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

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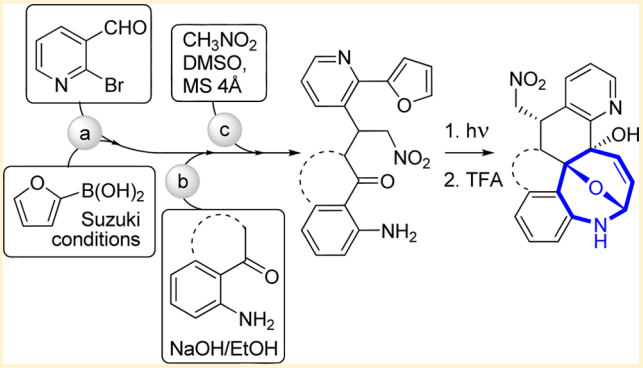
Supporting Information

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 photogeneration 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 anticancer 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,[9] Mizoroki−Heck reaction,[10] ring expansion,[11] cycloaddition,[12] and condensation[13] strategies. Most of these approaches, however, imply multistep synthesis; therefore, the development of new short synthetic pathways to the benzazocane scaffold is well justified.

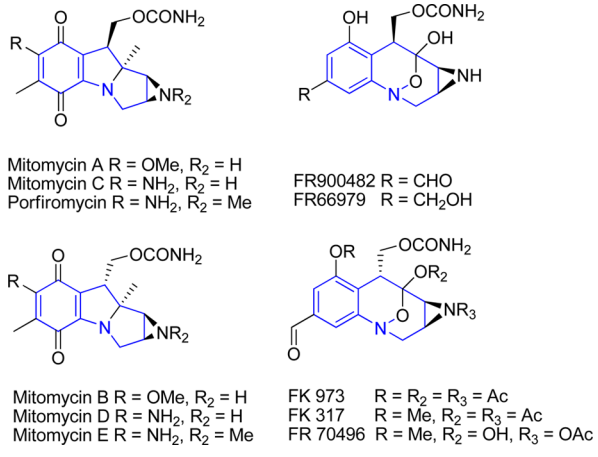


Figure 1. Some members of mitomycinoid alkaloids and their congeners.

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, ESIPT,[14] in aromatic *o*-amino ketones and aldehydes. Transient *C*-hydroxyazaxylylenes generated via ESIPT 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-ESIPT) approaches to azaxylylenes require exotic precursors such as benzosultams and benzoazetines and often occur

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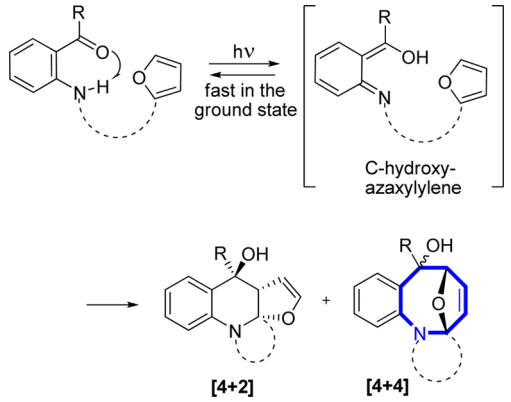
under the harsh conditions of flash vacuum pyrolysis;[15] thus, their utilization in the synthesis of delicate complex organic architectures remains very limited. An exception is Corey's mild generation of azaxylylenes via 1,4-dehydrochlorination of *o*-aminobenzyl chlorides.[16] However, azaxylylenes 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—*intra*molecular reactions of the ESIPT-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 *intra*molecularly with the appropriately tethered unsaturated pendants (Scheme 1).[17]

Scheme 1. Photogeneration of Azaxylylenes and Their Intramolecular Cycloadditions



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[18] both as 4π and less commonly as 2π[19] 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.[20] According to our recent experimental and theoretical mechanistic study,[21] it is likely that the intramolecular cycloaddition of azaxylylenes photogenerated via ESIPT 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 *o*-amino ketone core of the azaxylylene precursor.

In the current study we extend the scope to azaxylylenes derived *from o-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 ESIPT-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

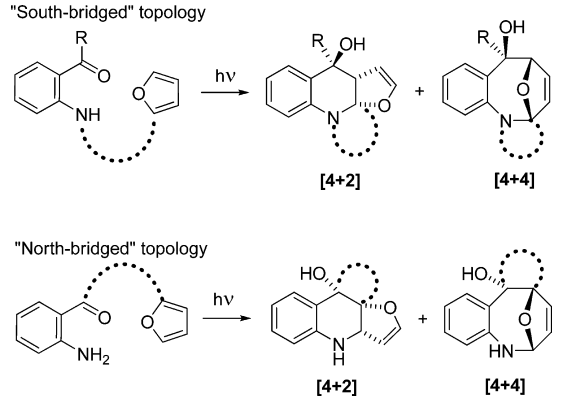


Figure 2. Original "south-bridged" and new "north-bridged" topology.

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 α 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 α 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.[22] The implemented pathway to the photoprecursors comprises two simple steps: aldol condensation of the *o*-furyl aromatic (or α-furyl vinyl) carboxaldehyde followed by the conjugate (Michael) addition of a nucleophile to the obtained α,β-unsaturated ketone. The starting aldehyde can be prepared by the Suzuki reaction of 2-furanboronic acid with the corresponding *o*- or β-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 obtained via the Suzuki reaction, the Michael nucleophile, and aromatic or α substitution in *o*-aminoacetophenone.

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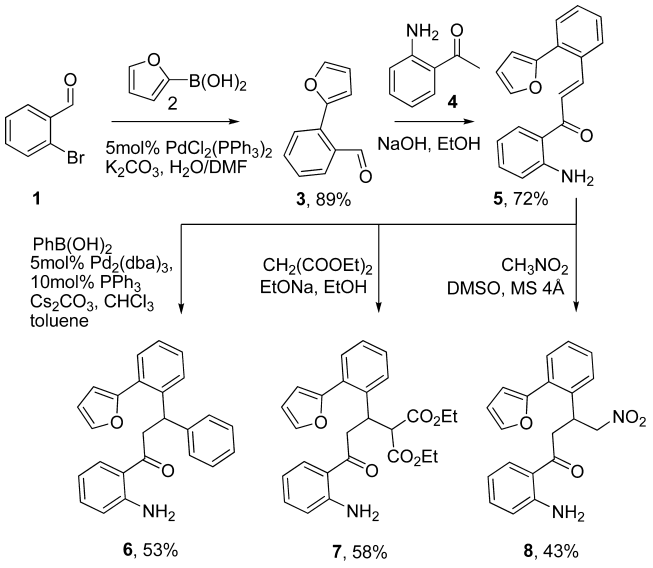
Scheme 2. Synthesis of the Initial Batch of Photoprecursors



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 $PdCl_2(PPh_3)_2$, yielded aldehyde **3**[23] (89%), which serves as the carbonyl component in the subsequent aldol condensation[24] with *o*-aminoacetophenone (**4**), giving chalcone **5**, a reactive Michael acceptor for a variety of nucleophiles, including nitromethane,[25] diethyl malonic ester,[26] and phenylboronic acid,[27] in a Pd^0-catalyzed reaction. Thus, the photoprecursors **6**–**8** are readily available in three simple steps in moderate to good yields.

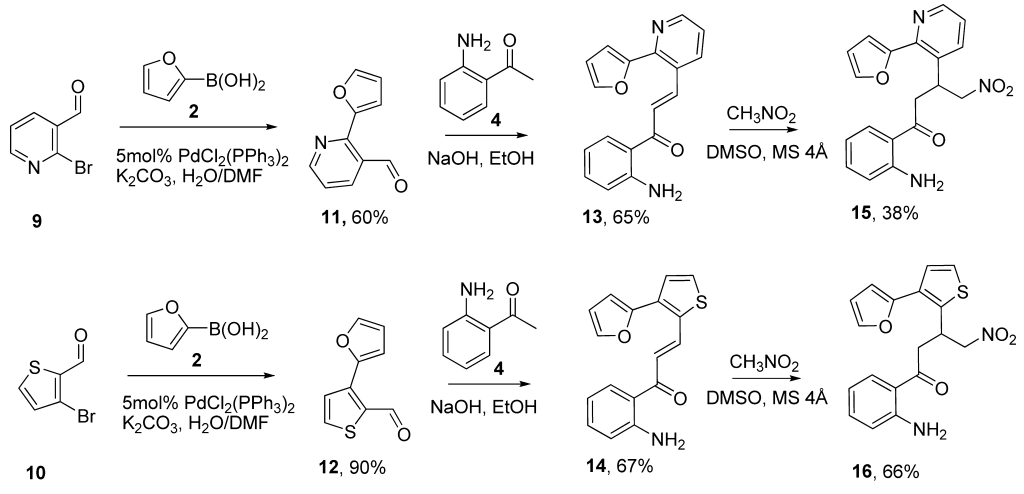
Similarly, heterocyclic analogues **15** and **16** were prepared, starting the sequence with 2-bromonicotinaldehyde (**9**) or 2-formyl-3-bromothiophene (**10**) (Scheme 3). In both of these cases, nitromethane was used as a Michael nucleophile.

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[28] from commercially available cyclic ketones on a multigram scale, using DMF and PBr_3. 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).

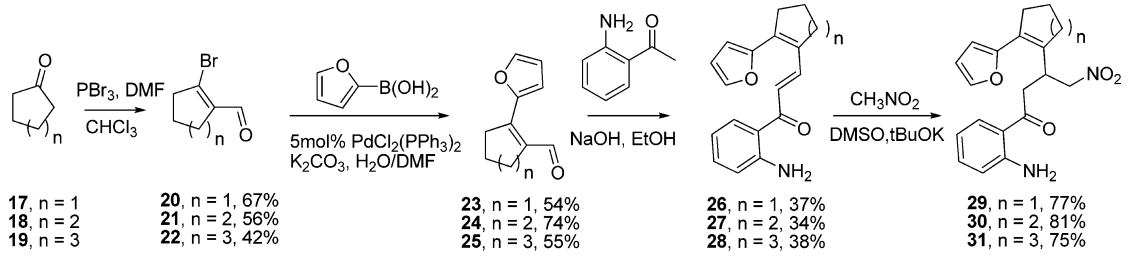
The photoprecursors, obtained as described above, have an (n,π^*) UV absorption maximum around 350 nm. Methanol was the solvent of choice for irradiation after a few solvent optimization runs. Irradiations were carried out with a Rayonet broad-band 300–400 nm UV source (RPR-3500 lamps). Curiously, irradiation 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 cycloaddition of the ESIPT-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

Scheme 3. Access to Photoprecursors Containing Heterocyclic Moieties



Scheme 4. Synthesis of Alicyclic Derivatives



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Scheme 5. Intramolecular Cycloadditions of Photogenerated Azaxylylenes

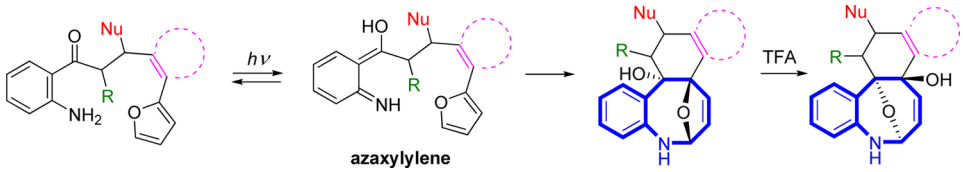
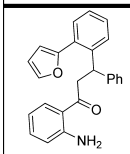
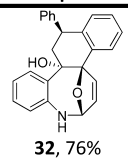
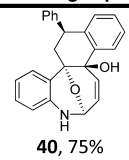
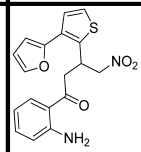
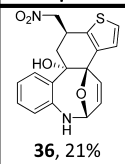
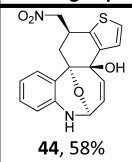
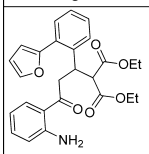
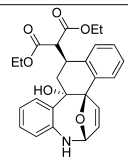
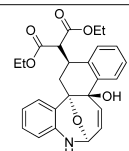
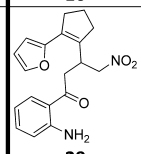
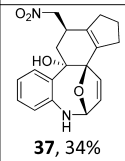
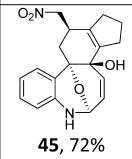
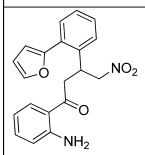
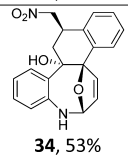
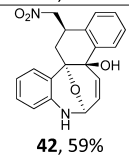
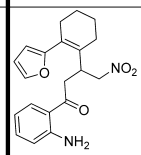
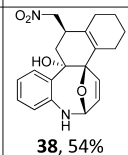
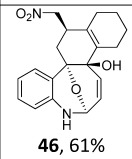
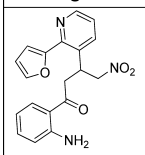
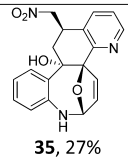
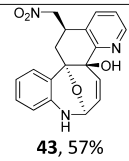
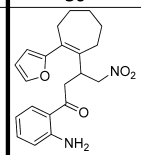
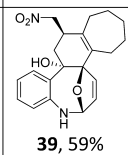
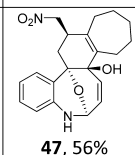


Table 1. Primary Photoproducts from the "North-Bridged" Photoprecursors and Their Acid-Catalyzed Rearrangement

Precursor	Photoproduct	Rearranged prod.	Precursor	Photoproduct	Rearranged prod.
 **6**	 **32**, 76%	 **40**, 75%	 **16**	 **36**, 21%	 **44**, 58%
 **7**	 **33**, 55%	 **41**, 72%	 **29**	 **37**, 34%	 **45**, 72%
 **8**	 **34**, 53%	 **42**, 59%	 **30**	 **38**, 54%	 **46**, 61%
 **15**	 **35**, 27%	 **43**, 57%	 **31**	 **39**, 59%	 **47**, 56%

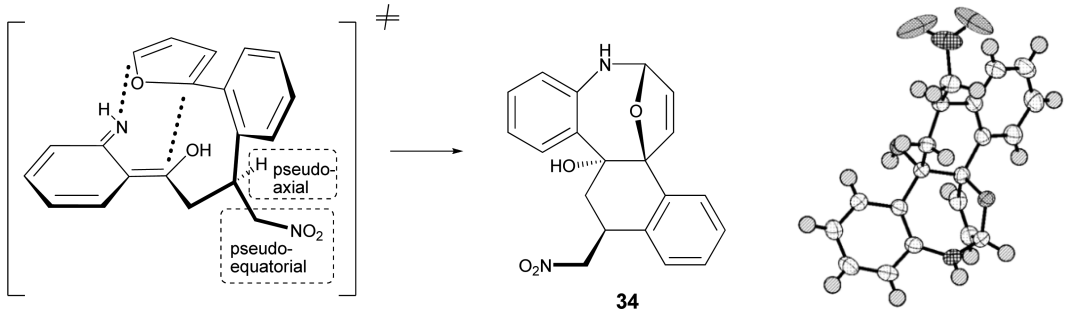


Figure 3. Nitromethyl moiety biasing the folding of the furanyl tether in the transition state, leading to the [4 + 4] intramolecular cycloadducts. The ORTEP structure of **34** is shown with 50% thermal ellipsoids.

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,[29] 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. ^{1}H NMR spectra of the

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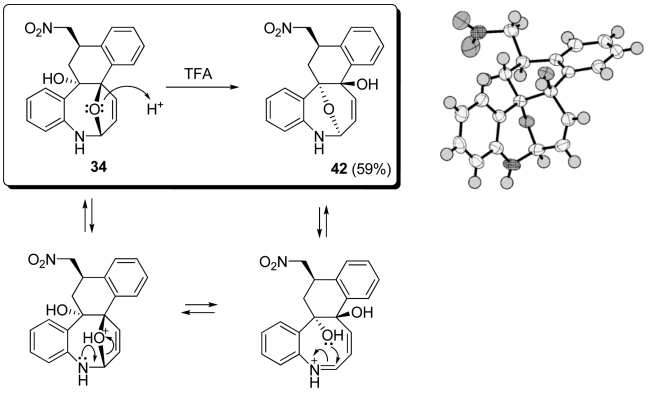
Scheme 6. Bicyclo[4.2.1] to [3.3.1] Rearrangement and the ORTEP Structure of 42[a]



[a]Shown with 50% thermal ellipsoids.

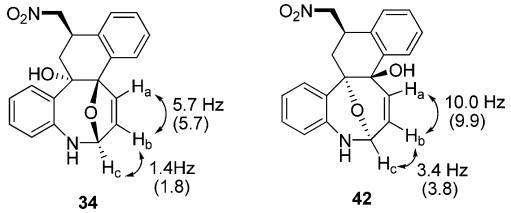


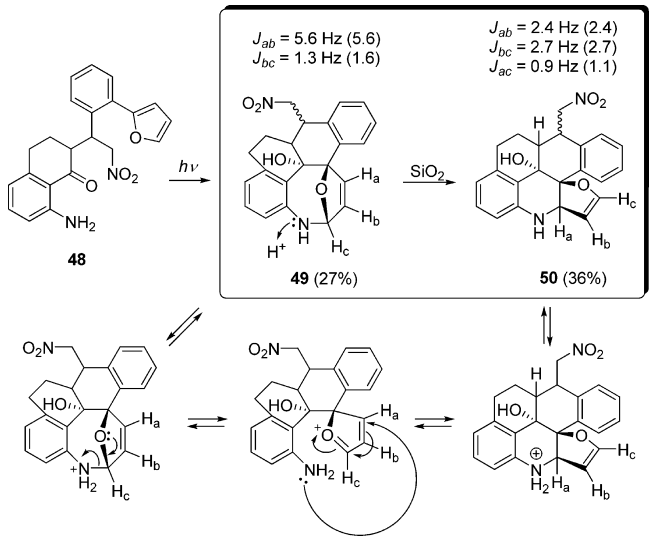
Figure 4. Experimental and calculated (in parentheses) proton spin–spin coupling constants (in Hz) for primary and rearranged products exemplified by compounds **34** and **42**.

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,[30] with the predicted constants, shown in Figure 4, matching the experimental values very well.

The only exception in this series was the rearrangement of photoproduct **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 ^{1}H NMR and COSY spectra. Protons H_a, H_b, and H_c (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 H_a and H_b protons and 1.3 Hz for H_b and H_c (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 J_{ab} = 2.4 Hz and J_{ac} = 0.9 Hz. Such a distinctive set of values has been observed earlier for [4 + 2] azaxylylene

Scheme 7. Rearrangement of Tetralone-Derived 49[a]

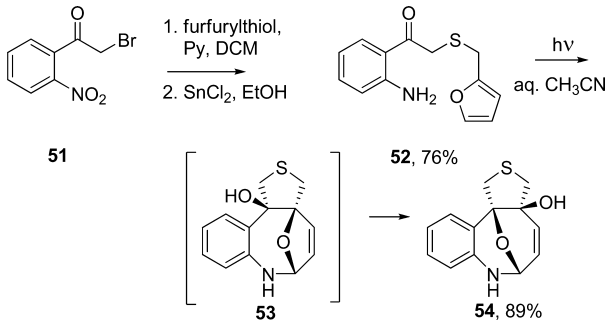


[a]Computed J values are given in parentheses.

cycloaddition 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 oxamorphan core. We identified a case in which this rearrangement occurs spontaneously during the photolysis. Sulfide **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,

Scheme 8. Spontaneous Post-Photochemical Rearrangement in Sulfide 52



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.

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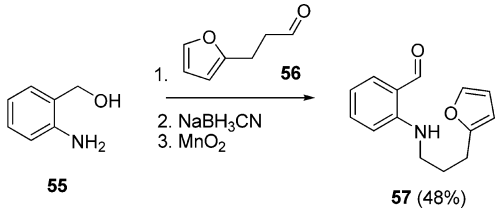
The observed rearrangement into the pyranose form is clearly facilitated by the fact that the aniline moiety is not acylated, resulting in a more stable iminium ion (Scheme 6) as the key intermediate in this rearrangement. Additional questions are whether this lack of N-acylation (or further electron-donating 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.

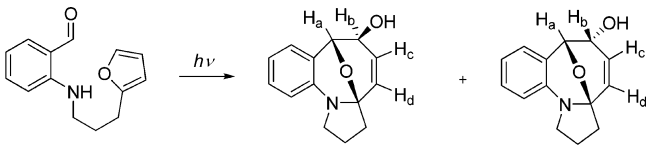
We therefore revisited the south-bridged structures, but instead of amide-forming coupling of the furan pendant we explored reductive amination to furnish alkylated *anilines*, not *anilides*. First, we synthesized the secondary amine **57**, through the sequence of reductive amination of 3-furylpropanal (**56**) with 2-aminophenylmethanol (**55**) and the oxidation of the benzylic alcohol with MnO_2 (Scheme 9).

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



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

Scheme 10. Irradiation of Alkylamine 57



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_{cd} = 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 α-hydroxy proton H_b: the syn isomer has the large constant J_{bc} = 5.2 Hz (calculated 5.1 Hz) and a small constant J_{ab} = 1.3 Hz (calculated 1.5 Hz); in contrast, the anti isomer has a small constant J_{bc} = 1.7 Hz (calculated 2.0 Hz) and a large constant J_{ab} = 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.

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 aldehydes 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 azaxylylene 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 photoproduct **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.[21] It also sets the product up for a subsequent Suzuki coupling,[31] 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 photoproduct **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 photoproduct, in addition to the two expected alkenyl 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

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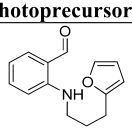
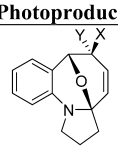
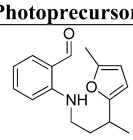
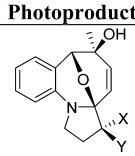
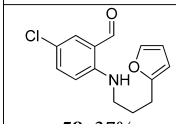
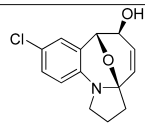
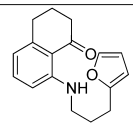
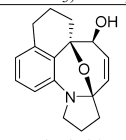
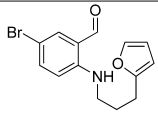
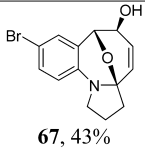
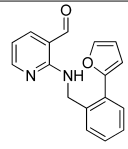
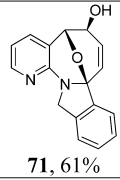
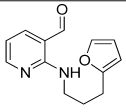
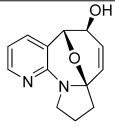
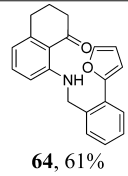
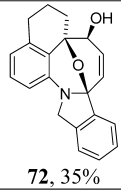
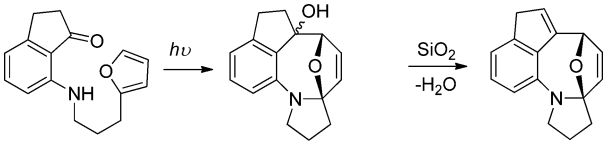
Table 2. South-Bridged Alkylamines[a]

Photoprecursor *	Photoproduct	Photoprecursor*	Photoproduct
 **57,** 48%	 **65a** X=OH, Y=H, 40% **65b**, X=H, Y=OH, 7%	 **61,** 63%	 **69a,** X=H, Y=CH_3, 36% **69b**, X=CH_3, Y=H, 33%
 **58**, 37%	 **66**, 57%	 **62**, 57%	 **70**, 47%
 **59**, 18%	 **67**, 43%	 **63**, 21%	 **71**, 61%
 **60**, 45%	 **68**, 62%	 **64**, 61%	 **72**, 35%

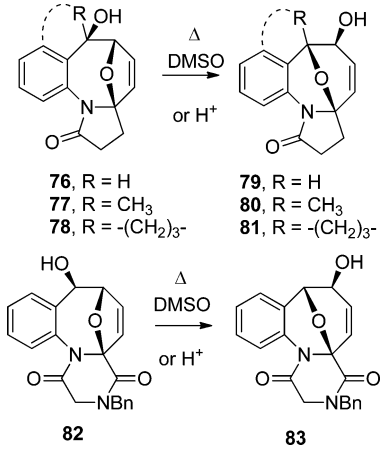
[a]The asterisk indicates that the yields for synthesis of photoprecursors **57**−**61** and **63** are given over two steps: reductive amination and benzylic alcohol oxidation.

Scheme 11. Spontaneous Dehydration of the Primary Photoproduct 74



73 **74** **75**, 67%

Scheme 12. [4.2.1] → [3.3.1] Rearrangement in Amides



76, R = H
77, R = CH_3
78, R = -$(CH_2)_3$-

79, R = H
80, R = CH_3
81, R = -$(CH_2)_3$-

82 **83**

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]

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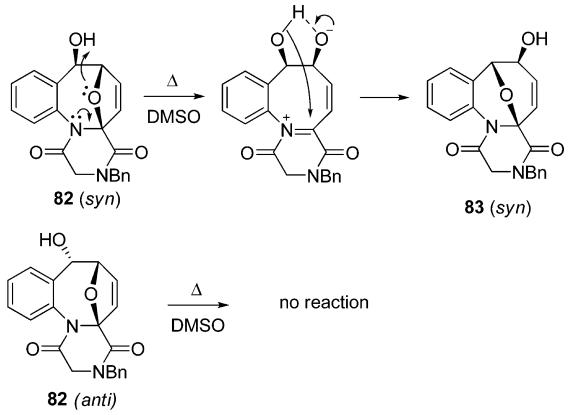
Scheme 13. Thermal Rearrangement: Anti vs Syn Reactivity



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 benzophenone 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 $CDCl_3$ 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 (10.2 mmol) in chloroform (10 mL) 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 $NaHCO_3$ (100 mL) and brine (100 mL), dried over $MgSO_4$, and concentrated in vacuo.[28]

1-Bromo-2-formyl-1-cyclopentene[32] ***(20)***. Following the general procedure for the Vilsmeier−Haack reaction from 0.86 g (10.2 mmol) of cyclopentanone, 1.20 g (67%) of the title compound was obtained, which was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.93 (s, 1H), 2.93 (m, 2H), 2.56 (m, 2H), 2.04 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 189.3, 141.5, 140.0, 42.6, 29.3, 21.4.

1-Bromo-2-formyl-1-cyclohexene[32] ***(21)***. Following the general procedure for the Vilsmeier−Haack reaction from 1.00 g (10.2 mmol) of cyclohexanone, 1.08 g (56%) of the title compound was obtained, which was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.05 (s, 1H), 2.77 (m, 2H), 2.30 (m, 2H), 1.79 (m, 2H), 1.71 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.8, 143.6, 135.3, 38.8, 25.0, 24.3, 21.1.

1-Bromo-2-formyl-1-cycloheptene[33] ***(22)***. Following the general procedure for the Vilsmeier−Haack reaction reaction from 1.34 g (10.2 mmol) of cycloheptanone, 0.87 g (42%) of the title compound was obtained, which was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.95 (s, 1H), 3.04 (m, 2H), 2.52 (m, 2H), 1.82 (m, 2H), 1.69 (m, 2H), 1.48 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.3, 148.3, 140.5, 44.3, 31.4, 25.7, 25.2, 24.8.

General Procedure for Suzuki Coupling. Under a nitrogen atmosphere, α-formyl aryl (or cycloalkyl) halide (10 mmol), arylboronic acid (12 mmol), K_2CO_3 (30 mmol), and $PdCl_2(PPh_3)_2$, (5 mol %, 350 mg) were suspended in DMF/H_2O (15 mL/1.5 mL). The resulting solution was stirred at 110 °C until the completion of the reaction. After it was cooled to room temperature, the resulting mixture was filtered through a short path of silica gel. The filtrate was then extracted several times with EtOAc/Et_2O (1/1). The combined organic layer was washed with brine (3 × 10 mL) and dried over $MgSO_4$. The reaction mixture was then concentrated in vacuo, and the crude residue was purified by silica gel column chromatography if necessary (petroleum ether/EtOAc) to afford the coupling products.[23]

2-(Furan-2-yl)cyclopent-1-enecarbaldehyde[34] ***(23)***. Following the general procedure for Suzuki coupling from 2.40 g (13.71 mmol) of **20**, 1.20 g (54%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.61 (s, 1H), 7.60 (d, J = 1.6 Hz, 1H), 6.63 (d, J = 3.4 Hz, 1H), 6.53 (dd, J = 3.4, 1.8 Hz, 1H), 2.94 (m, 2H), 2.77 (m, 2H), 1.99 (p, J = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.2, 151.0, 145.3, 144.8, 137.4, 114.0, 111.8, 36.0, 31.1, 21.7.

2-(Furan-2-yl)cyclohex-1-enecarbaldehyde[34] ***(24)***. Following the general procedure for Suzuki coupling from 1.20 g (6.34 mmol) of **21**, 0.83 g (74%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.14 (s, 1H), 7.55 (s, br, 1H), 6.54 (d, J = 3.3 Hz, 1H), 6.50 (m, 1H), 2.63 (m, 2H), 2.41 (m, 2H), 1.77 (m, 2H), 1.69 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.5, 151.9, 144.1, 143.8, 135.8, 113.1, 111.5, 29.19, 23.0, 22.1, 21.4.

2-(Furan-2-yl)cyclohept-1-enecarbaldehyde ***(25)***. Following the general procedure for Suzuki coupling from 2.10 g (10.3 mmol) of **22**, 1.08 g (55%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.97 (s, 1H), 7.57 (dd, J = 1.8, 0.6 Hz, 1H), 6.55 (d, J = 3.4 Hz, 1H), 6.51 (dd, J = 3.4, 1.8 Hz, 1H), 2.81 (m, 2H), 2.65 (m, 2H), 1.85 (m, 2H), 1.70 (dt, J = 11.6, 6.1 Hz, 2H), 1.52 (p, J = 6.0 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.6, 151.9, 150.5, 144.7, 141.8, 114.8, 111.7, 33.9, 32.2, 26.0, 25.9, 25.3.

2-(Furan-2-yl)benzaldehyde[35] ***(3)***. Following the general procedure for Suzuki coupling from 0.92 g (4.97 mmol) of 2-bromobenzaldehyde (**1**), 0.76 g (89%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.41 (s, 1H), 8.00 (m, 1H), 7.71 (m, 1H), 7.65 (m, 2H), 7.47 (m, 1H), 6.66 (m, 1H), 6.59 (dd, J = 3.4, 1.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.4, 151.1, 144.0, 133.6, 133.4, 133.1, 128.4, 128.1, 128.0, 111.9, 111.3.

2-(Furan-2-yl)nicotinaldehyde[36] ***(11)***. Following the general procedure for Suzuki coupling from 0.92 g (4.97 mmol) of nicontinaldehyde (**9**), 0.52 g (60%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.72 (d, 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), 7.35 (m, 1H), 7.23 (dd, J = 3.5, 0.7 Hz, 1H), 6.66 (dd, J = 3.5, 1.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.9, 153.4, 150.0, 152.6, 145.3, 136.2, 128.2, 122.3, 113.8, 112.4.

3-(Furan-2-yl)thiophene-2-carbaldehyde[37] ***(12)***. Following the general procedure for Suzuki coupling from 1.00 g (5.23 mmol) of 3-bromo-thiophene-2-carbaldehyde (**10**), 0.84 g (90%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.50 (d, J = 1.2 Hz, 1H), 7.68 (dd, J = 5.1, 1.2 Hz, 1H), 7.60 (dd, J = 1.8, 0.7 Hz, 1H), 7.36 (m, 1H), 6.80 (dd, J = 3.4, 0.6 Hz, 1H), 6.57 (dd, J = 3.4, 1.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): 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.*[24] 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.[38] Ethanolic solutions (10 mL) of equimolar amounts of 2′-aminoacetophenone (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 ***(13)***. 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. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.70 (dd, J = 4.7, 1.6 Hz, 1H), 8.29 (d, J = 15.5 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). ^{13}C NMR (126 MHz, $CDCl_3$): δ

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191.2, 152.2, 151.2, 150.1, 144.3, 140.2, 135.6, 134.6, 132.1, 131.1, 128.5, 126.7, 122.0, 118.6, 117.4, 115.9, 113.5, 112.0.

*(E)-1-(2-Aminophenyl)-3-(3-(furan-2-yl)thiophen-2-yl)prop-2-en-1-one (**14**).* Following the general procedure B for aldol condensation from 0.36 g (2.02 mmol) of **12**, 0.40 g (67%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48 (dd, J = 15.1, 0.8, 1H), 7.88 (dd, J = 8.1, 1.3 Hz, 1H), 7.58 (dd, J = 1.8, 0.7 Hz, 1H), 7.49 (d, J = 15.2 Hz, 1H), 7.35 (dd, J = 5.3, 0.7 Hz, 1H), 7.31 (m, 1H), 7.30 (d, J = 5.3 Hz, 1H), 6.73 (m, 2H), 6.65 (dd, J = 3.4, 0.6 Hz, 1H), 6.53 (dd, J = 3.4, 1.8 Hz, 1H), 6.37 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 190.9, 151.0, 150.2, 142.8, 135.1, 134.4, 134.3, 133.8, 130.9, 127.8, 126.9, 123.0, 119.1, 117.3, 115.9, 111.6, 109.3.

*(E)-1-(2-Aminophenyl)-3-(2-(furan-2-yl)phenyl)prop-2-en-1-one (**5**).* Following the general procedure A for aldol condensation from 0.24 g (1.39 mmol) of **3**, 0.29 g (72%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (d, J = 15.4 Hz, 1H), 7.92 (dd, J = 8.4, 1.4 Hz, 1H), 7.76 (dd, J = 7.9, 1.1 Hz, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.59 (m, 1H), 7.57 (d, J = 15.5 Hz, 1H), 7.48 (td, J = 7.6, 1.3 Hz, 1H), 7.39 (m, 1H), 7.31 (m, 1H), 6.73 (m, 2H), 6.56 (m, 2H), 6.39 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.6, 152.0, 151.1, 142.9, 142.2, 134.4, 133.0, 131.1, 131.1, 129.6, 127.8, 127.7, 127.6, 125.1, 119.0, 117.3, 115.9, 111.9, 111.0.

*(E)-1-(2-Aminophenyl)-3-(2-(furan-2-yl)cyclohex-1-en-1-yl)prop-2-en-1-one (**27**).* Following the general procedure A for aldol condensation from 0.80 g (4.54 mmol) of **24**, 0.45 g (34%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.24 (d, J = 15.3 Hz, 1H), 7.84 (m, 1H), 7.52 (dd, J = 1.7, 0.6 Hz, 1H), 7.28 (m, 1H), 7.14 (d, J = 15.3 Hz, 1H), 6.70 (m, 2H), 6.47 (dd, J = 3.4, 1.8 Hz, 1H), 6.44 (d, J = 3.3 Hz, 1H), 6.30 (m, 2H), 2.61 (m, 2H), 2.50 (m, 2H), 1.78 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.6, 153.8, 150.7, 143.2, 142.7, 134.7, 133.9, 131.0, 130.9, 121.8, 119.6, 117.2, 115.7, 111.5, 111.3, 29.1, 26.5, 22.3, 22.2.

*(E)-1-(2-Aminophenyl)-3-(2-(furan-2-yl)cyclopent-1-en-1-yl)prop-2-en-1-one (**26**).* Following the general procedure B for aldol condensation from 1.20 g (7.39 mmol) of **23**, 0.75 g (37%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 (d, J = 15.2 Hz, 1H), 7.84 (dd, J = 8.4, 1.4 Hz, 1H), 7.59 (d, J = 1.3 Hz, 1H), 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). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.3, 152.3, 150.8, 143.7, 138.5, 136.3, 134.2, 133.9, 131.0, 124.5, 119.5, 117.2, 115.8, 111.3, 111.2, 35.6, 33.7, 21.9.

*(E)-1-(2-Aminophenyl)-3-(2-(furan-2-yl)cyclohept-1-en-1-yl)prop-2-en-1-one (**28**).* 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. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.16 (d, J = 15.2 Hz, 1H), 7.84 (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 (h, J = 7.5, 6.7 Hz, 2H), 1.65 (dq, J = 17.1, 5.8 Hz, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): 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, 112.6, 111.5, 32.8, 32.0, 29.9, 26.3, 25.9.

(E)-8-Amino-2-(2-(furan-2-yl)benzylidene)-3,4-dihydronaphthalen-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. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (m, 2H), 7.53 (dd, 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 (d, J = 8.3 Hz, 1H), 6.54 (dd, J = 3.4, 0.7 Hz, 1H), 6.49 (m, 2H), 2.92 (m, 2H), 2.87 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 190.2, 152.1, 151.8, 145.0, 142.3, 137.1, 135.3, 134.5, 132.7, 130.6, 129.7, 128.3, 126.8, 126.4, 115.9, 115.6, 115.0, 111.9, 110.8, 30.4, 27.1.

Procedure for Addition of Phenyl Boronic Acid to Enones.[27] Enone (1.0 mmol), arylboronic acid (2.0 mmol), $Pd_2(dba)_3$ (5 mol %, 0.05 mmol), PPh_3 (10 mol %, 0.10 mmol), Cs_2CO_3 (1.0 mmol, 0.32 g), and $CHCl_3$ (0.01 mL) in toluene (2 mL) were heated to 80 °C for 24 h. The mixture was concentrated and purified via chromatography.

*1-(2-Aminophenyl)-3-(2-(furan-2-yl)phenyl)-3-phenylpropan-1-one (**6**).* Following the procedure for addition of boronic acids from 0.27 g (0.93 mmol) of **5**, 0.18 g (53%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (dd, J = 8.4, 1.4 Hz, 1H), 7.61−7.55 (m, 1H), 7.54−7.49 (m, 1H), 7.31−7.23 (m, 6H), 7.18 (dd, J = 13.1, 7.1 Hz, 3H), 6.69−6.61 (m, 2H), 6.52−6.43 (m, 2H), 6.19 (s, 2H), 5.42 (dd, J = 8.2, 6.4 Hz, 1H), 3.82 (dd, J = 17.1, 8.4 Hz, 1H), 3.65 (dd, J = 17.1, 6.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.7, 153.4, 150.4, 144.0, 142.2, 142.1, 134.2, 130.9, 130.5, 129.4, 128.4, 128.3, 128.3, 127.9, 126.3, 126.1, 118.0, 117.3, 115.7, 111.2, 108.8, 45.3, 41.8. HRMS (ESI): calcd for $C_{25}H_{22}NO_2^+$ (MH^+) 368.1645, found 368.1650.

Procedure for Addition of Diethyl Malonate.[26] To a solution of 1 mmol of chalcone and 5 mL of diethyl malonate in 25 mL of ethanol was added 0.25 g of sodium in 2.5 mL of ethanol, the mixture was refluxed for 2 h, quenched with NH_4Cl, and extracted with ether, and the extract was dried over Na_2SO_4, concentrated, and chromatographed.

*Diethyl 2-(3-(2-Aminophenyl)-1-(2-(furan-2-yl)phenyl)-3-oxopropyl)malonate (**7**).* Following the procedure for addition of diethyl malonate from 0.30 g (1.03 mmol) of **5**, 0.27 g (58%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80 (dd, J = 8.1, 1.2 Hz, 1H), 7.51 (dd, J = 7.4, 1.7 Hz, 1H), 7.45 (m, 1H), 7.40 (m, 1H), 7.25 (m, 3H), 6.69 (d, J = 3.3 Hz, 1H), 6.62 (m, 1H), 6.59 (d, J = 8.3 Hz, 1H), 6.47 (dd, J = 3.3, 1.8 Hz, 1H), 6.13 (s, 2H), 4.83 (td, J = 8.6, 5.2 Hz, 1H), 4.18 (dq, J = 10.7, 7.1 Hz, 1H), 4.13 (dq, J = 10.8, 7.5, 7.0 Hz, 1H), 4.00 (m, 2H), 3.94 (d, J = 8.6 Hz, 1H), 3.60 (dd, J = 16.2, 5.2 Hz, 1H), 3.48 (dd, J = 16.2, 8.6 Hz, 1H), 1.20 (t, J = 7.1 Hz, 3H), 1.04 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.7, 168.5, 168.0, 153.1, 150.3, 142.1, 138.5, 134.1, 131.2, 130.9, 129.4, 128.1, 127.5, 126.9, 117.9, 117.1, 115.7, 111.3, 108.9, 61.4, 61.3, 57.0, 42.7, 36.7, 13.9, 13.7. HRMS (ESI): calcd for $C_{26}H_{27}LiNO_6^+$ (MLi^+) 456.1993, found 456.2001.

Procedure for Addition of Nitromethane. *Procedure C.*[25a] A mixture of chalcone (0.3 mmol) and nitromethane (1.5 mmol) in DMSO (1 mL) in the presence of MS 4 Å (100 mg) was stirred at room temperature under an argon atmosphere. After 12 h, the reaction mixture was quenched with a phosphate buffer (pH 7, 20 mL). The organic materials were extracted with ethyl acetate and dried over anhydrous $MgSO_4$. If necessary, the product was purified with flash chromatography.

Procedure D.[25b] To a mixture of chalcone (0.3 mmol) and nitromethane (1 mL) in DMSO (5 mL) was added 0.3 mmol of tBuOK. After 12 h at room temperature the reaction mixture was quenched with saturated aqueous NH_4Cl. The organic materials were extracted with ethyl acetate and dried over anhydrous $MgSO_4$. If necessary, the product was purified with flash chromatography.

*1-(2-Aminophenyl)-3-(2-(furan-2-yl)phenyl)-4-nitrobutan-1-one (**8**).* Following general procedure C for addition of nitromethane from 0.10 g (0.35 mmol) of **5**, 0.05 g (43%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (dd, J = 8.1, 1.3 Hz, 1H), 7.56 (m, 2H), 7.36 (m, 4H), 6.65 (m, 3H), 6.55 (dd, J = 3.3, 1.9 Hz, 1H), 6.25 (s, 2H), 4.81 (m, 3H), 3.51 (dd, J = 17.3, 5.1 Hz, 1H), 3.39 (dd, J = 17.3, 8.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.8, 153.1, 150.5, 142.6, 137.1, 134.7, 130.8, 130.8, 130.1, 128.8, 127.6, 126.7, 117.4, 117.4, 115.9, 111.5, 109.0, 79.0, 42.0, 35.8. HRMS (ESI): calcd for $C_{20}H_{19}N_2O_4^+$ (MH^+) 351.1339, found 351.1343.

*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. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73 (m, 1H), 7.42 (m, 1H), 7.28 (m, 1H), 6.66 (m, 2H), 6.41 (dd, 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). ^{13}C NMR (126 MHz, $CDCl_3$): 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, 108.5, 78.0, 40.0, 34.7, 34.4, 33.8, 22.0. HRMS (ESI): calcd for $C_{19}H_{21}N_2O_4^+$ (MH^+) 341.1496, found 341.1497.

*1-(2-Aminophenyl)-3-(2-(furan-2-yl)cyclohex-1-en-1-yl)-4-nitrobutan-1-one (**30**).* Following general procedure D for addition of nitromethane from 0.43 g (1.47 mmol) of **27**, 0.42 g (81%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (dd, J = 8.2, 1.3 Hz, 1H), 7.35 (m, 1H), 7.27 (m, 1H), 6.65 (m, 2H), 6.38 (dd, J = 3.3, 1.8 Hz, 1H), 6.29 (m, 3H), 4.61 (m, 3H), 3.24 (dd, J = 16.3, 4.9 Hz, 1H),

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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). ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.5, 154.2, 150.5, 141.2, 134.6, 132.5, 131.0, 126.4, 117.5, 117.4, 115.8, 110.7, 107.8, 77.5, 40.0, 37.8, 29.3, 25.6, 22.4, 22.4. HRMS (ESI): calcd for $C_{20}H_{23}N_2O_4^+$ (MH^+) 355.1652, found 355.1653.

*1-(2-Aminophenyl)-3-(2-(furan-2-yl)cyclohept-1-en-1-yl)-4-nitrobutan-1-one (**31**).* Following the general procedure D for nitromethane addition from 0.20 g (0.65 mmol) of **28**, 0.18 g (75%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (dd, J = 8.2, 1.4, 1H), 7.34 (dd, J = 1.8, 0.7, 1H), 7.29 (m, 1H), 6.66 (dd, J = 8.3, 0.9 Hz, 1H), 6.63 (ddd, J = 8.2, 7.1, 1.1 Hz, 1H), 6.38 (dd, J = 3.3, 1.8, Hz 1H), 6.27 (s, 2H), 6.24 (dd, J = 3.3, 0.7 Hz, 1H), 4.57 (m, 3H), 3.18 (dd, J = 16.0, 4.9 Hz, 1H), 3.06 (dd, J = 16.0, 8.3 Hz, 1H), 2.51 (m, 2H), 2.37 (m, 2H), 1.81 (m, 2H), 1.57 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.4, 154.6, 150.6, 141.3, 138.3, 134.6, 133.5, 130.9, 117.4, 117.4, 115.8, 110.7, 107.9, 77.5, 39.9, 38.8, 33.7, 32.2, 29.2, 26.6, 26.1. HRMS (ESI): calcd for $C_{21}H_{25}N_2O_4^+$ (MH^+) 369.1809, found 369.1811.

*1-(2-Aminophenyl)-3-(3-(furan-2-yl)thiophen-2-yl)-4-nitrobutan-1-one (**16**).* Following general procedure C for nitromethane addition from 0.35 g (1.19 mmol) of **14**, 0.28 g (66%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): 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), 3.59 (dd, J = 17.4, 6.2 Hz, 1H), 3.52 (dd, J = 17.4, 7.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.1, 150.6, 150.2, 141.9, 136.7, 134.8, 130.8, 129.2, 127.5, 123.7, 117.5, 117.4, 115.9, 111.4, 107.3, 79.5, 42.6, 33.9. HRMS (ESI): calcd for $C_{18}H_{17}N_2O_4S^+$ (MH^+) 357.0904, found 357.0903.

*1-(2-Aminophenyl)-3-(2-(furan-2-yl)pyridin-3-yl)-4-nitrobutan-1-one (**15**).* Following general procedure C for addition of nitromethane from 0.35 g (1.21 mmol) of **13**, 0.16 g (38%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.59 (dd, J = 4.6, 1.5 Hz, 1H), 7.70 (m, 2H), 7.60 (m, 1H), 7.31 (m, 1H), 7.23 (dd, J = 8.0, 4.6 Hz, 1H), 7.14 (d, J = 3.4 Hz, 1H), 6.66 (m, 2H), 6.61 (dd, J = 3.4, 1.8 Hz, 1H), 6.26 (s, 2H), 5.09 (m, 1H), 4.91 (dd, J = 12.9, 6.4 Hz, 1H), 4.87 (dd, J = 12.9, 7.1 Hz, 1H), 3.54 (dd, J = 17.4, 6.1 Hz, 1H), 3.49 (dd, J = 17.4, 7.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.3, 153.5, 150.6, 148.4, 148.0, 143.6, 135.2, 134.8, 131.6, 130.7, 122.4, 117.5, 117.3, 115.9, 112.0, 111.9, 78.6, 41.2, 34.7. HRMS (ESI): calcd for $C_{19}H_{18}N_3O_4^+$ (MH^+) 352.1297, found 352.1299.

*8-Amino-2-(1-(2-(furan-2-yl)phenyl)-2-nitroethyl)-3,4-dihydronaphthalen-1(2H)-one (**48**).* Following general procedure D for addition of nitromethane from 0.24 g (0.76 mmol) of (*E*)-1-(2-aminophenyl)-3-(2-(furan-2-yl)phenyl)prop-2-en-1-one, 0.11 g (38%) of the title compound was obtained as a mixture of diastereomers that could not be separated. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (m, 2H), 7.43 (d, J = 3.8 Hz, 2H), 7.36 (m, 1H), 7.17 (m, 1H), 6.59 (d, J = 3.3 Hz, 1H), 6.51 (m, 2H), 6.40 (m, 3H), 5.23 (m, 1H), 4.88 (dd, J = 13.1, 9.4 Hz, 1H), 4.56 (td, J = 9.7, 4.6 Hz, 1H), 2.76 (m, 1H), 2.69 (m, 2H), 1.80 (m, 1H), 1.64 (dtd, J = 13.6, 8.2, 5.1 Hz, 1H). HRMS (ESI): calcd for $C_{22}H_{21}N_2O_4^+$ (MH^+) 377.1496, found 377.1494.

General Procedure for Reductive Amination. To a solution of substituted aniline (1 mmol) in MeOH (10 mL) at 0 °C was added NaOAc (2 equiv), glacial acetic acid (4 equiv), the corresponding aldehyde (1.5 equiv), and $NaCNBH_3$ (1.1 equiv). The solution was warmed slowly to room temperature over 1 h. The mixture was then filtered through a plug of silica gel and washed with 1% glacial acetic acid in ethyl acetate. The solution was then washed with brine, dried (Na_2SO_4), and concentrated to afford the crude material, which was then purified with flash chromatography.

General Procedure for Oxidation with MnO_2. Benzylic alcohol (1 equiv) was dissolved in DCM, 7 equiv of MnO_2 was added, and the mixture was stirred overnight and then filtered through a plug of Celite, concentrated, and purified using flash chromatography.

*2-((3-(Furan-2-yl)propyl)amino)benzaldehyde (**57**).* (1) (2-((3-(Furan-2-yl)propyl)amino)phenyl)methanol was prepared following the general procedure for reductive amination from 0.60 g (4.46 mmol) of 2-aminophenylmethanol with a yield of 0.78 g (73%) and used without further purification in the next step. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (dd, J = 1.8, 0.8 Hz, 1H), 7.25 (td, J = 7.9, 1.6 Hz, 1H), 7.09 (dd, J = 7.6, 1.6 Hz, 1H), 6.68 (m, 2H), 6.32 (dd, J = 3.1, 1.9 Hz, 1H), 6.05 (m, 1H), 4.68 (s, 2H), 3.24 (t, J = 7.0 Hz, 2H), 2.80 (t, J = 7.4 Hz, 2H), 2.04 (p, J = 7.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.4, 147.6, 141.0, 129.7, 129.2, 124.2, 116.3, 110.6, 110.2, 105.1, 64.9, 42.8, 27.7, 25.6.

(2) Following the general procedure for benzylic alcohol oxidation from 0.78 g (3.37 mmol) of (2-((3-(furan-2-yl)propyl)amino)phenyl)-methanol, 0.51 g (66%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.84 (s, 1H), 8.40 (s, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.41 (t, J = 7.8 Hz, 1H), 7.35 (s, 1H), 6.70 (m, 2H), 6.32 (s, 1H), 6.06 (m, 1H), 3.31 (m, 2H), 2.79 (t, J = 7.4 Hz, 2H), 2.06 (p, J = 7.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.9, 155.0, 150.7, 141.1, 136.7, 135.8, 118.4, 114.8, 110.8, 110.2, 105.4, 41.6, 27.4, 25.4. HRMS (ESI): calcd for $C_{14}H_{16}NO_2^+$ (MH^+) 230.1176, found 230.1176.

*5-Chloro-2-((3-(furan-2-yl)propyl)amino)benzaldehyde (**58**).* (1) (5-Chloro-2-((3-(furan-2-yl)propyl)amino)phenyl)methanol was prepared following the general procedure for reductive amination from 0.50 g (3.18 mmol) of 5-chloro-2-aminophenylmethanol with a yield of 0.48 g (57%) and used without further purification in the next step. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (dd, J = 1.8, 0.8 Hz, 1H), 7.18 (dd, J = 8.6, 2.5 Hz, 1H), 7.06 (d, J = 2.5 Hz, 1H), 6.58 (d, J = 8.7 Hz, 1H), 6.32 (dd, J = 3.1, 1.9 Hz, 1H), 6.05 (m, 1H), 4.77 (s, br, 1H), 4.63 (s, 2H), 3.20 (t, J = 7.0 Hz, 2H), 2.79 (t, J = 7.4 Hz, 2H), 2.03 (p, J = 7.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.2, 146.1, 141.0, 129.1, 128.7, 125.5, 120.8, 111.6, 110.2, 105.2, 64.3, 42.9, 27.6, 25.6.

(2) Following the general procedure for benzylic alcohol oxidation from 0.48 g (1.80 mmol) of (5-chloro-2-((3-(furan-2-yl)propyl)-amino)phenyl)methanol, 0.31 g (65%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.77 (s, 1H), 8.37 (s, 1H), 7.44 (d, J = 2.6 Hz, 1H), 7.34 (m, 2H), 6.64 (d, J = 9.1 Hz, 1H), 6.32 (dd, J = 3.1, 1.9 Hz, 1H), 6.06 (m, 1H), 3.28 (m, 2H), 2.78 (t, J = 7.3 Hz, 2H), 2.04 (p, J = 7.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.8, 154.7, 149.2, 141.2, 135.8, 135.2, 119.3, 118.9, 112.6, 110.2, 105.5, 41.8, 27.3, 25.3.

*5-Bromo-2-((3-(furan-2-yl)propyl)amino)benzaldehyde (**59**).* (1) (5-Bromo-2-((3-(furan-2-yl)propyl)amino)phenyl)methanol was prepared following the general procedure for reductive amination from 0.5 g (2.48 mmol) of 5-bromo-2-aminophenylmethanol with a yield of 0.34 g (44%) and used without further purification in the next step. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (dd, J = 1.8, 0.8 Hz, 1H), 7.31 (dd, J = 8.7, 2.4 Hz, 1H), 7.19 (d, J = 2.4 Hz, 1H), 6.54 (d, J = 8.7 Hz, 1H), 6.32 (dd, J = 3.1, 1.9 Hz, 1H), 6.05 (m, 1H), 4.77 (s, br, 1H), 4.62 (s, 2H), 3.19 (t, J = 7.0 Hz, 2H), 2.78 (t, J = 7.3 Hz, 2H), 2.02 (p, J = 7.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.2, 146.6, 141.0, 132.1, 131.5, 126.0, 112.1, 110.2, 107.7, 105.2, 64.3, 42.8, 27.5, 25.6.

(2) Following the general procedure for benzylic alcohol oxidation from 0.34 g (1.10 mmol) of (5-bromo-2-((3-(furan-2-yl)propyl)-amino)phenyl)methanol, 0.14 g (41%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.76 (s, 1H), 8.38 (s, 1H), 7.58 (d, J = 2.4 Hz, 1H), 7.45 (dd, J = 9.0, 2.4 Hz, 1H), 7.35 (d, J = 1.7 Hz, 1H), 6.60 (d, J = 9.0 Hz, 1H), 6.32 (dd, J = 3.1, 1.9 Hz, 1H), 6.06 (d, J = 3.0 Hz, 1H), 3.28 (m, 2H), 2.78 (t, J = 7.3 Hz, 2H), 2.04 (p, J = 7.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.7, 154.7, 149.5, 141.2, 138.4, 138.3, 119.5, 113.0, 110.2, 105.7, 105.5, 41.7, 27.3, 25.3. HRMS (ESI): calcd for $C_{14}H_{15}BrNO_2^+$ (MH^+) 308.0281, found 308.0280.

*2-((3-(Furan-2-yl)propyl)amino)nicotinaldehyde (**60**).* (1) (2-((3-(Furan-2-yl)propyl)amino)pyridin-3-yl)methanol was prepared following the general procedure for reductive amination from 0.28 g (2.25 mmol) of 2-amino-3-pyridinemethanol with a yield of 0.29 g (55%) and used without further purification in the next step. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 (dd, J = 5.1, 1.8 Hz, 1H), 7.33 (dd, J = 1.8, 0.8 Hz, 1H), 7.26 (dd, J = 7.1, 1.8 Hz, 1H), 6.54 (dd, J = 7.1, 5.1 Hz, 1H), 6.31 (dd, J = 3.1, 1.9 Hz, 1H), 6.05 (m, 1H), 5.41 (s, 1H), 4.61 (s, 2H), 3.56 (t, J = 7.0 Hz, 2H), 2.78 (t, J = 7.5 Hz, 2H), 2.04 (p, J = 7.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 157.6, 155.7, 147.8, 140.9, 135.9, 118.5, 111.7, 110.1, 105.0, 64.0, 40.7, 28.0, 25.7.

(2) Following the general procedure for benzylic alcohol oxidation from 0.15 g (0.65 mmol) of (2-((2-(furan-2-yl)benzyl)amino)pyridin-3-yl)methanol, 0.12 g (81%) of the title compound was obtained. ^{1}H

NMR (500 MHz, $CDCl_3$): δ 9.82 (s, 1H), 8.49 (s, 1H), 8.35 (dd, J = 4.8, 1.9 Hz, 1H), 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 Hz, 2H), 2.05 (p, J = 7.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.8, 157.8, 155.3, 155.0, 144.6, 141.0, 113.7, 111.4, 110.1, 105.1, 40.0, 27.8, 25.5. HRMS (ESI): calcd for $C_{13}H_{15}N_2O_2^+$ (MH^+) 231.1129, found 231.1128.

*2-((2-(Furan-2-yl)benzyl)amino)nicotinaldehyde (**63**).* (1) (2-((2-(Furan-2-yl)benzyl)amino)pyridin-3-yl)methanol was prepared following the general procedure for reductive amination from 0.28 g (2.25 mmol) of 2-amino-3-pyridinemethanol with a yield of 0.33 g (52%) and used without further purification in the next step. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.06 (m, 1H), 7.69 (dd, J = 7.7, 1.3 Hz, 1H), 7.49 (m, 2H), 7.33 (td, J = 7.6, 1.2 Hz, 1H), 7.27 (td, J = 7.8, 1.4 Hz, 1H), 7.22 (d, J = 7.1 Hz, 1H), 6.60 (d, J = 3.4 Hz, 1H), 6.52 (m, 1H), 6.46 (dd, J = 3.3, 1.8 Hz, 1H), 5.71 (t, J = 5.5 Hz, 1H), 4.83 (d, J = 5.4 Hz, 2H), 4.50 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 157.3, 153.0, 147.5, 142.2, 136.0, 135.8, 130.1, 129.7, 127.9, 127.9, 127.4, 118.9, 112.1, 111.5, 108.7, 63.5, 44.3.

(2) Following the general procedure for benzylic alcohol oxidation from 0.33 g (1.17 mmol) of (2-((2-(furan-2-yl)benzyl)amino)pyridin-3-yl)methanol, 0.13 g (40%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.83 (s, 1H), 8.83 (s, 1H), 8.37 (dd, J = 4.8, 1.9 Hz, 1H), 7.78 (dd, J = 7.5, 2.0 Hz, 1H), 7.67 (dd, J = 7.7, 1.4 Hz, 1H), 7.60 (d, J = 1.2 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.38−7.30 (m, 2H), 6.69 (dd, J = 7.5, 4.8 Hz, 1H), 6.61 (d, J = 3.3 Hz, 1H), 6.53 (dd, J = 3.3, 1.8 Hz, 1H), 5.01 (d, J = 5.9 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.7, 155.0, 153.2, 144.6, 142.4, 135.3, 130.0, 129.3, 128.0, 128.0, 127.4, 113.8, 111.7, 111.4, 108.6, 43.2, 29.7. HRMS (ESI): calcd for $C_{17}H_{15}N_2O_2^+$ (MH^+) 279.1128, found 279.1131.

*2-((3-(5-Methylfuran-2-yl)butyl)amino)benzaldehyde (**61**).* (1) (2-((3-(5-Methylfuran-2-yl)butyl)amino)phenyl)methanol was prepared following general procedure A for reductive amination from 0.52 g (3.48 mmol) of 3-(5-methyl-2-furyl)butanal and 0.28 g (2.32 mmol) of 2-aminophenylmethanol with a yield of 0.60 g (90%) and used in the oxidation step without further purification. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23 (td, J = 7.9, 1.6, 1H), 7.08 (m, 1H), 6.67 (m, 2H), 5.91 (d, J = 3.0, 1H), 5.88 (dd, J = 2.9, 1.0, 1H), 4.66 (s, 2H), 3.18 (m, 2H), 2.96 (h, J = 6.9, 1H), 2.29 (s, 3H), 2.02 (m, 1H), 1.90 (ddt, J = 13.4, 8.0, 6.6, 1H), 1.31 (d, J = 7.0, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 157.9, 150.3, 147.6, 129.6, 129.1, 124.2, 116.2, 110.5, 105.7, 104.5, 64.8, 41.4, 35.4, 31.2, 19.5, 13.5.

(2) Following the general procedure for benzilic alcohol oxidation from 0.60 g (2.32 mmol) of (2-((3-(5-methylfuran-2-yl)butyl)amino)-phenyl)methanol, 0.42 g (70%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.83 (s, 1H), 8.34 (s, 1H), 7.48 (dd, J = 7.7, 1.6 Hz, 1H), 7.39 (ddd, J = 8.5, 7.2, 1.2 Hz, 1H), 6.68 (m, 2H), 5.92 (d, J = 3.0 Hz, 1H), 5.88 (m, 1H), 3.24 (m, 2H), 2.95 (h, J = 6.9 Hz, 1H), 2.29 (s, 3H), 2.04 (dtd, J = 14.0, 8.2, 5.9 Hz, 1H), 1.92 (ddt, J = 13.4, 8.4, 6.6 Hz, 1H), 1.31 (d, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.9, 157.4, 150.8, 150.4, 136.7, 135.8, 118.3, 114.6, 110.8, 105.7, 104.7, 40.4, 35.0, 31.1, 19.5, 13.5. HRMS (ESI): calcd for $C_{16}H_{20}NO_2^+$ (MH^+) 258.1489, found 258.1486.

*8-((3-(Furan-2-yl)propyl)amino)-3,4-dihydronaphthalen-1(2H)-one (**62**).* Following the general procedure for reductive amination from 0.40 g (2.48 mmol) of 8-amino-1-tetralone, 0.38 g (57%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.34 (s, 1H), 7.34 (dd, J = 1.8, 0.8 Hz, 1H), 7.26 (m, 1H), 6.54 (d, J = 8.5 Hz, 1H), 6.42 (dd, J = 7.2, 0.9 Hz, 1H), 6.31 (dd, J = 3.1, 1.9 Hz, 1H), 6.06 (m, 1H), 3.27 (m, 2H), 2.89 (m, 2H), 2.80 (t, J = 7.4 Hz, 2H), 2.65 (m, 2H), 2.05 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 201.3, 155.2, 151.9, 146.7, 141.0, 134.9, 114.7, 114.3, 110.1, 109.1, 105.3, 41.8, 40.5, 31.3, 27.4, 25.5, 23.0. HRMS (ESI): calcd for $C_{17}H_{20}NO_2^+$ (MH^+) 270.1489, found 270.1492.

*8-((2-(Furan-2-yl)benzyl)amino)-3,4-dihydronaphthalen-1(2H)-one (**64**).* Following the general procedure for reductive amination from 0.36 g (2.32 mmol) of 8-amino-1-tetralone, 0.45 g (61%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.69 (s, 1H), 7.71 (dd, J = 7.7, 1.3 Hz, 1H), 7.57 (d, J = 1.7 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.35 (td, J = 7.5, 1.3 Hz, 1H), 7.29 (m, 1H), 7.19 (m, 1H), 6.57 (d, J = 3.3 Hz, 1H), 6.53 (dd, J = 3.3, 1.8 Hz, 1H), 6.44 (m, 2H), 4.65 (d, J = 5.7 Hz, 2H), 2.92 (m, 2H), 2.67 (m, 2H), 2.08 (p, J = 6.4 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 201.38, 152.93, 151.66, 146.61, 142.27, 135.08, 134.90, 129.60, 128.08, 128.06, 127.93, 127.24, 115.05, 114.88, 111.48, 109.64, 108.81, 45.50, 40.49, 31.25, 23.01. HRMS (ESI): calcd for $C_{21}H_{20}NO_2^+$ (MH^+) 318.1489, found 318.1482.

*7-((3-(Furan-2-yl)propyl)amino)-2,3-dihydro-1H-inden-1-one (**73**).* Following the general procedure for reductive amination from 0.32 g (2.32 mmol) of 7-amino-indan-1-one, 0.29 g (45%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (m, 3H), 6.61 (d, J = 7.3 Hz, 1H), 6.44 (d, J = 8.3 Hz, 1H), 6.31 (dd, J = 3.1, 1.9 Hz, 1H), 6.06 (m, 1H), 3.29 (m, 2H), 3.03 (m, 2H), 2.78 (m, 2H), 2.66 (m, 2H), 2.03 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 208.0, 156.9, 155.1, 148.6, 141.0, 136.8, 119.9, 112.1, 110.1, 107.0, 105.3, 41.5, 36.2, 27.5, 25.5, 25.4. HRMS (ESI): calcd for $C_{16}H_{18}NO_2^+$ (MH^+) 256.1333, found 256.1338.

*1-(2-Aminophenyl)-2-(furan-2-ylmethylthio)ethanone (**52**).* A 2.24 g portion of 2-bromo-2′-nitroacetophenone (**51**; 9.2 mmol) was dissolved in 30 mL of dichloromethane along with 1.08 g of 2-furylmercaptan (9.2 mmol) and 1.48 g of dry pyridine (18.4 mmol), and the reaction mixture was stirred for 1 h before it was quenched with 5% HCl solution (10 mL). The aqueous layer was then extracted with dichloromethane (2 × 20 mL), and the organic layers were combined and dried over anhydrous sodium sulfate. The organic layer was then concentrated to give 2.50 g (98%) of 1-(2-nitrophenyl)-2-(furan-2-ylmethylthio)ethanone. This was then dissolved in 100 mL of ethanol along with 5.23 g of tin(II) chloride (27.0 mmol) and heated to 70 °C under a nitrogen atmosphere for 2 h. Saturated sodium bicarbonate solution was added slowly until the solution reached pH 8, giving a thick milky white emulsion. This was filtered through a pad of Celite, and the filtrate was extracted with EtOAc (3 × 100 mL). The organic phase was washed with brine (2 × 50 mL) and then dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography to give 1.76 g (78%) of the title compound. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (dd, J = 8.2, 1.0 Hz, 1H), 7.40 (dd, J = 1.8, 0.7 Hz, 1H) 7.30 (dt J = 8.4, 1.3 Hz 1H), 6.69 (d, J = 8.4 Hz, 1H), 6.15 (dt J = 8.2, 1.0, 1H) 6.37−6.26 (m, 4H), 3.85 (s, 2H), 3.83 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): 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): calcd for $C_{13}H_{14}NO_2S^+$ (MH+) 248.0740, found 248.0743.

General Procedure for Photochemical Reactions. A 4 mmol portion of the photoprecursor was dissolved in 200 mL of methanol, and the solution was degassed and irradiated with RPR-3500 until the reaction was complete.

*Diethyl 2-(8b-Hydroxy-4,8b,9,10-tetrahydro-3H-3,14b-epoxybenzo[b]naphtho[2,1-d]azocin-10-yl)malonate (**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. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (dd, J = 8.1, 1.4, 1H), 7.31 (m, 3H), 7.23 (m, 1H), 7.10 (m, 1H), 6.89 (m, 1H), 6.63 (dd, J = 8.0, 1.1 Hz, 1H), 6.55 (d, J = 5.8 Hz, 1H), 5.94 (d, J = 2.8 Hz, 1H), 5.90 (dd, J = 5.8, 1.5 Hz, 1H), 4.73 (d, J = 3.5 Hz, 1H), 4.09 (m, 6H), 2.73 (dd, J = 14.1, 9.6 Hz, 1H), 2.10 (dd, J = 14.1, 7.2 Hz, 1H), 1.82 (s, 1H), 1.18 (t, J = 7.1 Hz, 3H), 1.09 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.8, 168.0, 139.1, 136.8, 136.6, 134.4, 132.8, 129.3, 128.7, 128.5, 128.3, 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): calcd for $C_{26}H_{27}NaNO_6^+$ (MNa^+) 472.1731, found 472.1737.

*10-Phenyl-4,8b,9,10-tetrahydro-3H-3,14b-epoxybenzo[b]-naphtho[2,1-d]azocin-8b-ol (**32**).* From 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. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87 (dd, J = 8.2, 1.5 Hz, 1H), 7.40 (dd, J = 7.6, 1.6 Hz, 1H), 7.26 (m, 7H), 7.12 (ddd, J = 8.1, 7.1, 1.6 Hz, 1H), 6.98 (d, J = 7.5 Hz, 1H), 6.92 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 6.68 (d, J = 5.7 Hz, 1H), 6.64 (dd, J = 8.0, 1.2, Hz 1H), 6.01 (s, 1H), 5.99 (dd, J = 5.7, 1.5 Hz, 1H), 4.79 (s, 1H), 4.49 (dd, J = 11.4, 6.6 Hz, 1H), 2.70 (ddd, J = 14.1, 11.6, 0.8 Hz, 2H), 2.28 (dd, J = 14.2, 6.6 Hz, 1H), 2.08 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 146.1, 140.1, 138.9, 136.1, 134.6, 132.5,

129.8, 129.6, 129.0, 128.5, 128.5, 128.2, 128.1, 126.7, 126.3, 120.1, 120.0, 89.8, 88.6, 83.1, 77.2, 44.1, 42.9. HRMS (ESI): calcd for $C_{25}H_{22}NO_2^+$ (MH^+) 368.1645, found 368.1649.

*10-(Nitromethyl)-4,8b,9,10-tetrahydro-3H-3,14b-epoxybenzo[b]-naphtho[2,1-d]azocin-8b-ol (**34**).* From 0.18 g (0.51 mmol) of **8**, following the general procedure for the photochemical reaction, 0.10 g (56%) of the title compound was obtained upon chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79 (dd, J = 8.1, 1.3, 1H), 7.41 (m, 2H), 7.34 (dd, J = 13.4, 6.9, 2H), 7.16 (m, 1H), 6.95 (m, 1H), 6.68 (m, 1H), 6.60 (d, J = 5.4, 1H), 5.95 (m, 2H), 4.83 (dd, J = 12.4, 4.8, 1H), 4.79 (s, 1H), 4.55 (dd, J = 12.4, 9.8, 1H), 4.10 (m, 1H), 2.40 (dd, J = 13.8, 8.8, 1H), 2.17 (dd, J = 14.2, 7.6, 1H), 1.86 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 138.9, 136.6, 134.5, 133.6, 132.1, 129.2, 128.9, 128.7, 128.7, 128.5, 127.9, 127.4, 120.3, 120.2, 89.9, 88.3, 82.2, 81.7, 37.7, 34.3. HRMS (ESI): calcd for $C_{20}H_{19}N_2O_4^+$ (MH^+) 351.1339, found 351.1342.

*14-(Nitromethyl)-8,12b,13,14-tetrahydro-7H-4b,7-epoxybenzo-[2,3]azocino[4,5-h]quinolin-12b-ol (**35**).* From 0.15 g (0.43 mmol) of **15**, following the general procedure for the photochemical reaction, 0.04 g (27%) of the title compound was obtained upon chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.61 (d, J = 3.9, 1H), 7.78 (dd, J = 8.1, 1.5 Hz, 1H), 7.65 (d, J = 7.9 Hz, 1H), 7.34 (dd, J = 7.9, 4.7 Hz, 1H), 7.18 (m, 1H), 6.96 (m, 1H), 6.73 (d, J = 5.8 Hz, 1H), 6.69 (dd, J = 8.0, 1.2 Hz, 1H), 6.03 (m, 1H), 5.96 (dd, J = 5.8, 1.6 Hz, 1H), 4.85 (br s, 1H), 4.79 (dd, J = 12.5, 5.2 Hz, 1H), 4.56 (dd, J = 12.5, 9.0 Hz, 1H), 4.13 (m, 1H), 2.43 (dd, J = 14.2, 9.3 Hz, 1H), 2.21 (dd, J = 14.1, 7.3 Hz, 1H), 1.91 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.7, 148.9, 139.1, 135.1, 133.4, 131.8, 130.7, 128.8, 128.6, 127.7, 123.8, 120.3, 120.3, 90.3, 89.6, 82.7, 80.7, 37.2, 33.7. HRMS (ESI): calcd for $C_{19}H_{17}NaN_3O_4^+$ (MNa^+) 374.1111, found 374.1111.

*13-(Nitromethyl)-7,11b,12,13-tetrahydro-6H-3b,6-epoxybenzo-[b]thieno [3′,2′:3,4]benzo[1,2-d]azocin-11b-ol (**36**).* From 0.19 g (0.53 mmol) of **16**, following the general procedure for the photochemical reaction, 0.04 g (21%) of the title compound was obtained upon chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (dd, J = 8.2, 1.4 Hz, 1H), 7.30 (m, 1H), 7.16 (m, 1H), 6.94 (m, 2H), 6.66 (dd, J = 8.1, 1.1 Hz, 1H), 6.56 (d, J = 5.8 Hz, 1H), 5.99 (dd, J = 5.8, 1.6 Hz, 1H), 5.94 (dd, J = 4.4, 1.4 Hz, 1H), 4.82 (s, 1H), 4.81 (dd, J = 12.7, 5.5 Hz, 1H), 4.48 (dd, J = 12.7, 8.9 Hz, 1H), 4.22 (m, 1H), 2.39 (ddd, J = 13.5, 10.5, 1.3 Hz, 1H), 2.27 (dd, J = 13.6, 6.0 Hz, 1H), 1.99 (d, J = 1.3 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 138.9, 137.3, 137.1, 133.2, 130.7, 130.2, 129.1, 128.8, 126.6, 124.9, 120.3, 120.2, 89.3, 86.2, 83.1, 80.2, 39.3, 32.9. HRMS (ESI): calcd for $C_{18}H_{17}N_2O_4S^+$ (MH^+) 357.0904, found 357.0907.

*10-(Nitromethyl)-3,4,8b,9,10,11,12,13-octahydro-3,13b-epoxybenzo[b]indeno[5,4-d]azocin-8b-ol (**37**).* From 0.68 g (2.00 mmol) of **29**, following the general procedure for the photochemical reaction, 0.23 g (34%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (dd, J = 8.1, 1.3 Hz, 1H), 7.13 (m, 1H), 6.91 (m, 1H), 6.63 (m, 1H), 6.44 (d, J = 5.5 Hz, 1H), 5.85 (m, 2H), 4.80 (d, J = 3.7 Hz 1H), 4.64 (dd, J = 12.3, 5.6 Hz, 1H), 4.25 (dd, 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). ^{13}C NMR (126 MHz, $CDCl_3$): δ 138.9, 137.9, 137.2, 133.2, 130.9, 130.4, 128.5, 128.3, 120.2, 120.0, 88.9, 86.3, 83.3, 78.5, 39.0, 33.5, 33.3, 31.9, 21.9. HRMS (ESI): calcd for $C_{19}H_{21}N_2O_4^+$ (MH^+) 341.1501, found 341.1500.

*10-(Nitromethyl)-4,8b,9,10,11,12,13,14-octahydro-3H-3,14b-epoxybenzo[b]naphtho[2,1-d]azocin-8b-ol (**38**).* From 0.39 g (1.10 mmol) of **30**, following the general procedure for the photochemical reaction, 0.21 g (54%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73 (dd, J = 8.2, 1.5 Hz, 1H), 7.11 (m, 1H), 6.89 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 6.61 (dd, J = 8.0, 1.2 Hz, 1H), 6.40 (m, 1H), 5.83 (m, 1H), 5.77 (dd, J = 5.8, 1.6 Hz, 1H), 4.77 (d, J = 4.3 Hz, 1H), 4.68 (dd, J = 11.9, 4.6 Hz, 1H), 4.26 (dd, J = 11.9, 9.5 Hz, 1H), 3.25 (m, 1H), 2.15 (dd, J = 13.9, 10.3 Hz, 1H), 2.07 (m, 4H), 1.95 (dd, J = 13.8, 6.2 Hz, 1H), 1.88 (m, 3H), 1.49 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 138.8, 133.6, 131.7, 131.4, 131.3, 129.8, 128.3, 127.7, 120.1, 120.0, 89.1, 88.2, 81.9, 78.8, 38.1, 37.0, 27.9, 26.2, 22.6, 22.4. HRMS (ESI): calcd for $C_{20}H_{23}N_2O_4^+$ (MH^+) 355.1652, found 355.1657.

*10-(Nitromethyl)-3,4,8b,9,10,11,12,13,14,15-decahydro-3,15b-epoxybenzo[b]cyclohepta[3,4]benzo[1,2-d]azocin-8b-ol (**39**).* From 0.17 g (0.46 mmol) of **31**, following the general procedure for the photochemical reaction, 0.10 g (59%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73 (dd, J = 8.2, 1.5 Hz, 1H), 7.11 (ddd, J = 8.1, 7.1, 1.6 Hz, 1H), 6.90 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 6.62 (dd, J = 8.0, 1.2 Hz, 1H), 6.41 (dd, J = 5.8, 0.5 Hz, 1H), 5.85 (s, 1H), 5.75 (dd, J = 5.8, 1.6 Hz, 1H), 4.76 (m, 1H), 4.68 (dd, J = 12.1, 3.7 Hz, 1H), 4.24 (dd, J = 12.0, 10.2 Hz, 1H), 3.26 (m, 1H), 2.32 (m, 2H), 2.25 (m, 2H), 2.12 (dd, J = 14.0, 9.3 Hz, 1H), 2.03 (s, 1H), 1.99 (dd, J = 14.0, 6.9 Hz, 1H), 1.82 (m, 2H), 1.62 (m, 2H), 1.51 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 138.8, 137.6, 137.6, 134.5, 131.8, 129.7, 128.2, 127.2, 120.1, 120.1, 89.2, 89.2, 81.7, 79.5, 38.2, 38.0, 32.1, 31.8, 30.1, 26.5, 26.2. HRMS (ESI): calcd for $C_{21}H_{25}N_2O_4^+$ (MH^+) 369.1809, found 369.1811.

*6-(Nitromethyl)-5,5a,5a1,6,13,14-hexahydro-4H-10b,13-epoxytetrapheno[1,12-bcd]azocin-5a1-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. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (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 (dd, J = 13.1, 8.1 Hz, 1H), 4.84 (dd, J = 13.1, 6.8 Hz, 1H), 4.12 (m, 2H), 2.76 (ddd, J = 16.6, 12.7, 4.4 Hz, 1H), 2.67 (dt, J = 16.7, 4.6 Hz, 2.3 Hz, 1H), 2.25 (dt, J = 13.9, 2.5 Hz, 1H), 1.34 (m, 2H), 0.80 (qd, J = 13.3, 4.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 141.9, 137.3, 136.8, 136.7, 134.3, 132.5, 128.2, 128.1, 127.8, 127.3, 125.4, 123.2, 122.7, 118.3, 91.7, 88.3, 82.7, 76.3, 46.0, 37.2, 29.0, 21.0. HRMS (ESI): calcd for $C_{22}H_{21}N_2O_4^+$ (MH^+) 377.1496, found 377.1496.

*10-(Nitromethyl)-4,8,9,9a,9a1,10-hexahydro-3aH-dibenzo[i,lmn]-furo[3,2-g]phenanthridin-9a1-ol (**50**).* From 0.11 g (0.29 mmol) of **48**, following the general procedure for the photochemical reaction, 0.04 g (36%) of the title compound and 0.03 g (27%) of **49** were obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53 (m, 1H), 7.40 (m, 2H), 7.30 (m, 1H), 7.10 (t, J = 7.7 Hz, 1H), 6.74 (m, 1H), 6.62 (d, J = 7.7 Hz, 1H), 6.24 (dd, J = 2.7, 0.9 Hz, 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), 4.04 (s, 1H), 3.98 (s, 1H), 2.89 (m, 3H), 2.05 (dq, J = 11.5, 3.6 Hz, 1H), 1.81 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 146.9, 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 $C_{22}H_{21}N_2O_4^+$ (MH^+) 377.1496, found 377.1495.

*9-Aza-10,11-benzo-5-hydroxy-2-oxa-3-thiatricyclo[6.3.1.0^{4,12}]-dodeca-6,10-diene (**54**).* A 0.31 g portion of **52** was dissolved in 50 mL of acetonitrile (5% H_2O 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 under reduced pressure and purified via flash chromatography, with a yield of 0.28 g (89%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (dd, J = 8.1, 1.3 Hz, 1H), 7.24, (dt, J = 8.1, 1.5 Hz, 1H), 6.97 (dt, J = 8.1, 1.3 Hz, 1H), 6.76, (dd, J = 8.0, 1.2 Hz, 1H), 6.31 (d, J = 9.8 Hz, 1H), 5.63 (dd, J = 9.8, 3.2 Hz, 1H), 5.50 (ddd, J = 5.0, 3.4, 0.6 Hz, 1H), 4.60−4.55 (m, 1H), 3.38 (d, J = 9.8 Hz, 1H), 3.07 (m, 2H), 2.91 (d, J = 9.8 Hz, 1H), 2.85 (t, J = 1.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): 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): calcd for $C_{13}H_{14}NO_2S$ (MH^+) 248.0740, found 248.0739.

General Procedure for Acid-Induced Rearrangemen. The photoproducts were dissolved in 5 mL of dichloromethane, 0.05 mL of trifluoroacetic 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-3,8b-epoxybenzo[b]-naphtho[2,1-d]azocin-10-yl)malonate (**41**).* From 47 mg (0.105 mmol) of **33**, 34 mg (72%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53 (m, 1H), 7.45 (dd, J = 7.9, 1.3 Hz, 1H), 7.28 (m, 3H), 7.20 (m, 1H), 6.94 (td, J = 7.8, 1.3 Hz, 1H), 6.79 (dd, J = 8.0, 1.2 Hz, 1H), 6.48 (d, J = 10.1 Hz, 1H), 5.59 (dd, 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 (dq, J = 10.7, 7.2 Hz, 1H), 4.19(dq, J = 10.7, 7.2 Hz, 1H), 4.11 (dq, J = 10.7, 7.2 Hz, 1H), 4.09 (dq, J = 10.7, 7.2 Hz, 1H), 4.02 (m, 1H), 3.58 (s, 1H), 3.28 (dd, J = 13.9, 11.3 Hz, 1H), 1.94 (dd, J = 13.8, 6.4 Hz, 1H), 1.27

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(t, J = 7.1 Hz, 3H), 1.14 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.6, 168.5, 140.5, 139.1, 135.2, 134.8, 129.0, 128.3, 128.1, 127.7, 127.1, 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]-naphtho[2,1-d]azocin-14b-ol (**40**).* From 120 mg (0.327 mmol) of **32**, 90 mg (75%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59 (dd, J = 7.9, 1.1 Hz, 1H), 7.37 (m, 3H), 7.29 (m, 4H), 7.20 (m, 2H), 6.90 (m, 2H), 6.81 (dd, J = 8.0, 1.1 Hz, 1H), 6.49 (d, J = 10.0 Hz, 1H), 5.68 (dd, J = 10.0, 3.4 Hz, 1H), 5.29 (d, J = 3.3 Hz, 1H), 4.55 (dd, J = 12.4, 5.0 Hz, 1H), 3.34 (s, 1H), 2.93 (m, 1H), 2.16 (dd, J = 13.6, 5.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 145.8, 139.2, 139.1, 138.7, 134.7, 129.4, 129.2, 128.6, 128.4, 128.3, 127.8, 127.5, 126.6, 126.5, 126.1, 124.7, 120.1, 118.7, 75.1, 74.9, 69.6, 42.5, 40.4. HRMS (ESI): calcd for $C_{25}H_{22}NO_2^+$ (MH^+) 368.1645, found 368.1648.

*10-(Nitromethyl)-4,9,10,14b-tetrahydro-3H-3,8b-epoxybenzo[b]-naphtho[2,1-d]azocin-14b-ol (**42**).* From 80 mg (0.228 mmol) of **34**, 47 mg (59%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (dd, J = 7.3, 2.2, 1H), 7.35 (m, 3H), 7.25 (m, 2H), 6.96 (m, 1H), 6.83 (m, 1H), 6.40 (d, J = 10.0 Hz, 1H), 5.66 (dd, J = 10.0, 3.4 Hz, 1H), 5.22 (d, J = 3.3, 1H), 5.05 (dd, J = 12.5 Hz, 4.8, 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 = 13.2, 5.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.3, 139.0, 134.2, 133.1, 129.6, 128.7, 128.2, 127.7, 127.5, 125.6, 125.2, 125.0, 120.4, 119.0, 80.1, 75.0, 74.0, 69.4, 34.6, 33.8. HRMS (ESI): calcd for $C_{20}H_{19}N_2O_4^+$ (MH^+) 351.1339, found 351.1341.

*14-(Nitromethyl)-7,8,13,14-tetrahydro-4bH-7,12b-epoxybenzo-[2,3]azocino[4,5-h]quinolin-4b-ol (**43**).* Following the general procedure for rearrangement, from 35 mg (0.099 mmol) of **35** 20 mg (57%) of the title compound was obtained upon chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.63 (d, J = 4.7, 1H), 7.80 (d, J = 8.0, 1H), 7.43 (dd, J = 8.1, 4.9 Hz, 1H), 7.39 (m, 1H), 7.24 (m, 1H), 6.95 (td, J = 7.8, 1.2 Hz, 1H), 6.81 (dd, J = 8.0, 1.0 Hz, 1H), 6.64 (d, J = 10.0 Hz, 1H), 5.74 (dd, J = 10.0, 3.4, 1H), 5.22 (d, J = 3.3 Hz, 1H), 4.94 (s, 1H), 4.92 (dd, J = 12.9, 5.2 Hz, 1H), 4.71 (m, 1H), 4.23 (dq, J = 12.0, 5.4 Hz, 1H), 2.82 (m, 1H), 2.14 (dd, J = 13.3, 5.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 158.1, 146.8, 138.5, 136.1, 133.1, 130.4, 128.6, 128.2, 125.8, 125.1, 123.3, 120.3, 118.7, 79.0, 75.3, 73.6, 70.3, 34.1, 33.2. HRMS (ESI): calcd for $C_{19}H_{18}N_3O_4^+$ (MH^+) 352.1292, found 352.1302.

*13-(Nitromethyl)-6,7,12,13-tetrahydro-3bH-6,11b-epoxybenzo-[b]thieno[3′,2′:3,4]benzo[1,2-d]azocin-3b-ol (**44**).* From 40 mg (0.112 mmol) of **36**, 23 mg (58%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (m, 2H), 7.30 (m, 1H), 7.25 (m, 1H), 7.12 (d, J = 5.2 Hz, 1H), 6.95 (m, 1H), 6.83 (dd, J = 8.0, 1.0 Hz, 1H), 6.24 (d, J = 10.0 Hz, 1H), 5.24 (d, J = 3.5 Hz, 1H), 4.90 (dd, J = 12.6, 5.2 Hz, 1H), 4.55 (dd, J = 12.6, 9.1 Hz, 1H), 4.17 (m, 1H), 2.70 (br s, 1H),2.64 (dd, J = 13.0, 11.3 Hz, 1H), 2.15 (dd, J = 13.1, 4.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.0, 138.4, 135.2, 132.7, 128.8, 127.5, 126.4, 125.7, 124.8, 124.7, 120.3, 119.0, 79.8, 74.9, 74.8, 68.7, 35.9, 32.9. HRMS (ESI): calcd for $C_{18}H_{17}N_2O_4S^+$ (MH^+) 357.0904, found 357.0906.

*10-(Nitromethyl)-3,4,9,10,11,12,13,13b-octahydro-3,8b-epoxybenzo[b]indeno[5,4-d]azocin-13b-ol (**45**).* From 180 mg (0.529 mmol) of **37**, 130 mg (72%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (m, 1H), 7.20 (m, 1H), 6.91 (m, 1H), 6.79 (dd, J = 8.0, 1.1 Hz, 1H), 5.93 (d, J = 10.0 Hz, 1H), 5.69 (dd, J = 10.0, 3.5 Hz, 1H), 5.25 (d, J = 3.5 Hz, 1H), 4.67 (dd, J = 12.2, 5.5 Hz, 1H), 4.34 (dd, J = 12.2, 8.8 Hz, 1H), 3.39 (m, 1H), 2.94 (s, 1H), 2.61 (dddd, J = 11.9, 9.0, 6.1, 3.9 Hz, 1H), 2.41 (m, 4H), 1.95 (m, 2H), 1.90 (dd, J = 13.2, 4.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 138.9, 138.1, 135.0, 132.4, 128.5, 127.6, 126.3, 125.3, 120.1, 118.9, 78.6, 75.2, 74.9, 68.9, 35.0, 33.3, 32.8, 31.1, 22.0. HRMS (ESI): calcd for $C_{19}H_{21}N_2O_4^+$ (MH^+) 341.1496, found 341.1500.

*10-(Nitromethyl)-4,9,10,11,12,13,14,14b-octahydro-3H-3,8b-epoxybenzo[b]naphtho[2,1-d]azocin-14b-ol (**46**).* From 180 mg (0.508 mmol) of **38**, 110 mg (61%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (m, 1H), 7.18 (td, J = 8.1, 1.4 Hz, 1H), 6.89 (td, J = 7.8, 1.2 Hz, 1H), 6.75 (dd, J = 8.0, 1.0 Hz, 1H), 5.99 (d, J = 10.1 Hz, 1H), 5.63 (dd, J = 10.1, 3.3 Hz, 1H), 5.23 (d, J = 3.2 Hz, 1H), 4.73 (dd, J = 12.0, 4.6 Hz, 1H), 4.34 (dd, J = 12.0, 9.2 Hz, 1H), 3.23 (m, 1H), 3.20 (s, 1H), 2.42 (m, 2H), 2.06 (m, 3H), 1.87 (m, 2H), 1.79 (dd, J = 13.2, 5.0 Hz, 1H), 1.45 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.0, 133.2, 133.1, 128.4, 128.0, 127.7, 126.1, 125.9, 120.1, 118.8, 78.6, 75.0, 74.2, 69.9, 36.6, 33.9, 27.5, 25.3, 22.5, 22.4. HRMS (ESI): calcd for $C_{20}H_{23}N_2O_4^+$ (MH^+) 355.1652, found 355.1659.

*10-(Nitromethyl)-3,4,9,10,11,12,13,14,15,15b-decahydro-3,8b-epoxybenzo[b]cyclohepta[3,4]benzo[1,2-d]azocin-15b-ol (**47**).* From 90 mg (0.244 mmol) of **39**, 50 mg (56%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (m, 2H), 7.19 (m, 1H), 6.91 (m, 2H), 6.76 (m, 1H), 6.03 (d, J = 10.1, 1H), 5.65 (dd, J = 10.1, 3.3 Hz, 1H), 5.23 (d, J = 3.2 Hz, 1H), 4.77 (dd, J = 12.0, 3.8 Hz, 1H), 4.33 (dd, J = 12.0, 9.6 Hz, 1H), 3.33 (dq, J = 10.0, 4.9 Hz, 1H), 2.40 (m, 2H), 2.28 (m, 3H), 1.87 (dd, J = 13.3, 5.4, 1H), 1.78 (m, 2H), 1.52 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.0, 138.4, 134.7, 132.9, 128.4, 127.6, 126.4, 126.0, 120.1, 118.8, 79.4, 74.9, 74.2, 70.5, 37.3, 34.5, 31.9, 30.7, 29.0, 26.8, 25.9 HRMS (ESI): calcd for $C_{21}H_{25}N_2O_4^+$ (MH^+) 369.1809, found 369.1816.

General Procedure for the Irradiation of Amines. An approximately 0.1−0.3 M solution of the photoprecursors in acetonitrile was irradiated in Pyrex or glass reaction vessels in a Rayonet reactor equipped with RPR-3500 UV lamps (broad-band 300−400 nm UV source with peak emission at 350 nm) until the reaction was complete.

*syn-2,3,6,7-Tetrahydro-1H-3a,7-epoxybenzo[g]pyrrolo[1,2-a]-azocin-6-ol (**65a**).* From 150 mg (0.44 mmol) of **57**, following the general procedure for irradiation of amines 60 mg (40%) of the title compound was obtained upon chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23 (m, 1H), 7.10 (m, 1H), 6.85 (td, J = 7.5, 1.1 Hz, 1H), 6.80 (d, J = 8.1 Hz, 1H), 5.99 (ddd, J = 9.8, 5.2 Hz, 1.1, 1H), 5.71 (d, J = 9.8 Hz, 1H), 5.08 (s, 1H), 3.97 (ddd, J = 10.6, 5.2, 1.3 Hz, 1H), 3.77 (ddd, J = 8.9, 7.4, 4.6 Hz, 1H), 3.43 (dt, J = 8.8, 7.2 Hz, 1H), 2.25 (m, 3H), 2.16 (m, 1H), 2.05 (dtd, J = 15.3, 7.5, 4.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 141.0, 132.1, 128.3, 125.9, 125.2, 121.4, 118.5, 116.9, 87.1, 77.7, 66.8, 50.3, 38.1, 22.5.

*anti-2,3,6,7-Tetrahydro-1H-3a,7-epoxybenzo[g]pyrrolo[1,2-a]-azocin-6-ol (**65b**).* From 150 mg (0.44 mmol) of **57**, following the general procedure for irradiation of amines 10 mg (7%) of the title compound was obtained upon chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (m, 1H), 7.20 (d, J = 7.5 Hz, 1H), 6.83 (m, 2H), 5.81 (dt, J = 10.0, 1.4 Hz, 1H), 5.56 (dd, J = 10.0, 2.2 Hz, 1H), 4.98 (d, J = 5.9 Hz, 1H), 4.67 (ddt, J = 9.9, 6.0, 2.0 Hz, 1H), 3.76 (ddd, J = 9.0, 7.5, 4.0 Hz, 1H), 3.36 (m, 1H), 2.27 (m, 1H), 2.16 (m, 2H), 2.04 (ddt, J = 11.4, 7.6, 4.0 Hz, 1H), 1.50 (d, J = 11.9, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 142.2, 130.2, 129.2, 128.7, 127.9, 117.8, 116.7, 87.2, 77.6, 73.9, 67.1, 50.4, 38.1, 22.7.

*9-Chloro-2,3,6,7-tetrahydro-1H-3a,7-epoxybenzo[g]pyrrolo[1,2-a]azocin-6-ol (**66**).* From 115 mg (0.44 mmol) of **58**, following the general procedure for irradiation of amines 65 mg (57%) of the title compound was obtained upon chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17 (dd, J = 8.6, 2.4 Hz, 1H), 7.07 (d, J = 2.3 Hz, 1H), 6.71 (d, J = 8.6 Hz, 1H), 6.00 (ddd, J = 9.8, 5.2, 1.0 Hz, 1H), 5.69 (d, J = 9.8 Hz, 1H), 5.03 (s, 1H), 3.94 (ddd, J = 10.6, 5.2, 1.3 Hz, 1H), 3.73 (ddd, J = 8.8, 7.4, 4.5 Hz, 1H), 3.39 (dt, J = 8.8, 7.2 Hz, 1H), 2.25 (m, 2H), 2.17 (m, 2H), 2.05 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.6, 131.9, 128.3, 125.6, 125.1, 123.5, 122.8, 118.0, 87.1, 77.4, 66.6, 50.3, 37.9, 22.5. HRMS (ESI): calcd for $C_{14}H_{15}ClNO_2^+$ (MH^+) 264.0786, found 264.0790.

*9-Bromo-2,3,6,7-tetrahydro-1H-3a,7-epoxybenzo[g]pyrrolo[1,2-a]azocin-6-ol (**67**).* From 124 mg (0.44 mmol) of **59**, following the general procedure for irradiation of amines 53 mg (43%) of the title compound was obtained upon chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (dd, J = 8.7, 2.4 Hz, 1H), 7.21 (d, J = 1.9 Hz, 1H), 6.66 (d, J = 8.6, 1H), 6.00 (ddd, J = 9.8, 5.2, 1.0 Hz, 1H), 5.69 (d, J = 9. Hz 8, 1H), 5.03 (s, 1H), 3.94 (ddd, J = 10.6, 5.2, 1.3 Hz, 1H), 3.72 (ddd, J = 8.8, 7.4, 4.5 Hz, 1H), 3.39 (dt, J = 8.8, 7.2 Hz, 1H), 2.24 (m, 2H), 2.17 (m, 2H), 2.05 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 140.0, 131.8, 131.2, 128.5, 125.1, 123.2, 118.3, 110.6, 87.0, 77.3, 66.6, 50.1, 37.9, 22.5. HRMS (ESI): calcd for $C_{14}H_{15}BrNO_2^+$ (MH^+) 308.0281, found 308.0287.

*6,9,10,11-Tetrahydro-5H-5,8a-epoxypyrido[3,2-g]pyrrolo[1,2-a]-azocin-6-ol (**68**).* From 210 mg (0.91 mmol) of **60**, following the

general procedure for irradiation of amines 130 mg (62%) of the title compound was obtained upon chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): 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, 7.6, 4.4 Hz, 1H), 3.72 (dt, J = 10.1, 7.3 Hz, 1H), 2.69 (s, 1H), 2.26 (m, 2H), 2.15 (m, 1H), 2.04 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): 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 $C_{13}H_{15}N_2O_2^+$ (MH^+) 231.1129, found 231.1127.

*syn-3,6-Dimethyl-2,3,6,7-tetrahydro-1H-3a,7-epoxybenzo[g]-pyrrolo[1,2-a]azocin-6-ol (**69a**).* From 165 mg (0.64 mmol) of **61**, following the general procedure for irradiation of amines 55 mg (33%) of the title compound was obtained upon chromatography together with 60 mg (36%) of **69b**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23 (m, 1H), 7.10 (m, 1H), 6.83 (td, J = 7.5, 1.2 Hz, 1H), 6.76 (dd, J = 8.1, 1.0 Hz, 1H), 5.88 (dd, J = 9.8, 1.2 Hz, 1H), 5.48 (d, J = 9.8 Hz, 1H), 4.77 (s, 1H), 3.75 (td, J = 9.3, 7.0 Hz, 1H), 3.41 (td, J = 9.1, 2.6 Hz, 1H), 2.78 (d, J = 1.0 Hz, 1H), 2.40 (dp, J = 11.1, 6.8 Hz, 1H), 2.05 (dtd, J = 12.0, 6.8, 2.6 Hz, 1H), 1.90 (m, 1H), 1.41 (d, J = 1.0 Hz, 3H), 1.17 (d, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 142.8, 133.7, 130.0, 128.2, 127.9, 121.4, 118.2, 117.8, 88.0, 80.5, 68.4, 51.9, 43.4, 30.6, 23.1, 12.4.

*anti-3,6-Dimethyl-2,3,6,7-tetrahydro-1H-3a,7-epoxybenzo[g]-pyrrolo[1,2-a]azocin-6-ol (**69b**).* From 165 mg (0.64 mmol) of **61** ,following the general procedure for irradiation of amines 60 mg (36%) of the title compound was obtained upon chromatography together with 55 mg (33%) of **69a**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 (td, J = 8.1, 1.4 Hz, 1H), 7.12 (d, J = 6.3 Hz, 1H), 6.75 (td, J = 7.5, 1.1 Hz, 1H), 6.67 (d, J = 8.1 Hz, 1H), 5.85 (m, 1H), 5.52 (d, J = 10.0 Hz, 1H), 4.83 (s, 1H), 3.66 (t, J = 7.8 Hz, 1H), 3.32 (ddd, J = 10.3, 8.7, 6.2 Hz, 1H), 2.76 (s, 1H), 2.40 (m, 1H), 2.24 (m, 1H), 1.79 (tdd, J = 12.3, 10.3, 7.9 Hz, 1H), 1.40 (s, 3H), 1.19 (d, J = 7.0, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 140.4, 131.5, 128.5, 128.3, 126.5, 118.9,116.5, 113.6, 88.4, 81.9, 68.7, 46.3, 42.9, 30.4, 23.5, 13.6.

*2,3,8,9,10,11-Hexahydro-1H-10a,13a-epoxynaphtho[1,8-fg]-pyrrolo[1,2-a]azocin-11-ol (**70**).* From 360 mg (1.34 mmol) of **62**, following the general procedure for irradiation of amines 170 mg (47%) of the title compound was obtained upon chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.14 (t, J = 7.8 Hz, 1H), 6.63 (m, 1H), 6.57 (d, J = 8.0 Hz, 1H), 6.06 (ddd, J = 9.7, 5.3, 0.6 Hz, 1H), 5.75 (d, J = 9.7 Hz, 1H), 3.87 (dd, J = 11.0, 5.3 Hz, 1H), 3.72 (ddd, J = 8.9, 7.6, 4.0 Hz, 1H), 3.38 (dt, J = 8.8, 7.2 Hz, 1H), 2.94 (ddd, J = 15.9, 10.6, 5.0 Hz, 1H), 2.84 (ddd, J = 17.4, 9.9, 5.4 Hz, 1H), 2.50 (ddd, J = 12.1, 6.6, 2.2 Hz, 1H), 2.24 (m, 1H), 2.11 (m, 4H), 1.95 (m, 1H), 1.75 (d, J = 11.1 Hz, 1H), 1.42 (td, J = 12.4, 7.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.8, 136.3, 131.5, 127.9, 126.2, 123.5, 118.6, 113.1, 87.4, 76.6, 64.5, 50.1, 38.0, 30.0, 26.3, 22.2, 16.0. HRMS (ESI): calcd for $C_{17}H_{20}NO_2^+$ (MH^+) 270.1489, found 270.1491.

*6,13-Dihydro-5H-5,8a-epoxypyrido[3′,2′:7,8]azocino[2,1-a]-isoindol-6-ol (**71**).* From 130 mg (0.46 mmol) of **63**, following the general procedure for irradiation of amines 80 mg (62%) of the title compound was obtained upon chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 (dd, J = 4.9, 1.7 Hz, 1H), 7.45 (m, 5H), 6.83 (m, 1H), 6.19 (ddd, J = 9.8, 5.2, 1.0 Hz, 1H), 5.84 (d, J = 9.8 Hz, 1H), 5.23 (s, 1H), 5.10 (d, J = 14.4 Hz, 1H), 4.95 (d, J = 14.4 Hz, 1H), 4.07 (d, J = 5.3 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 151.0, 148.4, 139.3, 138.4, 133.8, 131.4, 129.9, 128.0, 126.2, 123.4, 123.2, 116.0, 114.4, 89.7, 77.6, 66.4, 53.0. HRMS (ESI): calcd for $C_{17}H_{15}N_2O_2^+$ (MH^+) 279.1128, found 279.1133.

*2,3,4,11-Tetrahydro-1H-3a,6a-epoxynaphtho[1′,8′:6,7,8]azocino-[2,1-a]isoindol-4-ol (**72**).* From 400 mg (1.26 mmol) of **64** following the general procedure for irradiation of amines 140 mg (35%) of the title compound was obtained upon chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20 (d, J = 8.0 Hz, 1H), 7.94 (dt, J = 7.5, 0.9 Hz, 1H), 7.70 (td, J = 7.4, 1.1 Hz, 1H), 7.65 (dt, J = 7.6, 1.1 Hz, 1H), 7.62 (td, J = 7.4, 1.2 Hz, 1H), 7.37 (t, J = 7.9 Hz, 1H), 7.04 (m, 1H), 6.04 (dd, J = 9.8, 1.9 Hz, 1H), 5.66 (dd, J = 9.8, 1.9 Hz, 1H), 4.68 (dt, J = 12.0, 2.0 Hz, 1H), 3.11 (ddd, J = 17.6, 9.2, 3.1 Hz, 1H), 2.81 (dt, J = 17.5, 7.7 Hz, 1H), 2.45 (m, 2H), 2.23 (ddd, J = 12.5, 5.9, 2.9 Hz, 1H), 1.91 (m, 3H), 1.26 (d, J = 12.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 165.0, 143.9, 139.5, 133.2, 133.1, 132.4, 132.2, 130.5, 128.3, 127.2, 124.8, 124.2, 122.8, 120.4, 117.3, 85.1, 73.6, 35.2, 27.6, 17.5.

*3,6,7,8-Tetrahydro-1H-3,5a-epoxyindeno[1,7-fg]pyrrolo[1,2-a]-azocine (**75**).* From 203 mg (1.34 mmol) of **73**, following the general procedure for irradiation of amines 120 mg (67%) of the title compound was obtained upon chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.11 (m, 1H), 6.88 (m, 1H), 6.56 (d, J = 8.2 Hz, 1H), 6.10 (dd, J = 5.6, 2.0 Hz, 1H), 6.04 (t, J = 2.1 Hz, 1H), 5.75 (dd, J = 5.6, 1.2 Hz, 1H), 5.62 (s, 1H), 3.68 (m, 1H), 3.52 (m, 1H), 3.37 (m, 2H), 2.39 (m, 2H), 2.17 (m, 1H), 2.01 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 148.6, 146.5, 139.6, 134.5, 129.4, 128.9, 126.2, 121.7, 113.8, 113.6, 105.0, 80.9, 50.1, 38.7, 37.5, 22.1. HRMS (ESI): calcd for $C_{16}H_{16}NO^+$ (MH^+) 238.1226, found 238.1232.

General Procedure for the Rearrangement of Amides. A solution of the photoproduct 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.

*6-Hydroxy-2,3,6,7-tetrahydro-1H-3a,7-epoxybenzo[g]pyrrolo-[1,2-a]azocin-1-one (**79**).* From 12 mg of **76** following the general procedure for the rearrangement of amides 10 mg (83%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): 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), 3.98 (dd, J = 5.2, 1.1, 1H), 2.77 (m, 2H), 2.40 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 171.8, 132.4, 129.4, 128.6, 127.2, 125.4, 124.5, 123.4, 120.2, 86.4, 78.0, 66.8, 30.3, 29.8. HRMS (ESI): calcd for $C_{14}H_{14}NO_3^+$ (MH^+) 244.0969, found 244.0974.

6-Hydroxy-7-methyl-2,3,6,7-tetrahydro-1H-3a,7-epoxybenzo[g]-pyrrolo[1,2-a]azocin-1-one. From 10 mg of **77**, following the general procedure for the rearrangement of amides 9 mg (90%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): 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 (dd, J = 9.1, 7.3 Hz, 2H), 2.36 (m, 2H), 1.67 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 171.6, 132.0, 129.2, 129.1, 128.8, 128.2, 125.1, 124.5, 120.3, 86.9, 78.7, 68.5, 30.3, 29.8, 23.5. HRMS (ESI): calcd for $C_{15}H_{16}NO_3^+$ (MH^+) 258.1125, found 258.1126.

*11-Hydroxy-8,9,10,11-tetrahydro-1H-10a,13a-epoxynaphtho-[1,8-fg]pyrrolo[1,2-a]azocin-3(2H)-one (**81**).* From 10 mg of **78**, following the general procedure for the rearrangement of amides 9 mg (90%) of the title compound was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (d, J = 8.2, 1H), 7.27 (m, 1H), 6.96 (d, J = 7.5 Hz, 1H), 6.16 (dd, 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), 2.50 (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). ^{13}C NMR (126 MHz, $CDCl_3$): 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 $C_{17}H_{18}NO_3^+$ (MH^+) 284.1282, found 284.1284.

*syn-10-Hydroxy-3-benzyl-7,8-benzo-13-oxa-3,6-diazatricyclo-[7.3.1.0^{1,6}]trideca-7,11-diene-2,5-dione (**83**):* Compound **82** (0.5 g, 1.38 mmol) was dissolved in 5 mL of DMSO and heated to 150 °C for 44 h. The solvent was removed under reduced pressure and purified by flash chromatography, which afforded 0.41 g (82%) of the title compound. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (dd, 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 (dd, J = 7.7, 1.6 Hz, 1H), 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 (dd, J = 5.7, 1.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): 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 $C_{21}H_{19}N_2O_4^+$ (MH^+) 363.1340, found 363.1334.

■ 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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