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Unlocking the Potential of Phenacyl Protecting Groups – CO_2-Based Formation and Photocatalytic Release of Caged Amines

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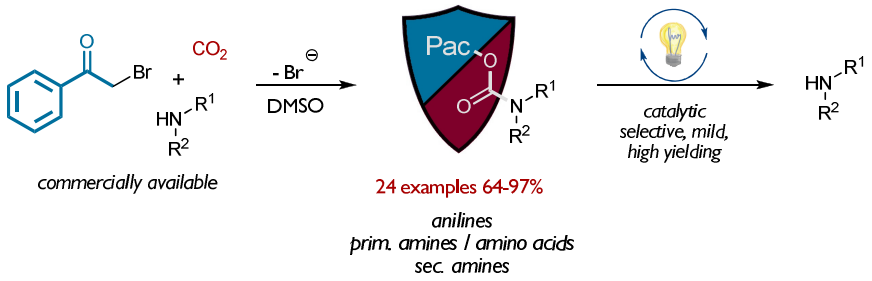
Supporting Information Placeholder



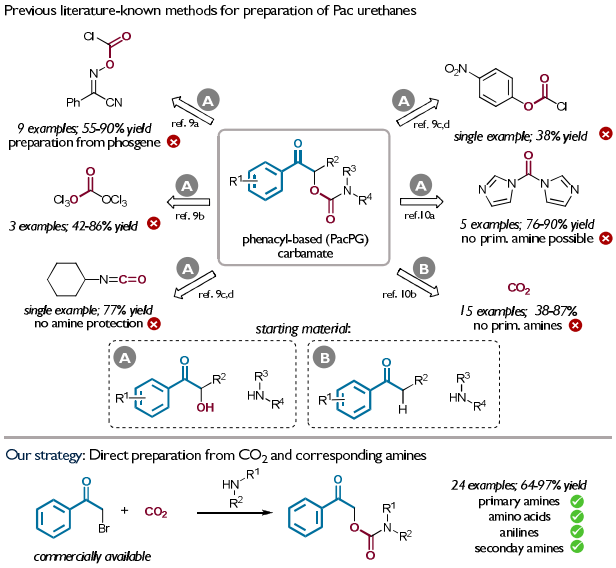
ABSTRACT: Orthogonal protection and deprotection of amines remain important tools in synthetic design as well as in chemical biology and material research applications. A robust, highly efficient and sustainable method for the formation of phenacyl based carbamate esters has been developed using CO_2 for the *in situ* preparation of the intermediate carbamates. Our mild and broadly applicable protocol allows for the formation of phenacyl urethanes of anilines, primary amines, including amino acids, and secondary amines in high to excellent yields. Moreover, we demonstrate the utility by a mild and convenient photocatalytic deprotection protocol using visible light. Key feature of the $[Ru(bpy)_3](PF_6)_2$-catalyzed method is the use of ascorbic acid as reductive quencher in a neutral, buffered, two-phase acetonitrile/water mixture granting fast and highly selective deprotection for all presented examples.

INTRODUCTION

In recent years organic synthesis has witnessed an increasing emphasis on efficiency, hence aiming at redox,[1a] atom,[1b] pot[1c] as well as step economy.[1d] Although this ultimately implies to minimize the use of protection/deprotection manipulations, accessing control over reactivity within multifunctional complex molecular systems is still a fundamental challenge in chemistry. Hence, powerful synthetic tools, such as activating,[2] directing[3] as well as protecting groups,[4] continue to be of essential importance and often play critical roles in multistep syntheses. Moreover, protecting groups (caging groups) are also widely applied in biological studies, analytics and polymer material sciences, whenever the controlled release of a certain molecular entity is required, being triggered by an external event.

From a practical point of view broadly applicable protecting groups need to meet a number of prerequisites. Starting from inexpensive and readily (preferably commercially) available precursors their introduction should proceed easily in an efficient and selective manner to provide stable protected products in high yields, allowing for purification, storage and a wide range of reaction conditions for further manipulations. For complex settings, such as multistep syntheses, polyfunctional molecules or late stage deprotections, orthogonality is of crucial importance. Therefore cleavage should also occur under mild, but highly selective conditions under which potentially generated by-products are non-reactive[5] and easy to separate. Catalytic deprotections,[6] but by far more significantly, photoremovable protecting groups (PRPG)[4b] fulfil quite a number of the aforementioned requirements and additionally offer the precise resolution for spatial and temporal control of deprotection by an external trigger. As a consequence photocleavable protecting groups are of crucial importance, but still limited to a small number of possible structural motifs.[4b]

Scheme 1. Strategies for the formation of Phenacyl (Pac) urethanes.



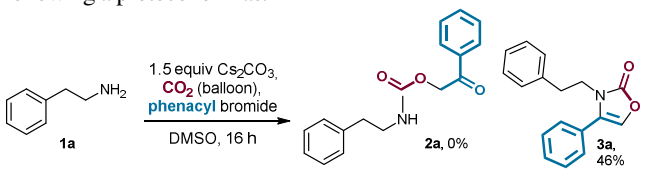
Especially phenacyl based (Pac) scaffolds have found widespread application for the design of photocleavable protecting groups, as, for example, their resulting Pac esters can be cleaved effectively with either UV light,[7] or, as recently documented, in a photocatalytic approach with visible light.[8] Besides the remarkable orthogonality of Pac protected carboxylic acids to common protecting group cleavage protocols (TFA, piperidine etc.) our photocatalytic cleavage mechanism grants tolerance to a great variety of functional groups.[8] But despite the excellent suitability of Pac as an orthogonal protecting group motif, until now Pac has mainly been used for the protection of carboxylic acids, while examples for amine protection remain rather scare,[9] not least due to the fact that typical transfer reagents such as its chloroformate or bicarbonate (Pac_2O) derivatives are not stable. In addition to the hence often required employment of harsh conditions and highly toxic and cumbersome chemicals like phosgene (and equivalents) for the formation of phenacyl urethanes,[10] the strongly limited substrate of all other reported protocols to secondary amine substrates is particularly problematic (Scheme 1, top).[11a] A general method to transfer the both photochemically and –catalytically cleavable, promising Pac motif as Pac urethane to amines (including amino acids) remains an unmet challenge.

Herein, we report an operationally simple, nontoxic and broadly applicable method for the synthesis of Pac urethanes from their corresponding amines with phenacyl bromide and CO_2 as phosgene replacing, abundant C1 building block. Additionally, we demonstrate the complete cleavage of all Pac carbamates by a convenient, mild and highly selective photocatalytic deprotection protocol mediated by visible light.[8]

RESULTS AND DISCUSSION

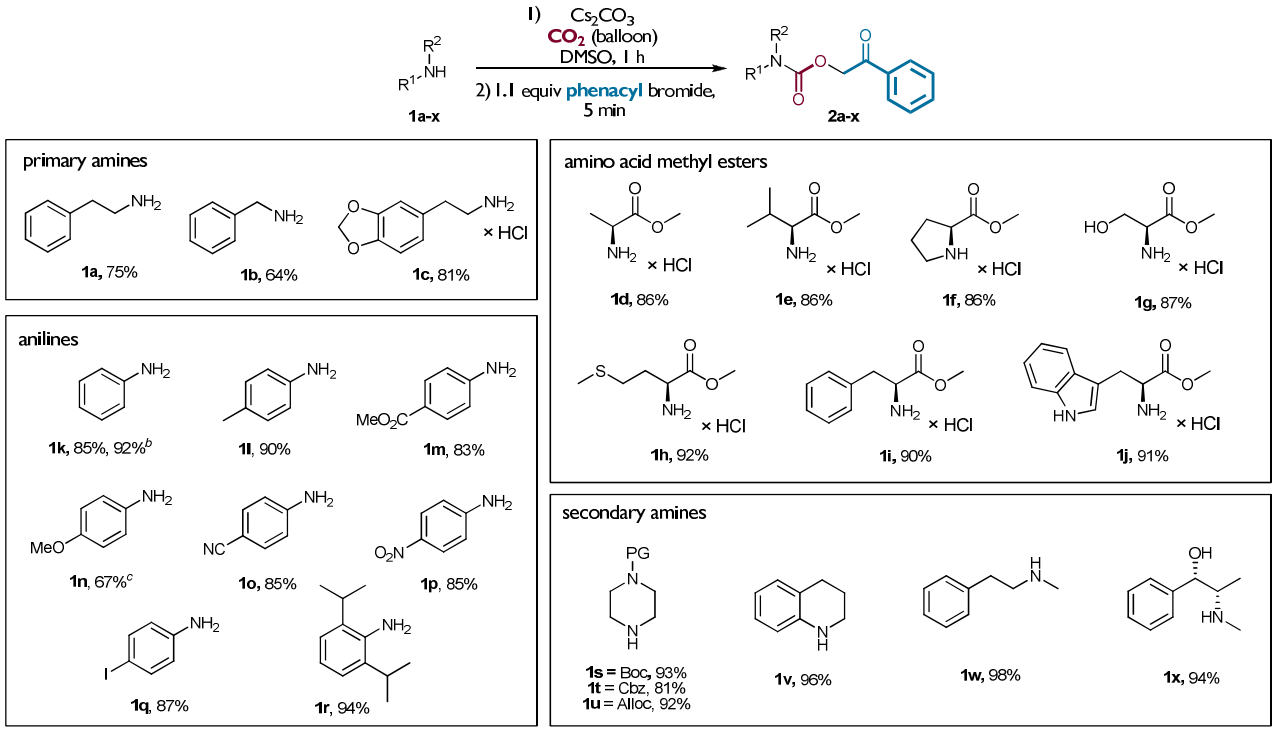
Pac carbamate protection of amines is often hampered by the well-documented, concurrent formation of undesired cyclized oxazolone byproducts (Scheme 2).[10d,12] A reaction of practical significance also would require mild conditions and chemoselective reagents without the production of excessive waste. Among the comprehensive literature describing different methods for the formation of urethanes in general (other than Pac),[4a] especially sustainable, CO_2-based methods have recently gained great interest.[13] Inspired by the procedures described by Jung[14] and following improved protocols by Hooker[15] and especially Das,[16] we questioned whether this strategy, employing solvents being saturated with CO_2, could be translated to the direct carbamate coupling of the challenging primary amines with phenacyl bromide (Scheme 2). Unfortunately, initial experiments carried out using phenacyl bromide instead of conventional alkyl halides referring to conditions detailed by Das afforded the same undesired cyclization product (**3a**) as observed by other groups before.[10d,12]

Scheme 2: Attempted formation of PacCO_2-phenethylamine **2a** following a protocol of Das.[16]



All our optimization efforts to alternatively employ different organic bases like DBU, DIPEA and Et_3N instead of Cs_2CO_3, also resulted in the formation of oxazolone **3a** as main product. Neither could the cyclization to **3a** be decreased by a solvent change to dichloromethane (DCM) or acetonitrile. Interestingly, an attempt to prepare the carbamic acid anion in *DMSO* with its subsequent trapping by phenacyl bromide in *DCM* to access Pac urethane **2a**, significantly increased the yield of oxazolone **3a** up to 100%.[17] Triggered by this instructive result, we reasoned anion stabilization to be of crucial importance for the successful transformation to the Pac urethane.

Scheme 3: Substrate scope for protection of various amines.[a]



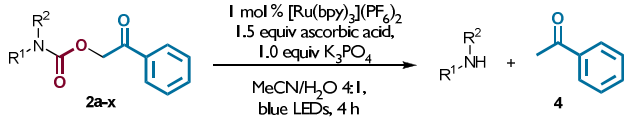
[a] Conditions for protection: 1.0 mmol amine (1.0 equiv), Cs_2CO_3 (1.0 equiv for primary amines; 2.0 equiv for HCl salts and secondary. amines, 1.5 equiv for anilines), phenacyl bromide (1.1 equiv), CO_2 in 5 mL DMSO; yield of isolated product. [b] large scale: 10 mmol. [c] Cs_2CO_3 (1.0 equiv).

By contrast to DCM, DMSO, which is also a good H-bond acceptor solvent, has no ability to function as H-bond donor[18a] and hence we assumed this to be beneficial for suppressing the base induced cyclization (starting with the deprotonation of Pac urethane **2a** and being strongly dependent on the stabilization of the corresponding anion).[18] As DMSO offers an outstanding solubility of Cs_2CO_3[19] as well as CO_2[20] and moreover Cs_2CO_3 has been used successfully for carbamate formations in previous literature,[21] additionally providing increased nucleophilicity of the corresponding deprotonated amines,[22] we considered the combination of Cs_2CO_3 in DMSO as most promising for the development of a new synthetic protocol. Specifically, we hypothesized that, instead of performing a screening focused on additives, solvent and reagent changes, the direct optimization of the reaction technique and conditions could be beneficial to facilitate the challenging formation of Pac urethanes from amines. We hence examined conditions to suppress the cyclization *via* concentration and especially timing effects. First, we minimized the amount of Cs_2CO_3 to 1.0 equiv in view of the base-promoted cyclization. Additionally, we dramatically shortened the indicated reaction time for the initial formation of the carbamic anion to 1 h using a balloon of CO_2 for bubbling through the solution for its saturation. After the subsequent addition of phenacyl bromide the formation of urethane **2a** in DMSO is very fast, so the reaction must be stopped after 5 minutes to avoid the detrimental cyclization to begin and the reaction to result in an inseparable mixture of oxazolone **3a** and Pac urethane **2a**.

With these optimized conditions in hand we next investigated the scope of our protocol for selective formation of Pac urethanes for a variety of different amines, including primary amines (**1a-c**), amino acids (**1d-j**), anilines (**1k-r**) and secondary amines (**1s-x**). We found the amount of Cs_2CO_3 to be strongly dependent on the respective substrate. While primary amines, that are the most susceptible substrates to the undesired cyclization, 1.0 equiv Cs_2CO_3 must not be exceeded, except for the direct usage of HCl salts (such as amino acid esters **1d-j**), where an extra of 1.0 equiv base is required for additional neutralization. Anilines (except for the electron rich anisidine (**1n**)) as well as secondary amines can be treated with 1.5 equiv respectively 2.0 equiv of Cs_2CO_3 to guarantee fast and full conversion to the intermediate carbamic anion. Application of this revised protocol allows for reproducible protection of *all different types of amines* as their corresponding Pac urethanes in short reaction times and good to excellent yields. As showcased for anilines our novel protection protocol tolerates electron donating effects (**1l, 1n**) and electron withdrawing effects (**1m, o, p**) and hence less nucleophilic amines as well as heavily sterically hindered amines (**1r**). Notably, the efficient protection of amines was not impeded by the presence of free alcohols (**1g, x**) or rather sensitive amino acids such as tryptophan (**1j**) and biogenic amines (**1a-c**). Furthermore, a series of piperazines bearing common protecting groups (Boc: **1s**, Cbz: **1t**, Alloc: **1u**) showed an unlimited stability under these conditions. With only three examples out of 24 resulting in yields below 80%, the broad substrate scope highlights the general applicability of our synthetic protocol for the Pac based protection of amines as urethanes.

With regard to the previous investigation of only single examples of Pac urethanes and their photochemical cleavage in literature[10,11a,12] that furthermore suffer from the typical inherent drawbacks of using UV light,[23] we decided to extend our recently reported, visible light mediated, photocatalytic deprotection method for Pac protected acids[8] to these Pac urethanes. Despite facing the additional challenge that a possible photoredox catalytic protocol would harbor the danger of an oxidation of the just released amines and therefore undesirable side reaction, we hoped to circumvent this problem based on our knowledge of this catalytical bond breakage.[8,24] We selected $[Ru(bpy)_3](PF_6)_2$ as a photocatalyst in combination with ascorbic acid as a reductive quencher in a neutral buffered two-phase acetonitrile/water mixture. Fortunately, this protocol proved to be efficient and concurrently mild enough to deprotect all examples showing full conversion and quantitative yields of acetophenone **4** (as determined by GC-FID, Table 1). Due to their volatility Boc protection served to facilitate the isolation of Pac urethane deprotected amino acid methylesters **5d-j** by adding Boc_2O and NaOH directly to the reaction mixture after irradiation. Using this formal re-protection we could successfully isolate all amino acids, with the exception of proline **5f** (71%) and serine **5g** (55%), in excellent yields (up to 98%). However, simple primary amines turned out to be most challenging: usage of the same re-protection strategy for isolation only afforded the corresponding amine derivative in poor yields (**6b**). Direct isolation as HCl salt could slightly increase the amount of isolated product to moderate yields (**6a**, **6c**).

Table 1. Photocatalytic Deprotection of Pac urethanes.[a]



protected entity	urethane	isolated as	yield
amino acids	**2d**	Boc-Ala-OMe (**5d**)	86%
	2e	Boc-Val-OMe (**5e**)	88%
	2f	Boc-Pro-OMe (**5f**)	71%
	2g	Boc-Ser-OMe (**5g**)	55%
	2h	Boc-Met-OMe (**5h**)	86%
	2i	Boc-Phe-OMe (**5i**)	98%
	2j	Boc-Trp-OMe (**5j**)	95%
primary amines	**2a**	HCl-amine (**6a**)	49%
	2b	Boc-amine (**6b**)	29%
	2c	HCl-amine (**6c**)	58%
anilines	**2k**	aniline (**1k-1r**)	83%
	2l		quant[b]
	2m		quant
	2n		81%
	2o		quant
	2p		0%
	2q		93%
	2r		quant[b]
secondary amines	**2s**	amine (**1s-1x**)	90%
	2t		92%
	2u		85%
	2v		78%
	2w		87%
	2x		32%

[a]Conditions: 0.5 mmol Pac-protected amine (1.0 equiv), 1 mol % $[Ru(bpy)_3](PF_6)_2$, ascorbic acid (1.5 equiv), K_3PO_4, (1.0 equiv) in 3 mL MeCN/H_2O 4:1, irradiated with blue LEDs, rt, 4 h; yield of isolated product. [b]yield determined by GC-FID with mesitylene as internal standard.

For the deprotection and direct isolation of anilines and secondary amines our protocol affords excellent yields for nearly all examples, except of pseudoephedrine (**1x)** and nitroaniline **1p**, being in good agreement with our recently published work[8] and the limitation of easily reducible aryl nitro groups for these conditions. Pseudoephedrine (**1x**) most probably suffers from isolation problems from the two-phase system due the free alcohol, as also observed for Boc-Ser-OMe (**5g**).

To further showcase the mildness and orthogonality of this protocol we successfully carried out a broad screening with a great variety of different additives to assess the functional group tolerance for Pac as a simulation of more complex systems (different functional groups, heterocycles etc.).[17] We also could assure that no oxidation problem occurs during this mild photoredox catalysis (e. g. dimethylaniline), and no additional limitations could be found within this screening.[17]

CONCLUSION

In summary, for the first time we have developed a high yielding synthetic strategy for the selective, mild and sustainable protection of primary amines, amino acids, anilines and secondary amines as Pac urethanes using CO_2 as phosgene replacing C1 building block. The utility of our Pac protection group strategy is completed by a broadly applicable, visible light photocatalytic protocol for the mild and selective deprotection.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all commercially available compounds were used as received without further purification. NMR spectra were recorded on a Varian Mercury plus 300 (300.08 MHz) and Varian Mercury plus 400 (400.00 MHz) using the solvent peak as internal reference ($CDCl_3$: δ H 7.26; δ C 77.0 and DMSO-d_6: δ H 2.51; δ C 39.5). Multiplicities are indicated, s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sept (septet), m (multiplet)); coupling constants (*J*) are in Hertz (Hz). Asterisks (*) indicate signal doubling due to formation of diastereomers or rotamers within the protection step. Mass spectra (MS ESI) were recorded using a Bruker APEX II FT-ICR. All reactions were monitored by thin-layer chromatography using Merck silica gel plates 60 F_{254}; visualization was accomplished with UV light and/or staining with appropriate stains. Flash chromatography procedures were performed on a Biotage® Isolera One using 10 g or 50 g Biotage® SNAP cartridge KP-Sil columns filled with Kieselgel 60 silica (size 40−63 µm). GC-FID spectra were recorded on a Thermo Scientific Trace 1310 gas chromatograph equipped with a Thermo Scientific TG-5MS column (5% diphenyl- and 95% dimethylpolysiloxane, 0.25 mm ID, 0.25 µm film thickness, length 30 m) using hydrogen as carrier gas and nitrogen as make-up gas. Melting points were recorded on a Büchi Melting point M-565 instrument. Absorption spectra were measured on a Shimadzu UV-1280 UV/VIS spectrometer. Irradiation was performed with eight OSLON LD H9GP deep blue (OSRAM®, λ = 455 nm) attached to a heat sink. The LEDs were operated at 700 mA. All reactions were carried out under a protective atmosphere of dry nitrogen using oven-dried glassware unless otherwise stated.

Experimental Details.

*General Procedure **A – Protection.*** The corresponding amine (1.0 equiv) and Cs_2CO_3 (1.0 equiv for primary amines; 2.0 equiv for ×HCl salts and secondary amines; 1.5 equiv for anilines) were added in a Schlenk tube and dissolved in dry DMSO (0.2 M). The tube was sealed with a septum and, while stirring for 1 h at room temperature, a balloon filled with CO_2 was bubbled through the reaction mixture. Then 2-bromo acetophenone (1.1 equiv) was added in one portion. After stirring of the reaction mixture for approx. 5 min (consumption of bromo acetophenone monitored by TLC) the reaction was quenched by the addition of water. The mixture was then extracted with DCM (3×) and the combined organic phases were washed with brine. After drying over Na_2SO_4 the solvent was removed in vacuo and the crude product was purified by flash chromatography to afford the corresponding urethane.

*General Procedure **B – Deprotection.*** $[Ru(bpy)_3](PF_6)_2$ (1.0 mol%), ascorbic acid (1.5 equiv), potassium triphosphate K_3PO_4 (1.0 equiv) and the protected aniline or amine (1.0 equiv) were added in a screw-capped reaction tube and dissolved in an acetonitrile/water mixture (4:1 v/v; 0.17 M). The mixture was irradiated with blue LEDs at room temperature under vigorous stirring for the time indicated.

For the isolation as amine×HCl: The reaction mixture was poured into a saturated solution of Na_2CO_3 and extracted with DCM (3×). The combined organic phases were extracted with HCl (1 M) (3×) and the aqueous phase was then basified with NaOH (3 M) (~ pH 13) and extracted again with DCM (3×). The combined organic phases were dried over Na_2SO_4, filtered and HCl in diethyl ether (conc.) was added until no further precipitation was formed. The solvent was then removed under reduced pressure.

For the isolation as Boc-protected amine: Di-*tert*-butyl dicarbonate (1.5 equiv) and sodium hydroxide (0.1 M, 1.5 equiv) were added to the reaction mixture. After stirring for 30 min the mixture was poured into water and extracted with DCM (3×). The organic layers were combined and dried over Na_2SO_4. Following filtration, the solvent was removed under reduced pressure and the residue was purified by column chromatography.

For the isolation as free amine by extraction: The reaction mixture was poured into a saturated solution of Na_2CO_3 and extracted with DCM (3×). The combined organic phases were extracted with HCl (1 M) (3×) and the aqueous phase was then basified with NaOH (3 M) (~ pH 13) and extracted again with DCM (3×). The combined organic phases were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure.

For the isolation as free amine by column chromatography: The reaction mixture was poured into water and extracted with DCM (3×). The water layer was basified with $NaHCO_3$ (aq.) and extracted again with DCM (1×). The organic layers were combined and dried over Na_2SO_4. Following filtration, the solvent was removed under reduced pressure and the residue was purified by column chromatography.

*3-Phenethyl-4-phenyloxazol-2(3H)-one (**3a**).* 121 mg phenethylamine (1.0 mmol, 1.0 equiv) and 658 mg Cs_2CO_3 (2.0 mmol, 2.0 equiv) were added in a Schlenk tube and dissolved in 5 mL DMSO. The tube was sealed with a septum and while stirring for 1 h at room temperature a balloon filled with CO_2 was bubbled through the reaction mixture. After that the reaction mixture was slowly added dropwise (syringe) to a stirred solution of 219 mg 2-bromo acetophenone (1.1 mmol, 1.1 equiv) in 5 mL DCM (round bottom flask). After stirring for 30 min the reaction mixture was poured into water and extracted with DCM (3×). The combined organic phases were washed with brine (1×) and dried over Na_2SO_4. After filtration the solvent was removed under reduced pressure and the resi-

due was purified by column chromatography (25 g silica gel, hexanes/acetone 3-30%) to afford 270 mg **3a** as a colorless solid (1.0 mmol, 100%); mp: 146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.38 (m, 3H), 7.27 – 7.20 (m, 3H), 7.19 – 7.08 (m, 2H), 7.02 – 6.98 (m, 2H), 6.77 (s, 1H), 3.93 – 3.81 (m, 2H), 2.94 – 2.85 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9, 137.4, 129.7, 129.5, 128.9, 128.8, 128.6, 128.5, 126.7, 126.4, 123.8, 43.6, 34.5. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{17}H_{15}NO_2Na$ 288.0995; Found: 288.0969.

*2-Oxo-2-phenylethyl phenethylcarbamate (**2a**).* According to **general procedure A** using 121 mg phenethylamine (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 212 mg (0.75 mmol, 75%) white solid; mp: 105 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.87 (m, 2H), 7.67 – 7.58 (m, 1H), 7.57 – 7.42 (m, 2H), 7.38 – 7.18 (m, 5H), 5.33 (s, 2H), 5.23 – 5.08 (m, 1H), 3.62 – 3.44 (m, 2H), 2.94 – 2.79 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.6, 155.7, 138.8, 134.4, 133.9, 128.9 (2C), 128.8, 127.9, 126.6, 66.4, 42.5, 36.1. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{17}H_{17}NO_3Na$ 306.1101; Found: 306.1099.

*Phenethylamine hydrochloride (**6a**).* According to **general procedure B** using 142 mg **2a** (0.50 mmol, 1.0 equiv) and irradiation for 3 h; yield after *isolation as amine×HCl*: 48.5 mg (0.24 mmol, 49%) white solid. ^{1}H NMR (300 MHz, D_2O) δ 7.53 – 7.32 (m, 5H), 3.31 (t, J = 7.3 Hz, 2H), 3.03 (t, J = 7.3 Hz, 2H).[25]

*2-Oxo-2-phenylethyl benzylcarbamate (**2b**).* According to **general procedure A** using 107 mg benzylamine (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 172 mg (0.64 mmol, 64%) white solid; mp: 109 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.90 (m, 2H), 7.65 – 7.56 (m, 1H), 7.52 – 7.44 (m, 2H), 7.39 – 7.26 (m, 5H), 5.36 (s, 2H), 5.32 (bs, 1H), 4.48 – 4.41 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 155.8, 138.2, 134.3, 133.8, 128.8, 128.7, 127.8, 127.6, 127.5, 66.5, 45.3. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{16}H_{15}NO_3Na$ 292.0944; Found: 292.0941.

*tert-Butyl benzylcarbamate (**6b**).* According to **general procedure B** using 135 mg **2b** (0.50 mmol, 1.0 equiv) and irradiation for 3 h; yield after isolation as *Boc-protected amine* (10 g silica gel, hexanes/acetone 3-30%) 29 mg (0.14 mmol, 29%) colorless oil.: ^{1}H NMR (300 MHz, $CDCl_3$) 7.47 – 7.20 (m, 5H), 4.88 (bs, 1H), 4.49 – 4.20 (m, 2H), 1.49 (s, 9H).

*2-Oxo-2-phenylethyl (2-(benzo[d][1,3]dioxol-5-yl)ethyl)-carbamate (**2c**)* According to **general procedure A** using 202 mg 3,4-methylenedioxyphenethylamine hydrochloride (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 265 mg (0.81 mmol, 81%) white solid; mp: 108 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.85 (m, 2H), 7.65 – 7.55 (m, 1H), 7.55 – 7.44 (m, 2H), 6.83 – 6.63 (m, 3H), 6.00 – 5.86 (m, 2H), 5.31 (s, 2H), 5.01 (bs, 1H), 3.51 – 3.36 (m, 2H), 2.77 (t, J = 6.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.6, 155.7, 148.0, 146.4, 134.4, 133.9, 132.5, 129.0, 127.9, 121.9, 109.3, 108.5, 101.0, 66.5, 42.7, 35.8. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{18}H_{17}NO_5Na$ 350.0999; Found: 350.0993.

*3,4-Methylenedioxyphenethylamine hydrochloride (**6c**).* According to **general procedure B** using 164 mg **1c** (0.50 mmol, 1.0 equiv) and irradiation for 3 h; yield after *isolation as amine×HCl:* 58 mg (0.29 mmol, 58%) white solid. ^{1}H NMR (300 MHz, D_2O) δ 6.95 – 6.79 (m, 3H), 6.03 – 5.93 (m, 2H), 3.25 (t, J = 7.2 Hz, 2H), 2.94 (t, J = 7.2 Hz, 2H).[25]

*Methyl ((2-oxo-2-phenylethoxy)carbonyl)alaninate (**2d**).* According to **general procedure A** using 140 mg L-alanine methyl ester hydrochloride (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 229 mg (0.86 mmol, 86%) white solid; mp: 84-88 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.89 (m, 2H), 7.66 – 7.60 (m, 1H), 7.54 – 7.47 (m, 2H), 5.69 – 5.57 (m, 1H), 5.50 – 5.23 (m, 2H), 4.56 – 4.37 (m, 1H), 3.80 (s, 3H), 1.49 (d, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 173.3, 155.0, 134.4, 134.0, 129.0, 127.9, 66.7, 52.6, 49.9, 18.7. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{13}H_{15}NO_5Na$ 288.0842; Found: 288.0841.

*Methyl (tert-butoxycarbonyl)alanate (**5d**).* According to **general procedure B** using 133 mg **1d** (0.50 mmol, 1.0 equiv) and irradiation for 3 h; yield after *isolation as Boc-protected amine* (10 g silica gel, hexanes/acetone 3-30%) 87 mg (0.43 mmol, 86%) colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.04 (bs, 1H), 4.38 – 4.25 (m, 1H), 3.74 (s, 3H), 1.44 (s, 9H), 1.38 (d, J = 7.2 Hz, 3H).

*Methyl ((2-oxo-2-phenylethoxy)carbonyl)valinate (**2e**).* According to **general procedure A** using 168 mg L-valine methyl ester hydrochloride (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 252 mg (0.86 mmol, 86%) white solid; mp: 65 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.88 (m, 2H), 7.68 – 7.55 (m, 1H), 7.53 – 7.42 (m, 2H), 5.61 – 5.49 (m, 1H), 5.46 – 5.20 (m, 2H), 4.37 – 4.26 (m, 1H), 3.76 (s, 3H), 2.27 – 2.08 (m, 1H), 1.00 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 172.3, 155.7, 134.4, 133.9, 129.0, 127.9, 66.8, 59.4, 52.3, 31.6, 19.0, 17.7. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{15}H_{19}NO_5Na$ 316.1155; Found: 316.1155.

*Methyl (tert-butoxycarbonyl)valinate (**5e**).* According to **general procedure B** using 147 mg 1e (0.50 mmol, 1.0 equiv) and irradiation for 3 h; yield after *isolation as Boc-protected amine* (10 g silica gel, hexanes/acetone 3-30%) 102 mg (0.44 mmol, 88%) colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.01 (d, J = 8.7 Hz, 1H), 4.26 – 4.16 (m, 1H), 3.73 (s, 3H), 2.17 – 2.06 (m, 1H), 1.44 (s, 9H), 0.95 (d, J = 6.9 Hz, 3H), 0.89 (d, J = 6.8 Hz, 3H).

*2-Methyl 1-(2-oxo-2-phenylethyl) pyrrolidine-1,2-dicarboxylate (**2f**).* According to **general procedure A** using 166 mg L-proline methyl ester hydrochloride (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 250 mg (0.86 mmol, 86%) colorless gum. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 – 7.82 (m, 2H), 7.64 – 7.55 (m, 1H), 7.53 – 7.41 (m, 2H), 5.57 – 5.14 (m, 2H), 4.57 – 4.36 (m, 1H), 3.75 (2 s, Σ 3H), 3.72 – 3.52 (m, 2H), 2.39 – 2.18 (m, 1H), 2.12 – 1.89 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2*, 173.1*, 154.2*, 134.4, 133.7, 128.8, 127.7, 66.8, 59.3*, 52.3*, 47.0*, 30.9*, 24.3*. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{15}H_{17}NO_5Na$ 314.0999; Found: 314.0993.

*1-(tert-Butyl) 2-methyl pyrrolidine-1,2-dicarboxylate (**5f**).* According to **general procedure B** using 146 mg **2f** (0.50 mmol, 1.0 equiv) and irradiation for 3 h; yield after *isolation as Boc-protected amine* (10 g silica gel, hexanes/ethyl acetate 3-30%) 80.8 mg (0.35 mmol, 71%) colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.34 – 4.12 (m, 1H), 3.72 (2 s, Σ 3H), 3.59 – 3.33 (m, 2H), 2.28 – 2.08 (m, 1H), 1.99 – 1.80 (m, 3H), 1.43 (2 s, Σ 9H).

*Methyl ((2-oxo-2-phenylethoxy)carbonyl)serinate (**2g**).* According to **general procedure A** using 156 mg L-serine

methyl ester hydrochloride (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 244 mg (0.87 mmol, 87%) white solid; mp: 99-102 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.84 (m, 2H), 7.65 – 7.55 (m, 1H), 7.55 – 7.43 (m, 2H), 6.20 – 6.09 (m, 1H), 5.51 – 5.20 (m, 2H), 4.55 – 4.41 (m, 1H), 4.12 – 3.96 (m, 2H), 3.80 (s, 3H), 2.59 (bs, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 173.3, 155.0, 134.4, 134.0, 129.0, 127.9, 66.7, 52.6, 49.9, 18.7. HRMS (ESI) m/z: [M + Na]$^+$: Calcd for $C_{13}H_{15}NO_6Na$ 304.0792; Found: 304.0777.

*Methyl (tert-butoxycarbonyl)serinate (**5g**).* According to **general procedure B** using 141 mg **2g** (0.50 mmol, 1.0 equiv) and irradiation for 3 h; yield after *isolation as Boc-protected amine* (silica gel, hexanes/acetone 3-30%) 60 mg (0.27 mmol, 55%) colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (bs, 1H), 4.38 (bs, 1H), 4.01 – 3.85 (m, 2H), 3.78 (s, 3H), 2.50 – 2.16 (m, 1H), 1.45 (s, 9H).

*Methyl ((2-oxo-2-phenylethoxy)carbonyl)methioninate (**2h**).* According to **general procedure A** using 150 mg L-methionine methyl ester hydrochloride (0.75 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 225 mg (0.69 mmol, 92%) white solid; mp: 60-63 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 – 7.86 (m, 2H), 7.71 – 7.57 (m, 1H), 7.57 – 7.41 (m, 2H), 5.90 – 5.76 (m, 1H), 5.54 – 5.20 (m, 2H), 4.66 – 4.48 (m, 1H), 3.79 (s, 3H), 2.60 (t, J = 7.3 Hz, 2H), 2.25 – 1.99 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 172.3, 155.3, 134.3, 134.0, 129.0, 127.9, 66.8, 53.4, 52.7, 32.0, 29.9, 15.6. HRMS (ESI) m/z: [M + Na]$^+$: Calcd for $C_{15}H_{19}NO_5SNa$ 348.0876; Found: 348.0884.

*Methyl (tert-butoxycarbonyl)methioninate (**5h**).* According to **general procedure B** using 163 mg **2h** (0.50 mmol, 1.0 equiv) and irradiation for 3 h; yield after *isolation as Boc-protected amine* (10 g silica gel, hexanes/acetone 3-30%) 113 mg (0.43 mmol, 86%) colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.20 – 5.09 (m, 1H), 4.51 – 4.39 (m, 1H), 3.78 (s, 3H), 2.56 (t, J = 7.4 Hz, 2H), 2.22 – 2.08 (m, 1H), 2.12 (s, 3H), 2.02 – 1.91 (m, 1H), 1.47 (s, 9H).

*Methyl ((2-oxo-2-phenylethoxy)carbonyl)phenylalaninate (**2i**).* According to **general procedure A** using 216 mg L-phenylalanine methyl ester hydrochloride (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 307 mg (0.90 mmol, 90%) white solid; mp: 70-78 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.87 (m, 2H), 7.65 – 7.57 (m, 1H), 7.55 – 7.43 (m, 2H), 7.35 – 7.26 (m, 3H), 7.20 – 7.15 (m, 2H), 5.57 – 5.43 (m, 1H), 5.40 – 5.22 (m, 2H), 4.75 – 4.63 (m, 1H), 3.73 (s, 3H), 3.24 – 3.10 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.0, 171.6, 154.9, 135.5, 134.3, 133.8, 129.4, 128.8, 128.6, 127.8, 127.2, 66.6, 55.0, 52.4, 38.1. HRMS (ESI) m/z: [M + Na]$^+$: Calcd for $C_{19}H_{19}NO_5Na$ 364.1155; Found: 364.1152.

*Methyl (tert-butoxycarbonyl)phenylalaninate (**5i**).* According to **general procedure B** using 171 mg **2i** (0.50 mmol, 1.0 equiv) and irradiation for 3 h; yield after *isolation as Boc-protected amine* (10 g silica gel, hexanes/ethyl acetate 3-30%) 137 mg (0.49 mmol, 98%) colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.23 (m, 3H), 7.18 – 7.07 (m, 2H), 4.96 (d, J = 8.3 Hz, 1H), 4.64 – 4.51 (m, 1H), 3.71 (s, 3H), 3.16 – 2.99 (m, 2H), 1.41 (s, 9H).

*Methyl ((2-oxo-2-phenylethoxy)carbonyl)tryptophanate (**2j**).* According to **general procedure A** using 255 mg D-tryptophan methyl ester hydrochloride (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 347 mg (0.91 mmol, 91%) white solid; mp: 64-70 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (bs, 1H), 7.95 – 7.85 (m, 2H), 7.65 – 7.55 (m, 2H), 7.52 – 7.44 (m, 2H), 7.38 – 7.32 (m, 1H), 7.22 – 7.08 (m, 3H), 5.68 – 5.59 (m, 1H), 5.46 – 5.16 (m, 2H), 4.82 – 4.64 (m, 1H), 3.68 (s, 3H), 3.35 (d, J = 5.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 172.1, 155.0, 136.1, 134.2, 133.8, 128.8, 127.7, 127.5, 123.3, 122.1, 119.6, 118.6, 111.2, 109.6, 66.5, 54.5, 52.4, 27.8. HRMS (ESI) m/z: [M + Na]$^+$: Calcd for $C_{21}H_{20}N_2O_5Na$ 403.1264; Found: 403.1261.

*Methyl (tert-butoxycarbonyl)tryptophanate (**5j**).* According to **general procedure B** using 191 mg **2j** (0.50 mmol, 1.0 equiv) and irradiation for 3 h; yield after *isolation as Boc-protected amine* (10 g silica gel, hexanes/acetone 3-30%) 152 mg (0.48 mmol, 95%) colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.59 – 7.53 (m, 1H), 7.37 – 7.32 (m, 1H), 7.22 – 7.16 (m, 1H), 7.16 – 7.09 (m, 1H), 7.00 – 6.94 (m, 1H), 5.15 – 5.05 (m, 1H), 4.71 – 4.60 (m, 1H), 3.67 (s, 3H), 3.35 – 3.23 (m, 2H), 1.36 (s, 9H).

*2-Oxo-2-phenylethyl phenylcarbamate (**2k**).* According to **general procedure A** using 931 mg aniline (10.0 mmol, 1.0 equiv); yield after column chromatography (100 g silica gel, hexanes/acetone 3-30%): 2.36 g (9.2 mmol, 92%) white solid; mp: 152 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 – 7.91 (m, 2H), 7.67 – 7.58 (m, 1H), 7.56 – 7.46 (m, 2H), 7.45 – 7.37 (m, 2H), 7.34 – 7.27 (m, 2H), 7.12 – 6.96 (m, 2H), 5.42 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.0, 152.7, 137.5, 134.2, 134.0, 129.1, 128.9, 127.8, 123.8, 118.8, 66.5. HRMS (ESI) m/z: [M + Na]$^+$: Calcd for $C_{15}H_{13}NO_3Na$ 278.0788; Found: 278.0786.

*Aniline (**1k**).* According to **general procedure B** using 128 mg **2k** (0.50 mmol, 1.0 equiv) and irradiation for 3 h; yield after *isolation as amine by column chromatography* (10 g silica gel, hexanes/acetone 9:1) 38.4 mg (0.41 mmol, 83%) pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.10 (m, 2H), 6.83 – 6.65 (m, 3H), 3.49 (bs, 2H).

*2-Oxo-2-phenylethyl p-tolylcarbamate (**2l**).* According to **general procedure A** using 214 mg *p*-toluidine (2.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 484 mg (1.8 mmol, 90%) white solid; mp: 154 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.91 (m, 2H), 7.66 – 7.57 (m, 1H), 7.53 – 7.46 (m, 2H), 7.33 – 7.26 (m, 2H), 7.17 – 7.08 (m, 2H), 7.03 – 6.95 (m, 1H), 5.41 (s, 2H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 152.8, 138.0, 133.9, 129.5, 128.9, 127.8, 124.6, 119.0, 66.4, 20.8. HRMS (ESI) m/z: [M + Na]$^+$: Calcd for $C_{16}H_{15}NO_3Na$ 292.0944; Found: 292.0942.

*p-Toluidine (**1l**).* According to **general procedure B** using 135 mg **2l** (0.50 mmol, 1.0 equiv) and irradiation for 3 h; yield (> 99%) determined by GC-FID with mesitylene as internal standard.

*Methyl 4-(((2-oxo-2-phenylethoxy)carbonyl)amino)benzoate (**2m**).* According to **general procedure A** using 151 mg methyl 4-aminobenzoate (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 254 mg (0.83 mmol, 83%) white solid; mp: 150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.90 (m, 4H), 7.69 – 7.59 (m, 1H), 7.56 – 7.44 (m, 4H), 7.22 (s, 1H), 5.44 (s, 2H), 3.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.9, 166.7, 152.4, 141.9, 134.2, 134.0, 130.9, 129.0, 127.8, 125.1, 117.8, 66.6, 52.0. HRMS (ESI) m/z: [M + Na]$^+$: Calcd for $C_{17}H_{15}NO_5Na$ 336.0842; Found: 336.0835.

*Methyl 4-aminobenzoate (**1m**).* According to **general procedure B** using 157 mg **2m** (0.50 mmol, 1.0 equiv) and irradiation for 2.5 h; yield after *isolation as amine by column chromatography* (10 g silica gel, hexanes/acetone 3-30%) 76 mg (0.50 mmol, quantitative) colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.80 (m, 2H), 6.69 – 6.58 (m, 2H), 4.03 (bs, 2H), 3.85 (s, 3H).

*2-Oxo-2-phenylethyl (4-methoxyphenyl)carbamate (**2n**).* According to **general procedure A** using 123 mg methyl *p*-anisidine (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 191 mg (0.67 mmol, 67%) white solid; mp: 162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 7.89 (m, 2H), 7.69 – 7.60 (m, 1H), 7.55 – 7.48 (m, 2H), 7.41 – 7.22 (m, 2H), 6.93 – 6.77 (m, 3H), 5.43 (s, 2H), 3.88 – 3.78 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) 193.2, 159.1, 134.2, 133.9, 128.9, 128.7, 127.8, 120.8, 114.5, 114.3, 66.4, 55.5. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{16}H_{15}NO_4Na$ 308.0893; Found: 308.0890.

*p-Anisidine (**1n**).* According to **general procedure B** using 143 mg **2n** (0.50 mmol, 1.0 equiv) and irradiation for 4 h; yield after *isolation as amine by column chromatography* (10 g silica gel, hexanes/acetone 3-30%) 50 mg (0.40 mmol, 81%) pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 – 6.73 (m, 2H), 6.73 – 6.61 (m, 2H), 3.77 (s, 3H), 3.47 (s, 2H).

*2-Oxo-2-phenylethyl (4-cyanophenyl)carbamate (**2o**).* According to **general procedure A** using 118 mg 4-aminobenzonitrile (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 237 mg (0.85 mmol, 85%) white solid; mp: 156-171 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.92 (m, 2H), 7.68 – 7.59 (m, 3H), 7.57 – 7.49 (m, 4H), 7.17 (s, 1H), 5.45 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.9, 152.4, 141.9, 134.5, 134.0, 133.5, 129.2, 127.9, 119.0, 118.7, 106.7, 66.8. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{16}H_{12}N_2O_3Na$ 303.0740; Found: 303.0731.

*4-Aminobenzonitrile (**1o**).* According to **general procedure B** using 140 mg **2o** (0.50 mmol, 1.0 equiv) and irradiation for 2 h; yield after *isolation as amine by column chromatography* (10 g silica gel, hexanes/acetone 3-30%) 59 mg (0.50 mmol, quantitative) colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.37 (m, 2H), 6.69 – 6.61 (m, 2H), 4.14 (s, 2H).

*2-Oxo-2-phenylethyl (4-nitrophenyl)carbamate (**2p**).* According to **general procedure A** using 138 mg 4-nitroaniline (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 254 mg (0.85 mmol, 85%) pale yellow solid; mp: 155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.21 (m, 2H), 8.02 – 7.94 (m, 2H), 7.71 – 7.64 (m, 1H), 7.63 – 7.59 (m, 2H), 7.58 – 7.52 (m, 2H), 5.50 (s, 2H).[26] ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 164.4, 150.9, 135.0, 134.3, 134.1, 131.2, 129.1, 127.9, 123.7, 67.2. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{15}H_{12}N_2O_5Na$ 323.0638; Found: 323.0605.

*2-Oxo-2-phenylethyl (4-iodophenyl)carbamate (**2q**).* According to **general procedure A** using 219 mg 4-iodoaniline (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 326 mg (0.87 mmol, 87%) white solid; mp: 173-186 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.89 (m, 2H), 7.68 – 7.58 (m, 3H), 7.56 – 7.46 (m, 2H), 7.23 – 7.15 (m, 2H), 6.92 (s, 1H), 5.42 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.8, 152.5, 137.9, 137.4, 134.1, 128.9, 127.8, 120.7, 110.0, 86.7, 66.5. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{15}H_{12}N_2O_5Na$ 403.9754; Found: 403.9753.

*4-Iodoaniline (**1q**).* According to **general procedure B** using 191 mg **2q** (0.50 mmol, 1.0 equiv) and irradiation for 2.5 h; yield after *isolation as amine by column chromatography* (10 g silica gel, hexanes/acetone 3-30%) 101 mg (0.46 mmol, 93%) colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.31 (m, 2H), 6.62 – 6.33 (m, 2H), 3.68 (bs, 2H).

*2-Oxo-2-phenylethyl (2,6-diisopropylphenyl)carbamate (**2r**).* According to **general procedure A** using 177 mg 2,6-diisopropylaniline (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 318 mg (0.94 mmol, 94%) white solid; mp: 116 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.83 (m, 2H), 7.65 – 7.56 (m, 1H), 7.53 – 7.41 (m, 2H), 7.34 – 7.28 (m, 1H), 7.23 – 7.15 (m, 2H), 6.28, 5.96 (2 bs, Σ 1H), 5.42, 5.26 (2 s, Σ 2H), 3.50 – 3.37, 3.33 – 3.18 (2 m, Σ 2H), 1.33 – 1.19 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.3, 154.6, 147.0*, 134.4, 133.8*, 130.3, 128.8, 128.5, 127.8*, 123.6, 66.8, 28.6*, 23.7*. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{21}H_{25}NO_3Na$ 362.1727; Found: 362.1722.

*2,6-Diisopropylaniline (**1r**).* According to **general procedure B** using 170 mg **2r** (0.50 mmol, 1.0 equiv) and irradiation for 2 h; yield ((> 99%) determined by GC-FID with mesitylene as internal standard.

*2-Oxo-2-phenylethyl 4-(3,3-dimethylbutanoyl)piperazine-1-carboxylate (**2s**).* According to **general procedure A** using 186 mg 1-Boc-piperazine (1.0 mmol, 1.0 equiv); yield after column chromatography (silica gel, hexanes/acetone 3-30%): 323 mg (0.93 mmol, 93%) white solid; mp: 123 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.89 (m, 2H), 7.67 – 7.57 (m, 1H), 7.56 – 7.44 (m, 2H), 5.36 (s, 2H), 3.66 – 3.42 (m, 8H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 154.7, 154.6, 134.3, 133.8, 128.9, 127.7, 80.2, 66.9, 43.9, 28.4. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{18}H_{24}N_2O_5Na$ 371.1577; Found: 371.1570.

*1-Boc-piperazine (**1s**).* According to **general procedure B** using 174 mg **2s** (0.50 mmol, 1.0 equiv) and irradiation for 2 h; yield after *isolation as amine by extraction*: 84 mg (0.45 mmol, 90%) colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.48 – 3.37 (m, 4H), 2.89 – 2.76 (m, 4H), 2.02 (bs, 1H), 1.46 (s, 9H).

*1-Benzyl 4-(2-oxo-2-phenylethyl) piperazine-1,4-dicarboxylate (**2t**).* According to **general procedure A** using 220 mg benzyl piperazine-1-carboxylate (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 295 mg (0.81 mmol, 81%) white solid; mp: 90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.87 (m, 2H), 7.65 – 7.56 (m, 1H), 7.53 – 7.45 (m, 2H), 7.41 – 7.30 (m, 5H), 5.36 (s, 2H), 5.16 (s, 2H), 3.66 – 3.45 (m, 8H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.3, 155.3, 154.8, 136.6, 134.4, 134.0, 129.0, 128.7, 128.3, 128.1, 127.9, 67.6, 67.1, 43.7. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{21}H_{22}N_2O_5Na$ 405.1421; Found: 405.1419.

*Benzyl piperazine-1-carboxylate (**1t**).* According to **general procedure B** using 191 mg **2t** (0.50 mmol, 1.0 equiv) and irradiation for 2 h; yield after *isolation as amine by extraction*: 101 mg (0.46 mmol, 92%) colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.28 (m, 5H), 5.13 (s, 2H), 3.58 – 3.45 (m, 4H), 2.95 – 2.79 (m, 4H), 2.47 (bs, 1H).

*1-Allyl 4-(2-oxo-2-phenylethyl) piperazine-1,4-dicarboxylate (**2u**).* According to **general procedure A** using 170 mg allyl piperazine-1-carboxylate (1.0 mmol, 1.0 equiv); yield

after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 305 mg (0.92 mmol, 92%) white solid; mp: 98 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.86 (m, 2H), 7.65 – 7.56 (m, 1H), 7.54 – 7.45 (m, 2H), 5.94 (ddt, *J* = 17.3, 10.8, 5.6 Hz, 1H), 5.36 (s, 2H), 5.34 – 5.20 (m, 2H), 4.62 (dt, *J* = 5.6, 1.5 Hz, 2H), 3.70 – 3.41 (m, 8H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 155.1, 154.8, 134.3, 134.0, 132.9, 129.0, 127.8, 117.9, 67.1, 66.4, 43.7. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{17}H_{20}N_2O_5Na$ 355.1264; Found: 355.1256.

*Allyl piperazine-1-carboxylate (**1u**).*[27] According to **general procedure B** using 166 mg **2u** (0.50 mmol, 1.0 equiv) and irradiation for 2 h; yield after *isolation as amine by extraction* 72 mg (0.42 mmol, 85%) colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.03 – 5.86 (m, 1H), 5.37 – 5.12 (m, 2H), 4.68 – 4.50 (m, 2H), 3.60 – 3.35 (m, 4H), 2.95 – 2.74 (m, 4H), 2.17 (bs, 1H).

*2-Oxo-2-phenylethyl 3,4-dihydroquinoline-1(2H)-carboxylate (**2v**).* According to **general procedure A** using 136 mg 1,2,3,4-tetrahydroquinoline (1.0 mmol, 1.0 equiv); yield after column chromatography (silica gel, hexanes/acetone 3-30%): 283 mg (0.96 mmol, 96%) pale yellow solid; mp: 69 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.91 (m, 2H), 7.85 – 7.80 (m, 1H), 7.65 – 7.58 (m, 1H), 7.53 – 7.46 (m, 2H), 7.20 – 7.14 (m, 1H), 7.13 – 7.08 (m, 1H), 7.06 – 7.00 (m, 1H), 5.44 (s, 2H), 3.88 (t, *J* = 6.1 Hz, 2H), 2.82 (t, *J* = 6.6 Hz, 2H), 2.01 (p, *J* = 6.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.3, 154.4, 138.1, 134.4, 133.9, 130.4, 129.0, 128.7, 127.9, 126.2, 124.4, 124.1, 67.2, 45.2, 27.4, 23.6. HRMS (ESI) m/z: $[M + H]^+$: Calcd for $C_{18}H_{17}NO_3H$ 296.1281; Found: : 296.1282.

*1,2,3,4-Tetrahydroquinoline (**1v**).* According to **general procedure B** using 148 mg **2v** (0.50 mmol, 1.0 equiv) and irradiation for 16 h; yield yield after *isolation as amine by extraction*: 52 mg (0.39 mmol, 78%) pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 – 6.91 (m, 2H), 6.65 – 6.57 (m, 1H), 6.51 – 6.45 (m, 1H), 3.48 (bs, 1H), 3.34 – 3.27 (m, 2H), 2.77 (t, *J* = 6.4 Hz, 2H), 2.00 – 1.90 (m, 2H).

*2-oxo-2-phenylethyl methyl(phenethyl)carbamate (**2w**).* According to **general procedure A** using 219 mg *N*-methylphenethylamine (1.0 mmol, 1.0 equiv); yield after column chromatography (silica gel, hexanes/acetone 3-30%): 290 mg (0.98 mmol, 98%) pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.88 (m, 2H), 7.66 – 7.56 (m, 1H), 7.56 – 7.44 (m, 2H), 7.38 – 7.18 (m, 5H), 5.39 – 5.27 (m, 2H), 3.68 – 3.47 (m, 2H), 3.04 – 2.81 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.7, 155.7, 139.2, 134.6, 133.8, 129.0, 128.9, 128.6, 127.9, 126.5, 66.9, 51.6*, 35.6*, 34.7*. HRMS (ESI) m/z: $[M + Na]^+$: Calcd for $C_{18}H_{19}NO_3Na$ 320.1257; Found: 320.1252.

*N-Methyl-phenethylamine (**1w**).* According to **general procedure B** using 149 mg **2w** (0.50 mmol, 1.0 equiv) and irradiation for 16 h; yield after *isolation as amine by extraction*: 59 mg (0.44 mmol, 87%) pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.23 (m, 5H), 2.93 – 2.83 (m, 4H), 2.48 (s, 3H), 1.76 (bs, 1H).

*2-Oxo-2-phenylethyl (1-hydroxy-1-phenylpropan-2-yl)(methyl)carbamate (**2x**).* According to **general procedure A** using 165 mg pseudoephedrine (1.0 mmol, 1.0 equiv); yield after column chromatography (25 g silica gel, hexanes/acetone 3-30%): 306 mg (0.94 mmol, 94%) pale yellow resin. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.87 (m, 2H), 7.67 – 7.56 (m, 1H), 7.54 – 7.43 (m, 2H), 7.43 – 7.27 (m, 5H), 5.72 – 5.25 (m, 2H), 4.70 – 4.53 (m, 1H), 4.50 – 4.16 (m, 1H), 3.75, 3.20 (2 bs, Σ 1H) 2.97 (s, 3H), 1.10 – 1.00 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.5*, 156.2, 142.0*, 134.1*, 128.8, 128.5, 127.9, 127.8, 127.0, 126.9, 76.0, 66.8*, 59.1*, 30.6*, 15.0*. HRMS (ESI) m/z: $[M + H]^+$: Calcd for $C_{19}H_{21}NO_4H$ 328.1543; Found: 328.1539.

*Pseudoephedrine (**1x**).* According to **general procedure B** using 149 mg **2x** (0.46 mmol, 1.0 equiv) and irradiation for 3 h; yield after *isolation as amine by extraction*: 25 mg (0.15 mmol, 32%) white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.25 (m, 5H), 4.19 (d, *J* = 8.2 Hz, 1H), 2.80 – 2.49 (m, 3H), 2.45 (s, 3H), 0.95 (d, *J* = 6.4 Hz, 3H).

ASSOCIATED CONTENT

Supporting Information

Additional data for a functional group tolerance survey and copies of ^{1}H NMR and ^{13}C NMR spectra for all new compounds (PDF). This material is available free of charge *via* the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.

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