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Continued Exploration of Trifunctional Alkyl 4-Chloro-2-diazo-3-oxobutanoates: Streamlined Entry into [1,2,3]Triazolo[5,1-*c*][1,4]-benzoxazines and [1,2,3]Triazolo[5,1-*c*][1,4]benzoxazepines

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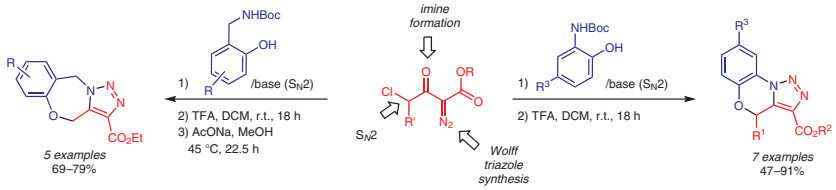

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Abstract Further exploration of the trifunctional character of previously introduced alkyl 4-chloro-2-diazo-3-oxobutanoates in reactions with *N*-protected substituted *o*-aminophenols followed by deprotection provided a convenient entry into [1,2,3]triazolo[5,1-*c*][1,4]benzoxazines, which are of high medicinal importance, as documented in the literature. The same approach applied to *N*-protected substituted *o*-(aminomethyl)phenols afforded [1,2,3]triazolo[5,1-*c*][1,4]benzoxazepines, which are practically unexplored compounds from a medicinal chemistry perspective. The syntheses start with S_N2-type alkylation of the phenol. Removal of the protecting group triggers imine formation followed by Wolff 1,2,3-triazole synthesis.

Key words diazo compounds, multicenter reactions, nucleophilic substitution, domino reactions, Wolff 1,2,3-triazole synthesis, benzoxazines, benzoxazepines

Similar to multicomponent reactions, which are known for their efficiency, the engagement of multiple reactive centers in reagents participating in a two-component transformation allows molecular complexity to be built up rapidly and in atom-economical fashion.[1] Ring-forming processes based on one bifunctional reagent reacting with another are rather common. Such reactions typically involve the formation of two new chemical bonds via an initial intermolecular event followed by intramolecular ring closure.[2] In contrast, reagents with multiple reactive centers that can generate more than two new chemical bonds through a domino process[3] are much less widespread.[4]

Recently, we introduced trifunctional 4-chloro-2-diazo-3-oxobutanoates **1a**,**b**, which are capable of interacting with nucleophile-bearing primary amines to furnish fused 1,2,3-triazoles via a tandem of bimolecular nucleophilic substitution, imine formation, and the Wolff 1,2,3-triazole synthesis. This was demonstrated in reactions with vicinal *N*,*S*-bis-nucleophiles and led to the formation of bicyclic 6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]thiazines **2**.[5] These reactions proceeded with good to excellent yields (67–96%), and no fragmentation of the β-oxo-α-diazocetate moiety (known to be triggered by nucleophilic primary amines[6]) was observed. Encouraged by this initial success, we were keen to extend this methodology to other bis-nucleophilic partners such as phenols bearing an amino functionality (in a protected form to ensure the selectivity of the initial S_N2 event[7]) attached to the *ortho* position of the phenyl ring, either directly or via a 1–2 carbon linker. This was seen as a potentially streamlined entry into 1,2,3-triazolo-fused tricycles **3** featuring a variably sized oxa-ring (Scheme 1). Herein, we report on the realization of this strategy.

o-Aminophenols (and other phenols investigated in this work) could not be directly used in the reactions with **1a**,**b** because, under basic conditions (required to activate the phenolic substrates), the β-dicarbonyl diazo reagents undergo deacetylative fragmentation, as was observed previously.[5] *o*-Aminophenol and its *p*-substituted derivatives were Boc-protected by using a literature procedure,[8] and the resulting products **4a**–**e** were obtained in excellent yields. Doubly protected product **4f** was synthesized from 2,4-diaminophenol dihydrochloride by using sodium bicarbonate as a base. Carboxamide **4g** was obtained from carboxylic acid **4e** by amidation. Boc-protected *o*-hydroxybenzylamines **5a**–**e** were synthesized by reductive amination of the respective benzaldehydes with *tert*-butyl carbamate by

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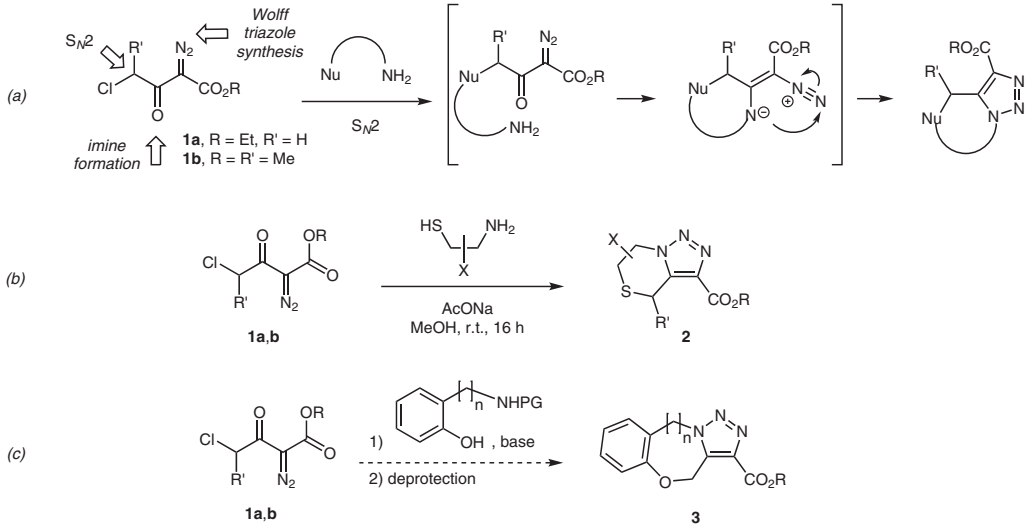


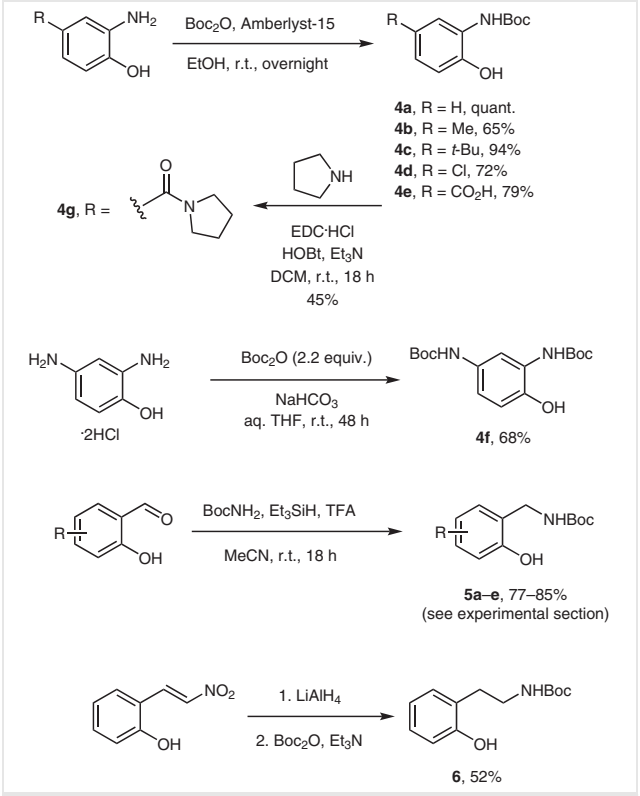
Scheme 1 (a) Interaction of trifunctional reagents **1a**,**b** with nucleophile-bearing primary amines; (b) tandem assembly of 6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]thiazines **2** reported previously;[5] (c) approach to tricycles **3** explored in this work

using triethylsilane as the reducing agent.[9] Finally, Boc-protected *o*-hydroxyphenethylamine (**6**) was synthesized in two steps from 2-(2-nitrovinyl)phenol as described in the literature (Scheme 2).[10,11]

For the suitably protected phenols **4a–d**,**f**,**g**, **5a–e**, and **6**, initial S_N2-type coupling with trifunctional reagents **1a**,**b** was envisioned as the next step. After brief experimentation involving variation of the solvent, base, reaction temperature, and additives, we arrived at an optimal protocol that allowed alkylation of all of the above phenols in fair to good yields (Table 1).

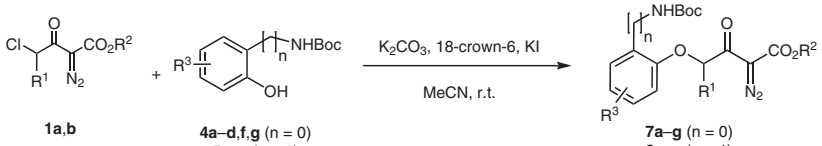
Not unexpectedly, alkylation of Boc-protected *o*-aminophenols **4a–d**,**f**,**g** was generally higher yielding and proceeded over a shorter period of time than that of benzylamines **5a–e** and phenethylamine **6**. Compound **1b** was a markedly less efficient alkylator than **1a** (*cf*. entries 4 and 7, Table 1).

With compounds **7a–g**, **8a–e**, and **9** in hand, we proceeded to remove the Boc protecting group; we reasoned that this would liberate the primary amine and trigger the tandem imine formation and the subsequent Wolff 1,2,3-triazole synthesis (Scheme 1a). Indeed, for *o*-aminophenol-derived substrates **7a–g**, treatment with 10 equiv. of TFA in DCM at room temperature over 18 h resulted in removal of the Boc group and formation of [1,2,3]triazolo[5,1-*c*]-[1,4]benzoxazines **10a–g** in good to excellent yields (Scheme 3).



Scheme 2 Preparation of starting phenols **4a–d**,**f**,**g**, **5a–e**, and **6**; HOBt: 1-hydroxy-1*H*-benzotriazole

Table 1 Alkylation of Phenols **4a–d,f,g**, **5a–e**, and **6**



Entry	Phenol	**1**	Time (h)	Product	Yield (%)
1	**4a**	**1a**	6	**7a**	75
2	**4b**	**1a**	6	**7b**	79
3	**4c**	**1a**	6	**7c**	75
4	**4d**	**1a**	6	**7d**	83
5	**4f**	**1a**	6	**7e**	73
6	**4g**	**1a**	31	**7f**	42
7	**4d**	**1b**	51	**7g**	40
8	**5a**	**1a**	24	**8a**	58
9	**5b**	**1a**	24	**8b**	54
10	**5c**	**1a**	24	**8c**	72

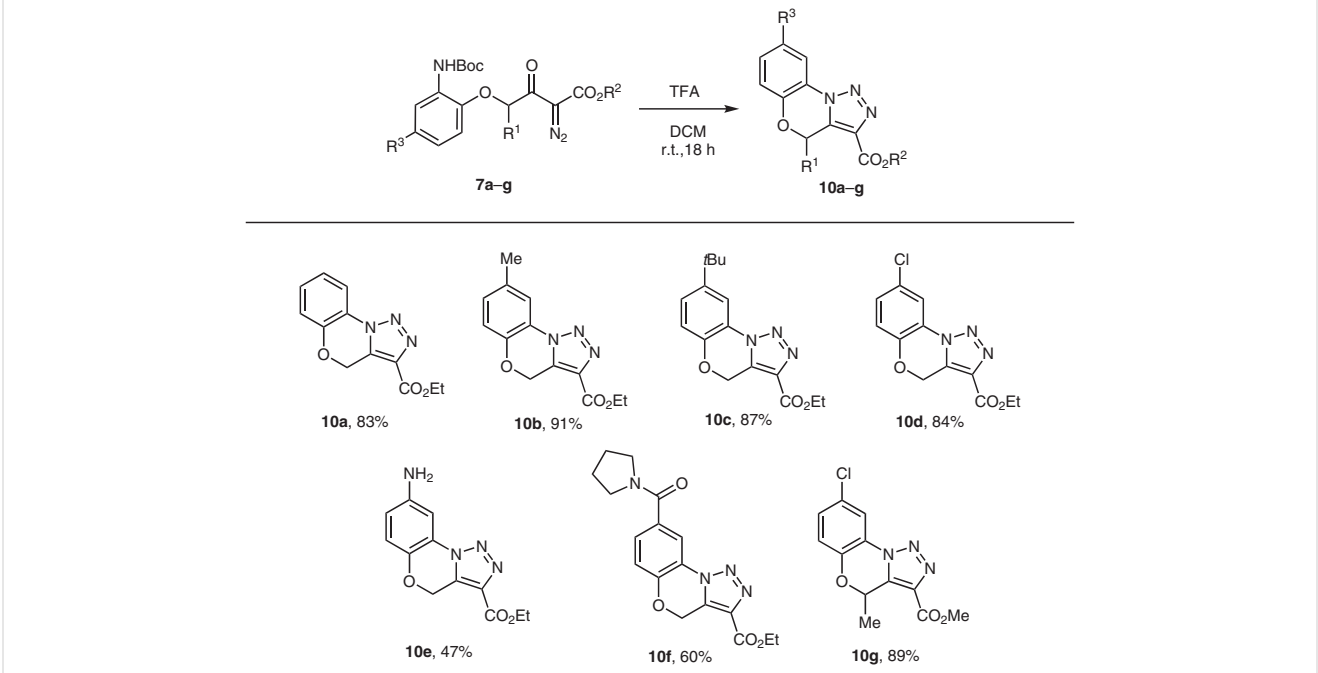
Table (continued)

Entry	Phenol	1	Time (h)	Product	Yield (%)
11	**5d**	**1a**	15	**8d**	65
12[a]	**5e**	**1a**	15	**8e**	41
13	**6**	**1a**	15.5	**9**	53

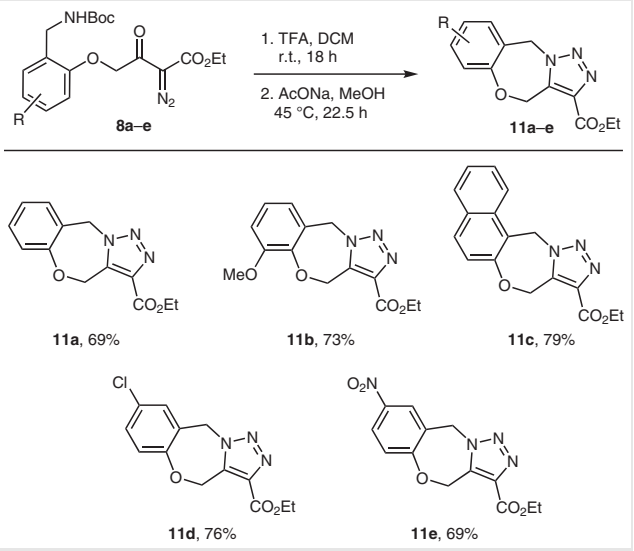
[a] An equal volume of DMF was added to aid solubility of **5e**.

The medicinal relevance of the [1,2,3]triazolo[5,1-*c*][1,4]benzoxazine scaffold (typically assembled via an intramolecular azide–alkyne click reaction[12]) is undisputable. For example, this core is central to Glaxo's 5-$HT_{1A/B/D}$ antagonists[13] and mGluR5 receptor antagonists,[14] developed as antidepressants/anxyolytics, Shionogi's HIV replication inhibitors[15] and Takeda's thrombin receptor antagonists.[16]

Under the same conditions that proved efficient in affording **10a–g**, removal of the Boc protecting group from benzylamines **8a–e** liberated a more basic alkylamino functionality that was strongly protonated by TFA, which did not allow the reaction to proceed further. This problem was solved by neutralizing the TFA with sodium acetate (added as a solution in methanol); this led, at elevated temperature, to a slow and gradual formation of the expected [1,2,3]triazolo[5,1-*c*][1,4]benzoxazepines **11a–e**, which were isolated in good yields (Scheme 4).



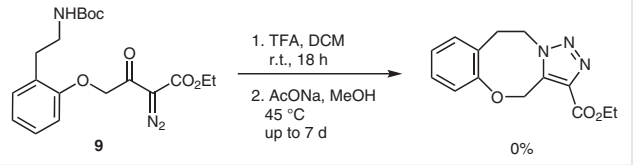
Scheme 3 Synthesis of [1,2,3]triazolo[5,1-c][1,4]benzoxazines **10a–g**



Scheme 4 Synthesis of [1,2,3]triazolo[5,1-*c*][1,4]benzoxazepines **11a–e**

The [1,2,3]triazolo[5,1-*c*][1,4]benzoxazepine scaffold is a lot scarcer than [1,2,3]triazolo[5,1-*c*][1,4]benzoxazines. It has only sporadically appeared in the literature,[17] and therefore, little is known of the associated biological activity, except for hints of a weak antibacterial and antifungal activity.[17d]

Unfortunately, all attempts to assemble a homologous ring system by exposing compound **9** to the same conditions failed, even with a reaction time of several days. This is possibly a result of unfavorable entropy associated with the formation of an eight-membered ring (Scheme 5).[18]



Scheme 5 Attempted assembly of the benzo[*g*][1,2,3]triazolo[5,1-*c*]-[1,4]oxazocine ring system

In summary, we have extended the trifunctional reactivity of the previously reported alkyl 4-chloro-2-diazo-3-oxobutanoates to *O,N*-bis-nucleophilic substrates. These were engaged in ring-forming processes, in *N*-Boc-protected form, in two steps. Initially, S_N2-type displacement of the chlorine atom generated phenoxy-substituted precursors that were isolated. Removal of the Boc protecting group with TFA from anilinic substrates triggered cascade imine formation and Wolff 1,2,3-triazole synthesis. This afforded [1,2,3]triazolo[5,1-*c*][1,4]benzoxazines, which are well characterized from a medicinal chemistry perspective. Deprotection of the more basic benzylamines required the TFA salt to be neutralized by sodium acetate. This resulted in the slow, high-yielding formation of [1,2,3]triazolo[5,1-*c*][1,4]benzoxazepines, a much scarcer ring system that remains to be studied with respect to biological activity. Although the approach was found to be unsuitable for the construction of the benzo[*g*][1,2,3]triazolo[5,1-*c*][1,4]oxazocine ring system, these findings significantly expand the scope of cascade transformations achievable with the aid of trifunctional alkyl 4-chloro-2-diazo-3-oxobutanoates.

All commercial reagents and solvents were used without further purification, unless otherwise noted. NMR spectroscopic data were recorded with a 400 MHz spectrometer (400.13 MHz for ^{1}H and 100.61 MHz for ^{13}C) in $CDCl_3$ and in DMSO-d_6 and were referenced to residual solvent proton signals (δ_H = 7.26 and δ_H = 2.50, respectively) and solvent carbon signals (δ_C = 77.0 and δ_C = 39.5, respectively). All chemical shifts are reported in parts per million (ppm). Abbreviations used in the description of resonances are: s (singlet), d (doublet), t (triplet), q (quartet), br (broad), and m (multiplet). Coupling constants (*J*) are quoted to the nearest 0.1 Hz. Mass spectra were recorded with a HRMS-ESI-qTOF spectrometer (electrospray ionization mode). Melting points were determined with a Stuart SMP 50 melting point apparatus in open capillary tubes. Analytical thin-layer chromatography was performed on UV-254 silica gel plates with appropriate eluents. Compounds were visualized with short-wavelength UV light. Flash column chromatography was performed by using silica gel Merck grade 60 (0.040–0.063 mm) 230–400 mesh (isocratic or gradient elution as indicated).

Preparation of Starting Materials

tert-Butyl carbamate,[19] 2-(2-nitrovinyl)phenol,[20] ethyl 4-chloro-2-diazo-3-oxobutanoate (**1a**), and methyl 4-chloro-2-diazo-3-oxopentanoate (**1b**)[5] were prepared according to literature procedures. Data for the obtained compounds were in accordance with the literature data.

N-Boc-Protected 2-Aminophenols 4a–e; General Procedure 1 (GP1)[8]

The appropriate aminophenol (6.1 mmol) was added to a stirred mixture of Amberlyst-15 (10% w/w) and di-*tert*-butyl dicarbonate (1.45 g, 6.7 mmol) in ethanol (6 mL) at room temperature. Stirring was continued overnight. After completion of the reaction, the catalyst was filtered off and the solvent was evaporated in vacuo. The residue was dissolved in $CHCl_3$ (30 mL) and washed with water (3 × 30 mL). The organic phase was dried over Na_2SO_4, filtered, and evaporated to dryness to afford the corresponding *N*-Boc-protected 2-aminophenol.

The spectral data for *tert*-butyl (2-hydroxyphenyl)carbamate (**4a**) (1.91 g, quant.),[21] *tert*-butyl (2-hydroxy-5-methylphenyl)carbamate (**4b**) (1.71 g, 65%),[22] and *tert*-butyl (5-chloro-2-hydroxyphenyl)carbamate (**4d**) (1.77 g, 72%)[21] thus obtained were in accordance with the literature data.

tert-Butyl (5-(*tert*-Butyl)-2-hydroxyphenyl)carbamate (4c)

Following GP1, 2-amino-4-(*tert*-butyl)phenol (1 g, 6.1 mmol), Boc_2O (1.45 g, 6.7 mmol), and Amberlyst-15 (100 mg) in ethanol (6 mL) gave *tert*-butyl (5-(*tert*-butyl)-2-hydroxyphenyl)carbamate (**4c**) as a light brown solid (1.51 g, 94%); mp 102.5–103.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (br s, 1 H, NH), 7.13–7.01 (m, 2 H), 6.93 (d, *J* = 8.5 Hz, 1 H, 3-Ar), 6.68 (br s, 1 H, OH), 1.55 (s, 9 H, $C(CH_3)_3$ (Boc)), 1.30 (s, 9 H, $C(CH_3)_3$ (*t*Bu-Ph)).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 155.22, 145.39, 143.79, 124.66, 122.85, 118.77, 118.66, 82.03, 34.07, 31.46 (3 C, $C(CH_3)_3$), 28.28 (3 C, $C(CH_3)_3$).

HRMS (ESI +ve): *m*/*z* calcd for $C_{15}H_{23}NO_3$ [M + Na]$^+$: 288.1570; found: 288.1571.

3-((*tert*-Butoxycarbonyl)amino)-4-hydroxybenzoic acid (4e)

Following GP1, 3-amino-4-hydroxybenzoic acid (1.0 g, 6.3 mmol), Boc_2O (1.57 g, 7 mmol), and Amberlyst-15 (100 mg) in ethanol (6.5 mL) were used. In this case, flash chromatography was performed (acetone as the eluent), which gave 3-((*tert*-butoxycarbonyl)amino)-4-hydroxybenzoic acid (**4e**) as a colorless solid (1.27 g, 79%); mp 168.7–169.7 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.45 (br s, 1 H, COOH), 10.62 (br s, 1 H, OH), 8.28 (d, *J* = 2.0 Hz, 1 H, 2-Ar), 7.87 (s, 1 H, NH), 7.52 (dd, *J* = 8.4, 2.2 Hz, 1 H, 6-Ar), 6.89 (d, *J* = 8.4 Hz, 1 H, 5-Ar), 1.47 (s, 9 H, $C(CH_3)_3$).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 167.66, 153.21, 151.92, 126.62, 126.03, 122.56, 121.90, 114.96, 79.89, 28.49 (3 C, $C(CH_3)_3$).

HRMS (ESI +ve): *m*/*z* calcd for $C_{12}H_{15}NO_5$ [M + Na]$^+$: 276.0842; found: 276.0847.

Di-*tert*-butyl (4-Hydroxy-1,3-phenylene)dicarbamate (4f)

A solution of $NaHCO_3$ (2.17 g, 25.9 mmol) in water (25 mL) was added to a stirred solution of 2,4-diaminophenol dihydrochloride (1.00 g, 5.1 mmol) in THF (25 mL). Stirring was continued for 15 min at room temperature, and Boc_2O (2.33 g, 10.7 mmol) was added. The reaction mixture was stirred for 48 h at room temperature. THF was removed in vacuo, then the water was extracted with DCM (3 × 30 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain di-*tert*-butyl (4-hydroxy-1,3-phenylene)dicarbamate (**4f**) as a light lilac solid (1.11 g, 68%); mp 81.4–82.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (br s, 1 H), 7.41 (br s, 1 H), 6.89 (d, *J* = 8.5 Hz, 1 H, 5-Ar), 6.83 (dd, *J* = 8.7, 2.5 Hz, 1 H, 6-Ar), 6.65 (br s, 1 H), 6.34 (br s, 1 H), 1.54 (s, 9 H, $C(CH_3)_3$), 1.52 (s, 9 H, $C(CH_3)_3$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 154.71, 153.39, 143.17, 131.17, 126.05, 118.57, 116.34, 112.52, 81.85, 80.50, 28.35 (3 C, $C(CH_3)_3$), 28.25 (3 C, $C(CH_3)_3$).

HRMS (ESI +ve): *m*/*z* calcd for $C_{16}H_{24}N_2O_5$ [M + Na]$^+$: 347.1577; found: 347.1579.

tert-Butyl (2-Hydroxy-5-(pyrrolidine-1-carbonyl)phenyl)carbamate (4g)[23]

EDC?HCl (360 mg, 1.78 mmol), HOBt (301 mg, 1.78 mmol), Et_3N (248 µL, 1.78 mmol), and pyrrolidine (147 µL, 1.78 mmol) were added to a stirred solution of 3-((*tert*-butoxycarbonyl)amino)-4-hydroxybenzoic acid (**4e**) (443 mg, 1.75 mmol) in DCM (10 mL). The reaction mixture was stirred for 18 h at room temperature and then diluted with DCM (20 mL). The reaction mixture was washed with water (2 × 15 mL) and brine (15 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain *tert*-butyl (2-hydroxy-5-(pyrrolidine-1-carbonyl)phenyl)carbamate (**4g**) as a colorless solid (242 mg, 45%); mp 196.9–197.8 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.20 (s, 1 H, OH), 7.86–7.84 (m, 2 H, 6-Ar and NH overlapping), 7.09 (dd, *J* = 8.3, 2.1 Hz, 1 H, 4-Ar), 6.84 (d, *J* = 8.2 Hz, 1 H, 3-Ar), 3.49–3.39 (t, *J* = 6.4 Hz, 4 H, $(CH_2)_2$, pyrrolidine), 1.83 (br s, 4 H, $(CH_2)_2$, pyrrolidine), 1.47 (s, 9 H, $C(CH_3)_3$).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 168.60, 153.28, 149.02, 128.24, 126.26, 123.46, 120.63, 114.71, 79.86, 49.66, 46.48, 28.50 (3 C, $C(CH_3)_3$), 26.53, 24.37.

HRMS (ESI +ve): *m*/*z* calcd for $C_{16}H_{22}N_2O_4$ [M + Na]$^+$: 329.1472; found: 329.1472.

tert-Butyl (2-Hydroxybenzyl)carbamates 5a–e; General Procedure 2 (GP2)[9]

The appropriate salicylaldehyde (2.5 mmol), Et_3SiH (1.198 mL, 7.34 mmol), and TFA (0.371 mL, 4.85 mmol) were added to a solution of *tert*-butylcarbamate (852 mg, 7.27 mmol) in CH_3CN (11 mL), and the reaction mixture was stirred at room temperature for the indicated time. Organic solvent was removed in vacuo, then the residue was dissolved in DCM (15 mL) and washed with a sat. solution of $NaHCO_3$ (2 × 20 mL) and brine (20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain corresponding *tert*-butyl (2-hydroxybenzyl)carbamate.

The data for *tert*-butyl (2-hydroxybenzyl)carbamate (**5a**) (359 mg, 65%) were in accordance with the literature data.[24]

tert-Butyl (2-Hydroxy-3-methoxybenzyl)carbamate (5b)

Following GP2, 2-hydroxy-3-methoxybenzaldehyde (380 mg, 2.5 mmol) and other reagents were used in the indicated quantities with a reaction time of 20 h. Yield 532 mg (84%); colorless solid; mp 136.3–136.9 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.88–6.77 (m, 4 H, Ar and OH overlapping), 5.16 (br s, 1 H, NH), 4.33 (d, *J* = 6.3 Hz, 2 H, ArCH_2), 3.90 (s, 3 H, OCH_3), 1.46 (s, 9 H, $C(CH_3)_3$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 156.68, 147.21, 144.19, 124.93, 121.84, 119.57, 110.47, 79.84, 56.05, 40.33 (ArCH_2), 28.41 (3 C, $C(CH_3)_3$).

HRMS (ESI +ve): *m*/*z* calcd for $C_{13}H_{19}NO_4$ [M + Na]$^+$: 276.1206; found: 276.1208.

tert-Butyl ((2-Hydroxynaphthalen-1-yl)methyl)carbamate (5c)

Following GP2, 2-hydroxy-1-naphthaldehyde (430 mg, 2.5 mmol) and other reagents were used in the indicated quantities with a reaction time of 3 d. Yield 578 mg (85%); beige solid; mp 140.2–140.9 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.57 (s, 1 H, OH), 7.82 (d, *J* = 8.3 Hz, 1 H, Ar), 7.79 (d, *J* = 8.4 Hz, 1 H, Ar), 7.76 (d, *J* = 8.9 Hz, 1 H, Ar), 7.52 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1 H, Ar), 7.36 (ddd, *J* = 8.0, 6.8, 1.1 Hz, 1 H, Ar), 7.26 (d, *J* = 8.9 Hz, 1 H, Ar), 5.47 (t, *J* = 6.8 Hz, 1 H, NH), 4.69 (d, *J* = 6.7 Hz, 2 H, ArCH_2), 1.45 (s, 9 H, $C(CH_3)_3$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 158.79, 154.11, 133.00, 129.97, 129.08, 128.92, 126.80, 123.00, 121.22, 120.46, 116.67, 81.30, 35.54 (ArCH_2), 28.31 (3 C, $C(CH_3)_3$).

HRMS (ESI +ve): *m*/*z* calcd for $C_{16}H_{19}NO_3$ [M + Na]$^+$: 296.1257; found: 296.1254.

tert-Butyl (5-Chloro-2-hydroxybenzyl)carbamate (5d)

Following GP2, 5-chloro-2-hydroxybenzaldehyde (390 mg, 2.5 mmol) and other reagents were used in the indicated quantities with a reaction time of 16 h. Yield 524 mg (82%); colorless solid; mp 133.3–134.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.06 (br s, 1 H, OH), 7.17 (dd, *J* = 8.6, 2.6 Hz, 1 H, 4-Ar), 7.05 (d, *J* = 2.6 Hz, 1 H, 6-Ar), 6.89 (d, *J* = 8.6 Hz, 1 H, 3-Ar), 5.28 (br s, 1 H, NH), 4.20 (d, *J* = 6.7 Hz, 2 H, ArCH_2), 1.47 (s, 9 H, $C(CH_3)_3$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 158.49, 154.48, 130.10, 129.52, 126.44, 124.22, 119.19, 81.60, 40.93 (ArCH_2), 28.28 (3 C, $C(CH_3)_3$).

HRMS (ESI +ve): *m*/*z* calcd for $C_{12}H_{16}ClNO_3$ [M + Na]$^+$: 280.0711; found: 280.0708.

tert-Butyl (2-Hydroxy-5-nitrobenzyl)carbamate (5e)

Following GP2, 2-hydroxy-5-nitrobenzaldehyde (420 mg, 2.5 mmol) and other reagents were used in the indicated quantities with a reaction time of 26 h. After completion of the reaction, the mixture was left to stand overnight in a freezer (–18 °C). The solid was isolated by suction and carefully rinsed with DCM (2 × 5 mL) and CH_3CN (4 mL). Yield 516 mg (77%); colorless solid; mp 181.0–181.6 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.21 (br s, 1 H, OH), 8.04 (dd, *J* = 8.8, 2.9 Hz, 1 H, 4-Ar), 8.00 (d, *J* = 2.9 Hz, 1 H, 6-Ar), 7.42 (t, *J* = 6.2 Hz, 1 H, NH), 6.97 (d, *J* = 8.9 Hz, 1 H, 3-Ar), 4.12 (d, *J* = 6.2 Hz, 2 H, ArCH_2), 1.42 (s, 9 H, $C(CH_3)_3$).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 161.55, 156.42, 140.00, 127.91, 124.70, 123.55, 115.43, 78.61, 38.56 (ArCH_2), 28.67 (3 C, $C(CH_3)_3$).

HRMS (ESI +ve): *m*/*z* calcd for $C_{12}H_{16}N_2O_5$ [M + Na]$^+$: 291.0951; found: 291.0949.

tert-Butyl (2-Hydroxyphenethyl)carbamate (6)[10,11]

$LiAlH_4$ (366 mg, 9.65 mmol) was suspended in dry THF (3.5 mL) in a 25 mL round-bottom flask equipped with a pressure-equalizing dropping funnel, a condenser, and a drying tube. A solution of 2-(2-nitrovinyl)phenol (486 mg, 2.92 mmol) in dry THF (7 mL) was added dropwise (over 1.5 h) to a stirred and cooled (0 °C) suspension of $LiAlH_4$ (avoid boiling the solvent!). After completion of the dropwise addition, the reaction mixture was stirred for another 10 min at 0 °C, then for 2 h at room temperature. The reaction mixture was cooled to 0 °C, and then H_2O (10 mL) was added. To this mixture, 10% HCl (20 mL) was added and washed with EtOAc (2 × 10 mL). The combined organic layers were extracted with 10% HCl (3 × 10 mL). The combined aqueous layers were treated with tartaric acid (4 equiv., 1770 mg), the pH value was adjusted to 10 with concd. aq. NH_3, and the aqueous layers were extracted with $CHCl_3$ (6 × 10 mL). The organic phase was dried over Na_2SO_4. The solvent was removed under reduced pressure to afford crude (2-hydroxyphenethyl)amine, which was used in the next step without any purification. A solution of this crude material (257 mg), di-*tert*-butyldicarbonate (422 mg, 1.87 mmol), NEt_3 (0.261 mL, 1.87 mmol) in H_2O (1.9 mL), and THF (4.5 mL) was stirred overnight at room temperature. The THF was then removed by rotary evaporation, and the aqueous residue was extracted with ethyl acetate (3 × 8 mL). The organic phase was dried over Na_2SO_4. The solvent was removed under reduced pressure. The residue was purified by column chromatography to obtain the title compound as a yellowish crystals (366 mg, 52%); mp 78.5–79.7 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (br s, 1 H, OH), 7.14 (ddd, *J* = 7.66, 7.60, 1.51 Hz, 1 H, 4-Ar), 7.08 (dd, *J* = 7.5, 1.7 Hz, 1 H, 6-Ar), 6.89 (dd, *J* = 7.95, 1.10 Hz, 1 H, 3-Ar), 6.84 (ddd, *J* = 7.43, 7.39, 1.08 Hz, 1 H, 5-Ar), 4.98 (br s, 1 H, NH), 3.35 (q, *J* = 6.7 Hz, 2 H, $ArCH_2CH_2$), 2.86 (t, *J* = 7.1 Hz, 2 H, $ArCH_2CH_2$), 1.48 (s, 9 H, $C(CH_3)_3$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 157.07, 155.00, 130.54, 127.97, 124.83, 120.07, 115.97, 80.08 ($C(CH_3)_3$), 40.96 ($ArCH_2CH_2$), 31.32 ($ArCH_2CH_2$), 28.41 (3 C, $C(CH_3)_3$).

HRMS (ESI +ve): *m*/*z* calcd for $C_{13}H_{19}NO_3$ [M + Na]$^+$: 260.1257; found: 260.1259.

Compounds 7a–g; General Procedure 3 (GP3)

The appropriate *N*-Boc-protected aminophenol **4** (1.5 mmol), K_2CO_3 (311 mg, 2.25 mmol), and 18-crown-6 (40 mg, 0.15 mmol) were dissolved in HPLC-grade MeCN (6 mL) and stirred at room temperature for 15 min. KI (25 mg, 0.15 mmol) and the appropriate 4-chloro-2-diazo-3-oxobutanoate (as a solution in 1 mL of HPLC-grade CH_3CN, 286 mg, 1.5 mmol) were added, and the reaction mixture was stirred at room temperature for 6 h (TLC control). The organic solvent was removed in vacuo. The residue was dissolved in DCM (10 mL) and washed with H_2O (2 × 15 mL) and brine (15 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain the corresponding alkylation product.

Ethyl 4-(2-((*tert*-Butoxycarbonyl)amino)phenoxy)-2-diazo-3-oxobutanoate (7a)

Following GP3, *tert*-butyl (2-hydroxyphenyl)carbamate (**4a**) (320 mg, 1.53 mmol), ethyl 4-chloro-2-diazo-3-oxobutanoate (**1a**) (292 mg, 1.53 mmol), and other reagents in corresponding quantities were used to give ethyl 4-(2-((*tert*-butoxycarbonyl)amino)phenoxy)-2-diazo-3-oxobutanoate (**7a**) as a yellowish solid (417 mg, 75%); mp 124.2–125.6 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.1 Hz, 1 H, 3-Ar), 7.61 (br s, 1 H, NH), 7.00 (ddd, *J* = 7.9, 7.7, 1.5 Hz, 1 H, 5-Ar), 6.93 (ddd, *J* = 7.8, 7.6, 1.7 Hz, 1 H, 4-Ar), 6.82 (dd, *J* = 8.0, 1.5 Hz, 1 H, 6-Ar), 5.21 (s, 2 H, $OCH_2C(O)$), 4.36 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 1.55 (s, 9 H, $C(CH_3)_3$), 1.38 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, CDCl3): δ = 187.31, 161.08, 152.92, 146.64, 129.46, 122.62, 122.24, 118.98, 113.23, 80.19, 75.24 ($C=N_2$), 72.84, 61.98, 28.39 (3 C, $C(CH_3)_3$), 14.32.

HRMS (ESI +ve): *m*/*z* calcd for $C_{17}H_{21}N_3O_6$ [M + Na]$^+$: 386.1323; found: 386.1312.

Ethyl 4-(2-((*tert*-Butoxycarbonyl)amino)-4-methylphenoxy)-2-diazo-3-oxobutanoate (7b)

Following GP3, *tert*-butyl (2-hydroxy-5-methylphenyl)carbamate (**4b**) (335 mg, 1.5 mmol), ethyl 4-chloro-2-diazo-3-oxobutanoate (**1a**) (286 mg, 1.5 mmol), and other reagents in corresponding quantities were used to give ethyl 4-(2-((*tert*-butoxycarbonyl)amino)phenoxy)-2-diazo-3-oxobutanoate (**7b**) as a beige solid (449 mg, 79%); mp 98.3–98.6 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (br s, 1 H), 7.62 (br s, 1 H), 6.75–6.70 (m, 2 H, 5-Ar and 6-Ar overlapping), 5.18 (s, 2 H, $OCH_2C(O)$), 4.35 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 2.30 (s, 3 H, ArCH_3), 1.55 (s, 9 H, $C(CH_3)_3$), 1.37 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.59, 161.08, 152.98, 144.68, 132.33, 129.18, 122.58, 119.54, 113.35, 80.12, 75.20 ($C=N_2$), 73.21, 61.95, 28.39 (3 C, $C(CH_3)_3$), 21.07 ($ArCH_3$), 14.32.

HRMS (ESI +ve): *m*/*z* calcd for $C_{18}H_{23}N_3O_6$ [M + Na]$^+$: 400.1479; found: 400.1474.

Ethyl 4-(2-((*tert*-Butoxycarbonyl)amino)-4-(*tert*-butyl)phenoxy)-2-diazo-3-oxobutanoate (7c)

Following GP3, *tert*-butyl (5-(*tert*-butyl)-2-hydroxyphenyl)carbamate (**4c**) (400 mg, 1.5 mmol), ethyl 4-chloro-2-diazo-3-oxobutanoate (**1a**) (286 mg, 1.5 mmol), and other reagents in corresponding quantities

were used to give ethyl 4-(2-((*tert*-butoxycarbonyl)amino)-4-(*tert*-butyl)phenoxy)-2-diazo-3-oxobutanoate (**7c**) as a beige solid (472 mg, 75%); mp 107.1–108.3 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (br s, 1 H), 7.59 (br s, 1 H), 6.94 (dd, *J* = 8.5, 2.4 Hz, 1 H, 5-Ar), 6.74 (d, *J* = 8.5 Hz, 1 H, 6-Ar), 5.19 (s, 2 H, $OCH_2C(O)$), 4.35 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 1.56 (s, 9 H, $C(CH_3)_3$ (Boc)), 1.37 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.33 (s, 9 H, $C(CH_3)_3$ (*t*Bu-Ph)).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.61, 161.08, 152.93, 145.62, 144.55, 128.90, 118.87, 116.54, 112.82, 79.99, 75.21 (C=N_2), 73.09, 61.95, 34.51, 31.50 (3 C, $C(CH_3)_3$), 28.45 (3 C, $C(CH_3)_3$), 14.33.

HRMS (ESI +ve): *m*/*z* calcd for $C_{21}H_{29}N_3O_6$ [M + Na]$^+$: 442.1949; found: 442.1947.

Ethyl 4-(2-((*tert*-Butoxycarbonyl)amino)-4-chlorophenoxy)-2-diazo-3-oxobutanoate (7d)

Following GP3, *tert*-butyl (5-chloro-2-hydroxyphenyl)carbamate (**4d**) (370 mg, 1.5 mmol), ethyl 4-chloro-2-diazo-3-oxobutanoate (**1a**) (286 mg, 1.5 mmol), and other reagents in corresponding quantities were used to give ethyl 4-(2-((*tert*-butoxycarbonyl)amino)-4-(*tert*-butyl)phenoxy)-2-diazo-3-oxobutanoate (**7d**) as a beige solid (502 mg, 83%); mp 87.4–88.1 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (br s, 1 H), 7.61 (br s, 1 H), 6.89 (dd, *J* = 8.6, 2.5 Hz, 1 H, 5-Ar), 6.73 (d, *J* = 8.7 Hz, 1 H, 6-Ar), 5.20 (s, 2 H, $OCH_2C(O)$), 4.36 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 1.56 (s, 9 H, $C(CH_3)_3$), 1.38 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.00, 161.02, 152.56, 145.12, 130.52, 127.88, 121.71, 118.81, 114.09, 80.71, 75.27 (C=N_2), 72.99, 62.05, 28.33 (3 C, $C(CH_3)_3$), 14.33.

HRMS (ESI +ve): *m*/*z* calcd for $C_{17}H_{20}ClN_3O_6$ [M + Na]$^+$: 420.0933; found: 420.0929.

Ethyl 4-(2,4-Bis((*tert*-butoxycarbonyl)amino)phenoxy)-2-diazo-3-oxobutanoate (7e)

Following GP3, di-*tert*-butyl (4-hydroxy-1,3-phenylene)dicarbamate (**4f**) (490 mg, 1.5 mmol), ethyl 4-chloro-2-diazo-3-oxobutanoate (**1a**) (286 mg, 1.5 mmol), and other reagents in corresponding quantities were used to give ethyl 4-(2,4-bis((*tert*-butoxycarbonyl)amino)phenoxy)-2-diazo-3-oxobutanoate (**7e**) as a colorless solid (526 mg, 73%); mp 157.9–158.4 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 2.6 Hz, 1 H, 3-Ar), 7.69 (br s, 1 H), 7.24 (br s, 1 H), 6.78 (d, *J* = 8.8 Hz, 1 H, 6-Ar), 6.40 (br s, 1 H), 5.17 (s, 2 H, $OCH_2C(O)$), 4.35 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 1.54 (s, 9 H, $C(CH_3)_3$), 1.51 (s, 9 H, $C(CH_3)_3$), 1.37 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.62, 161.05, 152.96, 152.82, 142.73, 133.35, 129.95, 114.36, 112.69, 109.93, 80.36, 80.20, 75.24 (C=N_2), 73.60, 61.98, 28.36 (3 C, $C(CH_3)_3$), 28.34 (3 C, $C(CH_3)_3$), 14.32.

HRMS (ESI +ve): *m*/*z* calcd for $C_{22}H_{30}N_4O_8$ [M + Na]$^+$: 501.1956; found: 501.1968.

Ethyl 4-(2-((*tert*-Butoxycarbonyl)amino)-4-(pyrrolidine-1-carbonyl)phenoxy)-2-diazo-3-oxobutanoate (7f)

Following GP3, *tert*-butyl (2-hydroxy-5-(pyrrolidine-1-carbonyl)phenyl)carbamate (**4g**) (150 mg, 0.49 mmol), K_2CO_3 (135 mg, 0.98 mmol), 18-crown-6 (13 mg, 0.05 mmol), KI (8 mg, 0.05 mmol), and ethyl 4-chloro-2-diazo-3-oxobutanoate (**1a**) (140 mg, 0.73 mmol) were used in HPLC-grade CH_3CN (5 mL) for a reaction time of 31 h. Yield 94 mg (42%); brownish wax; mp 106.8–107.6 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (br s, 1 H), 7.55 (br s, 1 H), 7.19 (dd, *J* = 8.4, 2.1 Hz, 1 H, 5-Ar), 6.81 (d, *J* = 8.4 Hz, 1 H, 6-Ar), 5.24 (s, 2 H, $OCH_2C(O)$), 4.37 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 3.57 (dt, *J* = 42.0, 6.6 Hz, 4 H, pyrrolidine), 2.00–1.84 (m, 4 H, pyrrolidine), 1.55 (s, 9 H, $C(CH_3)_3$), 1.39 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 186.79, 169.26, 161.04, 152.70, 147.38, 131.31, 128.70, 121.93, 117.75, 112.59, 80.45, 75.32 (C=N_2), 72.44, 62.06, 28.37 (3 C, $C(CH_3)_3$), 14.33.

HRMS (ESI +ve): *m*/*z* calcd for $C_{22}H_{28}N_4O_7$ [M + Na]$^+$: 483.1850; found: 483.1862.

Methyl 4-(2-((*tert*-Butoxycarbonyl)amino)-4-chlorophenoxy)-2-diazo-3-oxopentanoate (7g)

Following GP3, *tert*-butyl (5-chloro-2-hydroxyphenyl)carbamate (**4d**) (300 mg, 1.23 mmol), K_2CO_3 (255 mg, 1.85 mmol), 18-crown-6 (33 mg, 0.12 mmol), KI (20 mg, 0.12 mmol), and methyl 4-chloro-2-diazo-3-oxopentanoate **1b** (235 mg, 1.23 mmol) were used in HPLC-grade CH_3CN (3 mL). In this case, the reaction temperature was 30 °C and the reaction time was 51 h. Yield 198 mg (40%); beige solid; mp 115.4–116.2 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (br s, 1 H), 7.55 (br s, 1 H), 6.85 (dd, *J* = 8.6, 2.6 Hz, 1 H, 5-Ar), 6.69 (d, *J* = 8.7 Hz, 1 H, 6-Ar), 5.76 (q, *J* = 6.7 Hz, 1 H, $CHCH_3$), 3.89 (s, 3 H, OCH_3), 1.63 (d, *J* = 6.7 Hz, 3 H, $CHCH_3$), 1.56 (s, 9 H, $C(CH_3)_3$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 190.72, 161.07, 152.57, 144.32, 130.59, 127.74, 121.71, 118.86, 114.58, 80.71, 77.17 ($CHCH_3$), 75.54 (C=N_2), 52.58, 28.34 (3 C, $C(CH_3)_3$) 18.17 ($CHCH_3$).

HRMS (ESI +ve): *m*/*z* calcd for $C_{17}H_{20}ClN_3O_6$ [M + Na]$^+$: 420.0933; found: 420.0943.

Compounds 8a–e and 9; General Procedure 4 (GP4)

The appropriate *N*-Boc-protected salicylamine (0.63 mmol), K_2CO_3 (131 mg, 0.95 mmol), and 18-crown-6 (17 mg, 0.064 mmol) were dissolved in HPLC-grade CH_3CN (2 mL) and stirred at room temperature for 15 min. KI (11 mg, 0.066 mmol) and ethyl 4-chloro-2-diazo-3-oxobutanoate (as a solution in 1 mL of HPLC-grade CH_3CN, 145 mg, 0.76 mmol) were added, and the reaction mixture was stirred at room temperature for the indicated time (TLC control). The organic solvent was removed in vacuo. The residue was dissolved in DCM (15 mL) and washed with H_2O (2 × 10 mL) and brine (10 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain the corresponding alkylation product.

Ethyl 4-(2-(((*tert*-Butoxycarbonyl)amino)methyl)phenoxy)-2-diazo-3-oxobutanoate (8a)

Following GP4, *tert*-butyl (2-hydroxybenzyl)carbamate (**5a**) (140 mg, 0.63 mmol) and other reagents were used in the indicated quantities with a reaction time of 24 h. Yield 138 mg (58%); colorless solid; mp 60.4–61.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 7.5 Hz, 1 H, 3-Ar), 7.22 (ddd, *J* = 7.86, 7.80, 1.74 Hz, 1 H, 5-Ar), 6.96 (ddd, *J* = 7.46, 7.44, 1.07 Hz, 1 H, 4-Ar), 6.79 (dd, *J* = 8.2, 0.9 Hz, 1 H, 6-Ar), 5.67 (br s, 1 H, NH), 5.22 (s, 2 H, $OCH_2C(O)$), 4.45–4.30 (m, 4 H, $ArCH_2$ and OCH_2CH_3 overlapping), 1.46 (s, 9 H, $C(CH_3)_3$), 1.39 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.13, 161.13, 156.17, 156.09, 130.06, 128.54, 128.02, 121.67, 111.57, 78.94, 75.31 (C=N_2), 71.02, 61.95, 40.72 ($ArCH_2$), 28.47 (3 C, $C(CH_3)_3$), 14.33.

HRMS (ESI +ve): *m*/*z* calcd for $C_{18}H_{23}N_3O_6$ [M + H]$^+$: 378.1660; found: 378.1660.

Ethyl 4-(2-(((*tert*-Butoxycarbonyl)amino)methyl)-6-methoxyphenoxy)-2-diazo-3-oxobutanoate (8b)

Following GP4, *tert*-butyl (2-hydroxy-3-methoxybenzyl)carbamate (**5b**) (160 mg, 0.63 mmol) and other reagents were used in the indicated quantities with a reaction time of 24 h. Yield 138 mg (54%); pale green oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.02 (dd, *J* = 7.91, 7.82 Hz, 1 H, 4-Ar), 6.96 (d, *J* = 7.5 Hz, 1 H, Ar), 6.85 (dd, *J* = 8.1, 1.7 Hz, 1 H, Ar), 5.65 (br s, 1 H, NH), 5.25 (s, 2 H, $OCH_2C(O)$), 4.41 (d, *J* = 6.2 Hz, 2 H, $ArCH_2$), 4.32 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 3.86 (s, 3 H, OCH_3), 1.45 (s, 9 H, $C(CH_3)_3$), 1.36 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 188.46, 161.10, 156.10, 151.64, 145.76, 132.83, 124.07, 121.77, 111.93, 78.99, 75.25, 75.07 (C=N_2), 61.75, 55.90, 40.57 ($ArCH_2$), 28.44 (3 C, $C(CH_3)_3$), 14.31.

HRMS (ESI +ve): *m*/*z* calcd for $C_{19}H_{25}N_3O_7$ [M + H]$^+$: 408.1765; found: 408.1765.

Ethyl 4-((1-(((*tert*-Butoxycarbonyl)amino)methyl)naphthalen-2-yl)oxy)-2-diazo-3-oxobutanoate (8c)

In this case, 1.5 equiv. of ethyl 4-chloro-2-diazo-3-oxobutanoate and 2 equiv. of K_2CO_3 were used. Following GP4, *tert*-butyl ((2-hydroxynaphthalen-1-yl)methyl)carbamate (**5c**) (173 mg, 0.63 mmol), K_2CO_3 (175 mg, 1.27 mmol), 18-crown-6 (17 mg, 0.064 mmol), KI (11 mg, 0.066 mmol), and ethyl 4-chloro-2-diazo-3-oxobutanoate (181 mg, 0.95 mmol) were used in HPLC-grade CH_3CN (3 mL) with a reaction time of 24 h. Yield 196 mg (72%); colorless solid; mp 122.2–123.1 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (d, *J* = 8.6 Hz, 1 H, Ar), 7.80–7.77 (m, 2 H, Ar), 7.56 (dd, *J* = 7.56, 7.42 Hz, 1 H, Ar), 7.39 (ddd, *J* = 8.0, 6.8, 1.1 Hz, 1 H, Ar), 7.16 (d, *J* = 9.1 Hz, 1 H, Ar), 5.56 (t, *J* = 5.2 Hz, 1 H, NH), 5.37 (s, 2 H, $OCH_2C(O)$), 4.92 (d, *J* = 5.6 Hz, 2 H, $ArCH_2$), 4.38 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 1.46 (s, 9 H, $C(CH_3)_3$), 1.39 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.67, 161.13, 156.00, 153.98, 132.84, 129.68, 129.59, 128.28, 127.14, 124.08, 123.89, 121.27, 113.73, 78.90, 75.30 (C=N_2), 72.01, 61.97, 34.92 ($ArCH_2$), 28.48 (3 C, $C(CH_3)_3$), 14.34.

HRMS (ESI +ve): *m*/*z* calcd for $C_{22}H_{25}N_3O_6$ [M + Na]$^+$: 450.1636; found: 450.1647.

Ethyl 4-(2-(((*tert*-Butoxycarbonyl)amino)methyl)-4-chlorophenoxy)-2-diazo-3-oxobutanoate (8d)

Following GP4, *tert*-butyl (5-chloro-2-hydroxybenzyl)carbamate (**5d**) (163 mg, 0.63 mmol) and other reagents were used in the indicated quantities with a reaction time of 15 h. Yield 169 mg (65%); colorless solid; mp 79.8–81.1 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (br s, 1 H, 3-Ar, overlapping with $CDCl_3$), 7.17 (dd, *J* = 8.7, 2.7 Hz, 1 H, 5-Ar), 6.71 (d, *J* = 8.8 Hz, 1 H, 6-Ar), 5.56 (br s, 1 H, NH), 5.19 (s, 2 H, $OCH_2C(O)$), 4.40–4.34 (m, 4 H, OCH_2CH_3 and $ArCH_2$ overlapping), 1.47 (s, 9 H, $C(CH_3)_3$), 1.39 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 186.80, 161.08, 156.07, 154.67, 129.85, 129.60, 128.06, 126.45, 112.85, 79.43, 75.36 (C=N_2), 71.26, 62.02, 40.43 ($ArCH_2$), 28.42 (3 C, $C(CH_3)_3$), 14.33.

HRMS (ESI +ve): *m*/*z* calcd for $C_{18}H_{22}ClN_3O_6$ [M + Na]$^+$: 434.1089; found: 434.1098.

Ethyl 4-(2-(((*tert*-Butoxycarbonyl)amino)methyl)-4-nitrophenoxy)-2-diazo-3-oxobutanoate (8e)

Following GP4, *tert*-butyl (2-hydroxy-5-nitrobenzyl)carbamate (**5e**) (170 mg, 0.63 mmol) and other reagents were used in the indicated quantities. In this case, because of the poor solubility of **5e** in CH_3CN, the reaction was performed in a mixture of CH_3CN (1.5 mL) and dry DMF (1.5 mL). The reaction time was 15 h. Yield 110 mg (41%); brownish solid; mp 97.7–98.4 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (d, *J* = 2.8 Hz, 1 H, 3-Ar), 8.15 (dd, *J* = 9.0, 2.8 Hz, 1 H, 5-Ar), 6.81 (d, *J* = 9.1 Hz, 1 H, 6-Ar), 5.42 (br s, 1 H, NH), 5.32 (s, 2 H, $OCH_2C(O)$), 4.46 (d, *J* = 6.2 Hz, 2 H, $ArCH_2$), 4.39 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 1.48 (s, 9 H, $C(CH_3)_3$), 1.40 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 185.64, 161.03, 160.70, 155.93, 141.92, 129.30, 124.69 (2 C), 111.12, 79.70, 75.49 (C=N_2), 71.16, 62.18, 40.01 ($ArCH_2$), 28.39 (3 C, $C(CH_3)_3$), 14.34.

HRMS (ESI +ve): *m*/*z* calcd for $C_{18}H_{22}N_4O_8$ [M + Na]$^+$: 445.1330; found: 445.1333.

Ethyl 4-(2-(2-((*tert*-Butoxycarbonyl)amino)ethyl)phenoxy)-2-diazo-3-oxobutanoate (9)

Following GP4, *tert*-butyl (2-hydroxyphenethyl)carbamate **6** (150 mg, 0.63 mmol) and other reagents were used in the indicated quantities with a reaction time of 15.5 h. Yield 130 mg (53%); pale green oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19–7.16 (m, 2 H, Ar), 6.94 (ddd, *J* = 7.47, 7.45 1.06 Hz, 1 H, Ar), 6.74 (d, *J* = 8.44 Hz, 1 H, Ar), 5.20 (s, 2 H, $OCH_2C(O)$), 4.99 (br s, 1 H, NH), 4.37 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 3.44 (td, *J* = 6.05, 5.89 Hz, 2 H, $ArCH_2CH_2$), 2.92 (t, *J* = 6.6 Hz, 2 H, $ArCH_2CH_2$), 1.43 (s, 9 H, $C(CH_3)_3$), 1.39 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.04, 161.17, 156.16, 156.01, 131.09, 128.26, 127.57, 121.53, 111.30, 78.77, 75.25 (C=N_2), 70.80, 61.92, 30.79 ($ArCH_2CH_2$), 28.41 (3 C, $C(CH_3)_3$), 28.38 ($ArCH_2CH_2$), 14.34.

HRMS (ESI +ve): *m*/*z* calculated for $C_{19}H_{25}N_3O_6$ [M + Na]$^+$: 414.1636; found: 414.1638.

Alkyl 4*H*-Benzo[*b*][1,2,3]triazolo[1,5-*d*][1,4]oxazine-3-carboxylates 10a–g; General Procedure 5 (GP5)

TFA (0.386 mL, 5 mmol) was added to a solution of the appropriate alkyl 4-(2-((*tert*-butoxycarbonyl)amino)phenoxy)-2-diazo-3-oxobutanoate **7a–g** (0.5 mmol) in DCM (4 mL), and the reaction mixture was stirred at room temperature for 18 h. The organic solvent was washed with a sat. solution of $NaHCO_3$ (2 × 4 mL) and H_2O (4 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the corresponding alkyl 4*H*-benzo[*b*][1,2,3]triazolo[1,5-*d*][1,4]oxazine-3-carboxylate.

Ethyl 4*H*-Benzo[*b*][1,2,3]triazolo[1,5-*d*][1,4]oxazine-3-carboxylate (10a)

Following GP5, ethyl 4-(2-((*tert*-butoxycarbonyl)amino)phenoxy)-2-diazo-3-oxobutanoate (**7a**) (182 mg, 0.5 mmol) and the indicated amount of TFA were used to obtain the title compound as a brown solid (102 mg, 83%); mp 130.5–131.8 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (dd, *J* = 8.0, 1.6 Hz, 1 H, 9-Ar), 7.35 (ddd, *J* = 8.0, 7.9, 1.6 Hz, 1 H, 7-Ar), 7.23–7.12 (m, 2 H, 8-Ar and 6-Ar overlapping), 5.66 (s, 2 H, $ArOCH_2$), 4.49 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 1.47 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.63, 145.22, 134.86, 131.49, 129.76, 123.17, 123.16, 117.89, 116.95, 62.22, 61.61, 14.32.

HRMS (ESI +ve): *m*/*z* calcd for $C_{12}H_{11}N_3NaO_3$ [M + Na]$^+$: 268.0693; found: 268.0681.

Ethyl 8-Methyl-4*H*-benzo[*b*][1,2,3]triazolo[1,5-*d*][1,4]oxazine-3-carboxylate (10b)

Following GP5, ethyl 4-(2-((*tert*-butoxycarbonyl)amino)-4-methylphenoxy)-2-diazo-3-oxobutanoate (**7b**) (190 mg, 0.5 mmol) and the indicated amount of TFA were used to obtain the title compound as a brownish solid (119 mg, 91%); mp 110.9–111.7 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 2.1 Hz, 1 H, 9-Ar), 7.13 (dd, *J* = 8.5, 2.1 Hz, 1 H, 7-Ar), 7.04 (d, *J* = 8.4 Hz, 1 H, 6-Ar), 5.61 (s, 2 H, ArOC*H*$_2$), 4.48 (q, *J* = 7.1 Hz, 2 H, OC*H*$_2$CH$_3$), 2.41 (s, 3 H, ArC*H*$_3$), 1.47 (t, *J* = 7.1 Hz, 3 H, OCH$_2$C*H*$_3$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.67, 143.01, 134.81, 133.20, 131.60, 130.29, 122.86, 117.56, 117.15, 62.14, 61.57, 20.77, 14.32.

HRMS (ESI +ve): *m*/*z* calcd for $C_{13}H_{13}N_3NaO_3$ [M + Na]$^+$: 282.0849; found: 282.0846.

Ethyl 8-(*tert*-Butyl)-4*H*-benzo[*b*][1,2,3]triazolo[1,5-*d*][1,4]oxazine-3-carboxylate (10c)

Following GP5, ethyl 4-(2-((*tert*-butoxycarbonyl)amino)-4-(*tert*-butyl)phenoxy)-2-diazo-3-oxobutanoate (**7c**) (210 mg, 0.5 mmol) and the indicated amount of TFA were used to obtain the title compound as a brown solid (132 mg, 87%); mp 97.6–99.1 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 2.4 Hz, 1 H, 9-Ar), 7.36 (dd, *J* = 8.7, 2.4 Hz, 1 H, 7-Ar), 7.08 (d, *J* = 8.6 Hz, 1 H, 6-Ar), 5.61 (s, 2 H, ArOC*H*$_2$), 4.49 (q, *J* = 7.1 Hz, 2 H, OC*H*$_2$CH$_3$), 1.47 (t, *J* = 7.1 Hz, 3 H, OCH$_2$C*H*$_3$), 1.39 (s, 9 H, C(CH$_3$)$_3$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.71, 146.87, 142.90, 134.82, 131.65, 126.74, 122.75, 117.34, 113.90, 62.14, 61.58, 34.73, 31.32 (3 C, C(*C*H$_3$)$_3$), 14.33.

HRMS (ESI +ve): *m*/*z* calcd for $C_{16}H_{19}N_3NaO_3$ [M + Na]$^+$: 324.1319; found: 324.1315.

Ethyl 8-Chloro-4*H*-benzo[*b*][1,2,3]triazolo[1,5-*d*][1,4]oxazine-3-carboxylate (10d)

Following GP5, ethyl 4-(2-((*tert*-butoxycarbonyl)amino)-4-chlorophenoxy)-2-diazo-3-oxobutanoate (**7d**) (200 mg, 0.5 mmol) and the indicated amount of TFA were used to obtain the title compound as a beige solid (118 mg, 84%); mp 139.6–140.8 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 2.4 Hz, 1 H, 9-Ar), 7.30 (dd, *J* = 8.8, 2.5 Hz, 1 H, 7-Ar, overlapping with $CDCl_3$), 7.10 (d, *J* = 8.8 Hz, 1 H, 6-Ar), 5.65 (s, 2 H, ArOC*H*$_2$), 4.48 (q, *J* = 7.1 Hz, 2 H, OC*H*$_2$CH$_3$), 1.46 (t, *J* = 7.2 Hz, 3 H, OCH$_2$C*H*$_3$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.44, 143.68, 135.11, 131.37, 129.65, 128.31, 123.55, 119.13, 117.10, 62.41, 61.74, 14.31.

HRMS (ESI +ve): *m*/*z* calcd for $C_{16}H_{19}N_3NaO_3$ [M + Na]$^+$: 302.0303; found: 302.0301.

Ethyl 8-Amino-4*H*-benzo[*b*][1,2,3]triazolo[1,5-*d*][1,4]oxazine-3-carboxylate (10e)

TFA (0.576 mL, 7.5 mmol) was added to a solution of ethyl 4-(2,4-bis((*tert*-butoxycarbonyl)amino)phenoxy)-2-diazo-3-oxobutanoate (**7e**) (240 mg, 0.5 mmol) in DCM (4 mL), and the reaction was stirred at room temperature overnight. The organic solvent was removed in vacuo. The residue was dissolved in EtOAc (10 mL) and washed with a sat. solution of $NaHCO_3$ (2 × 10 mL) and H_2O (10 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the title compound as a beige solid (62 mg, 47%); mp 207.8–208.7 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 2.7 Hz, 1 H, 9-Ar), 6.97 (d, *J* = 8.7 Hz, 1 H, 6-Ar), 6.65 (dd, *J* = 8.8, 2.7 Hz, 1 H, 7-Ar), 5.54 (s, 2 H, ArOC*H*$_2$), 4.48 (q, *J* = 7.1 Hz, 2 H, OC*H*$_2$CH$_3$), 3.76 (br s, 2 H, NH$_2$), 1.46 (t, *J* = 7.1 Hz, 3 H, OCH$_2$C*H*$_3$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.71, 142.41, 137.55, 134.75, 132.04, 123.69, 118.60, 116.12, 103.02, 62.04, 61.54, 14.32.

HRMS (ESI +ve): *m*/*z* calcd for $C_{12}H_{12}N_4O_3$ [M + Na]$^+$: 283.0802; found: 283.0807.

Ethyl 8-(Pyrrolidine-1-carbonyl)-4*H*-benzo[*b*][1,2,3]triazolo[1,5-*d*]-[1,4]oxazine-3-carboxylate (10f)

Following GP5, ethyl 4-(2-((*tert*-butoxycarbonyl)amino)-4-(pyrrolidine-1-carbonyl)phenoxy)-2-diazo-3-oxobutanoate (**7f**) (63 mg, 0.137 mmol) and TFA (0.105 mL, 1.37 mmol) were used in DCM (1.1 mL). In this case, the reaction time was 23 h. Yield 28 mg (60%); beige solid; mp 167.4–168.3 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.13 (d, *J* = 2.0 Hz, 1 H, 9-Ar), 7.59 (dd, *J* = 8.5, 2.0 Hz, 1 H, 7-Ar), 7.27 (d, *J* = 8.4 Hz, 1 H, 6-Ar), 5.78 (s, 2 H, ArOC*H*$_2$), 4.36 (q, *J* = 7.0 Hz, 2 H, OC*H*$_2$CH$_3$), 3.49 (t, *J* = 6.5 Hz, 4 H, pyrrolidine), 1.88 (p, *J* = 6.3, 5.9 Hz, 4 H, pyrrolidine), 1.35 (t, *J* = 7.1 Hz, 3 H, OCH$_2$C*H*$_3$).

^{13}C NMR (101 MHz, DMSO-*d*6): δ = 166.78, 160.26, 146.38, 134.77, 132.62, 132.13, 129.31, 122.53, 117.94, 115.88, 62.99, 61.56, 49.48, 46.66, 26.51, 24.35, 14.54.

HRMS (ESI +ve): *m*/*z* calcd for $C_{12}H_{12}N_4O_3$ [M + Na]$^+$: 365.1220; found: 365.1229.

Methyl 8-Chloro-4-methyl-4*H*-benzo[*b*][1,2,3]triazolo-[1,5-*d*][1,4]oxazine-3-carboxylate (10g)

Following GP5, methyl 4-(2-((*tert*-butoxycarbonyl)amino)-4-chlorophenoxy)-2-diazo-3-oxopentanoate **7g** (125 mg, 0.314 mmol) and TFA (0.241 mL, 3.14 mmol) were used in DCM (2 mL) to afford the title compound as a beige solid (78 mg, 89%); mp 151.2–152.3 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 2.5 Hz, 1 H, 9-Ar), 7.31 (dd, *J* = 8.8, 2.5 Hz, 1 H, 7-Ar, overlapping with $CDCl_3$), 7.10 (d, *J* = 8.7 Hz, 1 H, 6-Ar), 6.13 (q, *J* = 6.8 Hz, 1 H, C*H*CH$_3$), 4.02 (s, 3 H, OCH$_3$), 1.62 (d, *J* = 6.8 Hz, 3H, CHC*H*$_3$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.91, 142.01, 135.25, 134.22, 129.80, 127.98, 122.93, 119.84, 116.96, 69.93, 52.46, 19.72.

HRMS (ESI +ve): *m*/*z* calcd for $C_{12}H_{10}ClN_3O_3$ [M + Na]$^+$: 302.0303; found: 302.0310.

Ethyl 4*H*,10*H*-Benzo[*f*][1,2,3]triazolo[5,1-*c*][1,4]oxazepine-3-carboxylates 11a–e; General Procedure 6 (GP6)

TFA (0.141 mL, 1.84 mmol) was added to a solution of the appropriate ethyl 4-(2-(((*tert*-butoxycarbonyl)amino)methyl)phenoxy)-2-diazo-3-oxobutanoate **8a–e** (0.18 mmol) in DCM (1.2 mL), and the reaction mixture was stirred at room temperature for 18 h. The organic solvent was removed in vacuo. The residue was dissolved in MeOH (2 mL), and AcONa (121 mg, 1.47 mmol) was added. The reaction mixture was stirred at 45 °C for 22.5 h (TLC control). The MeOH was evaporated in vacuo. The residue was dissolved in DCM (5 mL) and washed with a sat. solution of $NaHCO_3$ (2 × 5 mL) and H_2O (5 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the corresponding ethyl 4*H*,10*H*-benzo[*f*][1,2,3]triazolo[5,1-*c*][1,4]oxazepine-3-carboxylate.

Ethyl 4*H*,10*H*-Benzo[*f*][1,2,3]triazolo[5,1-*c*][1,4]oxazepine-3-carboxylate (11a)

Following GP6, ethyl 4-(2-(((*tert*-butoxycarbonyl)amino)methyl)phenoxy)-2-diazo-3-oxobutanoate (**8a**) (70 mg, 0.18 mmol) and other reagents in the indicated quantities were used. In this case, the crude product was purified by column chromatography to obtain the title compound as a brownish solid (33 mg, 69%); mp 102.1–103.3 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 (ddd, *J* = 7.76, 7.75, 1.68 Hz, 1 H, 7-Ar), 7.40 (dd, *J* = 7.5, 1.6 Hz, 1 H, 9-Ar), 7.29–7.26 (m, 1 H, 6-Ar, overlapping with $CDCl_3$), 7.22 (ddd, *J* = 7.6, 7.5, 1.2 Hz, 1 H, 8-Ar), 5.72 (s, 2 H), 5.53 (s, 2 H), 4.41 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 1.42 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.10, 157.97, 138.84, 135.96, 131.32, 129.12, 128.34, 125.65, 121.85, 68.07, 61.28, 51.25, 14.33.

HRMS (ESI +ve): *m*/*z* calcd for $C_{13}H_{13}N_3O_3$ [M + Na]$^+$: 282.0849; found: 282.0849.

Ethyl 6-Methoxy-4*H*,10*H*-benzo[*f*][1,2,3]triazolo[5,1-*c*][1,4]oxazepine-3-carboxylate (11b)

Following GP6, ethyl 4-(2-(((*tert*-butoxycarbonyl)amino)methyl)-6-methoxyphenoxy)-2-diazo-3-oxobutanoate (**8b**) (75 mg, 0.18 mmol) and other reagents in the indicated quantities were used to afford the title compound as a colorless solid (39 mg, 73%); mp 121.1–122.3 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.16 (dd, *J* = 8.4, 7.6 Hz, 1 H, Ar), 7.03 (dd, *J* = 8.5, 1.5 Hz, 1 H, Ar), 6.97 (dd, *J* = 7.6, 1.4 Hz, 1 H, Ar), 5.71 (s, 2 H), 5.53 (s, 2 H), 4.41 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 3.94 (s, 3 H, OCH_3), 1.41 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.05, 152.24, 146.10, 139.04, 136.00, 130.26, 126.07, 120.34, 113.69, 67.58, 61.24, 56.05, 51.13, 14.34.

HRMS (ESI +ve): *m*/*z* calcd for $C_{14}H_{15}N_3O_4$ [M + Na]$^+$: 312.0955; found: 312.0960.

Ethyl 8*H*,13*H*-Naphtho[1,2-*f*][1,2,3]triazolo[5,1-*c*][1,4]oxazepine-9-carboxylate (11c)

Following GP6, ethyl 4-((1-(((*tert*-butoxycarbonyl)amino)methyl)naphthalen-2-yl)oxy)-2-diazo-3-oxobutanoate (**8c**) (79 mg, 0.18 mmol) and other reagents in the indicated quantities were used to afford the title compound as a beige solid (45 mg, 79%); mp 146.7–147.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 8.5 Hz, 1 H, Ar), 7.94 (d, *J* = 8.7 Hz, 1 H, Ar), 7.90 (d, *J* = 8.2 Hz, 1 H, Ar), 7.64 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1 H, Ar), 7.52 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1 H, Ar), 7.42 (d, *J* = 8.8 Hz, 1 H, Ar), 6.19 (s, 2 H), 5.60 (s, 2 H), 4.41 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 1.41 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.09, 156.16, 138.91, 136.00, 131.75, 131.44, 130.72, 128.93, 127.75, 125.72, 123.12, 122.38, 120.77, 67.92, 61.28, 45.56, 14.33.

HRMS (ESI +ve): *m*/*z* calcd for $C_{17}H_{15}N_3O_3$ [M + Na]$^+$: 332.1006; found: 332.1008.

Ethyl 8-Chloro-4*H*,10*H*-benzo[*f*][1,2,3]triazolo[5,1-*c*][1,4]oxazepine-3-carboxylate (11d)

Following GP6, ethyl 4-(2-(((*tert*-butoxycarbonyl)amino)methyl)-4-chlorophenoxy)-2-diazo-3-oxobutanoate (**8d**) (76 mg, 0.18 mmol) and other reagents in the indicated quantities were used to afford the title compound as a beige solid (41 mg, 76%); mp 154.4–155.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.39 (m, 2 H, Ar), 7.21 (d, *J* = 9.2 Hz, 1 H, Ar), 5.67 (s, 2 H), 5.52 (s, 2 H), 4.41 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 1.41 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.01, 156.43, 138.50, 136.08, 131.17, 130.76, 129.75, 129.13, 123.30, 68.09, 61.38, 50.73, 14.31.

HRMS (ESI +ve): *m*/*z* calcd for $C_{13}H_{12}ClN_3O_3$ [M + Na]$^+$: 316.0459; found 316.0461.

Ethyl 8-Nitro-4*H*,10*H*-benzo[*f*][1,2,3]triazolo[5,1-*c*][1,4]oxazepine-3-carboxylate (11e)

Following GP6, ethyl 4-(2-(((*tert*-butoxycarbonyl)amino)methyl)-4-nitrophenoxy)-2-diazo-3-oxobutanoate (**8e**) (78 mg, 0.18 mmol) and other reagents in the indicated quantities were used to afford the title compound as a beige solid (39 mg, 69%); mp 163.9–164.9 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.35–8.30 (m, 2 H, 7-Ar and 9-Ar overlapping), 7.43–7.37 (m, 1 H, 6-Ar), 5.83 (s, 2 H), 5.66 (s, 2 H), 4.44 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 1.44 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 162.49, 160.87, 144.45, 137.52, 136.47, 127.82, 126.77, 125.11, 123.11, 66.81, 61.57, 50.63, 14.29.

HRMS (ESI +ve): *m*/*z* calcd for $C_{13}H_{12}N_4O_5$ [M + Na]$^+$: 327.0700; found: 327.0700.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/a-1348-9031. Copies of the ^{1}H and ^{13}C NMR spectra are included.

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