 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.77$ (m, 6H; $CH_2CH_2CH_2$), 2.59 (m, 2H; $COCH_2$), 3.94 (m, 2H; NCH_2), 7.04 (d, $J = 8.1$ Hz, 1Ar-H), 7.09 (t, $J = 7.5$ Hz, 1Ar-H), 7.21 (d, $J = 7.7$ Hz, 1Ar-H), 7.32 ppm (t, $J = 8.1$ Hz, 1Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.6$, 28.6, 29.5 (CH_2), 39.0 ($COCH_2$), 43.8 (NCH_2), 118.1, 124.9, 128.0, 130.5, 135.6 (Ar-C), 169.5 (CON), 176.9 ppm ($COCH_2$); EI-HRMS: *m/z* calcd for $C_{14}H_{15}N_3O_2$: 258.1117, found: 258.1116; MS (EI): *m/z* (%): 258 (4) [M^+], 230 (100); yield: 20%.

General procedure for the synthesis of 1,4-benzodiazepin-5-ones (7{1,9–11}): The triphenylphosphine polystyrene (4 equiv) was distended with dry toluene (8 mL) in a glass vial sealed under argon. A solution of the azide **6**{1,9–11} (1 equiv) in dry toluene was injected into the suspension. The reaction mixture was shaken at RT for 1 h and then heated at 100°C for 132 h. After cooling, the resin was separated by filtration and washed with dichloromethane. The filtrate was concentrated to dryness to give the benzodiazepines **7**{1,9–11}.

2,3-Dihydro-1*H*-pyrrolo[2,1-*b*]quinazolin-9-one (deoxyvasicinone) 7{1,9}: R_f: 0.03 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.21$ (q, 2H; $NCH_2CH_2CH_2$), 3.10 (t, $J = 7.8$ Hz, 2H; $NCH_2CH_2CH_2$), 4.13 (t, $J = 7.1$ Hz, 2H; $NCH_2CH_2CH_2$), 7.35–8.22 ppm (m, 4Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 19.5$ ($NCH_2CH_2CH_2$), 32.5 ($NCH_2CH_2CH_2$), 46.5 ($NCH_2CH_2CH_2$), 120.5, 126.2, 126.4, 126.7, 134.1, 149.1 (Ar-C), 159.4 (CO), 160.9 ppm (N=*C*); EI-HRMS: *m/z* calcd for $C_{11}H_{10}N_2O$: calcd 186.0793; found: 186.0789; MS (EI): *m/z* (%): 186 (90) [M^+], 185 (100); purity: 82% (by GC); yield: 99%.

6,7,8,9-Tetrahydropyrido[2,1-*b*]quinazolin-11-one 7{1,10}: R_f: 0.1 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.87$ (q, 2H; $NCH_2CH_2CH_2CH_2$), 1.93 (q, 2H; $NCH_2CH_2CH_2CH_2$), 2.93 (t, $J = 6.6$ Hz, 2H; $NCH_2CH_2CH_2CH_2$), 4.00 (t, $J = 6.0$ Hz, 2H; $NCH_2CH_2CH_2CH_2$), 7.25–8.19 ppm (m, 4Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 19.3$ ($NCH_2CH_2CH_2CH_2$), 22.0 ($NCH_2CH_2CH_2CH_2$), 31.8 ($NCH_2CH_2CH_2CH_2$), 42.2 ($NCH_2CH_2CH_2CH_2CH_2$), 120.4, 126.0, 126.3, 126.6, 134.1, 147.3 (Ar-C), 154.9 (CO), 162.1 ppm (N=*C*); EI-HRMS: *m/z* calcd for $C_{12}H_{12}N_2O$: 200.095; found: 200.095; MS (EI): *m/z* (%): 200 (100) [M^+]; purity: 96% (by GC); yield: 99%.

7,8,9,10-Tetrahydro-6*H*-azepino[2,1-*b*]quinazolin-12-one 7{1,11}: R_f: 0.2 (Cyclohexane/AcOEt 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.77$ (m, 6H; $NCH_2CH_2CH_2CH_2CH_2$), 3.00 (m, 2H; $NCH_2CH_2CH_2CH_2CH_2$), 4.31 (m, 2H; $NCH_2CH_2CH_2CH_2CH_2$), 7.20–8.19 ppm (m, 4Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 25.4$, 28.1, 29.57 ($NCH_2CH_2CH_2CH_2CH_2$), 37.7 ($NCH_2CH_2CH_2CH_2CH_2$), 42.9 ($NCH_2CH_2CH_2CH_2CH_2$), 120.2, 126.3,

126.7, 127.0, 134.1, 147.4 (Ar-C), 159.7 (CO), 161.9 ppm (N=*C*); EI-HRMS: *m*/*z* calcd for $C_{13}H_{14}N_2O$: 214.1106; found: 214.1107; MS (EI) *m*/*z* (%): 214 (100) [M^+]; purity: 91% (by GC); yield: 99%.

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