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Synthesis of photocaged diamines and their application in photoinduced self-assembly

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Abstract

The photochemical cleavage of covalent bonds is an important strategy in protection group chemistry, as well as for the triggering of chemical events posterior to the application of the physicochemical stimulus. Photocages allow the arresting and traceless liberation of a chemical entity, which can be broadly applied as a functional control element in materials chemistry and the life sciences in general. Among the best studied and most versatile light-sensitive protecting groups known to date rank the *o*-nitrobenzyl derivatives, entities which are easily introduced to amines, thiols, and alcohols. Their photolability relies on a phototautomerisation-induced cleavage mechanism, a phenomenon largely dependent on the substitution pattern of the aromatic ring in the *o*-nitrophenyl-moiety. Although well described and studied in detail for the protection of amino groups of different nature, the photocaging of aliphatic diamines has not been described in detail to date. Because of their interesting properties as synthons in supramolecular and polymer chemistry alike, we wish to describe the efficient photocaging of diamines with *o*-nitrobenzyl derivatives, their photocleavage behavior over time, as well as their application in a photoinduced templated self-assembly reaction towards cyclic imines.

KEYWORDS

diamines, imine formation, photocaging, photochemistry, physicochemical stimuli, self-assembly

1 | INTRODUCTION

The exploitation of light energy as a driving force for chemical transformations is of exceptional utility, since it allows for the spatiotemporal control of reactivity on-demand, resulting in triggerable chemical reactions and their associated functions.[1] Many light sources offer the exact control of their emitted wavelengths, discrete operational areas, and highly exact exposure times, rendering them perfect tools for applications in organic chemistry, material sciences, and medicine alike.[2] Photochemical organic reactions can basically be distinguished as irreversible (eg, photochemical bond cleavages) and reversible transformations (eg, light-induced isomerizations).[3] Whereas reversible reactions are commonly applied in complex systems chemistry, dynamic materials, biomedical gating processes, and photopharmacology,[4] irreversible reactions are more common in light-controlled polymerizations or as photocleavable protection groups.[5] *o*-Nitrobenzyl derivatives are among the most common irreversibly light-cleaved molecules, and their invention is dating back to reports by Barltrop et al,[6] and since then, they were widely applied, greatly improved, and mechanistically studied by various laboratories.[7] The simplicity and straightforward synthetic manipulation render them

perfect for photoprotection in organic chemistry or as highly efficient control elements in on/off and off/on processes.[8] The mechanism involved in their photocleavage relies on a phototautomerism (see Scheme 1), initiated by (i) a light-induced hydrogen transfer from the benzylic substituent in *o*-position to the NO_2-group, resulting in (ii) an *aci*-nitro-intermediate in *Z*- or *E*-form, with the (iii) *E-aci*-nitro species cyclizing irreversibly into a 5-membered ring. This bicyclic intermediate finally ring opens into a transient nitroso-alcohol, releasing the previously protected molecule from the benzylic position, resulting in the deprotected entity and an *o*-nitrosobenzaldehyde as a by-product.[9]

Therefore, it is no surprise that electron-donating substituents in the aromatic ring facilitate the reaction, and the most commonly applied *o*-nitrobenzyl derivatives bear the 4,5-MeO-substitution pattern or other electron rich groups (see Scheme 1, right hand side).[10]

Despite the fact that the photochemical properties, quantum yields, and reactivities of differently substituted *o*-nitrobenzyl derivatives are well studied,[7a] we were intrigued by their application towards the photocaging of diamines, as they are representing viable substrates in polymerizations and self-assembly reactions alike.[11]

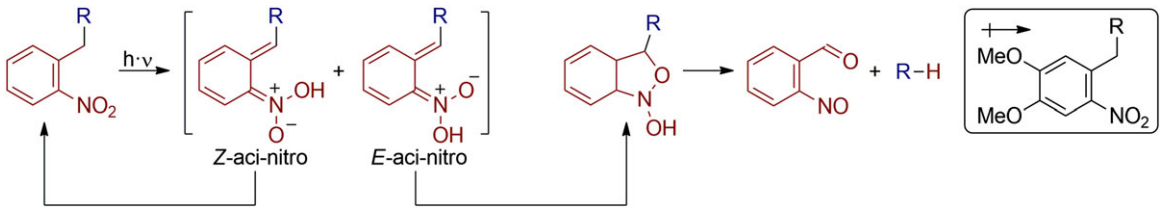
2 | EXPERIMENTAL

2.1 | Materials and apparatus

Solvents (anhydrous and nonanhydrous) and commercial starting materials were used as received. Reactions were monitored by thin layer chromatography (TLC) carried out on silica gel plates (Merck 60F-254) using UV light for visualization. Column chromatography was carried out with standard silica gel on normal phase (Merck 60, particle size 0.040 to 0.063 mm). Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker DPX 300 (300 MHz for ^{1}H, 75 MHz for ^{13}C) spectrometer at 25°C using residual protonated solvent signals as internal standards for ^{1}H and ^{13}C spectra (^{1}H: δ ($CDCl_3$) = 7.26 ppm, ^{13}C: δ ($CDCl_3$) = 77.16 ppm). The splitting patterns are abbreviated as follows: singlet (s), doublet (d), multiplet (m), and broad singlet (bs). UV/VIS spectra were recorded using quartz cuvettes on a Varian Cary 50 spectrophotometer, equipped with a thermostated cell holder at 25 ± 0.1°C. For irradiation experiments, ThorLabs LEDs (365 and 405 nm) were applied, coupled with a collimator and optical fiber to direct and concentrate light beams onto the sample solutions. Ultraperformance liquid chromatography coupled to mass spectrometry detection (UPLC-MS) was performed with a Waters Alliance system (gradient mixture of acetonitrile/water) equipped with Acquity UPLC columns. The Waters system consisted of a Waters Separations Module 2695, a Waters Diode Array Detector 996, an LCT Premier XE mass spectrometer, and a Waters Mass Detector ZQ 2000.

2.1.1 | 2-Nitrobenzyl(4-nitrophenyl) carbonate

4.28 g (1.3 Eq, 21.23mmol) 4-nitrophenyl chloroformate was dissolved in 100 mL dry THF and subsequently cooled to 0°C. Then, 1.71 mL (1.3 Eq, 21.23mmol) pyridine was added to the solution dropwise and the mixture left stirring for 30 minutes. Subsequently, 2.50 g (1.0 Eq, 16.33mmol) of 2-nitrobenzyl alcohol dissolved in 50 mL dry THF was added over 10 minutes and the resulting mixture left stirring for 16 hours at room temperature. Then, 100 mL CH_2Cl_2 was added to the mixture and then transferred to a separation funnel and washed with 1M HCl (3 × 50 mL) and brine (1 × 80 mL). The aqueous layer was reextracted with CH_2Cl_2 (2 × 50 mL) and the unified organic phases dried over $MgSO_4$. The solvent was removed in vacuo and the crude product purified by recrystallization from a mixture of ethyl acetate/petrol ether 40-60 and washed with cold petrol ether, giving 4.54 g (14.23mmol, 87% yield) of an off-white solid. Analytics: ^{1}H-NMR (300 MHz, $CDCl_3$) δ [ppm]: 5.74 (s, 2H, —CH_2O—), 7.42 (d, 2H, ^3J = 9.2 Hz, Ar-H), 7.55-7.62 (m, 1H, Ar-H), 7.71-7.77 (m, 2H, Ar-H), 8.20 (d, 1H, ^3J = 8.8 Hz), 8.29 (d, 2H, ^3J = 9.2 Hz, Ar-H). ^{13}C-NMR



SCHEME 1 Photochemical cleavage of *o*-nitrobenzyl derivatives with transient species; most efficiently cleaved *o*-nitrobenzyl derivative because of electron-donating substitutions (box on right hand side)

(75 MHz, $CDCl_3$) δ [ppm]: 67.5, 121.9, 125.5, 125.7, 129.2, 129.7, 130.7, 134.3, 145.7, 147.5, 152.2, 155.5. UV-VIS (λ_{max}): 265 nm.

2.1.2 | 4,5-Dimethoxy-2-nitrobenzyl(4-nitrophenyl)carbonate

3.07 g (1.3 Eq, 15.24mmol) 4-nitrophenyl chloroformate was dissolved in 100 mL dry THF and subsequently cooled to 0°C. Then, 1.23 mL (1.3 Eq, 15.24mmol) pyridine was added to the solution dropwise and the mixture left stirring for 30 minutes. Subsequently, 2.50 g (1.0 Eq, 11.73mmol) of 4,5-dimethoxy-2-nitrobenzyl alcohol dissolved in 50 mL dry THF was added over 10 minutes and the resulting mixture left stirring for 16 hours at room temperature. Then, 100 mL CH_2Cl_2 was added to the mixture and then transferred to a separation funnel and washed with 1M HCl (3 × 50 mL) and brine (1 × 80 mL). The aqueous layer was reextracted with CH_2Cl_2 (2 × 50 mL) and the unified organic phases dried over $MgSO_4$. The solvent was removed in vacuo and the crude product purified by recrystallization from a mixture of ethyl acetate/petrol ether 40-60 and washed with cold petrol ether, giving 3.43 g (9.07mmol, 77% yield) of a slightly yellow solid. Analytics: ^{1}H-NMR (300 MHz, $CDCl_3$) δ [ppm]: 3.98 (s, 3H, CH_3O—), 4.02 (s, 3H, CH_3O—), 5.71 (s, 2H, —CH_2O—), 7.10 (s, 1H, Ar-H), 7.41 (d, 2H, ^3J = 9.2 Hz, Ar-H), 7.77 (s, 1H, Ar-H), 8.29 (d, 2H, ^3J = 9.2 Hz, Ar-H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ [ppm]: 56.6, 56.7, 67.8, 108.5, 110.7, 121.9, 125.2, 125.5, 140.1, 145.6, 148.9, 152.2, 153.8, 155.5. UV-VIS (λ_{max}): 246 nm, 343 nm.

2.1.3 | (3,4,5-trimethoxy-2-nitrophenyl)-methanol

3.0 g (1.0 Eq, 11.06mmol) methyl-3,4,5-trimethoxy-2-nitrobenzoate were dissolved in 50 mL dry toluene under an atmosphere of argon and cooled to −20°C (ice-NaCl mixture). Subsequently, a solution of DIBAL-H in toluene (1.2M, 1.25 Eq, 13.27mmol, 11.06 mL) was added slowly over 10 minutes. The reaction was left stirring for 2 hours at room temperature, after which the mixture was treated with MeOH, diluted with H_2O, and transferred to a separation funnel. The reaction was extracted with ethyl acetate (3 × 100 mL) and the unified extracts dried over $MgSO_4$, filtered, and evaporated to dryness. The resulting crude material was purified by column chromatography (ethyl acetate/petrol ether 40-60, 1:3), resulting in a yellow solid (1.55 g, 6.37mmol, 58% yield). Analytics: ^{1}H-NMR (300 MHz, $CDCl_3$) δ [ppm]: 3.89 (s, 3H, CH_3O—), 3.93 (s, 3H, CH_3O—), 3.90 (s, 3H, CH_3O—), 4.62 (s, 2H, —CH_2O—), 6.83 (s, 1H, Ar-H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ [ppm]: 56.4, 61.3, 61.6, 62.6, 106.9, 130.0, 138.4, 142.1, 147.0, 155.8.

2.1.4 | 3,4,5-trimethoxy-2-nitrobenzyl(4-nitrophenyl)carbonate

1.2 g (1.3 Eq, 6.41mmol) 4-nitrophenyl chloroformate was dissolved in 30 mL dry THF and subsequently cooled to 0°C. Then, 0.52 mL (1.3 Eq, 6.41mmol) pyridine was added to the solution dropwise and the mixture left stirring for 30 minutes. Subsequently, 1.20 g (1.0 Eq, 4.94mmol) of 3,4,5-trimethoxy-2-nitrobenzyl alcohol dissolved in 20 mL dry THF was added over 10 minutes and the resulting mixture left stirring for 16 hours at room temperature. Then, 100 mL CH_2Cl_2 was added to the mixture and then transferred to a separation funnel and washed with 1M HCl (3 × 20 mL) and brine (1 × 40 mL). The aqueous layer was reextracted with CH_2Cl_2 (2 × 30 mL) and the unified organic phases dried over $MgSO_4$. The solvent was removed in vacuo and the crude product purified by column chromatography over silica gel with ethyl acetate/petrol ether 40-60 mixtures (5:1 to 1:1), resulting in the product in quantitative amounts as a slightly yellow solid. Analytics: ^{1}H-NMR (300 MHz, $CDCl_3$) δ [ppm]: 3.91 (s, 3H, CH_3O—), 3.94 (s, 3H, CH_3O—), 4.00 (s, 3H, CH_3O—), 5.30 (s, 2H, —CH_2O—), 6.80 (s, 1H, Ar-H), 7.38 (d, 2H, ^3J = 9.3 Hz, Ar-H), 8.27 (d, 2H, ^3J = 9.3 Hz, Ar-H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ [ppm]: 56.6, 61.3, 62.6, 66.5, 107.7, 121.9, 123.0, 125.5, 126.3, 143.3, 145.6, 147.2, 152.2, 155.4, 155.5. UV-VIS (λ_{max}): 265 nm, 340 nm.

2.1.5 | Bis(4,5-dimethoxy-2-nitrobenzyl) ((ethane-1,2-diylbis (oxy))bis (ethane-2,1-diyl))-di-carbamate

54.2 mg (55 μL, 0.366mmol, 1.0 Eq) 2,2'-(ethane-1,2-diylbis-(oxy))-diethanamine and 304.6 mg (0.805mmol, 2.2 Eq) 4,5-dimethoxy-2-nitrobenzyl-(4-nitrophenyl)-carbonate were dissolved in 19 mL dry CH_3CN. Subsequently, 104.1 mg (137 μL, 0.805mmol, 2.2 Eq) DIPEA were added and the resulting mixture stirred at reflux overnight. The solvent was evaporated to dryness and purified by column chromatography on SiO_2 (cyclohexane/ethyl acetate 1:1), giving the title compound in quantitative amounts as a slight yellow solid. Analytics: ^{1}H-NMR (300 MHz, $CDCl_3$) δ [ppm]: 3.38-3.42 (m, 4H, —CH_2—), 3.56-3.58 (m, 4H, —CH_2—), 3.61 (bs, 4H, —CH_2—), 3.93 (s, 6H, CH_3O—), 3.95 (s, 6H, CH_3O—), 5.46 (bs, 6H, —CH_2O— and —NH—), 6.97 (s, 2H, Ar-H), 7.66 (s, 2H, Ar-H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ

[ppm]: 41.0, 56.5, 63.7, 70.1, 70.4, 108.2, 110.6, 128.0, 140.0, 148.2, 153.6, 156.1. MS (ESI+) m/z: 627.214 ($M + H^+$), calcd. 610.215. UV-VIS (λ_{max}): 346 nm.

2.1.6 | Bis(2-nitrobenzyl)((ethane-1,2-diylbis (oxy))bis (ethane-2,1-diyl)) dicarbamate

54.2 mg (55 μL, 0.366mmol, 1.0 Eq) 2,2′-(ethane-1,2-diylbis (oxy))-diethanamine and 256.3 mg (0.805mmol, 2.2 Eq) 2-nitrobenzyl-(4-nitrophenyl)-carbonate were dissolved in 20 mL dry CH_3CN. Subsequently, 104.1 mg (137 μL, 0.805mmol, 2.2 Eq) DIPEA were added and the resulting mixture stirred at reflux overnight. The solvent was evaporated to dryness and purified by column chromatography on SiO_2 (cyclohexane/ethyl acetate 1:1), giving 159 mg (0.314mmol, 86 % yield) of the title compound as a slight yellow solid. Analytics: ^{1}H-NMR (300 MHz, $CDCl_3$) δ [ppm]: 3.38-3.41 (m, 4H, —CH_2—), 3.56-3.59 (m, 4H, —CH_2—), 3.61 (bs, 4H, —CH_2—), 5.47-5.53 (m, 6H, —CH_2O— and —NH—), 7.42-7.45 (m, 2H, Ar-H), 7.55-7.57 (m, 2H, Ar-H) 7.59-7.62 (m, 2H, Ar-H),8.05 (d, J = 8.2 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ [ppm]: 41.0, 63.4, 70.0, 70.4, 125.0, 128.6, 128.9, 133.7, 147.4, 156.0. MS (ESI+) m/z: 524.16 ($M + H_2O$), 507.14 ($M + H^+$). UV-VIS (λ_{max}): 265 nm.

2.1.7 | Bis(3,4,5-trimethoxy-2-nitrobenzyl) ((ethane-1,2-diylbis (oxy))bis (ethane-2,1-diyl))di-carbamate

54.2 mg (55 μL, 0.366mmol, 1.0 Eq) 2,2'-(ethane-1,2-diylbis-(oxy))-diethanamine and 304.6 mg (0.805mmol, 2.2 Eq) 4,5-dimethoxy-2-nitrobenzyl-(4-nitrophenyl)-carbonate were dissolved in 20 mL dry CH_3CN. Subsequently 104.1 mg (137 μL, 0.805mmol, 2.2 Eq) DIPEA were added and the resulting mixture stirred at reflux overnight. The solvent was evaporated to dryness and purified by column chromatography on SiO_2 (cyclohexane/ethyl acetate 1:1), giving 245 mg (0.358mmol, 98 % yield) of the title compound as a slight yellow solid. Analytics: ^{1}H-NMR (300 MHz, $CDCl_3$) δ [ppm]: 3.33-3.36 (m, 4H, —CH_2—), 3.52-3.54 (m, 4H, —CH_2—), 3.58 (bs, 4H, —CH_2—), 3.87 (s, 6H, CH_3O—), 3.89 (s, 6H, CH_3O—), 3.95 (s, 6H, CH_3O—), 5.07 (s, 4H, —CH_2O), 5.38 (bs, 2H, NH—), 6.72 (s, 2H, Ar-H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ [ppm]: 41.0, 56.4, 61.3, 62.5, 70.0, 70.4, 107.5, 125.4, 139.0, 142.5, 146.7, 155.2, 155.9. MS (ESI+) m/z: 704.24 ($M + H_2O$), 687.24 ($M + H^+$). UV-VIS (λ_{max}): 255 nm, 360 nm.

2.1.8 | Bis(4,5-dimethoxy-2-nitrobenzyl) (oxybis (ethane-2,1-diyl))dicarbamate

49.0 mg (50 μL, 0.471mmol, 1.0 Eq) 2,2'-oxydiethanamine and 391.6 mg (1.035mmol, 2.2 Eq) 4,5-dimethoxy-2-nitrobenzyl-(4-nitrophenyl)-carbonate were dissolved in 24 mL dry CH_3CN. Subsequently, 133.8 mg (176 μL, 1.035mmol, 2.2 Eq) DIPEA were added and the resulting mixture stirred at reflux overnight. The solvent was evaporated to dryness and purified by column chromatography on SiO_2 (cyclohexane/ethyl acetate 1:1), giving 257 mg (0.441mmol, 94 % yield) of the title compound as a slight yellow solid. Analytics: ^{1}H-NMR (300 MHz, DMSO) δ [ppm]: 3.16-3.20 (m, 4H, —CH_2—), 3.42-3.44 (m, 4H, —CH_2—), 3.86 (s, 6H, CH_3O—), 3.88 (s, 6H, CH_3O—), 5.31 (s, 4H, —CH_2O—), 7.16 (s, 2H, Ar-H), 7.49-7.51 (m, 2H, —NH—), 7.67 (s, 2H, Ar-H). ^{13}C-NMR (75 MHz, DMSO) δ [ppm]: 56.1, 56.2, 62.4, 68.9, 108.1, 110.5, 127.9, 139.2, 147.7, 153.3, 155.8. MS (ESI+) m/z: 583.187 ($M + H^+$), calcd. 583.189. UV-VIS (λ_{max}): 346 nm.

3 | RESULTS AND DISCUSSION

The incorporation of photocaged molecules into a system designed to self-assemble renders light an ideal trigger to start the chemical reaction, or more general, to trigger the associated event. To introduce the *o*-nitrobenzyl group to amines, the most common strategy leads through the corresponding *p*-nitrophenyl-(PNP)-carbonates, since the PNP-group represents an excellent leaving group upon nucleophilic attacks.[12] To pursue our endeavors, we synthesized different (mainly electron-rich) candidates from commercially available *o*-nitrobenzyl alcohols and *p*-nitrophenyl chloroformate. This simple one-pot procedure with pyridine as an activating agent gave the corresponding products **1**-**3** in good to excellent yields (see Figure 1, left side). Since we were intrigued by the results of Cummings and Krafft[13] on the virtual unreactivity of the 3,4,5-MeO-substituted *o*-nitrobenzyl-group, we synthesized the related carbonate **3** in two steps from the ester as well (see Figure 1, top right) to gain more insight into these molecules.[14]

First, we studied the synthesized carbonates by UV-spectroscopy (in CH_3CN as a solvent) to corroborate the aforementioned reactivity trends. The unsubstituted carbonate **1** shows an absorption maximum at λ = 265 nm, and the 4,5-MeO-substituted **2** two maxima at λ = 246 and 343 nm, respectively, with a curve fading further into the 400 nm range. The 3,4,5-MeO-derivative **3** shows a maximum at λ = 265 nm and a slightly wider shoulder into the 400 nm range as compared with **1**, nevertheless with much lower intensities than **2** (at equal concentration in

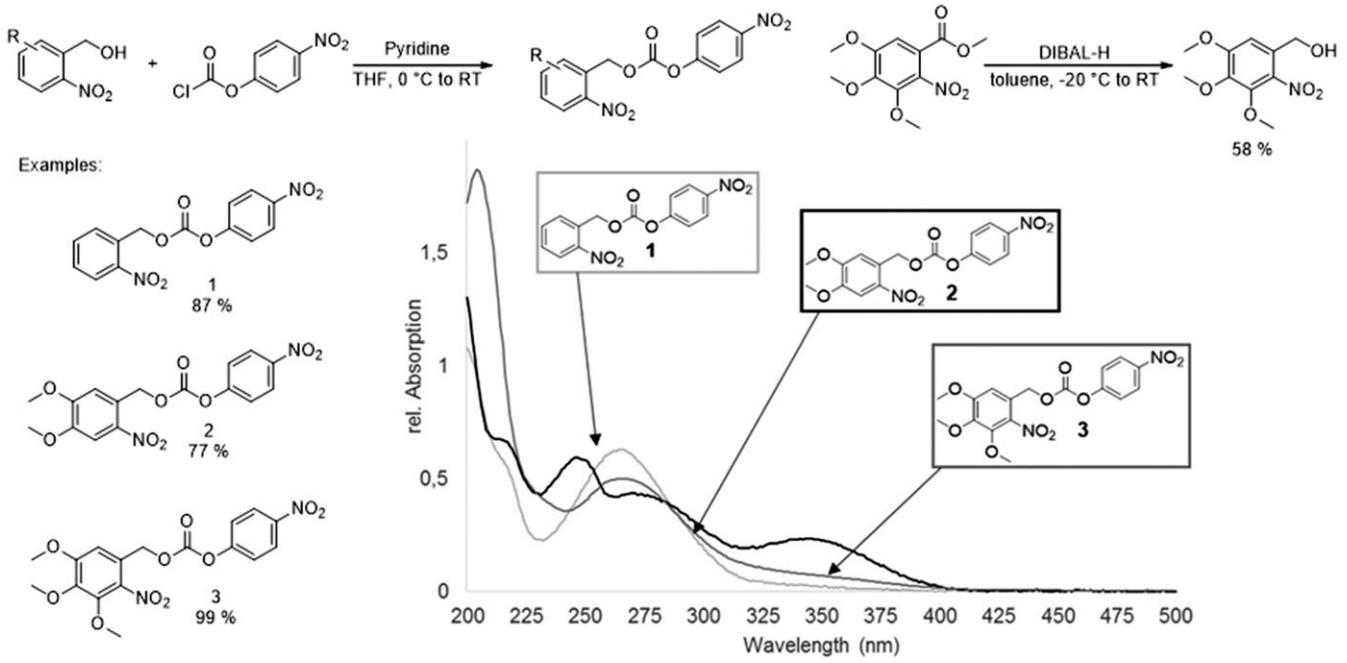


FIGURE 1 Synthesis of differently substituted *o*-nitrobenzyl-(PNP)-carbonates **1**-**3** and their corresponding UV-spectra

CH_3CN). Considering these absorption spectra, it was no surprise that **1** and **2** also performed substantially better in photocleavage experiments when irradiated with a 365 nm LED light under constant reaction control. Carbonate **2** was the most efficiently cleaved candidate as indicated by the initial spectral change, whereas **3** showed virtually no change even after 30 minutes of irradiation at a wavelength of 365 nm, very much in line with the previous results reported by Cummings and Krafft.[13]

Considering our goal of the implementation of a photoinduced templated self-assembly reaction of iminoid macrocycles, we turned our attention to the development of a synthetic protocol for the photoprotection of different aliphatic diamines. We deemed the commercially available 2,2′-(ethane-1,2-diylbis-(oxy))-diethanamine as the most appropriate for the templated self-assembly of macrocycles following different reports by Haussmann et al,[15] although we synthesized photocaged ethylenediamine and 2,2′-oxydiethaneamine as well. Oxygen-containing diamines are generally more favorable for templated self-assembly reactions, since they add multiple coordination sites for metal centers into a system. The synthetic protocol we developed involves the corresponding *p*-nitrophenyl-carbonates **1**-**3** and the respective diamines, using Hünig's base (DIPEA) as a base, under refluxing conditions in acetonitrile. This protocol gave us the resulting products **4**-**6** in good to excellent yields (see Figure 2).

From the respective UV absorption spectra, it became very clear that candidate **5** is the most viable for photoinduced release applications, since it shows a strong absorption maximum at $\lambda = 346$ nm. As expected from previous studies and our own results, the 3,4,5-MeO-substituted derivate **6** did not show any significant absorption maximum in the UV/VIS range. In the photocleavage experiments of the corresponding photocaged diamines, we compared their light-induced photo deprotection over time (see Figure 3). It was no surprise that **4** and **5** performed significantly better than **6** (see Figure 3, top vs bottom right), with candidate **5** being superior to **4** as shown by the faster initial spectral change rate, indicating a more efficient liberation of the diamine and better availability for a following self-assembly reaction in the tentative supramolecular assembly application. The absorption spectrum of **5** and its fading into the 400 nm range possibly opens up the photocleavage in the visible light range, a theory we could actually prove by using a 405 nm LED light in the photo uncaging experiment (see Figure 3, bottom left). This fact is especially interesting for applications in medicine, where light of longer wavelengths is vital for its application in tissue, allowing for a deeper tissue penetration as a function of longer wavelengths.[16]

With these results in hand, we turned our attention towards the application of photocaged diamines in photoinduced self-assembly reactions with dialdehydes in a reversible condensation fashion. We chose an experimental setup with commercially available 2,6-pyridinedialdehyde,[17] our photoprotected diamine **5**, and Zn $(OTf)_2$ as a templating metal source, since it is easily available and compatible with in situ NMR experiments. As a first reaction, we carried out a control experiment to exclude the existence of background reactions of any type. For this purpose, we mixed the 2,6-pyridinedialdehyde,

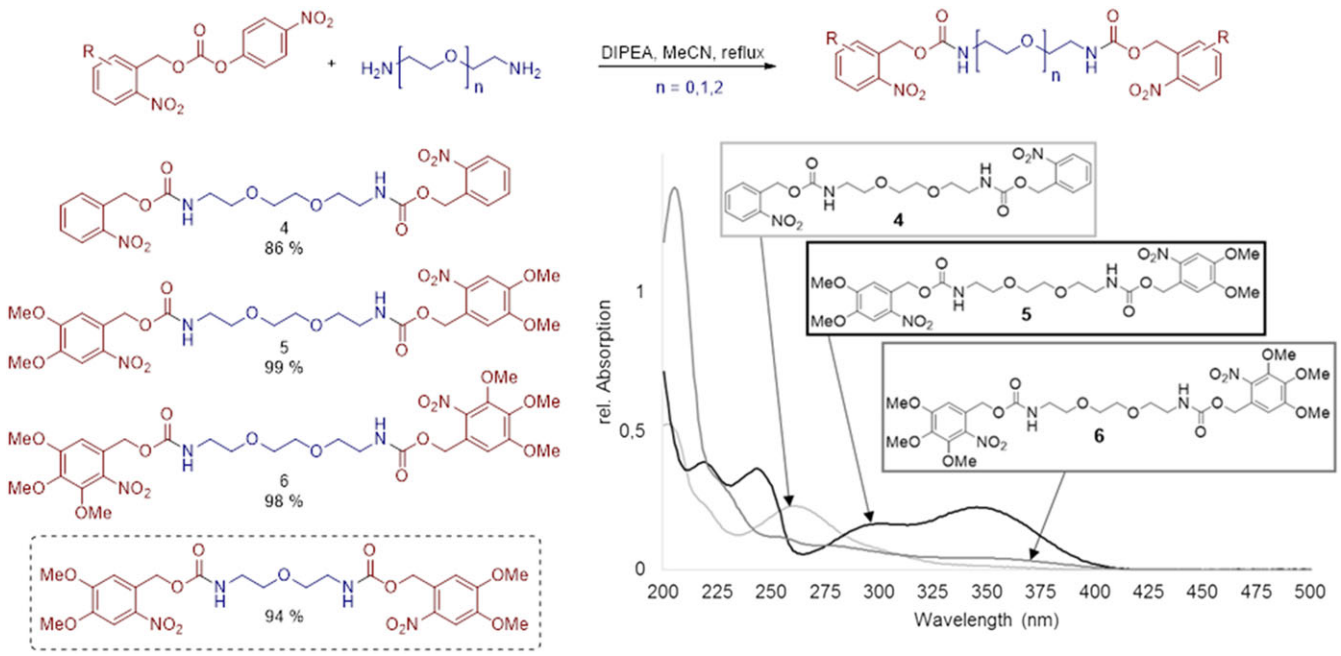


FIGURE 2 Synthesis of different photocaged diamines **4**-**6** and corresponding UV-spectra

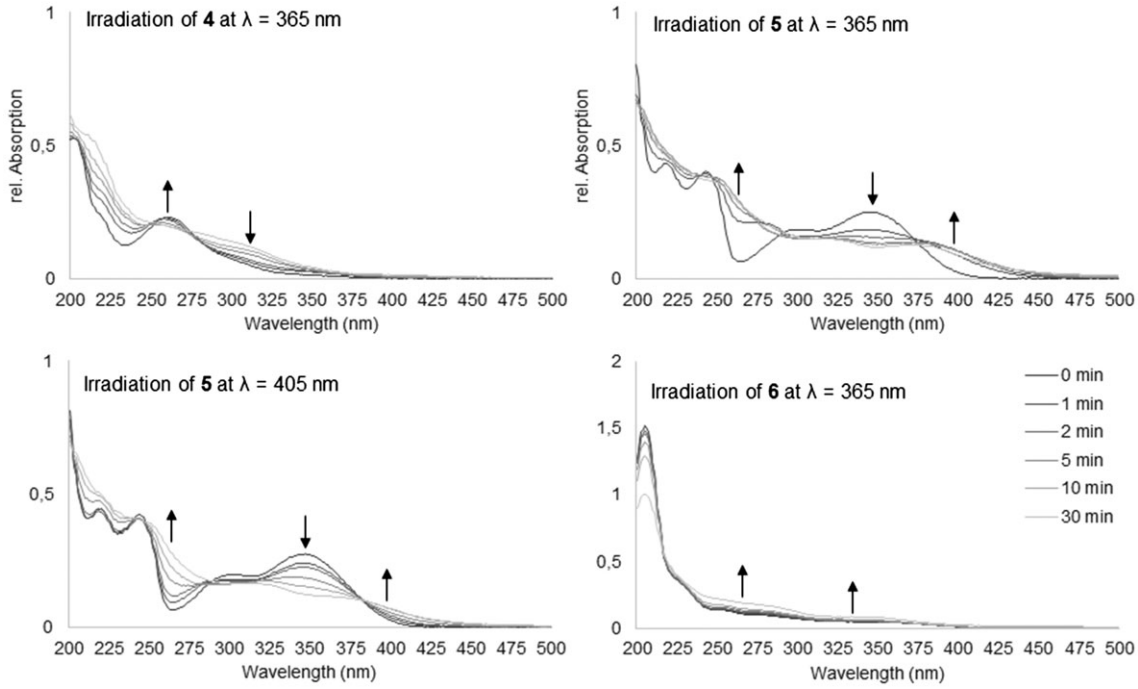


FIGURE 3 Photocleavage of caged diamines **4**,**5**, and **6** over time and at different wavelengths (365 vs 405 nm)

photocaged diamine **5**, and $Zn(OTf)_2$ in equimolar amounts in a 1:1 mixture of $CDCl_3/CD_3CN$ at 0.2M concentration. The resulting ^{1}H-NMR spectrum virtually resembles the reactants, without additional aldehyde or aromatic peaks indicative for any significant background reaction (see Figure 4a).

The next experiment we carried out was the stoichiometric mixture of 2,6-pyridinedialdehyde, free 2,2'-(ethane-1,2-diylbis (oxy))-diethanamine, and $Zn(OTf)_2$ in equimolar amounts in a 1:1 mixture of $CDCl_3/CD_3CN$ at 0.2M concentration. After heating this mixture to 60°C for equilibration of the reversible reaction, we obtained a ^{1}H-NMR-spectrum

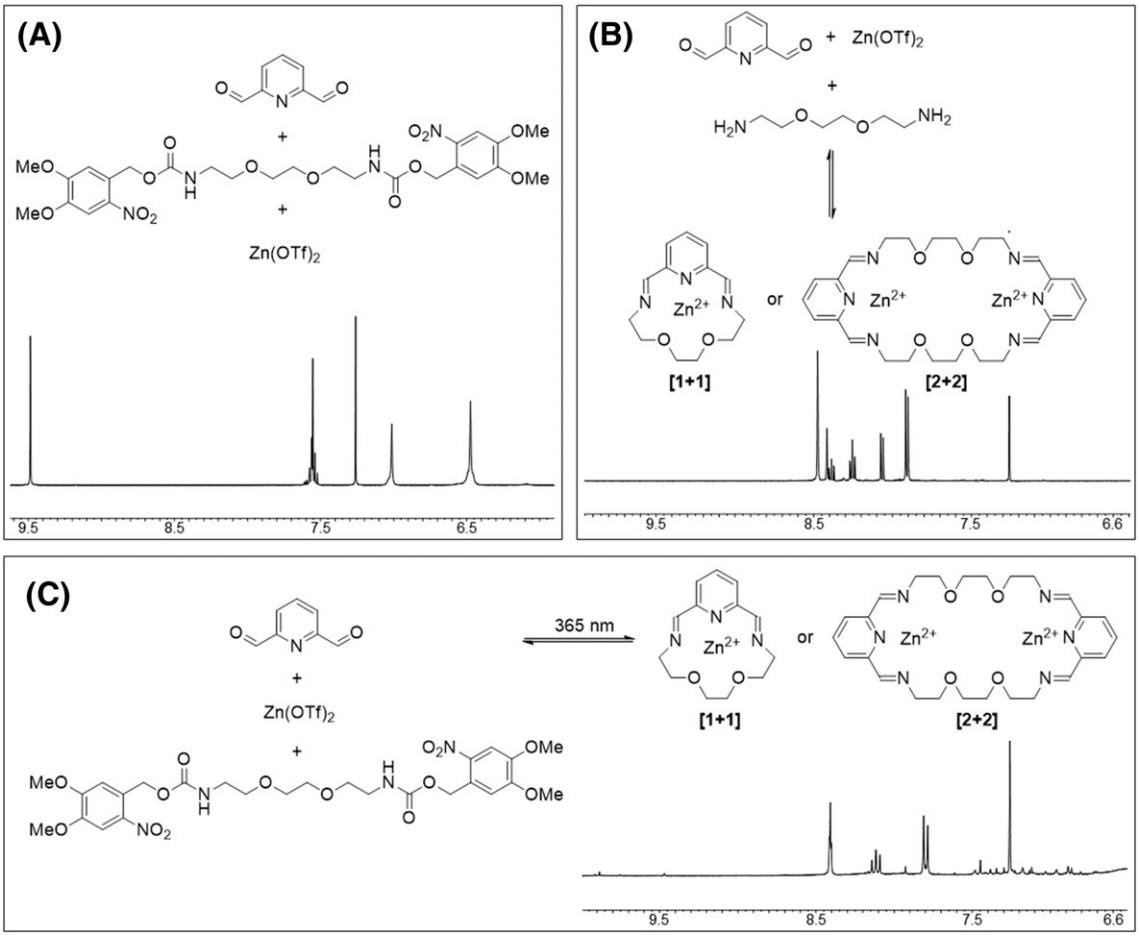


FIGURE 4 A photoinduced self-assembly reaction featuring (a) background reaction of dialdehyde, photocaged diamine **5**, and Zn $(OTf)_2$; (b) reaction of dialdehyde, noncaged diamine, and Zn $(OTf)_2$; and (c) dialdehyde, photocaged diamine **5**, and Zn $(OTf)_2$ after irradiation with UV light of $\lambda = 365$ nm

of a mixture of two major species. These peaks are likely indicative for [n + n]-macrocycles, and the clean nature of the NMR-spectrum shows that the reaction mixture is approaching to or had reached an equilibrium state (see Figure 4b).

Finally, in an experiment otherwise identical to the one reported in Figure 4a, we irradiated the corresponding sample with an LED of $\lambda = 365$ nm for 200 minutes, then equilibrated the mixture at 60°C for 1 hour, and subsequently analyzed the ^{1}H-NMR-spectrum. We were pleased to find a clean and virtually identical spectrum of one of the species observed in the spectrum of Figure 4b. Although we were not able to clearly identify whether a [1 + 1]- or a [2 + 2]-macrocycle was formed, previous reports on similar molecules indicate that strain renders formations of [2 + 2]-macrocycle more likely.[15a] In any case, it became quite clear that the effect of diamine photocaging was beneficiary for an ordered formation of dialdehyde/diamine adducts. One can presume that the consecutive liberation of the diamine leads through pathways involving Zn-coordinated intermediates.

4 | CONCLUSIONS

In summary, we demonstrated the potential of *o*-nitrobenzyl derivatives as photosensitive protection groups for synthetically important diamines. Our utilization of these molecules in self-assembly reactions triggered by light is showcasing only one possible application of photocaged diamines. Many other diamines of aromatic and aliphatic nature are important building blocks in systems chemistry and materials, thus rendering the application of light perfect to trigger these systems. Although we did focus on regular *o*-nitrobenzyl derivatives in this study, the fact that photocages cleavable at longer wavelengths are developed regularly enables the application of photocaged diamines in life sciences for the future.

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