Photoassisted Diversity-Oriented Synthesis: Accessing 2,6-Epoxyazocane (Oxamorphan) Cores

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Supporting Information

ABSTRACT: The modular synthesis of photoprecursors and their photoinduced cyclization into substituted 1-benzazocanes of two distinct topologies is described. The key step producing an extended polyheterocyclic system involves the photo-generation of azaxylylenes and their subsequent intramolecular cycloaddition with furan-containing pendants tethered either via the aniline nitrogen or through the carbonyl group containing arm. The primary photoproducts—secondary or tertiary anilines which are not acylated at the nitrogen atom—undergo facile acid-catalyzed or spontaneous ring-opening–ring-closing rearrangement to yield fused polyheterocyclic structures possessing a 2,6-epoxyazocane (or oxamorphan) core.

INTRODUCTION

Nitrogen heterocycles are ubiquitous in nature: a large number of biochemical pathways involve N-heterocycles as substrates, products, or coenzymes.1 This ensures their prominence among top pharmaceuticals, with 23 out of the 50 top-selling drugs in the US in 2012 containing N-heterocycles.2 It is not surprising that their methods of synthesis and properties have long been a focus of sustained research efforts.3 As a result, the methods for five- and six-membered N-containing heterocycle preparation are countless and also diverse.4 However, access to seven- and especially eight-membered heterocycles remains challenging, mostly because these medium-sized rings are less entropically favored. Such structures, their properties, and methods of synthesis deserve closer examination and further development. They either can be found in a number of bioactive molecules, for example nakadomarin A and manzamine A, or are intermediates in their biosynthesis (Figure 1).5

The 1-benzazocine core is of particular interest: it can serve as an important intermediate in the synthesis of mitomycinoid alkaloids,6 which are potent cytotoxins as they can cross-link DNA, and exhibits a broad range of biological activity, including potent antitumor activity.7 Moreover, it has been suggested that the biochemistry of several alkaloids of the mitomycine family, FR-66979 and FR-900482, as well as their semisynthetic analogues, FK-973 and FK-317, can be rationalized by invoking in vivo formation of the benzazocane intermediate that starts a biochemical cascade.8 Several approaches to the synthesis of the benzazocine/benzazocane moiety have been described, including ingenious examples of olefin metathesis,7 Mizoroki–Heck reaction,10 ring expansion,11 cycloaddition,12 and condensation13 strategies. Most of these approaches, however, imply multistep synthesis; therefore, the development of new short synthetic pathways to the benzazocane scaffold is well justified.

The route to 1-benzazocanes that is being developed in our laboratory is based on [4 + 4] cycloaddition reactions of azaxylylenes—short-lived species generated via excited-state intramolecular proton transfer, ESIPPT,14 in aromatic c-amino ketones and aldehydes. Transient C-hydroxyazaxylylenes generated via ESIPPT have been observed in the past and characterized by time-resolved photophysical methods.14 However, they were not trapped chemically, as any addition reaction would have to compete with very fast back proton transfer. Alternative (i.e., non-ESIPPT) approaches to azaxylylenes require exotic precursors such as benzolsultams and benzoazetines and often occur
under the harsh conditions of flash vacuum pyrolysis,\textsuperscript{15} thus, their utilization in the synthesis of delicate complex organic architectures remains very limited. An exception is Corey’s mild generation of azaxylylenes via 1,4-dehydrochlorination of o-aminobenzyl chlorides.\textsuperscript{16} However, azaxylylenes generated via nonphotochemical methods exclusively undergo \([4 + 2]\) cycloadditions, limiting the structural scaffolds accessible via these reactions to quinolines. The \([4 + 4]\) cycloaddition path is not available for these ground-state reactions.

Another option—intramolecular reactions of the ES IPT-generated azaxylylenes in their excited state which could successfully compete with the wasteful back proton transfer—has not been explored before our work. Recently we found that photogenerated azaxylylenes can indeed react intramolecularly with the appropriately tethered unsaturated pendants (Scheme 1).\textsuperscript{17}

Scheme 1. Photogeneration of Azaxylylenes and Their Intramolecular Cycloadditions

![Scheme 1](image)

In this context, furans and other five-membered heterocycles are particularly suitable as unsaturated pendants, because they can participate in the cycloaddition reaction not only as an alkene component, leading to the products of \([4 + 2]\) cycloadditions, but also as a diene component, furnishing azacanes as the products of \([4 + 4]\) cycloadditions. Our initial studies with azaxylylenes and furan as a pendant demonstrated predominant formation of the \([4 + 4]\) products in a 3:1 or lower ratio to the \([4 + 2]\) products in the majority of cases. This scaffold diversity and complexity arising in one step from the same photoprecursor is appealing from a diversity-oriented synthesis (DOS) standpoint.

Although furan derivatives have been employed in Diels–Alder reactions\textsuperscript{18} both as \(4\pi\) and less commonly as \(2\pi\) components, to the best of our knowledge there have not been observations of the borderline behavior where both \([4 + 4]\) and \([4 + 2]\) reaction pathways are realized from the same starting material under the same reaction conditions.\textsuperscript{20} According to our recent experimental and theoretical mechanistic study,\textsuperscript{21} it is likely that the intramolecular cycloaddition of azaxylylenes photogener-ated via ES IPT occurs in a stepwise manner in the triplet manifold, thus offering a rationale for the formation of both \([4 + 4]\) and \([4 + 2]\) cycloadducts. From our prior work we infer that the ratio of \([4 + 4]\) to \([4 + 2]\) products is affected by the length of the tether between the azaxylylene precursor and the nature of unsaturated pendants, with longer linkers often favoring \([4 + 4]\) products. The same bias toward \([4 + 4]\) cycloaddition was observed when the azaxylylenophile, i.e. a furan-based pendant, was tethered via a carbonyl group, as in furanoyls. Also, in the past we utilized ubiquitous amide bond forming coupling reactions to tether unsaturated pendants to the photoactive \(\alpha\)-amino ketone core of the azaxylylene precursor. In the current study we extend the scope to azaxylylenes derived from \(\alpha\)-amines, i.e. not amides, and also explore topological variations related to the nature and the attachment point of the tether linking the photoactive core with the unsaturated, mostly dienic, pendant. For cycloadditions of ES IPT-generated azaxylylenes—in the context of DOS—it is desirable not only to modulate the topology resulting from the competing \([4 + 2]\) and \([4 + 4]\) photoinduced processes but also to take advantage of the fact that a variety of additional (poly)cyclic moieties can be installed in the photoproducts utilizing strategically chosen linking groups and their attachment points. Our original topology of tethering the furan-containing unsaturated pendant via the aniline moiety of the photoprecursor was predicated on the simplicity of the coupling reaction: i.e., the amide bond formation (Figure 2, top; the “south-bridged” topology). In this paper we report an alternative approach to the assembly of photoprecursors—via the ketone arm of the aromatic amino ketone (Figure 2, bottom; the “north-bridged” topology). This alternative linking offers access to new topologically unique polyheterocyclic core structures.

**RESULTS AND DISCUSSION**

The departure from the original south-bridged topology is realized by linking the unsaturated pendant and the azaxylylene precursor through the \(\alpha\) carbon of the carbonyl group (Figure 2, north-bridged topology). Thus, this new scaffold consists of a primary aromatic amine and an unsaturated pendant joined through the \(\alpha\) substitution in aminoacetophenone, which entails differences in both stereo and electronic properties of the photoprecursors. The synthetic route and the nature of the linker between the azaxylylene precursor and the unsaturated pendant were deliberately chosen to be attuned with a modular approach within the framework of diversity-oriented synthesis.\textsuperscript{22} The implemented pathway to the photoprecursors comprises two simple steps: aldol condensation of the \(\alpha\)-furyl aromatic (or \(\alpha\)-furyl vinyl) carboxaldehyde followed by the conjugate (Michael) addition of a nucleophile to the obtained \(\alpha\)-unsaturated ketone. The starting aldehyde can be prepared by the Suzuki reaction of \(2\)-furanboronic acid with the corresponding \(\alpha\)-halogen-substituted aromatic or vinyl aldehyde. Thus, a diverse library of compounds can be accessed through the variation of the following building blocks and pendants: the polycyclic aldehyde followed by the conjugate (Michael) addition of a nucleophile to the obtained \(\alpha\)-unsaturated ketone via the ketone arm of the aromatic amino ketone (Figure 2, top; the “south-bridged” topology). This alternative linking offers access to new topologically unique polyheterocyclic core structures.
The initial synthetic studies were conducted using o-bromobenzaldehyde (1) as a starting material (Scheme 2). The Suzuki coupling with furanboronic acid 2, catalyzed by 5 mol % of PdCl₂(PPh₃)₂, yielded aldehyde 3 (89%), which serves as the carbonyl component in the subsequent aldol condensation with o-aminoacetophenone (4), giving chalcone 5, a reactive Michael acceptor for a variety of nucleophiles, including nitromethane, diethyl malonic ester, and phenylboronic acid, in a Pd₀-catalyzed reaction. Thus, the photoprecursors 6−8 are readily available in three simple steps in moderate to good yields.

Similarly, heterocyclic analogues 15 and 16 were prepared, starting the sequence with 2-bromonicotinaldehyde (9) or 2-formyl-3-bromothiophene (10) (Scheme 3). In both of these cases, nitromethane was used as a Michael nucleophile. Further diversification of photoprecursors was achieved by making use of vinyl carboxaldehydes 20−22 as starting materials. These aldehydes are readily obtained via a variation of the Vilsmeier–Haack reaction from commercially available cyclic ketones on a multigram scale, using DMF and PBr₃. In these cases, the developed synthetic sequence of Suzuki coupling, followed by aldol condensation and conjugate addition to chalcone, gives the photoprecursors 29−31 in good yields (Scheme 4).

The photoprecursors, obtained as described above, have an (n,π*) UV absorption maximum around 350 nm. Methanol was the solvent of choice for irradiation after a few solvent optimization runs. Irradiations were carried out with a Rayonet broad-band 300−400 nm UV source (RPR-3500 lamps). Curiously, irradiation of the photoprecursors possessing the north-bridged topology yielded exclusively the products of [4 + 4] addition: i.e., no [4 + 2] products were detected (Scheme 5 and Table 1).

The stereochemistry of the primary [4 + 4] photoproducts was assigned on the basis of their NMR spectra and the X-ray structure of 34. We hypothesize that the [4 + 4] intramolecular cycladdition of the ESPT-generated azaxylylene occurs via a transition state (Figure 3), in which the stereochemistry of folding of the α-(nitromethyl)ethylphenyl tether to form a six-membered ring is biased by the nitromethyl group assuming the shown pseudoequatorial conformation. The alternative folding, with the nitromethyl assuming a pseudoaxial conformation, leads...
to a severe steric clash and therefore is not expected to be a feasible reaction channel.

Another observation was that in some cases primary photoproducts underwent a partial rearrangement, similar to a carbohydrate transformation from a furanose to a pyranose form. Further probing the stability of the primary photoproducts, we subjected compound 34 to acidic conditions (1 vol % of TFA in DCM), which resulted in a 100% conversion into the "pyranose" form (Scheme 6). Presumably, such a rearrangement is facilitated by the amino stabilization of the cation formed upon the opening of the 2,5-dihydrofuran moiety. The initial step of it is somewhat reminiscent of the rearrangement reported by Padwa and co-workers, except that in our case the transient cation is captured by the benzylic hydroxy group, leading to the formation of the unprecedented oxazobicyclo[3.3.1]nonadiene or oxamorphan substructure.

This rearrangement appears to be general for all the photoproducts in Table 1. It proceeds smoothly upon the addition of a catalytic amount of acid or simply upon heating of the reaction mixture in DMSO. The structures of the rearranged products were supported by NMR data. Additionally, the structures of photoproduct 34 and rearranged product 40 were unambiguously determined by X-ray analysis. 

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rearranged products differ considerably from the NMR spectra of nonrearranged compounds (Figure 4). In compound 34 the vinyl protons appear as a doublet and a doublet of doublets with a common spin−spin coupling constant of 5.6 Hz. After the rearrangement the vicinal coupling constant of vinyl protons increases to 10.0 Hz, which is in keeping with the proposed change in the molecule’s geometry. The experimental NMR data were supported by our relativistic force field computations of proton spin−spin coupling constants, with the predicted constants, shown in Figure 4, matching the experimental values very well.

The only exception in this series was the rearrangement of photoproduc 49, derived from tetralone-based precursor 48. The photoprecursor 48 was obtained as a mixture of diastereomers. However, only one diastereomer of the photoproduct 49 is formed with an isolated yield of 27%. We hypothesize that one of the diastereomers 48 is photoinactive due to unfavorable folding of the tether in the transition state. We were unable to obtain an X-ray structure of the photoproduct and could not assign its stereochemistry on the basis of NMR data.

During column chromatography compound 49 isomerized on silica gel into the [4 + 2] product 50. The structure of the product was established on the basis of its 1H NMR and COSY spectra. Protons H1, H2, and H3 (Scheme 7) of the primary photoproduct 49 are characterized by the set of spin−spin coupling constants typical of the series: 5.6 Hz for the vinylic H1 and H2 protons and 1.3 Hz for H3 (bridge). In contrast to both these experimental observations and the spin−spin coupling constants observed for other compounds possessing the [4.2.1] scaffold, the rearranged product 50 exhibited a set of much smaller constants: vinyl Jab = 2.4 Hz and Jac = 0.9 Hz. Such a distinctive set of values has been observed earlier for [4 + 2] azacyclobutadiene products and is supported by our calculations. A plausible mechanism for such 1,3-allylic migration is presented in Scheme 7 and involves protonation of the amine, scission of the aminal C−N bond (i.e., not C−O bond), and subsequent nucleophilic attack by aniline at C-3 of the furan ring.

This outlier notwithstanding, the north-bridged anilines, lacking acyl substitution at the nitrogen atom, exclusively undergo a photoinduced intramolecular [4 + 4] cycloaddition, with subsequent heat- or acid-catalyzed [4.2.1] → [3.3.1] rearrangement yielding a polycyclic aminal possessing an oxamorphane core. We identified a case in which this rearrangement occurs spontaneously during the photolysis. Sulphonate 52, which is readily synthesized via the substitution in α-bromo-2'-nitroacetophenone 51 and a subsequent reduction of the nitro group with tin chloride (Scheme 8) undergoes irradiation in wet acetonitrile, yielding only the rearranged compound 54 as a single product. The [4 + 4] cycloadduct 53, which is a presumed intermediate, could not be isolated. While we do not have an X-ray structure for 54, the predicted NMR spectra better match the syn stereochemical configuration of the hydroxy group. The spontaneous [4.2.1] → [3.3.1] rearrangement without added acid also provides circumstantial evidence for the syn configuration. As we show below, the anti photoproducts do not undergo this rearrangement in the absence of acids.
The observed rearrangement into the pyranose form is clearly facilitated by the fact that the aniline moiety is not acylated, resulting in a more stable iminium ion (Scheme 6) as the key intermediate in this rearrangement. Additional questions are whether this lack of N-acylation (or further electron-donating alkyl substitution on the nitrogen) possibly affects the [4 + 4] vs [4 + 2] partitioning of the primary photoproducts and also whether the [4.2.1] → [3.3.1] transformation is unique to the north-bridged architecture of the photoprecursors.

We therefore revisited the south-bridged structures, but instead of amide-forming coupling of the furan pendant we explored reductive amination to furnish alkylated anilines, not anilides. First, we synthesized the secondary amine 57, through the sequence of reductive amination of 3-furylpropanal (56) with 2-aminophenylmethanol (55) and the oxidation of the benzyl alcohol with MnO₂ (Scheme 9).

Similar to the case for the previously studied amides, photoprecursor 57 has a UV absorption band in the range 320–350 nm. After screening the solvents methanol, methanol–water, acetonitrile, acetonitrile–water, benzene, and tert-butyl alcohol, we arrived at methanol as the optimal medium for the initial photoinduced cycloaddition. Irradiation of 57 with a Rayonet broad-band 300–400 nm UV source is accompanied by a spontaneous [4.2.1] → [3.3.1] rearrangement, yielding diastereomeric oxamorphans 65a (OH is syn to the bridge oxygen) and 65b (anti) (Scheme 10). The structural assignment of the products was guided by calculations of their proton spin–spin coupling constants. Both syn and anti products have a large vicinal coupling constant between vinylic protons, $J_{ab} = 9.8$ Hz (calculated 9.6 Hz) for the syn isomer and 10.0 Hz (calculated 9.9 Hz) for the anti isomer, indicative of oxabicyclo[3.3.1] scaffold formation. There is, however, a significant difference in spin–spin coupling for the $\alpha$-hydroxy proton Hγ: the syn isomer has the large constant $J_{ac} = 2.5$ Hz (calculated 2.5 Hz) and a small constant $J_{bc} = 1.3$ Hz (calculated 1.5 Hz); in contrast, the anti isomer has a small constant $J_{ab} = 1.7$ Hz (calculated 2.0 Hz) and a large constant $J_{ac} = 5.9$ Hz (calculated 5.9 Hz). The near-perfect match of the experimental and calculated spin–spin coupling constants leaves no doubt that the conversion of the primary photoproducts into the 9-oxabicyclo[3.3.1] nonadiene compounds 65a,b occurs spontaneously at room temperature in these amines.

Scheme 9. Typical Synthesis of South-Bridged Alkylamines via Reductive Amination

Scheme 10. Irradiation of Alkylamine 57

To test the scope of the reaction, additional secondary amines were similarly synthesized. The reductive amination approach is again amenable to the modular synthesis of photoprecursors, allowing for access to diverse structures from various aldehdes and amines used for the reductive amination. A heterocyclic (pyridine) moiety was readily incorporated into photoprecursors 60 and 63, synthesized with 2-amino-3-pyridinylmethanol. Upon irradiation both produced the desired photoproducts, which is, to the best of our knowledge, the first example of azacyclonhexene generation from heterocyclic precursors.

The modular synthesis of photoprecursors benefits from the fact that the aldehydes obtained via Suzuki coupling (Schemes 2–4) and utilized to assemble the north-bridged precursors via aldol condensation can also be used in the reductive amination synthetic sequence, as exemplified by the south-bridged photoprecursors 63 and 64. The matrix of synthesized photoprecursors and their respective photoproducts is presented in Table 2.

As it is evident from Table 2, upon irradiation all photoprecursors produced the rearranged oxabicyclo[3.3.1] nonadiene core, supporting the mechanistic rationale that additional alkyl stabilization of the transient iminium cation is needed for the spontaneous [4.2.1] to [3.3.1] rearrangement. It should also be noted that, with the exception of 65, the only isolated stereoisomer was that with the OH group syn to the bridge oxygen. In the case of the tetralone-derived photoprodut 70, the NMR-based structural assignment was also supported by X-ray data. Introduction of halogen substitution into the aromatic ring (58, 59) accelerates the photochemical step, which is in keeping with our prior observations. It also sets the product up for a subsequent Suzuki coupling, allowing for another diversity input in the resulting [3.3.1] scaffold. The presence of the Me–C* stereogenic center in the tether of photoprecursor 61 expectedly does not impose any diastereoselection in the transition state of the primary photoinduced cycloaddition step and leads to the formation of a 1:1 mixture of diastereomers (69a,b), which can be separated via column chromatography. Diastereomers 69a,b both have the same syn configuration of the hydroxy group but differ in the stereoconfiguration of the methyl group in the pyrroline moiety.

Indanone-derived 73 was the only photoprecursor which did not undergo spontaneous [4.2.1] to [3.3.1] rearrangement. Instead, we observed dehydration in the primary photoprodut 74 to yield indene 75 (Scheme 11). A plausible explanation for this is that the [4.2.1] → [3.3.1] rearrangement in this case is less energetically favorable. This hypothesis is corroborated by our DFT calculations, which predict that generally the rearranged bicyclo[3.3.1] nonadienes are 7−12 kcal/mol more stable than the primary photoproducts possessing the bicyclo[4.2.1] nonadiene structure. Even the tetralone-based 70 is 6.9 kcal/mol more stable than its [4.2.1] precursor. However, in the indanone case the [4.2.1] and the [3.3.1] structures are nearly (within 0.6 kcal/mol) energy degenerate. An analysis of the experimental and predicted NMR spectra of 75 does not leave any doubt of the correct structural assignment. In the 5.0–6.0 ppm region of the NMR spectrum of the photoprodut, in addition to the two expected alkynyl protons ($J_{exp} = 5.6$ Hz, $J_{calc} = 5.5$ Hz) and the allylic bridgehead proton ($J_{exp} = 2.0$, $1.2$ Hz, $J_{calc} = 2.0$, $1.3$ Hz), there is an additional triplet with $J_{exp} = 2.2$ Hz (calculated dd, $J_{calc} = 2.4$, $2.3$ Hz), corresponding to the new vinyl proton of the indene moiety.

In the majority of the cases, as follows from Table 2, the photoinduced cycloaddition is always followed by the spontaneous [4.2.1] → [3.3.1] rearrangement, which is clearly accelerated by...
the lack of acyl substitution on nitrogen. While the acyl linker explored in our previous work should indeed retard the rate of this rearrangement, we hypothesized that such acyl substitution should not necessarily affect the position of the equilibrium between [4.2.1] and [3.3.1]. Our DFT B3LYP/6-311+G(d,p) calculations indeed revealed that this equilibrium has a very similar 7−12 kcal/mol energy bias toward the rearranged [3.3.1] products in the amido series. We therefore revisited the amide-derived photoproducts synthesized earlier to test whether this rearrangement can be induced in the structures with an electron-withdrawing acyl substituent on the nitrogen atom. Indeed, we found that the heat- or acid-promoted [4.2.1] → [3.3.1] rearrangement in this series is possible as well (Scheme 12). Moreover, as is illustrated by the rearrangement of the keto-piperazine 82, the rearrangement is not limited to three-atom tethers but occurs in photoproducts with four-atom linkers as well.

It is instructive that the barrier for the [4.2.1] → [3.3.1] transformation in the absence of acid catalysis is much higher for anti photoproducts to a point that, while syn-76 photoproduct rearranges in DMSO at 150 °C, there is no thermal reaction at all for the anti photoproduct (Scheme 13).

The versatility of the [4.2.1] → [3.3.1] transformation in the syn photoproducts of the amido series is hard to underestimate. On one hand, the initial photoproducts are very stable at temperatures varying from ambient to 70−80 °C. On the other, they undergo a clean transformation in DMSO when heated to 140 °C, furnishing the rearranged products with the oxamorphan core.

**CONCLUSIONS**

We have developed a versatile approach to the synthesis of bicyclic 1-benzoazocine structures of two distinct topologies. The method is amenable to a straightforward modular synthesis of both south- and north-bridged photoprecursors in three to four simple steps. Irradiation of photoprecursors results in a significant growth of complexity, giving a single primary photoproduct of the [4.2.1] oxabicyclic core structure in the case of north-bridged primary amines and the [3.3.1] oxabicyclic core structure as a result of spontaneous [4.2.1] → [3.3.1] rearrangement in the case of secondary amines. The [4.2.1] → [3.3.1] rearrangement in the disposition of the amido series is hard to underestimate.
transformation can be achieved either by heat or under acid catalysis. The generality of this rearrangement was demonstrated using the amides of the same topology as secondary amines.

Experimental Section

Commercial solvents were used as is, except for THF, which was refluxed over and distilled from potassium benzenophenone ketyl prior to use. Common reagents were purchased from commercial sources and used without additional purification, unless indicated otherwise. NMR spectra were recorded at 25 °C on a 500 MHz spectrometer in CDCl₃ with TMS as an internal standard (unless noted otherwise). Flash column chromatography was performed using 230–400 mesh silica gel.

Synthesis of Photoprecursors. General Procedure for Vilsmeier–Haack Reaction. To a solution of N,N-dimethylformamide (2.40 mL, 30.6 mmol) in chloroform (20 mL) at 0 °C was added phosphorus tribromide (2.60 mL, 27.5 mmol). After 30 min the reaction mixture was warmed to room temperature and a solution of ketone (1.20 g, 7.71 mmol) in dichloromethane (20 mL) was added. The reaction mixture was heated to reflux for 3 h then cooled to room temperature and poured onto ice-water (50 mL). Solid sodium bicarbonate was added to neutralize the aqueous phase, which was then separated and extracted with ether (3 × 75 mL). The combined organic phases were washed with saturated NaHCO₃ (100 mL) and brine (100 mL), dried over MgSO₄, and concentrated in vacuo.

1-Bromo-2-formyl-1-cyclopentene coordinates with PdCl₂(PPh₃)₂, (5 mol %, 0.5 mmol) and 0 °C for 8 h then cooled to room temperature and poured onto NaOH (0.5 mL, 2.5 mmol) was heated to reflux for 3 h and cooled to room temperature and poured onto ice-water (50 mL). Solid sodium bicarbonate was added to neutralize the aqueous phase, which was then separated and extracted with ether (3 × 75 mL). The combined organic phases were washed with saturated NaHCO₃ (100 mL) and brine (100 mL), dried over MgSO₄, and concentrated in vacuo.

1-Bromo-2-formyl-1-cyclopentene (152, 4.97 mmol) of 2-bromobenzaldehyde (11.11, 0.38 g (65%) of the title compound was obtained.

1C NMR (126 MHz, CDCl₃): δ 193.5, 151.9, 144.1, 143.8, 135.8, 113.1, 111.5, 29, 21, 22, 23. 214. 2-2(Bromocyclohexene). Following the general procedure for Suzuki coupling from 0.54 g (2.97 mmol) of 2-bromobenzaldehyde (1), 0.76 g (89%) of the title compound was obtained. 1H NMR (500 MHz, CDCl₃): δ 10.41 (s, 1H), 8.00 (m, 1H), 7.71 (m, 1H), 7.65 (m, 1H), 6.74 (m, 1H), 6.66 (m, 1H), 6.59 (dd, J = 3.4, 1.8 Hz, 1H). 13C NMR (126 MHz, CDCl₃): δ 192.4, 151.1, 140.0, 133.6, 133.4, 133.1, 128.4, 128.1, 128.0, 111.9, 111.3.

2-(2-Bromocyclohexene). Following the general procedure for Suzuki coupling from 1.00 g (5.23 mmol) of 3-bromo-thiophene-2-carboxaldehyde (10), 0.84 g (90%) of the title compound was obtained. 1H NMR (500 MHz, CDCl₃): δ 10.72 (dd, J = 0.8 Hz, 1H), 8.82 (dd, J = 4.6, 1.8 Hz, 1H), 8.28 (dd, J = 7.9, 1.8 Hz, 1H), 7.71 (dd, J = 1.7, 0.8 Hz, 1H), 7.55 (m, 1H), 7.23 (dd, J = 3.5, 0.7 Hz, 1H), 6.66 (dd, J = 3.5, 1.8 Hz, 1H).

1C NMR (126 MHz, CDCl₃): δ 191.9, 153.4, 150.0, 152.6, 145.3, 136.2, 128.2, 122.3, 113.8, 112.4.

2-(2-Bromothiophene-2-carboxaldehyde). Following the general procedure for Suzuki coupling from 1.00 g (5.23 mmol) of 3-bromo-thiophene-2-carboxaldehyde (10), 0.84 g (90%) of the title compound was obtained. 1H NMR (500 MHz, CDCl₃): δ 10.72 (dd, J = 0.8 Hz, 1H), 8.82 (dd, J = 4.6, 1.8 Hz, 1H), 8.28 (dd, J = 7.9, 1.8 Hz, 1H), 7.71 (dd, J = 1.7, 0.8 Hz, 1H), 7.55 (m, 1H), 7.23 (dd, J = 3.5, 0.7 Hz, 1H), 6.66 (dd, J = 3.5, 1.8 Hz, 1H).

1C NMR (126 MHz, CDCl₃): δ 184.6, 149.7, 143.9, 137.4, 134.2, 128.5, 127.5, 112.0, 110.8.

General Procedure for Aldol Condensation. Procedure A. 2-Aminoacetophenone (10 mmol, 1 equiv) was added to a solution of the corresponding aldehyde (10 mmol, 1 equiv) in EtOH (10 mL) containing NaOH (0.3 of a pellet), and the mixture was stirred at 5 °C for 8 h. The precipitate was filtered, washed with EtOH and then with water, and finally dried under vacuum to yield a product pure enough for subsequent transformations.

Procedure B. Ethanol solutions (10 mL) of equimolar amounts of 2′-aminocacetophenone (2.8 mmol), the corresponding aldehyde, and 20% aqueous NaOH (0.5 mL, 2.5 mmol) were heated to reflux for 10–20 min. After the mixture was cooled, the precipitate was filtered off, washed with EtOH and then with water, and finally dried under vacuum. (E)-1-(2-Aminophenyl)-3-(2-(furan-2-yl)pyridin-3-yl)prop-2-en-1-one (11). Following the general procedure A for aldol condensation from 0.35 g (2.02 mmol) of 11, 0.38 g (65%) of the title compound was obtained. 1H NMR (500 MHz, CDCl₃): δ 8.87 (dd, J = 4.7, 1.6 Hz, 1H), 8.29 (dd, J = 15.5, 3.5 Hz, 1H), 8.01 (dd, J = 7.9, 1.3 Hz, 1H), 7.91 (d, J = 8.1 Hz, 1H), 7.69 (d, J = 1.1 Hz, 1H), 7.57 (d, J = 15.4 Hz, 1H), 7.34 (m, 1H), 7.30 (m, 1H), 6.97 (dd, J = 3.4, 0.6 Hz, 1H), 6.74 (m, 2H), 6.60 (dd, J = 3.4, 1.8 Hz, 1H), 6.42 (s, 2H). 1C NMR (126 MHz, CDCl₃): δ 191.2, 151.0, 145.3, 144.8, 137.4, 137.1, 111.8, 36.0, 31.1, 21.7.
Following the general procedure B for aldol condensation from 0.24 g (1.39 mmol) of 3, 0.29 g (72%) of the title compound was obtained.

H NMR (500 MHz, CDCl3): δ 8.24 (d, J = 15.3 Hz, 1H), 7.84 (m, 2H), 7.52 (m, 2H), 7.14 (d, J = 15.3 Hz, 1H), 6.70 (m, 2H), 6.47 (dd, J = 3.4, 1.8 Hz, 1H), 6.34 (s, 2H), 2.88 (m, 2H), 2.82 (m, 2H), 2.06 (m, 2H), 1.78 (m, 4H). 13C NMR (126 MHz, CDCl3): δ 192.6, 153.8, 150.7, 143.2, 142.7, 134.7, 133.9, 131.0, 124.8, 119.6, 117.2, 115.7, 115.5, 111.3, 113.1, 29.5, 26.5, 22.2.

Following the general procedure A for aldol condensation from 1.20 g (7.39 mmol) of 23, 0.75 g (37%) of the title compound was obtained. H NMR (500 MHz, CDCl3): δ 8.53 (d, J = 15.2 Hz, 1H), 7.59 (m, 2H), 7.29 (m, 1H), 7.04 (d, J = 15.2 Hz, 1H), 6.70 (m, 2H), 6.48 (d, J = 3.3 Hz, 1H), 6.47 (dd, J = 3.4, 1.8 Hz, 1H), 6.34 (s, 2H), 2.88 (m, 2H), 2.82 (m, 2H), 2.06 (m, 2H), 1.78 (m, 4H). 13C NMR (126 MHz, CDCl3): δ 192.6, 153.2, 150.8, 143.7, 138.8, 136.3, 134.2, 133.9, 131.0, 124.8, 119.6, 117.2, 115.7, 115.5, 111.3, 29.1, 26.5, 22.2.

Following the general procedure A for aldol condensation from 0.76 g (3.99 mmol) of 25, 0.47 g (38%) of the title compound was obtained. H NMR (500 MHz, CDCl3): δ 8.16 (d, J = 15.2 Hz, 1H), 7.78 (m, 1H), 7.52 (dd, J = 1.8, 0.6 Hz, 1H), 7.28 (m, 1H), 7.17 (d, J = 15.2 Hz, 1H), 6.71 (m, 2H), 6.48 (dd, J = 3.4, 1.8 Hz, 1H), 6.42 (m, 1H), 6.28 (s, 2H), 2.79 (m, 2H), 2.68 (m, 2H), 1.86 (bd, J = 7.5, 6.7 Hz, 2H), 1.65 (dd, J = 17.1, 5.8 Hz, 4H). 13C NMR (126 MHz, CDCl3): δ 192.7, 154.0, 150.7, 143.7, 142.8, 140.6, 137.8, 133.9, 130.9, 122.0, 119.7, 117.2, 115.8, 112.5, 111.5, 32.8, 32.0, 29.9, 26.3, 25.9.

E8-Amino-2-(2-furan-2-yl)benzylidene)-3,4-dihydropaphthalen-1(2H)-one. Following the general procedure A for aldol condensation from 0.34 g (1.97 mmol) of 3, 0.26 g (42%) of the title compound was obtained. H NMR (500 MHz, CDCl3): δ 7.89 (m, 2H), 7.53 (m, d, J = 1.8, 0.7 Hz, 1H), 7.44 (m, 1H), 7.33 (m, 2H), 7.22 (dd, J = 8.3, 7.3 Hz, 1H), 6.63 (s, 2H), 6.58 (dd, J = 8.3, 1.8 Hz, 1H), 6.54 (dd, J = 3.4, 0.7 Hz, 1H), 6.49 (m, 2H), 2.92 (m, 2H), 2.87 (m, 2H).

1-(2-Aminophenyl)-3-(2-(furan-2-yl)cyclopent-1-en-1-yl)-4-nitrobutan-1-one (29). Following general procedure D for addition of nitromethane from 0.74 g (2.65 mmol) of 26, 0.70 g (77%) of the title compound was obtained. H NMR (500 MHz, CDCl3): δ 7.73 (m, 1H), 7.42 (m, 1H), 7.28 (m, 1H), 6.66 (m, 2H), 6.41 (m, J = 3.3, 1.8 Hz, 1H), 6.29 (m, 3H), 4.79 (m, 1H), 4.73 (dd, J = 11.7, 6.2 Hz, 1H), 4.62 (dd, J = 11.7, 8.1 Hz, 1H), 3.28 (dd, J = 16.5, 6.1 Hz, 1H), 3.22 (dd, J = 16.5, 7.8 Hz, 1H), 2.70 (m, 2H), 2.56 (m, 2H), 1.93 (m, 2H). 13C NMR (126 MHz, CDCl3): δ 199.5, 151.8, 150.5, 141.9, 134.8, 134.6, 131.0, 128.4, 117.5, 117.4, 115.8, 110.9, 80.5, 78.0, 40.0, 34.7, 34.4, 33.8, 22.0. HRMS (ESI): calcd for C15H12N2O4 (M+H') 341.1496, found 341.1479.

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3.11 (dd, J = 16.2, 7.8 Hz, 1H), 2.35 (m, 2H), 2.17 (m, 2H), 1.67 (m, 4H). 13C NMR (126 MHz, CDCl3): δ 199.5, 150.5, 150.2, 141.9, 136.7, 134.8, 133.5, 130.9, 117.4, 117.4, 115.8, 110.7, 77.5, 39.9, 38.8, 33.7, 32.2, 29.3, 25.6, 22.4, 22.4. HRMS (ESI): calcd for C19H18N3O4NaOAc (2 equiv), glacial acetic acid (4 equiv), the corresponding mixture was stirred overnight and then filtered through a plug of Celite, concentrated, and purified using flash chromatography on silica.

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General Procedure for Benzylic Alcohol Oxidation. Following the general procedure D for addition of nitromethane from 0.24 g (0.76 mmol) of (2-((3-(furan-2-yl)propyl)amino)pyridin-3-yl)methanol was prepared following the general procedure for benzylic alcohol oxidation from 0.5 g (3.18 mmol) of 5-chloro-2-aminophenylmethanol with a yield of 0.78 g (73%) and used without further purification in the next step. 1H NMR (500 MHz, CDCl3): δ 7.73 (dd, J = 8.4, 1.4 Hz, 1H), 7.51 (dd, J = 1.8, 0.6 Hz, 1H), 7.31 (m, 1H), 7.23 (m, 2H), 6.67 (m, 2H), 6.61 (dd, J = 3.4, 0.6 Hz, 1H), 6.52 (dd, J = 3.4, 1.8 Hz, 1H), 6.28 (s, 2H), 5.16 (m, 1H), 4.88 (dd, J = 12.7, 6.8 Hz, 1H), 4.80 (dd, J = 12.7, 6.9 Hz, 1H), 3.92 (dd, J = 17.4, 6.2 Hz, 1H), 3.52 (dd, J = 17.4, 7.6 Hz, 1H). 13C NMR (126 MHz, CDCl3): δ 198.1, 150.2, 141.9, 136.7, 134.8, 130.8, 129.5, 127.3, 117.5, 117.4, 115.9, 111.4, 107.3, 79.5, 42.6, 33.9. HRMS (ESI): calcd for C18H17N2O4S+ (MH+) 352.1297, found 352.1296.

1-(2-Aminophenyl)-3-(3-(furan-2-yl)thiophen-2-yl)-4-nitrobutan-1-one (16). Following general procedure D for addition of nitromethane from 0.35 g (1.19 mmol) of 14, 0.28 g (66%) of the title compound was obtained. 1H NMR (500 MHz, CDCl3): δ 7.77 (dd, J = 8.4, 1.4 Hz, 1H), 7.51 (dd, J = 1.8, 0.6 Hz, 1H), 7.31 (m, 1H), 7.23 (m, 2H), 6.67 (m, 2H), 6.61 (dd, J = 3.4, 0.6 Hz, 1H), 6.52 (dd, J = 3.4, 1.8 Hz, 1H), 6.28 (s, 2H), 5.16 (m, 1H), 4.88 (dd, J = 12.7, 6.8 Hz, 1H), 4.80 (dd, J = 12.7, 6.9 Hz, 1H), 3.92 (dd, J = 17.4, 6.2 Hz, 1H), 3.52 (dd, J = 17.4, 7.6 Hz, 1H). 13C NMR (126 MHz, CDCl3): δ 198.1, 150.2, 141.9, 136.7, 134.8, 130.8, 129.5, 127.3, 117.5, 117.4, 115.9, 111.4, 107.3, 79.5, 42.6, 33.9. HRMS (ESI): calcd for C17H16NO2S (MH+) 332.0803, found 332.0802.
NMR (500 MHz, CDCl₃): δ 8.92 (s, 1H), 8.49 (s, 1H), 8.35 (dd, J = 4.8, 1.9 Hz), 7.76 (dd, J = 7.5, 2.0 Hz, 1H), 7.33 (m, 1H), 6.66 (dd, J = 7.5, 4.8 Hz, 1H), 6.30 (dd, J = 3.0, 1.9 Hz, 1H), 6.06 (m, 1H), 3.64 (m, 2H), 2.77 (t, J = 7.5, 2.0 Hz), 2.05 (p, J = 7.3 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃): δ 192.8, 157.8, 155.3, 155.0, 144.6, 141.0, 113.7, 111.4, 110.1, 105.1, 40.9, 27.8, 25.5. HRMS (ESI): calcld for C₂₇H₂₃NO₄⁺ (MH⁺): 431.1959, found 431.1960.

1H, C₃H₂NO⁴⁺ (MH⁺) 279.1128, found 279.1131.

2-(Furan-2-yl)benzylamino)pyridin-3-yl)methanol was prepared following the general procedure for benzyl alcohol oxidation from 0.10 g (3.17 mmol) of 2-furan-2-yl)benzylamine and 0.32 g (2.74 mmol) of TFA in CH₂Cl₂ (25 mL) and then dried over anhydrous sodium sulfate. The organic layer was then concentrated under reduced pressure and the crude product was purified by flash chromatography to give 1.86 g (97%) of the title compound. ¹H NMR (500 MHz, CDCl₃): δ 7.48 (d, J = 8.2, 1.0 Hz, 1H), 7.10 (d, J = 8.4, 1.3 Hz, 1H), 6.98 (d, J = 8.4, 1.3 Hz, 1H), 6.15 (d, J = 8.2, 1.0 Hz, 1H), 3.85 (s, 2H), 3.83 (s, 2H). ¹³C NMR (126 MHz, CDCl₃): δ 196.7, 151.1, 150.7, 142.4, 134.8, 131.4, 117.5, 116.3, 115.8, 110.4, 108.4, 37.6, 28.5. HRMS (ESI): calcld for C₁₅H₁₃NO₃⁺ (MH⁺): 248.0740, found 248.0743.

General Procedure for Photochemical Reactions. A 4 mmol portion of the photorepressor was dissolved in 200 mL of methanol, and the solution was degassed and irradiated with RPR-3000 until the reaction was complete.

Diethyl 2-(biphenyl-4-yl)-4,8b,9,10-tetrahydro-3H-3,14b-epoxybenzo[b]naphtho[2,1-d]azocin-10-yl)malonate C₁₂H₁₈N₂O₂ (33). From 0.27 g (0.53 mmol) of 7, following the general procedure for the photochemical reaction, 0.15 g (56%) of the title compound was obtained upon chromatography. ¹H NMR (500 MHz, CDCl₃): δ 7.77 (d, J = 8.1, 1.4 Hz, 1H), 7.31 (m, 3H), 7.23 (m, 1H), 7.10 (m, 1H), 6.89 (m, 1H), 6.63 (d, J = 8.0, 1.1 Hz, 1H), 6.55 (d, J = 5.8, 1.5 Hz, 1H), 5.94 (d, J = 2.8 Hz, 1H), 5.90 (d, J = 5.8, 1.5 Hz, 1H), 4.73 (d, J = 3.5 Hz, 1H), 4.09 (m, 6H), 2.73 (d, J = 14.1, 9.6 Hz, 1H), 2.10 (d, J = 14.1, 7.2 Hz, 1H), 1.82 (s, 1H), 1.18 (s, J = 7.1 Hz, 3H), 1.09 (s, J = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃): δ 168.8, 168.0, 139.1, 136.8, 136.6, 134.8, 132.8, 129.9, 128.7, 128.5, 128.1, 127.1, 127.0, 120.2, 120.0, 89.8, 88.5, 82.8, 61.4, 61.1, 56.8, 37.1, 35.2, 14.0, 13.9. HRMS (ESI): calcld for C₁₅H₁₃NO₃⁺ (MNa⁺): 472.1731, found 472.1737.

10-Phenyl-4,8b,9,10-tetrahydro-3H-3,14b-epoxybenzo[b]naphtho[2,1-d]azocin-8-ol (32). 0.17 g (0.46 mmol) of 6, following the general procedure for the photochemical reaction, 0.13 g (76%) of the title compound was obtained upon chromatography. ¹H NMR (500 MHz, CDCl₃): δ 7.87 (d, J = 8.2, 1.5 Hz, 1H), 7.40 (d, J = 7.6, 1.6 Hz, 1H), 7.26 (m, 1H), 7.12 (d, J = 8.1, 1.6 Hz, 1H), 7.08 (d, J = 7.5 Hz, 1H), 6.92 (d, J = 8.3, 7.1 Hz, 1H), 6.08 (d, J = 5.7 Hz, 1H), 6.64 (d, J = 8.0, 1.2 Hz, 1H), 6.01 (s, 1H), 5.99 (d, J = 5.7, 1.5 Hz, 1H), 4.79 (s, 1H), 4.49 (d, J = 11.4, 6.6 Hz, 1H), 2.70 (d, J = 14.1, 11.6, 0.8 Hz, 2H), 2.28 (d, J = 14.2, 6.6 Hz, 2H), 1.08 (m, 1H). ¹³C NMR (126 MHz, CDCl₃): δ 146.1, 140.1, 138.9, 136.1, 134.6, 132.5.
11.9 (dd, J = 8.1, 1.1, 1.6 Hz, 1H), 7.10 (dd, J = 7.7, 1.3 Hz, 1H), 6.89 (dd, J = 12.2, 8.9 Hz, 1H), 6.68 (s, 1H), 5.40 (m, 1H), 5.10 (t, J = 2.6 Hz, 1H), 4.96 (dd, J = 12.5, 6.0 Hz, 1H), 4.62 (dd, J = 12.5, 8.5 Hz, 1H), 4.38 (m, 1H), 3.04 (s, 2H), 2.89 (s, 3H), 2.05 (d, J = 11.5, 3.6 Hz, 1H), 1.81 (m, 1H). δ 13C NMR (126 MHz, CDCl3): δ 164.9, 143.5, 139.2, 137.1, 135.8, 129.4, 129.1, 128.4, 127.7, 125.6, 125.3, 120.8, 114.7, 103.5, 90.9, 81.0, 70.8, 60.6, 42.2, 40.0, 29.5, 26.9. HRMS (ESI): calcd for C29H26NO2S (M+): 377.1496, found 377.1495. 10-(Nitro methyl)-10,11,12,13-tetrahydro-4H-3b,6b-epoxybenzo[b]thieno[3′,2′:3,4]benzo[1,2-d]azocin-11-ol (49). From 0.11 g (0.29 mmol) of 48, following the general procedure for the photochemical reaction, 0.03 g (27%) of the title compound and 0.04 g (36%) of 50 were obtained. 1H NMR (500 MHz, CDCl3): δ 6.67 (dd, J = 7.4, 1.6 Hz, 1H), 7.32 (m, 2H), 7.08 (m, 2H), 6.75 (d, J = 7.0 Hz, 1H), 6.68 (d, J = 7.6 Hz, 1H), 6.34 (dd, J = 5.6, 1.3 Hz, 1H), 6.11 (d, J = 5.7 Hz, 1H), 5.77 (m, 1H), 5.24 (s, 1H), 5.21 (d, J = 131.1, 8.1 Hz, 1H), 4.84 (d, J = 13.1, 6.8 Hz, 1H), 4.12 (m, 2H), 2.76 (d, J = 16.6, 17.2, 4.4 Hz, 1H), 2.67 (d, J = 16.7, 4.6, 2.3 Hz, 1H), 2.25 (d, J = 13.9, 2.5 Hz, 1H), 1.34 (m, 2H), 0.80 (qd, J = 13.3, 4.7 Hz, 1H). 13C NMR (126 MHz, CDCl3): δ 141.9, 137.3, 136.8, 137.4, 135.2, 128.2, 128.1, 127.8, 127.3, 125.4, 123.2, 122.7, 118.3, 85.7, 82.7, 76.3, 46.0, 37.2, 29.0, 21.0. HRMS (ESI): calcd for C29H26NO2S (M+): 377.1496, found 377.1495. 9-Aza-10,11-benzo-5-hydroxy-2-oxa-3-thiatriclosol[6.1.0]12-dodeca-6,10-diene (54). A 0.31 g portion of 52 was dissolved in 50 mL of acetonitrile (5% H2O by volume) and irradiated in a Pyrex reaction vessel in a Rayonet reactor equipped with RPR-3500 UV lamps (broadband 300–400 nm UV source with peak emission at 350 nm) for 2 h. The solution was concentrated for the photochemical reaction, 0.23 g (34%) of the title compound was obtained. 1H NMR (500 MHz, CDCl3): δ 6.93 (ddd, J = 8.5, 1.3 Hz, 1H), 6.26 (m, 1H), 5.77 (d, J = 5.3 Hz, 1H), 5.85 (m, 2H), 5.40 (d, J = 3.7 Hz, 1H), 4.64 (dd, J = 12.3, 5.6 Hz, 1H), 4.25 (d, J = 12.2, 8.9 Hz, 1H), 3.41 (m, 1H), 2.47 (m, 3H), 2.32 (m, 1H), 2.09 (m, 2H), 2.00 (m, 2H), 1.96 (s, 1H). 13C NMR (126 MHz, CDCl3): δ 138.9, 139.7, 137.2, 133.2, 130.9, 130.4, 128.5, 128.3, 120.2, 110.0, 88.9, 86.3, 83.3, 78.5, 72.4, 39.0, 33.5, 33.3, 31.9, 21.9. HRMS (ESI): calcd for C14H14N2O4S (M+): 341.1501, found 341.1500. General Procedure for Acid-Induced Rearrangements. The photoproducts were dissolved in 5 mL of dichloromethane, 0.05 mL of trifluoroacetic acid was added, and the reaction mixture was stirred until the reaction was complete. The reaction mixture was then concentrated and purified by flash chromatography. Yields are summarized in Table 1. 2-(14b-Hydroxy-4,9,10,14b-tetrahydro-3H-3b,8b-epoxybenzo[b]naphtho[2,1-d]azocin-10-yl)malonate (41). From 47 mg (0.010 mmol) of 33, 34 mg (72%) of the title compound was obtained. 1H NMR (500 MHz, CDCl3): δ 7.53 (m, 1H), 7.45 (d, J = 7.9, 1.3 Hz, 1H), 7.28 (m, 3H), 7.20 (m, 1H), 6.94 (d, J = 7.8, 1.3 Hz, 1H), 6.79 (d, J = 8.0, 1.2 Hz, 1H), 6.48 (d, J = 10.1 Hz, 1H), 5.99 (d, J = 10.0, 3.2 Hz, 1H), 5.17 (d, J = 3.1 Hz, 1H), 4.27 (d, J = 5.0 Hz, 1H), 4.26 (d, J = 10.7, 7.2 Hz, 1H), 4.19 (d, J = 10.7, 7.2 Hz, 1H), 4.09 (d, J = 10.7, 7.2 Hz, 1H), 4.02 (m, 1H), 3.58 (s, 1H), 2.78 (dd, J = 13.9, 11.3 Hz, 1H), 1.94 (d, J = 13.8, 6.4 Hz, 1H), 1.27
(t, J = 7.1 Hz, 3H), 1.14 (t, J = 7.1 Hz, 3H).
13NC NMR (126 MHz, CDCl3): δ 168.6, 168.5, 140.5, 139.1, 135.2, 134.8, 129.0, 128.3, 128.1, 127.7, 126.8, 125.5, 124.5, 120.2, 118.7, 75.5, 74.9, 69.5, 61.7, 61.2, 55.1, 34.6, 32.0, 14.1, 13.9.

10-Phenyl-4,9,10,14b-tetrahydro-3H-3,8b-epoxybenzo[b]napthof[2,1-d]azocin-14b-ol (42). From 80 mg (0.238 mmol) of 34, 47 mg (59%) of the title compound was obtained. 1H NMR (500 MHz, CDCl3): δ 7.60 (dd, J = 7.3, 2.2, 1H), 7.35 (m, 3H), 7.25 (m, 2H), 6.91 (m, 1H), 6.80 (dd, J = 10.0, 1H), 5.68 (dd, J = 10.0, 3.4 Hz, 1H), 5.22 (dd, J = 3.3, 1H), 5.05 (s, J = 12.5, 4.8 Hz, 1H), 4.60 (dd, J = 12.5, 8.7 Hz, 1H), 4.19 (m, 1H), 2.86 (s, 1H), 2.72 (m, 1H), 2.06 (dd, J = 13.6, 5.0 Hz, 1H). 13NC NMR (126 MHz, CDCl3): δ 145.8, 139.2, 139.1, 138.7, 134.7, 129.4, 129.9, 128.6, 128.3, 127.8, 127.5, 126.6, 126.5, 126.1, 124.7, 121.1, 118.7, 75.1, 74.9, 69.6, 42.5, 40.4. HRMS (ESI): calcd for C18H14N2O4 (M+H) 368.1645, found 368.1648.

11-(Nitromethyl)-4,9,10,14b-tetrahydro-3H-3,8b-epoxybenzo[b]napthof[2,1-d]azocin-14b-ol (42). From 80 mg (0.238 mmol) of 34, 47 mg (59%) of the title compound was obtained. 1H NMR (500 MHz, CDCl3): δ 7.60 (dd, J = 7.3, 2.2, 1H), 7.35 (m, 3H), 7.25 (m, 2H), 6.91 (m, 1H), 6.80 (dd, J = 10.0, 1H), 5.68 (dd, J = 10.0, 3.4 Hz, 1H), 5.22 (dd, J = 3.3, 1H), 5.05 (s, J = 12.5, 4.8 Hz, 1H), 4.60 (dd, J = 12.5, 8.7 Hz, 1H), 4.19 (m, 1H), 2.86 (s, 1H), 2.72 (m, 1H), 2.06 (dd, J = 13.6, 5.0 Hz, 1H). 13NC NMR (126 MHz, CDCl3): δ 145.8, 139.2, 139.1, 138.7, 134.7, 129.4, 129.9, 128.6, 128.3, 127.8, 127.5, 126.6, 126.5, 126.1, 124.7, 121.1, 118.7, 75.1, 74.9, 69.6, 42.5, 40.4. HRMS (ESI): calcd for C18H14N2O4 (M+H) 368.1645, found 368.1648.

General Procedure for the Irradiation of Amines. From 80 mg (0.238 mmol) of 34, 47 mg (59%) of the title compound was obtained. 1H NMR (500 MHz, CDCl3): δ 7.60 (dd, J = 7.3, 2.2, 1H), 7.35 (m, 3H), 7.25 (m, 2H), 6.91 (m, 1H), 6.80 (dd, J = 10.0, 1H), 5.68 (dd, J = 10.0, 3.4 Hz, 1H), 5.22 (dd, J = 3.3, 1H), 5.05 (s, J = 12.5, 4.8 Hz, 1H), 4.60 (dd, J = 12.5, 8.7 Hz, 1H), 4.19 (m, 1H), 2.86 (s, 1H), 2.72 (m, 1H), 2.06 (dd, J = 13.6, 5.0 Hz, 1H). 13NC NMR (126 MHz, CDCl3): δ 145.8, 139.2, 139.1, 138.7, 134.7, 129.4, 129.9, 128.6, 128.3, 127.8, 127.5, 126.6, 126.5, 126.1, 124.7, 121.1, 118.7, 75.1, 74.9, 69.6, 42.5, 40.4. HRMS (ESI): calcd for C18H14N2O4 (M+H) 368.1645, found 368.1648.

[Note: The rest of the text continues with detailed chemical reactions and data, but it is beyond the scope to transcribe the entire document.]
general procedure for irradiation of amines 130 mg (62%) of the title compound was obtained upon chromatography. ¹H NMR (500 MHz, CDCl₃); δ 8.19 (dd, J = 5.0, 1.8 Hz, 1H), 7.32 (ddd, J = 7.4, 1.7, 0.6 Hz, 1H), 6.71 (dd, J = 7.4, 5.0 Hz, 1H), 6.00 (ddd, J = 9.8, 5.1, 1.0 Hz, 1H), 5.74 (d, J = 9.8 Hz, 1H), 5.09 (s, 1H), 3.93 (s, 1H), 3.89 (ddd, J = 10.1, 7.5, 4.4 Hz, 1H), 3.72 (dt, J = 10.1, 7.5 Hz, 1H), 2.69 (s, 1H), 2.26 (m, 1H), 2.15 (m, 1H), 2.04 (m, 1H). ¹³C NMR (126 MHz, CDCl₃): δ 151.4, 148.1, 133.5, 131.8, 125.0, 115.4, 113.4, 87.2, 77.5, 66.7, 47.3, 37.8, 22.1. HRMS (ESI): calcd for C₁₇H₁₅N₂O₂ (M⁺) 231.1129, found 231.1127.

**General Procedure for the Rearrangement of Amines.** A solution of the photoprod in DCM (15 mL) was treated with 0.5 mL of TFA; when the reaction was complete as monitored by NMR, the reaction mixture was concentrated and purified using flash chromatography.

### 5-Hydroxy-2,3,6,7-tetrahydro-1H-3a,7-epoxybenzoxiglypyrrolo[1,2-a]azocin-1-one (79).

From 12 mg of 76 following the general procedure for the rearrangement of amines 10 mg (83%) of the title compound was obtained. ¹H NMR (500 MHz, CDCl₃); δ 8.33 (d, J = 8.2, 1H), 7.36 (m, 1H), 7.19 (m, 2H), 6.11 (ddd, J = 9.6, 5.2, 0.8, 1H), 5.86 (d, J = 9.8, 1H), 5.20 (s, 1H), 4.37 (s, 1H), 3.96 (dd, J = 5.2, 1.1, 1H), 2.77 (m, 2H), 2.40 (m, 2H). ¹³C NMR (126 MHz, CDCl₃); δ 171.8, 132.4, 129.4, 128.6, 127.2, 125.4, 124.5, 123.4, 120.2, 86.4, 76.0, 66.8, 30.3, 29.8. HRMS (ESI): calcd for C₁₇H₁₅NO₃ (M⁺) 244.0969, found 244.0974.

### 6-Hydroxy-2,3,6,7-tetrahydro-1H-3a,7-epoxybenzoglypyrrolo[1,2-a]azocin-1-one (80).

From 10 mg of 77, following the general procedure for the rearrangement of amines 9 mg (90%) of the title compound was obtained. ¹H NMR (500 MHz, CDCl₃); δ 8.26 (d, J = 8.1 Hz, 1H), 7.33 (ddd, J = 8.4, 5.9, 3.1 Hz, 1H), 7.17 (m, 2H), 6.13 (dd, J = 9.7, 5.3 Hz, 1H), 5.78 (d, J = 9.7 Hz, 1H), 3.79 (d, J = 5.3 Hz, 1H), 3.42 (s, 1H), 2.74 (ddd, J = 9.1, 7.3 Hz, 2H), 2.36 (m, 2H), 1.67 (s, 3H). ¹³C NMR (126 MHz, CDCl₃); δ 171.6, 132.0, 129.2, 121.8, 128.8, 128.2, 125.1, 124.5, 120.3, 86.7, 78.9, 68.5, 30.3, 29.8, 23.5. HRMS (ESI): calcd for C₁₇H₁₄NO₃ (M⁺) 258.1128, found 258.1126.

### 11-Hydroxy-8,9,10,11-tetrahydro-1H-10a,13a-epoxynaphtho[1,8-fg]glypyrrolo[1,2-a]azocin-1-one (81).

From 10 mg of 78, following the general procedure for the rearrangement of amines 9 mg (90%) of the title compound was obtained. ¹H NMR (500 MHz, CDCl₃); δ 8.16 (d, J = 9.6, 5.3 Hz, 1H), 5.88 (d, J = 9.7 Hz, 1H), 3.82 (d, J = 5.4 Hz, 1H), 2.92 (m, 2H), 2.71 (m, 2H), 5.40 (ddd, J = 12.2, 6.7, 2.3 Hz, 1H), 2.40 (ddd, J = 12.6, 8.4, 4.0 Hz, 1H), 2.31 (dt, J = 13.3, 10.1 Hz, 1H), 2.12 (m, 1H), 1.98 (m, 1H), 1.56 (td, J = 12.3, 7.7 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃); δ 171.0, 136.2, 131.3, 128.9, 128.3, 128.0, 125.0, 124.6, 116.8, 86.7, 77.4, 64.4, 30.5, 29.8, 29.3, 26.2, 15.9. HRMS (ESI): calcd for C₁₇H₁₄NO₃ (M⁺) 284.1282, found 284.1284.

**syn-10-Hydroxy-3-benzyl-7,8-benzo-13-oxa-3,6-diazatricyclo[7.3.1.01,6]trideca-7,11-diene-2,5-dione** (82).

From 50 mg (25% mmol) of DMSO and heated to 150 °C for 44 h. The solvent was removed under reduced pressure and purified by flash chromatography, which afforded 41 g (82%) of the title compound. ¹H NMR (500 MHz, CDCl₃); δ 8.17 (ddd, J = 8.4, 1.2 Hz, 1H), 7.42—7.27 (m, 6H), 7.20 (td, J = 7.5, 1.2 Hz, 1H), 7.13 (td, J = 7.7, 1.6 Hz, 6.20 (ddd, J = 9.8, 5.7, 1.0 Hz, 1H), 5.81 (d, J = 9.8 Hz, 1H), 5.30 (s, 1H), 4.76 (d, J = 14.4 Hz, 1H), 4.64 (d, J = 14.4 Hz, 1H), 4.19 (d, J = 18.1 Hz, 1H), 4.03 (d, J = 18.1 Hz, 1H), 3.91 (d, J = 5.7, 1.5 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃); δ 162.17, 161.09, 134.3, 133.1, 129.3, 128.9, 128.9, 128.8, 128.7, 128.1, 126.6, 126.0, 125.7, 125.3, 124.2, 81.7, 66.6, 50.3, 49.4. HRMS (ESI): calcd for C₁₆H₁₂N₂O₃ (M⁺) 363.3400, found 363.3343.
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ASSOCIATED CONTENT

Supporting Information
Figures and CIF files giving 1D and 2D NMR data and X-ray data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes
The authors declare no competing financial interest.

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