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Photochemical Protection of Amines with Cbz and Fmoc Groups

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Abstract: The photochemical conversion of amines into carbamates was achieved using *N*-Cbz-, *N*-Fmoc-, and *N*-Boc-5,7-dinitroindolines. This reaction allows the protection of amines in neutral medium. Primary and unhindered secondary amines were protected to yield their benzyloxycarbonyl- and 9-fluorenylmethoxycarbonyl derivatives efficiently, whereas bulky amines or anilines gave low yields or no product. On the other hand, the formation of *N*-Boc compounds, although possible, proceeded only with low yields.

The three most common protecting groups for amines are the benzyloxycarbonyl- (Z, Cbz, **1**),[1] the 9-fluorenylmethoxycarbonyl- (Fmoc, **2**),[2] and the *tert*-butoxycarbonyl- (Boc, **3**)[3] derived carbamates. Various reagents have been developed over the years that allow the introduction of these groups under basic conditions.[4] However, methods to protect amines in strictly neutral conditions are still scarce,[5] and we wish to disclose here a clean and exceptionally mild method to convert them into these useful carbamates. The work of Patchornik et al. has shown that it is possible to photochemically acylate amines to give amides under irradiation conditions at 360 nm.[6] This method was initially used by these authors as a carboxyl protecting group and later to assemble two peptidic units. We recently published an improved version of this reaction that allows a clean, mild, and practical preparation of amides.[7,8] The advantage of such an approach is, in addition to the perfectly neutral conditions, that it is possible to premix the reagents and *later* trigger the acylation by turning on the 350-nm light. This external control of the timing of events represents a great versatility for photoaffinity studies or in cascade reactions.[9]

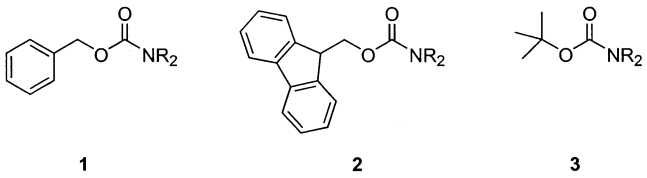
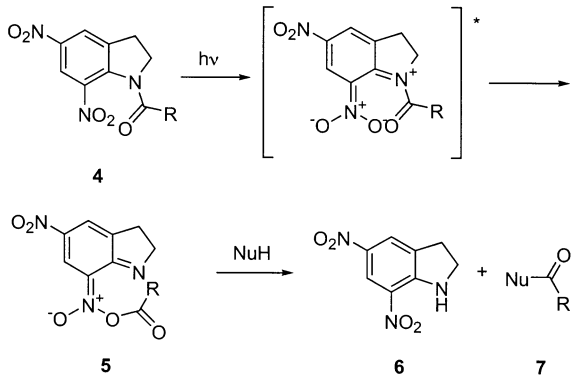


FIGURE 1. Commonly used carbamates.

SCHEME 1. Photochemical Acylation of Nucleophiles



The irradiation with UV light converts the normally inert species **4** into a highly reactive acyl-transfer intermediate (of tentative structure **5**), which is then trapped by the nucleophile, releasing the neutral indoline derivative **6** (Scheme 1).[10]

Preparation of the Acylating Agents. We anticipated that carbamates could be accessed by a similar mechanism, but our initial experiments were unsuccessful in both the preparation and photoacylation reaction. A Lewis acid promoted acylation of 5,7-dinitroindoline **6** proved to be inappropriate for the formation of the carbamates **4a**−**c**.[7] Whereas the anionic route was ineffective for the preparation of the amides,[7] it turned out that the carbamate **4a** was efficiently prepared by prior deprotonation of **6** with sodium hydride (1.5 equiv, THF, rt, 3 h), followed by the addition of benzyl chloroformate (1.5 equiv, rt, 3 h) (Scheme 2). Similarly, the Fmoc-derivative **4b** was prepared using 9-fluorenylmethyl chloroformate (1.2 equiv, 40 h) after deprotonation. On the other hand, the Boc-derivative **4c** was prepared by the reaction of **6** with Boc_2O (1.2 equiv, THF) in the presence of DMAP (0.1 equiv) at 60 °C for 3 h.[11]

Photoacylation Reactions. The protection of amines as *N*-Cbz derivatives proceeded smoothly upon irradia-

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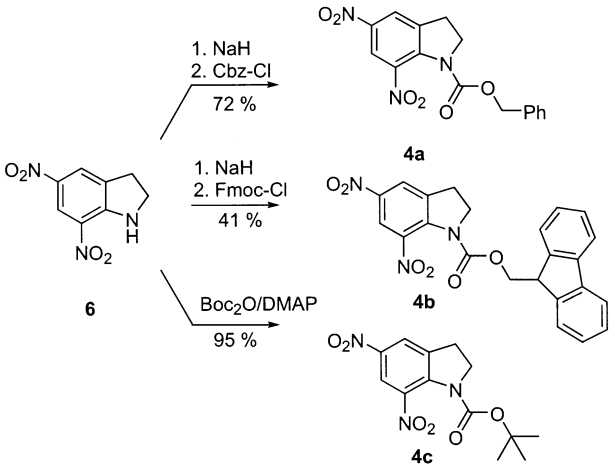
SCHEME 2. Preparation of Photoactivable Carbamates



SCHEME 3. Protection of Amines with the Cbz Group

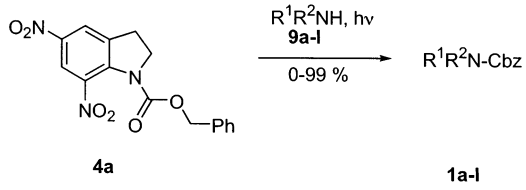


TABLE 1. Protection of Amines with the Cbz Group

entry	amine	R^1, R^2	yield[a]
1	**9a**	*n*-$C_{12}H_{25}$, H	99
2	**9b**	*c*-Hex, H	84
3	**9c**	PhCH(Me), H	86
4	**9d**	*n*-C_5H_{11}, *n*-C_5H_{11}	82
5	**9e**	-$(CH_2)_5$-	92
6	**9f**	*c*-Hex, *c*-Hex	24[b]
7	**9g**	PhCH(OH)CH(Me), Me	43[b]
8	**9h**	4-MeO(C_6H_4), H	0
9	**9i**	CH_2=$CHCH_2$, H	85
10	**9j**	$(CH_3)_2CHCH_2CH$(COOR), H	66[b]
11	**9k**	4-OH−C_6H_4−CH_2CH(COOR), H	33[b]
12	**9l**	$PhCH_2CH$(COOR), H	82

[a] Isolated yields (trituration). [b] Isolated yields (chromatography). R = allyl or ^{t}Bu.

tion for 3 h in a Rayonet apparatus using RPR-3500 lamps. We used a 1:1 mixture of amine and acylating agent **4a** in 1,2-dichloroethane at room temperature (Scheme 3). Most of the aliphatic (primary and secondary) unhindered amines we checked gave high yields of carbamate and no purification other than trituration with cyclohexane was necessary (Table 1). On the other hand, very bulky amines or poorly nucleophilic arylamines gave low yields or no reaction at all. In these cases, chromatography was necessary to purify the carbamates. Esters of amino acids gave satisfactory yields, except for the unprotected tyrosine ester **9k** (entries 10−12). No background reaction was observed in the absence of light (18 h, 40 °C).

The same reaction was also attempted to introduce the Boc group, by using the dinitroindoline derivative **4c** (Scheme 4), under slightly different conditions (1.5 equiv of **4c**, 9 h).

SCHEME 4. Protection of amines with the Boc group

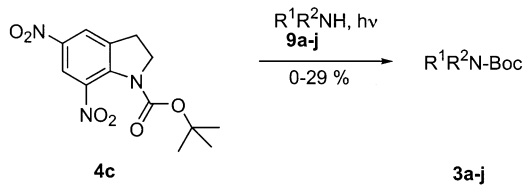


TABLE 2. Protection of Amines with the Boc Group

entry	amine	R^1, R^2	yield[a]
1	**9a**	*n*-$C_{12}H_{25}$, H	27
2	**9b**	*c*-Hex, H	29
3	**9c**	PhCH(Me), H	26
4	**9d**	*n*-C_5H_{11}, *n*-C_5H_{11}	0
5	**9e**	-$(CH_2)_5$-	0
6	**9j**	$(CH_3)_2CHCH_2CH$(COOR), H	24

[a] Isolated yields (chromatography).

SCHEME 5. Protection of Amines with the Fmoc Group

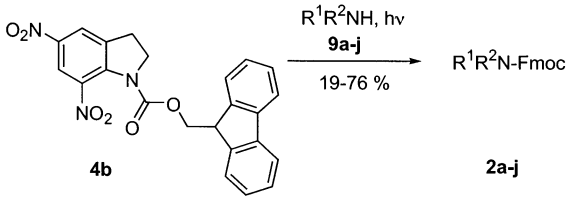


TABLE 3. Protection of Amines with the Fmoc Group

entry	amine	R^1, R^2	yield[a]
1	**9a**	*n*-$C_{12}H_{25}$, H	76
2	**9b**	*c*-Hex, H	65
3	**9d**	*n*-C_5H_{11}, *n*-C_5H_{11}	76
4	**9e**	-$(CH_2)_5$-	72
5	**9f**	*c*-Hex, *c*-Hex	19
6	**9j**	$(CH_3)_2CHCH_2CH$(COOR), H	65

[a] Isolated yields (chromatography).

In this case, mixed results were obtained (Table 2). Indeed, as a result of the lower stability of **4c**, only primary amines reacted, albeit in low yields (24−29%, entries 1−3 and 6). Secondary amines were also unsuccessful (entries 4 and 5). Again, no noticeable background reaction was observed in the absence of light (18 h, 40 °C).

Finally, we attempted to introduce the Fmoc group (Scheme 5). The typical reactivity pattern observed with the Cbz group was restored, albeit with slightly lower yields (Table 3). However, the poor solubility of **4b** required a higher temperature (65 °C, 3 h). Under these conditions, a slow background reaction was observed in the absence of light (ca. 30% decomposition of **4b** at 70 °C for 22 h).

It is interesting to note that with all three indolines **4a**−**c**, the photochemical reaction released the deacylated dinitroindoline **6**, which could be recycled. In contrast to the formation of amides,[7] variable amounts of the corresponding 7-nitrosoindoline **8** were also detected (identified by isolation and high-resolution MS). The amount of side-product seems proportional to the decrease in carbamate yield. This suggests a second, unproductive

reaction pathway. Nitroso-containing side-products have already been detected in related reactions, but no definite explanation is currently available.[10b,12] We are currently examining the mechanism of both productive and unproductive pathways.

In conclusion, we have shown that *N*-Cbz- and *N*-Fmoc-derived carbamates could easily and smoothly be prepared by photochemical acylation of amines. This should be useful to protect sensitive amines, for example, in the synthesis of peptides from unnatural amino acids. The *N*-Boc amines, on the other hand, could only be prepared in mediocre yields. It is interesting to note that while photo-*deprotection* of functional groups has been known for some time,[13] this is the first example of photo-*protection* of amines. A combined protection-deprotection approach is under development and will be reported in due course.

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded on a 500 or 400 MHz spectrometer with solvent used as a reference. For ^{13}C NMR, the number of hydrogen was determined by a DEPT sequence. Absorption bands of IR spectra are in cm^{-1}. Absorption bands of UV spectra are in nm. Mass spectra were recorded with EI (70 eV). All melting points are uncorrected. Photochemical irradiations were made in a Rayonet-RPR-100 photoreactor, in a quartz vessel, with 16 RPR-3500 lamps (at 350 nm). Purification by flash column chromatography (FC) was done on silica gel, with cyclohexane/AcOEt. Unless otherwise indicated, all commercial reagents were used without further purification.

1-Acetylindoline. A solution of indoline (4.00 g, 33.6 mmol) in acetic acid (56 mL) and acetyl chloride (14 mL) was stirred at 90 °C for 3 h. Evaporation of the volatiles gave 5.42 g (quantitative) of the pure product as a pale pink solid (mp 103−106 °C, lit. 102−104 °C). ^{1}H NMR ($CDCl_3$) major rotamer (84%) δ 8.23 (d, J = 8.1 Hz, 1H), 7.21 (m, 2H), 7.03 (t, J = 7.3 Hz, 1H), 4.07 (t, J = 8.5 Hz, 2H), 3.22 (t, J = 8.5 Hz, 2H), 2.25 (s, 3H); minor rotamer (16%) δ 8.23 (d, J = 8.1 Hz, 1H), 7.21 (m, 2H), 7.03 (t, J = 7.3 Hz, 1H), 4.16 (t, J = 8.3 Hz, 2H), 3.09 (t, J = 8.1 Hz, 2H), 2.46 (s, 3H). ^{13}C NMR ($CDCl_3$) major rotamer δ 168.7 (C), 142.8 (C), 131.1 (C), 127.4 (CH), 124.5 (CH), 123.5 (CH), 116.9 (CH), 48.7 (CH_2), 27.9 (CH_2), 24.2 (CH_3); minor rotamer δ 168.3 (C), 141.7 (C), 133.8 (C), 127.2 (CH), 125.8 (CH), 123.1 (CH), 114.0 (CH), 47.9 (CH_2), 26.8 (CH_2), 24.6 (CH_3). IR ($CHCl_3$) 3005.4, 1731.4, 1651.9, 1599.0, 1483.6, 1409.4. MS m/z (%) 161 (44, $M^{+\bullet}$), 119 (91), 118 (100), 91 (17). HR-MS 161.0847 ($C_{10}H_{11}NO$ calcd 161.0841).

1-Acetyl-5,7-dinitroindoline (4, R = Me).[14] 1-Acetylindoline (2.58 g, 16 mmol) was dissolved in a solution of sodium nitrate (4.08 g, 48 mmol) in trifluoroacetic acid (75 mL), and the mixture was stirred at room temperature for 20 h. It was then poured into ice-cold water. A yellow solid precipitated, which was filtered, washed with water, and dried. The filtrate was extracted with AcOEt; this organic layer was washed with saturated $NaHCO_3$ (until basic pH) and with brine, dried over $MgSO_4$, and evaporated. Both solids were purified by recrystallization in toluene/EtOH 1:1, to give 2.33 g (58%) of pure product as yellow crystals (mp 214−219 °C, lit. 216−217 °C). ^{1}H NMR (d_6-DMSO) δ 8.48 (m, 1H), 8.46 (m, 1H), 4.40 (t, J = 8.3 Hz, 2H), 3.37 (t, J = 8.2 Hz, 2H), 2.30 (s, 3H). ^{13}C NMR (d_6-DMSO) δ 169.3 (C), 142.6 (C), 139.9 (C), 139.2 (C), 138.2 (C), 123.6 (CH), 119.2 (CH), 50.5 (CH_2), 28.0 (CH_2), 23.3 (CH_3). IR ($CHCl_3$) 3099.5, 3035.7, 1697.7, 1609.0, 1548.1, 1534.6, 1461.8, 1438.1, 1385.4, 1344.1, 1302.3. UV (46 μM soln in MeCN) λ_{max} (ϵ) 202 (0.90), 224 (0.68), 349 (0.52). MS m/z (%) 251 (2, $M^{+\bullet}$), 209 (100), 163 (11), 117 (13), 89 (10). HR-MS 251.0553 ($C_{10}H_9N_3O_5$ calcd 251.0542).

5,7-Dinitroindoline 6. A mixture of 1-acetyl-5,7-dinitroindoline (1.07 g, 4.3 mmol), methanol, THF, and saturated K_2CO_3 was stirred at room temperature for 3 h. The precipitate was then filtered, washed with water, and dried in vacuo. More material was obtained by extracting the water layer with AcOEt. This organic layer was then washed with brine, dried over $MgSO_4$, and evaporated. The combined brown solid (mp 250−253 °C) yielded 883 mg (99%). ^{1}H NMR (d_6-DMSO) δ 9.05 (s, 1H), 8.55 (m, 1H), 7.97 (m, 1H), 3.89 (t, J = 8.5 Hz, 2H), 3.18 (t, J = 8.0 Hz, 2H). ^{13}C NMR (d_6-DMSO) δ 151.7 (C), 137.5 (C), 135.6 (C), 125.3 (C), 122.6 (CH), 121.2 (CH), 47.8 (CH_2), 26.6 (CH_2). IR ($CHCl_3$) 3442.5, 3015.9, 1630.7, 1525.6, 1433.1, 1318.0. UV (53 μM soln in MeCN) λ_{max} (ϵ) 193 (6.00), 211 (0.63), 264 (0.58), 364 (0.80). MS m/z (%) 209 (100, $M^{+\bullet}$), 163 (18), 117 (40), 89 (18), 63 (13). HR-MS 209.0444 ($C_8H_7N_3O_4$ calcd 209.0437).

***N*-Cbz-5,7-dinitroindoline 4a.** A mixture of 5,7-dinitroindoline (200 mg, 0.96 mmol) and NaH (~60%, 57.4 mg, 1.43 mmol) in 5 mL of dry THF was stirred at room temperature under Ar for 3 h. Benzyl chloroformate (200 μL, 1.43 mmol) was then added dropwise, and the resulting mixture was stirred at room temperature for 3 h. AcOEt was added, and the organic layer was washed with water and brine, dried over $MgSO_4$, and evaporated. Purification by FC (TLC R_f 0.49, cyclohexane/AcOEt 1:1) gave 237 mg (72%) of pure product as a brown solid (mp 132−135 °C). ^{1}H NMR ($CDCl_3$) δ 8.54 (m, 1H), 8.21 (m, 1H), 7.39 (5H), 5.24 (s, 2H), 4.36 (t, J = 8.6 Hz, 2H), 3.29 (t, J = 8.6 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 152.4 (C), 142.9 (C), 140.4 (C), 138.2 (C), 138.0 (C), 135.0 (C), 128.8 (C), 128.75 (CH), 128.7 (CH), 123.1 (CH), 120.1 (CH), 69.0 (CH_2), 50.5 (CH_2), 27.8 (CH_2). IR ($CHCl_3$) 3030.4, 1727.0, 1616.4, 1547.1, 1468.8, 1391.6, 1343.6, 1302.1. UV (52 μM soln in MeCN) λ_{max} (ϵ) 203 (1.30), 342 (0.58). MS m/z (%) 343 (7, $M^{+\bullet}$), 282 (64), 252 (14), 209 (5), 193 (56), 91 (100), 65 (70). HR-MS 343.0780 ($C_{16}H_{13}N_3O_6$ calcd 343.0804).

***N*-Fmoc-5,7-dinitroindoline 4b.** A mixture of 5,7-dinitroindoline (1.20 g, 5.74 mmol) and NaH (~60%, 344 mg, 8.60 mmol) in 30 mL of dry THF was stirred at room temperature under Ar for 3 h. 9-Fluorenylmethyl chloroformate (1.77 g, 6.84 mmol) was then added dropwise, as a solution in 10 mL dry THF, and the resulting mixture was stirred at room temperature for about 40 h. AcOEt and water were then added, and the precipitate was filtered and washed with water and AcOEt. Drying gave 1.02 g (41%) of the pure product as a yellow solid (decomp 270−275 °C). ^{1}H NMR ($CDCl_3$) δ 8.57 (m, 1H), 8.23 (m, 1H), 7.77 (d, J = 7.7 Hz, 2H), 7.57 (d, J = 7.2 Hz, 2H), 7.44 (t, J = 7.4 Hz, 2H), 7.35 (t, J = 7.0 Hz, 2H), 4.67 (d, J = 6.2 Hz, 2H), 4.30 (t, J = 6.2 Hz, 1H), 4.16 (t, J = 8.4 Hz, 2H), 3.23 (t, J = 8.5 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 152.6 (C), 143.2 (C), 143.1 (C), 141.4 (C), 140.4 (C), 138.1 (C), 138.05 (C), 128.0 (CH), 127.3 (CH), 124.9 (CH), 123.1 (CH), 120.2 (CH), 120.1 (CH), 68.8 (CH_2), 50.3 (CH_2), 47.0 (CH), 28.0 (CH_2). IR (KBr) 3088.9, 2955.6, 2900.0, 1723.7, 1611.1, 1550.0, 1522.2, 1394.4, 1336.1, 1293.9, 1192.6, 1039.0. UV (52 μM soln in MeCN) λ_{max} (ϵ) 208 (2.15), 265 (0.98), 289 (0.417), 300 (0.49), 342 (0.47). MS m/z (%) 431 (<1, $M^{+\bullet}$), 209 (8), 178 (100), 165 (9), 89 (7). HR-MS 209.0434 ($C_8H_7N_3O_4$ calcd 209.0437).

***N*-Boc-5,7-dinitroindoline 4c.** A mixture of 5,7-dinitroindoline (200 mg, 0.96 mmol), Boc_2O (250 mg, 1.15 mmol), and DMAP (11.7 mg, 0.10 mmol) in 10 mL of dry THF was stirred at 60 °C for 3 h. The reaction mixture was evaporated and extracted with AcOEt. This organic layer was washed with 10% HCl (twice) and brine, dried over Na_2SO_4, and evaporated, to give 280 mg (95%) of the pure product as a brown solid (mp 110−115 °C). ^{1}H NMR ($CDCl_3$) δ 8.58 (m, 1H), 8.20 (m, 1H), 4.31 (t, J = 8.5 Hz, 2H), 3.28 (t, J = 8.5 Hz, 2H), 1.51 (s, 9 H). ^{13}C NMR ($CDCl_3$) δ 151.2 (C), 142.4 (C), 140.9 (C), 138.3 (C), 137.6 (C), 123.2 (CH), 120.3 (CH), 84.4 (C), 50.7 (CH_2), 28.0 (CH_3), 27.7 (CH_2). IR ($CHCl_3$) 3033.3, 2983.1, 1718.5, 1616.7, 1545.7, 1371.8, 1335.7, 1311.5, 1152.9. UV (50 μM soln in MeCN) λ_{max} (ϵ) 200 (0.92), 222 (0.69), 345 (0.60). MS m/z (%) 309 (<1, $M^{+\bullet}$), 236 (2),

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209 (31), 163 (3), 117 (6), 57 (100). HR-MS 236.0303, 209.0434 ($C_9H_6N_3O_5$, $C_8H_7N_3O_4$ calcd 236.0308, 209.0437).

Typical Procedure for Photoprotection with Cbz. A solution of *N*-Cbz-5,7-dinitroindoline **4a** (0.07 mmol) and amine (0.07 mmol) in 7.5 mL of 1,2-dichloroethane was flushed with argon for 5 min. It was then irradiated at 350 nm for 3 h, under argon, with stirring and cooling by water. The volatiles were then evaporated, and the solid was triturated with warm cyclohexane; the evaporation of cyclohexane gave the carbamate, and the remaining brown solid was mostly 5,7-dinitroindoline. Some 5-nitro-7-nitrosoindoline was also formed.

***N*-Cbz-dodecylamine 1a.** Brown solid (mp 46−48 °C). ^{1}H NMR ($CDCl_3$) δ 7.39−7.30 (5H), 5.10 (s, 2H), 4.74 (br s, 1H), 3.19 (q, J = 6.6 Hz, 2H), 1.50 (2H), 1.26 (18 H), 0.89 (t, J = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 156.3 (C), 136.6 (C), 128.5 (CH), 128.09 (CH), 128.05 (CH), 66.5 (CH_2), 41.1 (CH_2), 31.9 (CH_2), 29.9 (CH_2), 29.61 (CH_2), 29.60 (CH_2), 29.55 (CH_2), 29.52 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 26.7 (CH_2), 22.7 (CH_2), 14.1 (CH_3). IR (neat) 3349.9, 2921.8, 2848.0, 1688.2, 1527.4, 1462.8, 1247.0, 1019.7, 726.8. MS *m*/*z* (%) 319 (1, $M^{+\bullet}$), 184 (3), 108 (100), 99 (16), 91 (84), 55 (13). HR-MS 319.2500 ($C_{20}H_{33}NO_2$ calcd 319.2511).

Typical Procedure for Photoprotection with Boc. A solution of *N*-Boc-5,7-dinitroindoline **4c** (0.10 mmol) and amine (0.07 mmol) in 7.5 mL of 1,2-dichloroethane was flushed with argon for 5 min. It was then irradiated at 350 nm for 9 h, under argon, with stirring and cooling by water. The volatiles were then evaporated, and the solid was triturated with warm cyclohexane; the evaporation of cyclohexane gave the impure carbamate, which was purified by FC (on silica gel, cyclohexane/AcOEt). The remaining brown solid was a mixture of 5,7-dinitroindoline and 5-nitro-7-nitrosoindoline **8**, which was purified by FC (TLC R_f 0.14, cyclohexane/AcOEt 2:1) to get a brown solid (mp 170−174 °C). ^{1}H NMR (d_6-DMSO) δ 10.50 (s, 1H), 9.33 (br s, 1H), 7.91 (s, 1H), 3.82 (t, J = 7.7 Hz, 2H), 3.05 (t, J = 7.9 Hz, 2H). ^{13}C NMR (d_6-DMSO) δ 151.9 (C), 138.8 (C), 136.3 (C), 122.4 (CH), 47.7 (CH_2), 25.4 (CH_2). IR (KBr) 3291.7, 2927.4, 2851.6, 1621.0, 1587.8, 1543.1, 1499.0, 1421.0, 1328.0, 1296.2, 1154.5, 1067.0, 731.0. MS *m*/*z* (%) 193 (100, $M^{+\bullet}$), 163 (65), 117 (72), 89 (27). HR-MS 193.0479 ($C_8H_7N_3O_3$ calcd 193.0487).

***N*-Boc-dodecylamine 3a.** Brown solid (mp 38−40 °C). TLC R_f 0.61 (cyclohexane/AcOEt 2:1). ^{1}H NMR ($CDCl_3$) δ 4.49 (br s, 1H), 3.11 (q, J = 6.3 Hz, 2H), 1.45 (11H), 1.27 (18H), 0.89 (t, J = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 156.0 (C), 79.0 (C), 40.7 (CH_2), 31.9 (CH_2), 30.1 (CH_2), 29.63 (CH_2), 29.61 (CH_2), 29.57 (CH_2), 29.33 (CH_2), 29.29 (CH_2), 28.4 (CH_3), 26.8 (CH_2), 22.7 (CH_2), 14.1 (CH_3). IR (neat) 3375.6, 2918.7, 2849.2, 1686.3, 1513.5, 1466.6, 1245.0, 1167.2. MS *m*/*z* (%) 230 (10), 185 (4), 184 (4), 74 (6), 59 (18), 57 (100).

Typical Procedure for Photoprotection with Fmoc. A solution of *N*-Fmoc-5,7-dinitroindoline **4b** (0.10 mmol) and amine (0.07 mmol) in 7.5 mL of 1,2-dichloroethane was flushed with argon for 5 min. It was then irradiated at 350 nm for 3 h, under argon, with stirring but no cooling (ca. 65 °C). The volatiles were then evaporated, and the solid was triturated with warm cyclohexane; the evaporation of cyclohexane gave the impure carbamate, which was purified by FC (on silica gel, cyclohexane/AcOEt). The remaining brown solid was a mixture of 5,7-dinitroindoline and 5-nitro-7-nitrosoindoline.

***N*-Fmoc-dodecylamine 2a.** Pale brown solid (mp 100−103 °C). TLC R_f 0.59 (cyclohexane/AcOEt 2:1). ^{1}H NMR ($CDCl_3$) δ 7.78 (d, J = 7.6 Hz, 2H), 7.61 (d, J = 7.5 Hz, 2H), 7.41 (t, J = 7.2 Hz, 2H), 7.32 (td, J = 7.5, 1.3 Hz, 2H), 4.73 (br s, 1H), 4.42 (d, J = 6.8 Hz, 2H), 4.23 (t, J = 6.7 Hz, 1H), 3.20 (q, J = 6.1 Hz, 2H), 1.51 (2H), 1.28 (18H), 0.90 (t, J = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 156.4 (C), 144.1 (C), 141.4 (C), 127.6 (CH), 127.0 (CH), 125.0 (CH), 119.9 (CH), 66.5 (CH_2), 47.4 (CH), 41.1 (CH_2), 31.9 (CH_2), 30.0 (CH_2), 29.64 (CH_2), 29.61 (CH_2), 29.58 (CH_2), 29.55 (CH_2), 29.33 (CH_2), 29.29 (CH_2), 26.8 (CH_2), 22.7 (CH_2), 14.1 (CH_3). IR (neat) 3333.1, 2920.0, 2851.8, 1688.2, 1537.1, 1451.9, 1265.1, 1154.7, 1028.2. MS *m*/*z* (%) 178 (100), 165 (7), 99 (2), 57 (3). HR-MS 407.2869 ($C_{27}H_{37}NO_2$ calcd 407.2824).

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Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectra for all compounds and characterization data for all compounds not described in the Experimental Section. This material is available free of charge via the Internet at http://pubs.acs.org.

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