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Intramolecular Photoassisted Cycloadditions of Azaxylylenes and Postphotochemical Capstone Modifications via Suzuki Coupling Provide Access to Complex Polyheterocyclic Biaryls

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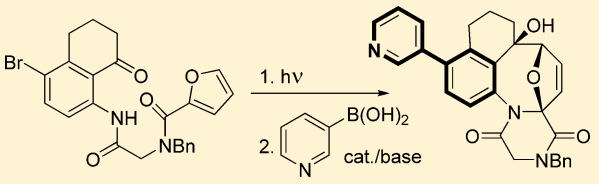
Supporting Information

ABSTRACT: Modular preassembly of azaxylylene photoprecursors, halogen-substituted in the aromatic ring, their intramolecular [4 + 4] or [4 + 2] cycloadditions to tethered unsaturated pendants, and subsequent postphotochemical capstone modification of the primary photoproducts via Suzuki coupling provides rapid access to diverse biaryls of unprecedented topology. This synthetic sequence allows for rapid growth of molecular complexity and is well aligned with methodology of Diversity-Oriented Synthesis.



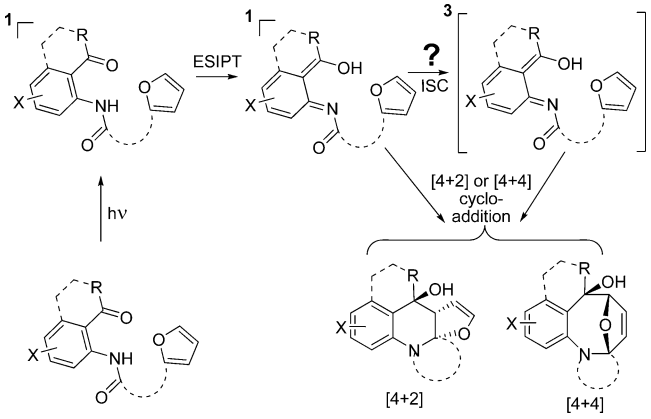
INTRODUCTION

Incorporation of key photochemical steps into synthetic sequences allow for dramatic increase in chemical complexity and rapid access to elaborate molecular architectures, rivaled by no other methods. This is especially true for inter- and intramolecular photocycloadditions,[1] which give rise to four- to eight-membered rings of complex topology ubiquitous in nature and perhaps promising from the medicinal chemistry standpoint.[2] Often photoreactions yield strained polycycles which can be further introduced into postphotochemical steps for added synthetic benefit. Photoinduced oxametathesis is one prominent example of such strain harvesting and utilization.[3] The most recent example is an elegant work by Porco and Stephenson[4] on a tandem dienone-photorearrangement-cycloaddition. The photoinduced step, inspired by Schultz' chemistry,[5] gives highly strained anti-Bredt polycycloalkenes, which react as dienophiles in the (ground state) postphotochemical step to further grow molecular complexity.

The current research focus in our laboratory is [4+n] cycloadditions of azaxylylenes,[6] short-lived species generated via the excited state intramolecular proton transfer (ESIPT) from *o*-formyl or acyl anilines, Scheme 1. Although azaxylylenes have been known for over half a century[7] and their photophysics is well-studied,[8] the synthetic utility of these intermediates remains largely underexplored, and is limited to the generation of azaxylylenes from exotic precursors,[7b] with the notable exception of the paper by Corey and Steinhagen describing a simple and efficient route to azaxylylenes from *o*-chloromethylanilines through base-induced elimination.[9] To the best of our knowledge, before our 2011 paper,[6a] azaxylylenes generated via ESIPT in aromatic *o*-aminoketones were not known to undergo cycloaddition reactions. One plausible reason for this could be the focus of the previous research efforts on *inter*- not *intra*molecular reactions.

We have found that intramolecular [4 + 4] or [4 + 2] cycloadditions of azaxylylenes to tethered unsaturated pendants

Scheme 1. Azaxylylene Formation via ESIPT and Their Intramolecular Cycloadditions



yield novel N,O,S-polyheterocycles,[6] demonstrating rapid growth of molecular complexity and diversity, fully in keeping with the central paradigm of diversity-oriented synthesis.[10] The synthesis of photoprecursors is straightforward and modular; they are assembled from readily (and in many cases—commercially) available starting materials in two to four simple steps such as amide bond formation, alkylation, acylation and oxidation, allowing for ready incorporation of multiple diversity inputs.

One of the questions for the current study focuses on whether it is possible to incorporate a high yielding postphotochemical step into this synthetic sequence to further increase the complexity of the product. The toolbox of a modern synthetic chemist is vast, and there are a number of options for postphotochemical transformations. According to

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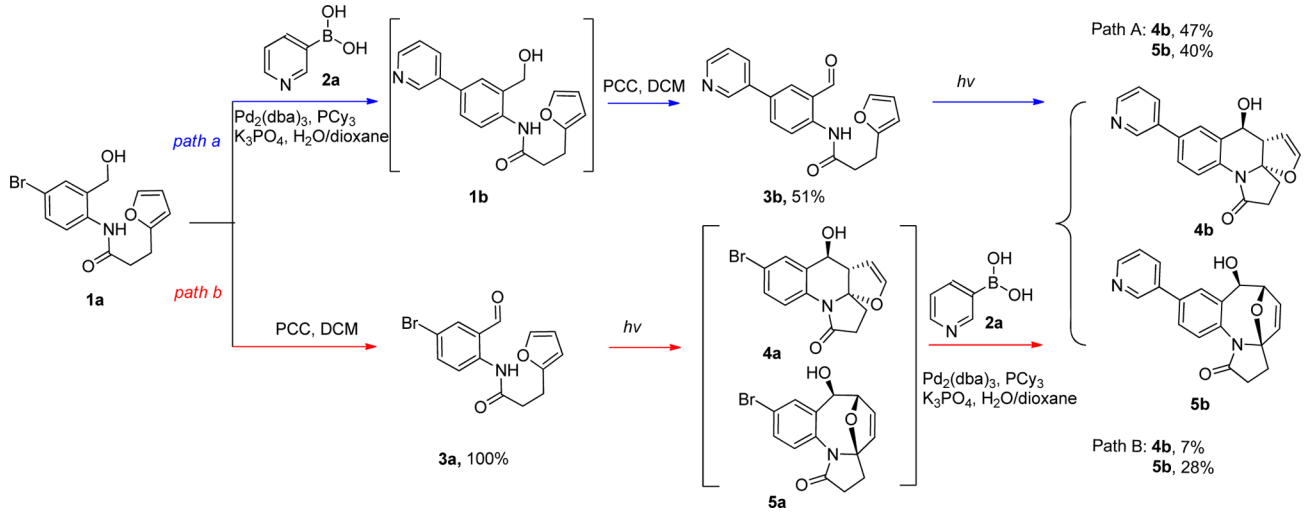
Scheme 2. Alternative Pathways To Install the Biaryl Moiety: Pre- or Postphotochemical



the comprehensive study published in 2011 by Roughley and Jordan,[11] the C−C bond forming reactions are the third most-widely used reaction, after alkylation/arylation or acylation of heteroatoms, employed by medicinal chemists in "the pursuit of drug candidates." These mostly sp^2-sp^2 cross-coupling reactions can be used to decorate the target N,O-polyheterocyclic structures with aryl- or hetaryl- pendants leading to biaryls, commonly found in various structures including natural products.[12] According to Roughley's survey, it is the Suzuki-Miyaura coupling that tops the list, accounting for more than 40% of all C−C bond forming reactions.

Besides a well-established methodology and a vast body of literature on the subject, the Suzuki reaction enjoys another advantage: the availability of starting materials. Synthetic pathways to both boronic acids and aryl halides are well-documented; many of these starting materials are commercially available. We rationalized that the Suzuki coupling could be an ideal starting point for the exploration of possible post-photochemical modifications, although in the context of the photoassisted synthesis it was not entirely clear whether the key photochemical step, i.e. the photoinduced intramolecular cycloaddition, should precede the Suzuki modification of the photoproduct or, alternatively, the Suzuki coupling should be performed on the photoprecursor which is subsequently photocyclized. In order to streamline the synthesis and make it amenable to modular-based approach, we introduced halogen into the phenyl ring of the azaxylylene photoprecursors and used commercially available aryl and heteroaryl boronic acids.

RESULTS AND DISCUSSION

Although transition metal catalyzed cross-coupling reactions are commonplace in modern synthesis, introduction of heterocyclic fragments still poses some challenges:[13] heteroaryl coupling partners may poison the catalyst, high temperatures required for the reaction may not be compatible with delicate starting materials or the product. Unprotected hydroxy or amino groups present additional difficulties due to the possibility of boroxines formation and competitive protodeboronation.[14] This results in an ongoing effort to optimize the catalyst, to lower the catalytic load and temperature, and to expand the scope of the reaction.[15] Anticipating such problems with complex photoproducts containing aminal moieties, hydroxy- and amido-groups, and reactive double bonds, we have investigated the two competing alternative approaches of incorporating the Suzuki reaction into the synthesis of novel scaffolds, Scheme 2: (i) the preassembly of the biaryl photoprecursor outfitted with the help of Suzuki coupling with a (hetero)aromatic moiety (*path a*, Scheme 2) or (ii) photoassisted synthesis of photoproducts halogenated in the aromatic ring, with subsequent Suzuki cross-coupling of these [4 + 4] and [4 + 2] products with (hetero)aromatic boronic acids (*path b*, Scheme 2). As this considerable extension of conjugation could potentially affect photoefficiency, the comparison of photochemical behavior of the two substrates and the feasibility of either synthetic pathway represented the first goal of this study.

5-Bromosubstituted alcohol **1a** was synthesized by acylation of 5-bromophenylmethanol with 2-furanpropanoyl chloride **6** and then carried through two pathways, Scheme 2. *Path A* consisted of Suzuki coupling followed by PCC oxidation to get the photoprecursor, while for the *path B* bromo alcohol **1a** was simply oxidized with PCC. Both photoprecursors, **3a** and **3b**, typical of *o*-formyl anilines, possess two characteristic emission bands in their fluorescence spectra: a band at 400 nm, corresponding to the fluorescence from the initial amide form, and a band at 540−550 nm attributable to excited state intramolecular proton transfer (ESIPT). Irradiations were carried out with a Rayonet broadband 300−400 nm UV source. The optimal irradiation media for compounds **3a** and **3b** were found to be 5% aqueous acetonitrile with the reactions proceeding faster in the presence of water. Both photoprecursors **3a** and **3b** gave stable polyheterocycles **4** and **5** as the products of the irradiation in the ratio of the [4 + 2] (**4**) to [4 + 4] (**5**) products of approximately 1:1. Interestingly, despite the presence of water capable of stabilizing azaxylylene due to hydrogen bonding, in contrast to our previous results only single stereo isomer of [4 + 4] (*syn*-**5**) and [4 + 2] (*anti*-**4**) is formed, where *syn*- and *anti*- refers to mutual arrangement of the benzylic hydroxy group in the quinolinole or benzoazacane rings, and furan's oxygen.

Compounds **4a** and **5a** were then subjected to Suzuki coupling under the same conditions as compound **1b**, yielding the mixture of **4b** and **5b** in the ratio of 1:4. Such a change in the ratios of [4 + 4] to [4 + 2] isomers is rationalized in terms of decreased stability and degradation of the [4 + 2] adduct under Suzuki coupling conditions. The yields of the [4 + 4] adducts over the three steps were comparable for both paths.

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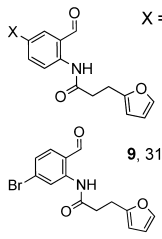
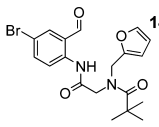
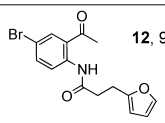
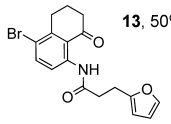
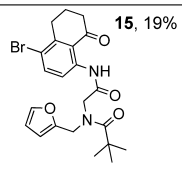
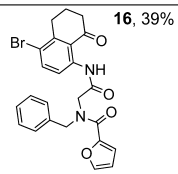
However, a closer examination revealed that the quantum efficiency of cycloaddition differs dramatically for halogen- and heterocycle-substituted photoprecursors, Table 1. While this fact has little effect on the preparative outcome of the synthetic sequence as long as the extended irradiation can compensate for lower quantum yields without causing unwanted side reactions, it does raise important mechanistic questions. The relative quantum yield experiment clearly shows that the QY of halogen-substituted photoprecursor **3a** is 3.7 times higher than that of **3b** bearing pyridine group, and 4.3 times higher than for azaxylylene precursor not substituted in the phenyl ring, **3e**. The explanation for this can probably be found in the mechanism of the reaction, Scheme 1. After the initial excitation and the excited-state proton transfer, the intramolecular cycloaddition of the formed azaxylylene can either proceed on the same singlet (S_1) hypersurface or, alternatively, the generated singlet excited azaxylylene can undergo intersystem crossing into the triplet state (T_1). The overall effect of the halogen substitution in the phenyl ring can presumably be dissected into (i) the electron withdrawing effect on both the ESIPT and on the rate of the inverse electron demand Diels–Alder step, or (ii) the heavy atom effect on the rate of intersystem crossing (especially in the case of Br as a substituent). To clarify the contribution of each of these factors further quantum yield studies were carried out, Table 1. Among the three halogen-substituted substrates **3a,c,d** the highest quantum yield was observed for the bromo-, followed by iodo- and chloro-substituted photoprecursors. Electronegativity decreases down a group in the Periodic Table, I < Br < Cl but the nuclear charge increases Cl < Br < I. Our experimental finding of the bell shaped rate dependence implies that the observed acceleration may be the result of a combined effect of the heavy atom and the electron-withdrawing effect, which also allows us to hypothesize that a triplet excited state might be involved in cycloadditions of photogenerated azaxylylenes. The detailed investigation of the underlying mechanism for the photochemical step is underway in our laboratory and will be reported elsewhere. On the basis of what we know so far it was decided to follow *path b* and to probe the scope of this photoassisted process, with Suzuki coupling as postphotochemical capstone.

Azaxylylene photoprecursors contain 2-acylaniline as the ESIPT-photoactive core, and furan as a tethered unsaturated pendant and azaxylylenophile. In the context of diversity-oriented synthesis the system can accommodate at least three diversity inputs: (i) identity and position of halogen

Table 1. Relative Quantum Yields for Selected 5-Substituted Photoprecursors

Photoprecursors	Relative quantum yield
3a, X = Br	(1.0)
3b, X = (3-Py)-	0.27
3c, X = Cl	0.45
3d, X = I	0.72
3e, X = H	0.23

Table 2. Matrix of Photoprecursors[a]

o-Formyl- or *o*-acyl-aniline	Linker: -CH_2CH_2-	Linker: -H_2C-N(-CH_2-)-C(=O)-C(=O)-	Linker: -H_2C-N(-C(=O)-)-C-
	 X = Br, **3a**, 53%; Py, **3b**, 51%; Cl, **3c**, 54%; I, **3d**, 34%; H, **3e**, 47% **9**, 31%	 **14**, 23%	
	 **12**, 93%		
	 **13**, 50%	 **15**, 19%	 **16**, 39%

[a]Isolated yields of photoprecursors are shown.

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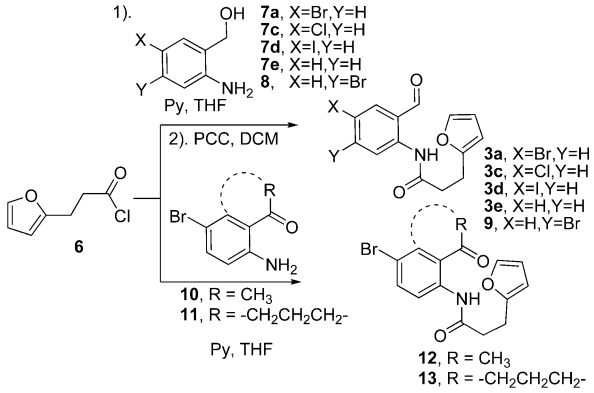
substitution in the aromatic ring, (ii) substituent on the carbonyl group of azaxylylene precursor, and (iii) the linker connecting the 2-acylaniline with furan. Such design makes it possible to implement modular approach and gain access to a diverse matrix of photoprecursors, Table 2. The synthesis of photoprecursors **3a−e, 9, 12−16** was carried out in a straightforward way as shown in Schemes 2 and 3. Upon

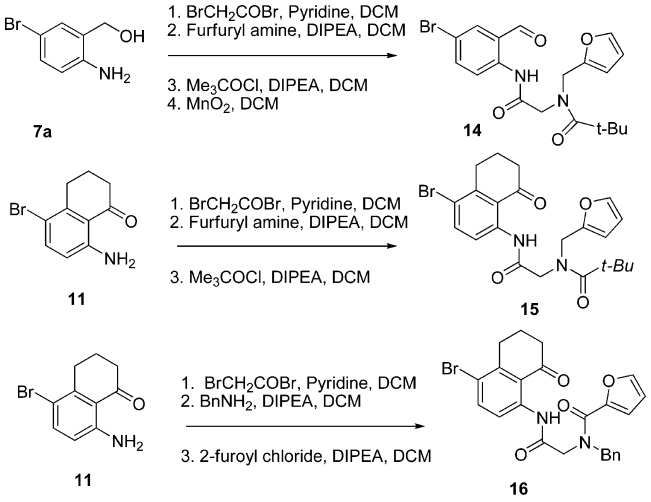
Scheme 3. General Synthesis of Photoprecursors



synthesis of halogen-substituted alcohols **7a,c-e, 8** or ketones **10,11** (see SI for the detailed description), they were introduced into reaction with furanpropanoyl chloride **6**. In case of ketones the immediate products of coupling, **12** or **13,** were directly used for irradiation, while the benzylic alcohols were first oxidized with PCC to yield the formyl-containing photoprecursor **3a,c-e**. The same result is achieved by the amide coupling of halogen-substituted methyl anthranilates with 2-furanpropanoyl chloride, followed by the reduction of the product to the corresponding benzylic alcohol with $LiAlH_4$, and its oxidation to aldehyde with PCC. The structure of the linker can be diversified via the peptoid synthesis-inspired[16] approach with bromoacetyl bromide. The initial product of bromoacetylation of alcohol **7a** or ketone **11** obtained in nearly quantitative yield was introduced into the reaction with benzyl or furfuryl amines, followed by acylation of the resulting secondary amine with furoyl or pivaloyl chlorides, respectively, Scheme 4.

In all cases the irradiation proceeded smoothly to give products of both [4 + 4] and [4 + 2] cycloaddition, Scheme 5, ratios and yields are compiled in Table 3. The average reaction time was under 5 h, and the reactions were highly diastereoselective as established by NMR analysis. The photoproducts were not isolated but rather introduced directly into palladium-catalyzed cross coupling to yield the expected biaryls, purified by column chromatography. The yields of the Suzuki-coupling step were found to be sensitive to the presence of additional heteroatoms: in two of the three cases the introduction of an additional amide fragment into the linker to form ketopiperazine resulted in complete degradation of the [4 + 2] photoproduct dihydrofuran after the coupling step, with a commensurate decrease of the overall yield to below 40%. The choice of catalysts, solvents and reaction time depended on the nature of arylboronic acid. In case of 3-pyridine boronic acid[17] **2a** the catalyst of choice was $Pd_2(dba)_3$ with PCy_3 as a ligand, and the catalyst load was as low as 0.9 mol %, while for reactions of 2-furyl- and 2-thienyl boronic[18] acids **2c** and **2d** 5 mol % of $Pd(PPh_3)_4$ was used. Moreover, while 3-pyridine- and phenyl-[19] boronic acids, **2a** and **2b,** reacted well with the

Scheme 4. Peptoid Synthesis-Based Diversification of the Linker



bromo-substituted substrates, reactions of furyl- and thienylboronic acids, **2c** and **2d**, required iodo-substituted substrates for the Suzuki coupling to occur at appreciable yields. Attempts to run the reaction under milder conditions using MIDA[20] boronates failed.

The structure and stereochemistry of Suzuki adducts was unambiguously established by XRay analysis of several representative examples and by the analysis of NMR spectra of the products. Of note is the rearrangement observed for furyl-substituted coupling product **5g**. The oxabicyclo[4.2.1]-nonene skeleton of the primary [4 + 4] photoproduct undergoes ring-opening and ring closure when subjected to silica during chromatography purification, yielding **29** containing oxabicyclo[3.3.1]nonane core, Scheme 6. Heating **5g** in DMSO also resulted in **29**. The mechanistic details of this rearrangement, the effect of functional groups and reaction conditions are currently under investigation.

■ CONCLUSIONS

Azaxylylenes generated from readily available halogen-substituted *o*-formyl or acyl anilines via photoinduced proton transfer undergo [4 + 4] or [4 + 2] intramolecular cycloadditions with high diastereoselectivity. The photoproducts are introduced into Suzuki reaction to yield structurally complex and topologically unprecedented heterocyclic biaryls. The whole photoassisted synthetic sequence, including the postphotochemical coupling, is well aligned with DOS.

■ EXPERIMENTAL SECTION

General Information. Common reagents and solvents were purchased from commercial sources and used as is, except for THF, which was refluxed over and distilled from potassium benzophenone ketyl prior to use. NMR spectra were recorded at 25 °C in $CDCl_3$ with TMS as an internal standard, unless noted otherwise. High resolution mass spectra were obtained on an *LC/MS/MS* system with triple quadrupole/TOF analyzer. Flash column chromatography was performed with 230−400 mesh silica gel using hexanes/EtOAc or DCM/methanol as an eluent.

2-Amino-5-bromobenzyl Alcohol[21] (7a). Methyl 2-amino-5-bromobenzoate (3.00 g, 13.0 mmol) in THF (9 mL) under nitrogen atmosphere was cooled to −41 °C. DIBAL-H (39.1 mL of a 1.0 M solution in hexanes, 43.0 mmol) was slowly added to the stirred

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Scheme 5

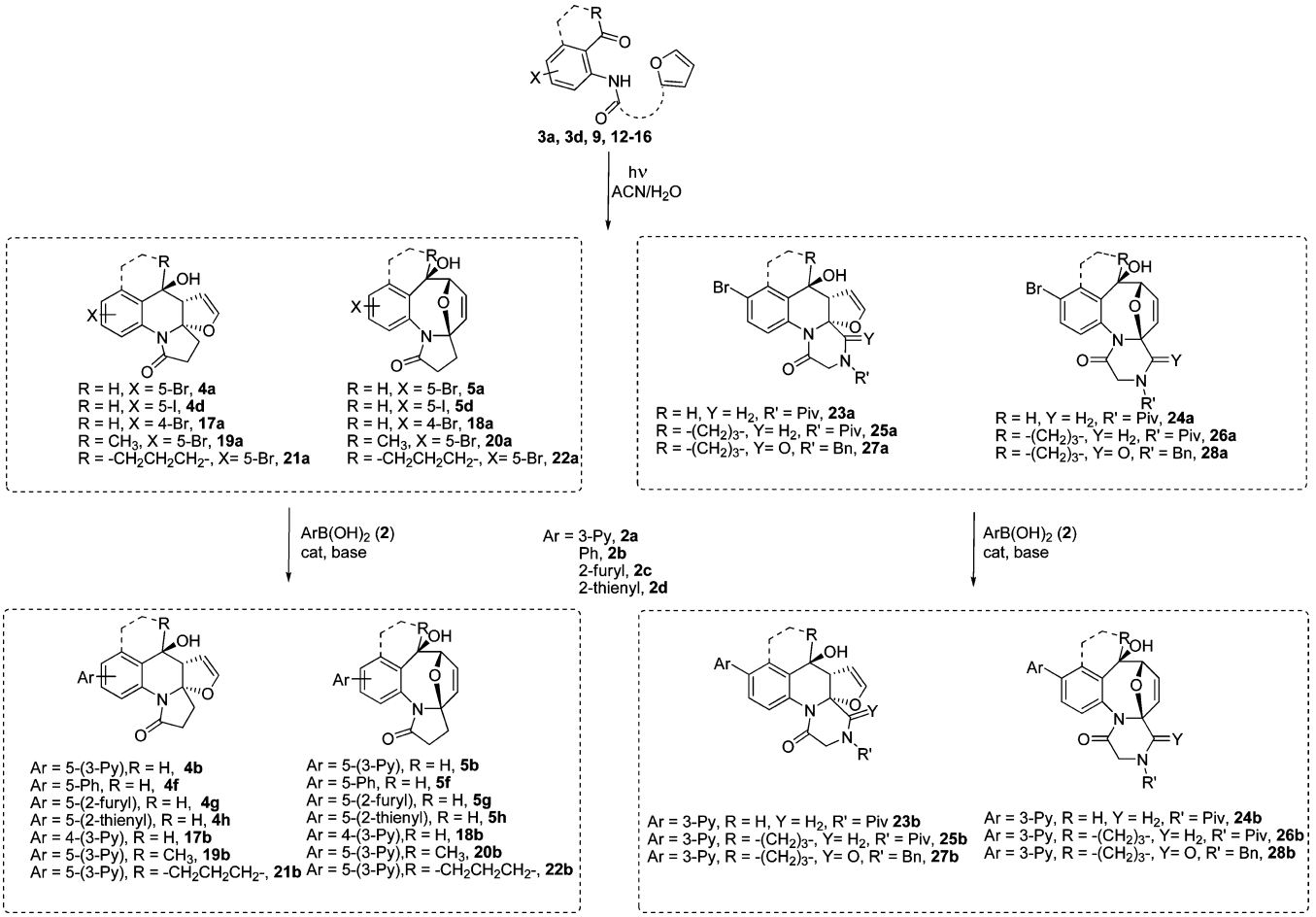
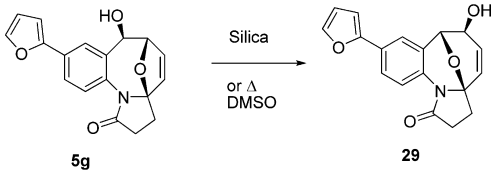


Table 3. Photoproduct Ratios and Isolated Yields of Postphotochemical Suzuki Couplings

Photoprecursor	Photoproducts ratio [4 + 2]:[4 + 4][a]	Suzuki coupling product from [4 + 2][b]	Suzuki coupling product from [4 + 4][b]
3a	**4a**:**5a** = 1:1	**4f**, 30%	**5f**, 44%
		4b, 7%	**5b**, 28%
3d	**4d**:**5d** = 1:1	**4g**, 17%	**5g**, 26%[c]
		4h, 27%	**5h**, 39%
9	**17a**:**18a** = 1:0.8	**17b**, 30%	**18b**, 24%
12	**19a**:**20a** = 1:1.1	**19b**, 28%	**20b**, 30%
13	**21a**:**22a** = 1:1.9	**21b**, 36%	**22b**, 16%
14	**23a**:**24a** = 1:1.4	**23b** 19%	**24b**, 12%
15	**25a**:**26a** = 1:1.5	**25b**, --	**26b**, 20%
16	**27a**:**28a** = 1:16	**27b**, --	**28b**, 36%

[a]determined by NMR of the reaction mixture after completion of irradiation. [b]isolated yields. [c]the primary [4 + 4] photoproduct rearranges from the bicyclo[4.2.1] to bicyclo[3.3.1] framework.

Scheme 6



solution. After maintaining at −41 °C for 1.5 h, the solution was allowed to reach room temperature and left to stir overnight. The solution was cooled in an ice water bath, quenched by a sequential addition of methanol and a sat. solution of sodium potassium tartrate, and the mixture was allowed to stir for 30 min. The organic phase was extracted with Et_2O (3 × 100 mL), and the solvent was removed under reduced pressure yielding 2.41 g (92%) of the product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (m, 2H), 6.61 (d, J = 8.3 Hz, 1H), 4.66 (d, J = 4.5 Hz, 2H), 4.22 (s, 2H).

4-Bromo-2-((trimethylsilyl)methyl)aniline (7a′). Chlorotrimethylsilane (1.16 mL, 9.14 mmol) was added to a stirred solution of 2-amino-5-bromobenzyl alcohol (**7a**) (1.68 g, 8.33 mmol) and triethylamine (2.32 mL, 16.6 mmol) in DCM (70 mL). The reaction mixture was stirred at room temperature overnight. The mixture was quenched with sat. aq. NH_4Cl (50 mL), the organic layer was separated, and the aqueous phase was extracted with DCM (3 × 100 mL). The organic fractions were combined, dried over Na_2SO_4, filtered, and the solvent was concentrated yielding 2.35 g (94%) of the

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product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (m, 2H), 6.57 (d, J = 8.2 Hz, 1H), 4.61 (s, 2H), 4.18 (s, 2H), 0.16 (s, 9H).

2-Amino-4-bromobenzyl Alcohol[22] (8). Methyl 2-amino-4-bromobenzoate[23] (1.14g, 4.95 mmol) in THF (5.5 mL) under nitrogen atmosphere was cooled to −41 °C. DIBAL-H (16.35 mL of a 1.0 M solution in hexanes, 16.35 mmol) was slowly added to the stirred solution. After remaining at −41 °C for 1.5 h, the solution was allowed to reach room temperature and left to stir overnight. The solution was cooled in an ice water bath, quenched by the sequential addition of methanol (35 mL) and a sat. solution of sodium potassium tartrate (70 mL), and the mixture was allowed to stir for 6 h. The organic phase was extracted with Et_2O (3 × 125 mL), and the solvent was removed under reduced pressure yielding 0.98 g of (2-amino-4-bromophenyl)methanol. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95 (d, J = 7.9 Hz, 1H), 6.88 (d, J = 1.9 Hz, 1H), 6.85 (dd, J = 7.9, 1.9 Hz, 1H), 4.66 (d, J = 5.1 Hz, 2H), 4.29 (s, 2H), 1.54 (m, 1H).

5-Bromo-2-((trimethylsilyloxy)methyl)aniline (8′). Chlorotrimethylsilane (0.69 mL, 5.4 mmol) was added to a stirred solution of (2-amino-4-bromophenyl)methanol (**8**) (0.98g 4.9 mmol) and triethylamine (1.36 mL, 9.75 mmol) in DCM (43 mL). The reaction mixture was stirred at room temperature overnight. The mixture was quenched with sat. aq. NH_4Cl (70 mL), the organic layer was separated, and the aqueous phase was extracted with DCM (3 × 100 mL). The organic fractions were combined, dried over Na_2SO_4, filtered, and the solvent was concentrated yielding 1.11 g of 5-bromo-2-((trimethylsilyloxy)methyl)aniline which was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (d, J = 7.8 Hz, 1H), 6.84 (d, J = 1.8 Hz, 1H), 6.82 (dd, J = 7.8, 1.9 Hz, 1H), 4.61 (s, 2H), 4.26 (s, 2H), 0.14 (s, 9H).

2-Amino-5-iodobenzyl Alcohol[24] (7d). Methyl 5-iodoanthranilate (3.00 g, 10.8 mmol) in THF (7.5 mL) under nitrogen atmosphere was cooled to −41 °C. DIBAL-H (32.7 mL of a 1.1 M solution in cyclohexane, 36 mmol) was slowly added to the stirred solution. After remaining at −41 °C for 1.5 h, the solution was allowed to reach room temperature and left to stir overnight. The solution was cooled in an ice water bath, quenched by the sequential addition of methanol, a sat. solution of sodium potassium tartrate, and the mixture was allowed to stir for 30 min. The organic phase was extracted with Et_2O (3 × 100 mL), and the solvent was removed under reduced pressure yielding 2.48 g (92%) of the product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (dd, J = 8.3, 2.2 Hz, 1H), 7.39 (d, J = 2.1 Hz, 1H), 6.51 (d, J = 8.3 Hz, 1H), 4.64 (d, J = 5.3 Hz, 2H), 4.24 (s, 2H).

4-Iodo-2-((trimethylsilyloxy)methyl)aniline (7d′). Chlorotrimethylsilane (0.49 mL, 3.8 mmol) was added to a stirred solution of 2-amino-5-iodobenzyl alcohol (**7d**) (0.87 g, 3.5 mmol) and triethylamine (0.98 mL, 7.0 mmol) in DCM (32 mL). The reaction mixture was stirred at room temperature overnight. The mixture was quenched with sat. aq. NH_4Cl (50 mL), the organic layer was separated, and the aqueous phase was extracted with DCM (3 × 100 mL). The organic fractions were combined, dried over Na_2SO_4, filtered, and the solvent was concentrated yielding 0.94 g (83%) of the product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (dd, J = 8.2, 2.2 Hz, 1H), 7.35 (d, J = 2.1 Hz, 1H), 6.47 (d, J = 8.3 Hz, 1H), 4.59 (s, 2H), 4.21 (s, 2H), 0.15 (s, 9H).

2-Amino-5-bromoacetophenone[25] (10). *o*-Aminoacetophenone (10 g, 73.96 mmol) was dissolved in Ac_2O, stirred for 2 h and concentrated. The residue was then dissolved in DCM, treated with Br_2 (6 mL), allowed to stir for 3 h, quenched with water, filtered, and the collected solid was washed with water. The solid residue was transferred to a round bottomed flask, dissolved in 2 M HCl (200 mL), and the solution was heated at 90 °C for 4 h. The solution was allowed to reach room temperature, basified to pH 12, extracted with EtOAc (3 × 50 mL), dried over Na_2SO_4, and concentrated yielding 13.5 g (85%) of the product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.35 (d, J = 8.8 Hz, 1H), 6.58 (d, J = 8.8, 0.9 Hz, 1H), 6.32 (s, 2H), 2.58 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.6, 149.1, 137.0, 134.1, 119.4, 119.0, 106.6, 27.8.

8-Amino-5-bromo-3,4-dihydronaphthalen-1(2*H*)-one (11). *(i). N-(4-Bromo-5,6,7,8-tetrahydronaphthalen-1-yl)acetamide.*[26] 5,6,7,8-Tetrahydro-1-naphthylamine (3.0 mL, 21.6 mmol) in EtOH (10 mL) was added dropwise to an ice-cooled solution of acetic anhydride (4.08 mL, 43.2 mmol) in EtOH (40 mL). The mixture was stirred for 16 h at room temperature. The solvent was concentrated to yield N-(5,6,7,8-tetrahydro-1-naphthyl)-acetamide as a white solid which was used without further purification ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.63 (d, J = 7.9, 1H), 7.15 (t, J = 7.8, 1H), 6.95 (d, J = 7.5, 1H), 6.89 (s, 1H), 2.81 (m, 2H), 2.62 (m, 2H), 2.23 (s, 3H), 1.87 (m, 2H), 1.80 (m, 2H). To a cooled solution of N-(5,6,7,8- tetrahydro-1-naphthyl)-acetamide in AcOH (55 mL) was slowly added a solution of Br_2 (3.36 mL, 65.2 mmol) in AcOH (4 mL) so that the temperature remained below 17 °C. The reaction mixture was then allowed to stir at room temperature for 24 h. The mixture was poured over ice water, the resulting suspension was filtered, and the collected solid was washed with water. The solid was dissolved in DCM (200 mL) and H_2O (50 mL), the organic phase was separated, and the aqueous phase was extracted with DCM (3 × 100 mL). The organic phases were combined, dried over Na_2SO_4, filtered, and the solvent was concentrated yielding 6.98 g (99.6%) of the product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 8.6 Hz, 1H), 7.43 (d, J = 8.6 Hz, 1H), 6.89 (s, 1H), 2.77 (m, 2H), 2.61 (m, 2H), 2.24 (s, 3H), 1.81 (m, 4H).

(ii). N-(4-Bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl)-acetamide. N-(4-bromo-5,6,7,8-tetra-hydronaphthalen-1-yl)acetamide (3.09 g, 11.5 mmol) in acetone (80 mL) and 15% aqueous $MgSO_4$ (1.90 g, 15.8 mmol in 11 mL of H_2O) was treated with $KMnO_4$ (5.47 g, 34.6 mmol) in portions. The mixture was allowed to stir for 12 h, filtered through Celite, and the solids were washed with $CHCl_3$ (100 mL) and H_2O (100 mL). The aqueous layer was extracted with $CHCl_3$ (4 × 100 mL). The organic fractions were combined, washed with brine, and dried over Na_2SO_4, and concentrated yielding 1.90 g (58.6%) of the desired product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.16 (s, 1H), 8.58 (d, J = 9.1 Hz, 1H), 7.72 (d, J = 9.1 Hz, 1H), 3.06 (t, J = 6.2 Hz, 2H), 2.72 (m, 2H), 2.25 (s, 3H), 2.14 (m, 2H). (iii) A stirred solution of N-(4-bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl)-acetamide (1.90 g, 6.74 mmol) in 6 M HCl (100 mL) was heated at 90 °C for 8 h. The mixture was cooled to room temperature and the volatiles were removed under vacuum. Ice was added to the mixture, followed by 2 M NaOH until pH of 8 was reached. The aqueous layer was extracted with EtOAc, the organic fractions were combined, washed with brine, dried, filtered and concentrated to give 1.26 g of the product (78.9%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, J = 8.9 Hz, 1H), 6.55 (s, 2H), 6.43 (d, J = 8.8 Hz, 1H), 2.96 (t, J = 6.2 Hz, 2H), 2.65 (m, 2H), 2.08 (m, 2H).

Synthesis of Photoprecursors. General Procedure for the Reaction of 2-Furanpropanoyl Chloride with Amines (A). A crude solution of *2-furanpropanoyl chloride* (1.2−1.5 equiv) in dry THF (25 mL) was added dropwise to an ice-cooled stirred solution of substituted anilines (1 equiv) and anhydrous pyridine (1.1 equiv) in THF (50 mL). The solution was allowed to reach room temperature and left to stir overnight. The reaction mixture was then diluted with water (100 mL), extracted with EtOAc (4 × 100 mL), the combined organic fractions were washed with 10% NaOH (100 mL), dried over Na_2SO_4, filtered, and concentrated. The product was purified when necessary using flash chromatography.

General Procedure for the Synthesis of *N*-(2-Acetylphenyl)-2-bromoacetamides (B). Bromoacetyl bromide (1.1 equiv) in dry DCM (10 mL) was slowly added to a stirred solution of amine (1 equiv), pyridine (1.1 equiv) in dry DCM (20 mL) at 0 °C under nitrogen atmosphere. The reaction mixture was left stirring overnight, then it was quenched with water (10 mL) and the aqueous phase was extracted with DCM (2 × 75 mL). Combined organic layers were dried over Na_2SO_4 and concentrated, giving the crude product, which was used further without purification

*N-(4-Chloro-2-formylphenyl)-3-(furan-2-yl)propanamide (**3c**).* General procedure **A** was followed using 2-furanpropanoyl chloride (**6**) (0.51 g, 3.2 mmol), 2-amino-5-chlorobenzyl alcohol (**7c**) (0.50 g, 3.2 mmol) and anhydrous pyridine (0.28 mL, 3.5 mmol) in THF (10 mL). The work-up and purification by flash chromatography yielded 0.67 g (2.4 mmol, 75%) of N-(4-chloro-2-(hydroxymethyl)phenyl)-3-(furan-2-yl)propanamide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.03 (d, J = 8.7 Hz, 1H), 7.36 (m, 1H), 7.31 (dd, J = 8.7, 2.4 Hz,

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1H), 7.20 (d, J = 2.4 Hz, 1H), 6.32 (t, J = 2.4 Hz, 1H), 6.11 (d, J = 3.2 Hz, 1H), 4.62 (d, J = 4.5 Hz, 2H), 3.11 (t, J = 7.4 Hz, 2H), 2.77 (t, J = 7.4 Hz, 2H), 2.07 (s, 1H). To a stirred solution of N-(4-chloro-2-(hydroxymethyl)phenyl)-3-(furan-2-yl)propanamide (0.67 g, 2.4 mmol) in dry DCM (100 mL) was added PCC (0.78 g, 3.6 mmol). The reaction mixture was left stirring overnight, filtered through a layer of silica gel, and evaporated yielding 0.64g (2.3 mmol, 72%) of **3c**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.08 (s, 1H), 9.88 (d, J = 0.7 Hz, 1H), 8.77 (d, J = 9.0 Hz, 1H), 7.66 (d, J = 2.5 Hz, 1H), 7.58 (dd, J = 9.1, 2.5 Hz, 1H), 7.34 (dd, J = 1.9, 0.9 Hz, 1H), 6.30 (dd, J = 3.2, 1.9 Hz, 1H), 6.09 (m, 1H), 3.11 (m, 2H), 2.84 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.3, 171.2, 153.8, 141.3, 139.3, 136.0, 135.0, 128.0, 122.5, 121.6, 110.2, 105.6, 36.5, 23.6.

*N-(4-Bromo-2-formylphenyl)-3-(furan-2-yl)propanamide (**3a**).* (i) General procedure **A** was followed using 2-furanpropanoyl chloride (**6**) (1.67 g, 10.5 mmol), methyl 2-amino-5-bromobenzoate (2.00 g, 8.6 mmol) and anhydrous pyridine (0.76 mL, 9.5 mmol). The work-up yielded 3.00 g (99%) of Methyl 5-bromo-2-(3-(furan-2-yl)-propanamido)benzoate. ^{1}H NMR (500 MHz, CDCl3) δ 11.05 (s, 1H), 8.68 (d, J = 9.1 Hz, 1H), 8.17 (d, J = 2.5 Hz, 1H), 7.65 (dd, J = 9.1, 2.5 Hz, 1H), 7.33 (dd, J = 1.9, 0.8 Hz, 1H), 6.29 (dd, J = 3.2, 1.9 Hz, 1H), 6.09 (m, 1H), 3.96 (s, 3H), 3.11 (m, 2H), 2.81 (m, 2H). ^{13}C NMR (126 MHz, CDCl3) δ 170.7, 167.6, 154.0, 141.3, 140.5, 137.4, 133.3, 122.1, 116.4, 114.8, 110.2, 105.5, 52.7, 36.7, 23.7.

(ii) To a suspension of $LiAlH_4$ (0.88 g, 23 mmol) in THF (12 mL) at −78 °C under nitrogen atmosphere was added methyl 5-bromo-2-(3-(furan-2-yl)propanamido)benzoate (4.29 g, 12.2 mmol) dissolved in THF (24 mL). The mixture was allowed to stir overnight, treated with water (1 mL), 10% NaOH (1 mL), followed by an additional allotment of water (3 mL), and dried over Na_2SO_4. The solvent was filtered and concentrated yielding 3.52 g of N-(4-bromo-2-(hydroxymethyl)phenyl)-3-(furan-2-yl)propanamide (**1a**) which was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.50 (s, 1H), 7.98 (d, J = 8.7 Hz, 1H), 7.45 (dd, J = 8.7, 2.4 Hz, 1H), 7.35 (m, 2H), 6.32 (dd, J = 3.1, 1.9 Hz, 1H), 6.11 (m, 1H), 4.61 (s, 2H), 3.10 (t, J = 7.4 Hz, 2H), 2.76 (t, J = 7.4 Hz, 2H), 2.21 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.4, 154.0, 141.3, 136.4, 131.9, 131.5, 131.4, 124.2, 116.9, 110.4, 105.8, 63.8, 36.2, 24.0. To the alcohol (3.52 g) in dry DCM (250 mL) was added PCC (2.63 g, 12.2 mmol). The reaction mixture was left stirring overnight, filtered through a layer of silica gel, and evaporated yielding 2.11 g of **3a** (54% over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.08 (s, 1H), 9.87 (s, 1H), 8.72 (d, J = 8.9 Hz, 1H), 7.80 (d, J = 2.4 Hz, 1H), 7.72 (dd, J = 9.0, 2.4 Hz, 1H), 7.34 (dd, J = 1.9, 0.9 Hz, 1H), 6.30 (dd, J = 3.2, 1.9 Hz, 1H), 6.09 (m, 1H), 3.11 (m, 2H), 2.84 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.2, 171.2, 153.8, 141.3, 139.8, 138.9, 138.0, 122.9, 121.9, 115.0, 110.2, 105.6, 36.5, 23.6. HRMS (ESI) calcd for $C_{14}H_{13}BrNO_3^+$ (MH^+) 322.0073, found 322.0067.

*N-(5-Bromo-2-formylphenyl)-3-(furan-2-yl)propanamide (**9**).* General procedure **A** was followed using 2-furanpropanoyl chloride (0.90 g, 5.7 mmol), 5-bromo-2-((trimethylsilyloxy)methyl)aniline (**8′**) (1.11 g, 4.05 mmol) and anhydrous pyridine (0.49 mL, 6.1 mmol). Upon work-up 1.27 g of N-(5-bromo-2-(hydroxymethyl)phenyl)-3-(furan-2-yl)propanamide was isolated, which was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.31 (d, J = 1.2 Hz, 1H), 7.35 (dd, J = 1.9, 0.9 Hz, 1H), 7.20 (dd, J = 8.1, 2.2 Hz, 1H), 7.02 (d, J = 8.1 Hz, 1H), 6.32 (dd, J = 3.2, 1.9 Hz, 1H), 6.10 (m, 1H), 4.60 (s, 2H), 3.08 (m, 2H), 2.75 (m, 2H). To N-(5-bromo-2-(hydroxymethyl)phenyl)-3-(furan-2-yl)propanamide (1.27 g, 3.71 mmol) in DCM (90 mL) was added PCC (4.80 g, 22.3 mmol). The reaction mixture was left stirring for 12 h, filtered through a layer of silica gel using EtOAc, the solvent was concentrated, and the mixture was subjected to flash chromatography yielding 0.40 g of **9** (24% over four steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.22 (s, 1H), 9.89 (s, 1H), 9.05 (d, 1H), 7.53 (d, J = 8.2 Hz, 1H), 7.39 (dd, J = 8.2, 1.8 Hz, 1H), 7.34 (dd, J = 1.9, 0.9 Hz, 1H), 6.30 (dd, J = 3.2, 1.9 Hz, 1H), 6.10 (m, 1H), 3.11 (m, 2H), 2.84 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.6, 171.3, 153.8, 141.4, 141.3, 136.8, 131.9, 126.3, 123.0, 120.2, 110.2, 105.6, 36.4, 23.5. HRMS (ESI) calcd for $C_{14}H_{13}BrNO_3^+$ (MH^+) 322.0073, found 322.0080.

*N-(2-Formyl-4-iodophenyl)-3-(furan-2-yl)propanamide (**3d**).* General procedure **A** was followed using 2-furanpropanoyl chloride (**6**) (0.79 g, 5.0 mmol), 4-iodo-2-((trimethylsilyloxy)methyl)aniline (**7d′**) (0.94 g, 2.9 mmol) and dry pyridine (0.40 mL, 5.0 mmol) in THF (10 mL). Upon work-up 0.90 g of N-(4-iodo-2-(hydroxymethyl)phenyl)-3-(furan-2-yl)propanamide was isolated which was used without further purification. ^{1}H NMR (500 MHz, CDCl3) δ 8.50 (s, 1H), 7.89 (d, J = 8.5 Hz, 1H), 7.65 (dd, J = 8.6, 2.1 Hz, 1H), 7.53 (d, J = 2.2 Hz, 1H), 7.36 (dd, J = 1.9, 0.9 Hz, 1H), 6.32 (dd, J = 3.2, 1.9 Hz, 1H), 6.10 (m, 1H), 4.60 (d, J = 5.7 Hz, 2H), 3.10 (t, J = 7.4 Hz, 2H), 2.76 (t, J = 7.4 Hz, 2H), 2.10 (s, 1H). To N-(4-iodo-2-(hydroxymethyl)phenyl)-3-(furan-2-yl)propanamide (0.90 g) in DCM (60 mL) was added PCC (3.15 g, 14.6 mmol). The reaction mixture was left stirring for 8h, filtered through a layer of silica gel using EtOAc, the solvent was concentrated, and the mixture was subjected to flash chromatography yielding 0.37 g of **3d** (34% over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.08 (s, 1H), 9.85 (s, 1H), 8.58 (d, J = 8.9 Hz, 1H), 7.97 (d, J = 2.2 Hz, 1H), 7.89 (dd, J = 8.9, 2.2 Hz, 1H), 7.33 (dd, J = 1.8, 0.9 Hz, 1H), 6.29 (dd, J = 3.2, 1.9 Hz, 1H), 6.09 (m, 1H), 3.11 (m, 2H), 2.83 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.2, 171.2, 153.8, 144.6, 144.1, 141.4, 140.4, 123.3, 122.0, 110.2, 105.6, 84.7, 36.6, 23.6. HRMS (ESI) calcd for $C_{14}H_{13}INO_3^+$ (MH^+) 369.9935, found 369.9945.

*N-(2-Acetyl-4-bromophenyl)-3-(furan-2-yl)propanamide (**12**).* General procedure **A** was followed using 2-furanpropanoyl chloride (**6**) (0.72 g, 2.8 mmol), 1-(2-amino-5-bromophenyl)ethanone (**10**) (0.30 g, 1.4 mmol) and anhydrous pyridine (0.17 mL, 2.1 mmol) yielding 0.45 g (93%) of **12**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.66 (s, 1H), 8.73 (d, J = 9.0 Hz, 1H), 8.01 (d, J = 2.4 Hz, 1H), 7.66 (dd, J = 9.1, 2.4 Hz, 1H), 7.33 (dd, J = 1.9, 0.8 Hz, 1H), 6.29 (dd, J = 3.2, 1.9 Hz, 1H), 6.08 (m, 1H), 3.10 (m, 2H), 2.81 (m, 2H), 2.68 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.6, 171.1, 154.0, 141.3, 139.9, 137.8, 134.0, 123.2, 122.6, 114.6, 110.2, 105.5, 36.7, 28.6, 23.7. HRMS (ESI) calcd for $C_{15}H_{15}BrNO_3^+$ (MH^+) 336.0230, found 336.0235.

*N-(4-Bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl)-3-(furan-2-yl)propanamide (**13**).* General procedure **A** was followed using 2-furanpropanoyl chloride (**6**) (3.8 mmol), 8-amino-5-bromo-3,4-dihydronaphthalen-1(2H)-one (**11**) (0.48 g, 2.0 mmol) and dry pyridine (0.18 mL, 2.2 mmol). Purification by flash chromatography yielded 0.38 g (50%) of **13**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.23 (s, 1H), 8.61 (d, J = 9.1 Hz, 1H), 7.72 (d, J = 9.1 Hz, 1H), 7.33 (dd, J = 1.9, 0.8 Hz, 1H), 6.29 (dd, J = 3.2, 1.9 Hz, 1H), 6.08 (m, 1H), 3.10 (m, 2H), 3.06 (t, J = 6.2 Hz, 2H), 2.82 (m, 2H), 2.72 (m, 2H), 2.14 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.0, 171.2, 154.1, 144.1, 141.3, 141.3, 138.8, 120.0, 119.7, 117.5, 110.2, 105.4, 40.1, 36.8, 31.4, 23.7, 21.7. HRMS (ESI) calcd for $C_{17}H_{17}BrNO_3^+$ (MH^+) 362.0386, found 362.0382.

*N-(2-(4-Bromo-2-formylphenylamino)-2-oxoethyl)-N-(furan-2-ylmethyl)pivalamide (**14**).* General procedure **B** was followed using 4-bromo-2-((trimethylsilyl)methyl)aniline (**7b′**) (2.28 g, 8.32 mmol), DIPEA (1.65 mL, 9.98 mmol) and bromoacetyl bromide (0.86 mL, 9.9 mmol). The work-up yielded 2-bromo-N-(4-bromo-2-(hydroxymethyl)phenyl)acetamide (3.07 g) which was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.51 (s, 1H), 8.02 (d, J = 8.7 Hz, 1H), 7.50 (dd, J = 8.7, 2.4 Hz, 1H), 7.39 (d, J = 2.3 Hz, 1H), 4.75 (s, 2H), 4.06 (s, 2H). To N-(4-bromo-2-(hydroxymethyl)-phenyl)acetamide (1.20 g) and DIPEA (0.71 mL, 4.1 mmol) in DCM (30 mL) was added furfuryl amine (0.49 mL, 5.5 mmol). The mixture was allowed to stir overnight, quenched with water (100 mL), the organic phase was separated, and the aqueous layer was extracted with DCM (3 × 100 mL). The combined organic fractions were washed with brine, dried over Na_2SO_4, filtered, and the solvent was concentrated yielding N-(4-bromo-2-(hydroxymethyl)phenyl)-2-(furan-2-ylmethylamino)acetamide (1.53 g crude) which was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.02 (d, J = 8.6 Hz, 1H), 7.45 (dd, J = 8.6, 2.4 Hz, 1H), 7.41 (d, J = 2.4 Hz, 1H), 7.39 (dd, J = 1.9, 0.8 Hz, 1H), 6.36−6.34 (m, 1H), 6.28−6.27 (m, 1H), 4.66 (s, 2H), 3.88 (s, 2H), 3.47 (s, 2H). To N-(4-bromo-2-(hydroxymethyl)phenyl)-2-(furan-2-ylmethylamino)-acetamide (1.08 g) and DIPEA (0.30 mL, 1.8 mmol) in DCM (100

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mL) was added pivaloyl chloride (0.19 mL, 1.5 mmol). The mixture was allowed to stir overnight, quenched with water (100 mL), the organic phase was separated, and the aqueous layer was extracted with DCM (3 × 100 mL). The combined organic fractions were dried over Na_2SO_4, filtered, and the solvent was concentrated. Purification by flash chromatography yielded 0.40 g of N-(2-((4-bromo-2-(hydroxymethyl)phenyl)amino)-2-oxoethyl)-N-(furan-2-ylmethyl)-pivalamide (29% over three steps). ^{1}H NMR (500 MHz, CDCl3) δ 9.11 (s, 1H), 7.88 (d, J = 8.7 Hz, 1H), 7.39 (dd, J = 8.7, 2.4 Hz, 1H), 7.37 (dd, J = 1.8, 0.8 Hz, 1H), 7.32 (d, J = 2.4 Hz, 1H), 6.36 (dd, J = 3.2, 1.9 Hz, 1H), 6.32 (m, 1H), 4.79 (s, 2H), 4.60 (d, J = 4.8 Hz, 2H), 4.10 (s, 2H), 3.48 (s, 1H), 1.39 (s, 9H). To a stirred solution of N-(2-((4-bromo-2-(hydroxymethyl)phenyl)amino)-2-oxoethyl)-N-(furan-2-ylmethyl)pivalamide (0.35 g, 0.83 mmol) in 40 mL of DCM was added MnO_2 (1.02 g, 11.7 mmol). After stirring for 24 h the solution was filtered through Celite and the solvent was concentrated yielding **14** (0.28 g, 0.67 mmol, 81%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.19 (s, 1H), 9.85 (d, J = 0.7 Hz, 1H), 8.68 (d, J = 9.0 Hz, 1H), 7.79 (d, J = 2.4 Hz, 1H), 7.70 (dd, J = 9.0, 2.4 Hz, 1H), 7.34 (dd, J = 1.8, 0.9 Hz, 1H), 6.33 (dd, J = 3.3, 1.8 Hz, 1H), 6.31 (dd, J = 3.3, 0.9 Hz, 1H), 4.87 (s, 2H), 4.17 (s, 2H), 1.45 (s, 9H).). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.8, 178.5, 168.7 149.7, 142.8, 139.3, 138.7, 137.9, 123.2, 122.0, 115.3, 110.5, 109.2, 52.2, 46.5, 39.2, 28.6. HRMS (ESI) calcd for $C_{19}H_{22}BrN_2O_4^+$ (MH^+) 421.0757, found 421.0757.

*N-(2-(4-Bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-ylamino)-2-oxoethyl)-N-(furan-2-ylmethyl)pivalamide (**15**).* General procedure **B** was followed using 8-amino-5-bromo-3,4-dihydronaphthalen-1(2H)-one (**11**) (1.15 g, 4.79 mmol), pyridine (0.77 mL, 9.56 mmol), bromoacetyl bromide (0.50 mL, 5.7 mmol) The work-up yielded 2-bromo-N-(4-bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl)-acetamide (1.67 g) which was used without further purification. ^{1}H NMR (500 MHz, CDCl3) δ 12.80 (s, 1H), 8.56 (d, J = 9.1 Hz, 1H), 7.76 (d, J = 9.1 Hz, 1H), 4.04 (s, 2H), 3.08 (t, J = 6.2 Hz, 2H), 2.76 (m, 2H), 2.16 (m, 2H). To 2-bromo-N-(4-bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl)acetamide (1.67 g) and DIPEA (1.21 mL, 6.95 mmol) in DCM (75 mL) was added furfuryl amine (0.61 mL, 0.67 mmol). The mixture was allowed to stir overnight, quenched with water (50 mL), the organic phase was separated, and the aqueous layer was extracted with DCM (3 × 100 mL). The combined organic fractions were washed with brine, dried over Na_2SO_4, filtered, and the solvent was concentrated yielding N-(4-bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl)-2-(furan-2-ylmethylamino)acetamide (1.60 g) which was used without further purification ^{1}H NMR (500 MHz, CDCl3) δ 12.85 (s, 1H), 8.66 (d, J = 9.1 Hz, 1H), 7.73 (d, J = 9.1 Hz, 1H), 7.38 (dd, J = 1.9, 0.9 Hz, 1H), 6.34 (dd, J = 3.2, 1.7 Hz, 1H), 6.29 (dd, J = 3.2, 0.8 Hz, 1H), 3.92 (s, 2H), 3.48 (s, 2H), 3.07 (t, J = 6.2 Hz, 2H), 2.73 (m, 2H), 2.14 (m, 2H). To N-(4-bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl)-2-(furan-2-ylmethylamino)acetamide (1.60 g) and DIPEA (0.96 mL, 5.5 mmol) in DCM (75 mL) was added pivaloyl chloride (0.68 mL, 5.5 mmol). The mixture was allowed to stir overnight, quenched with water (75 mL), the organic phase was separated, and the aqueous layer was extracted with DCM (3 × 100 mL). The combined organic fractions were dried over Na_2SO_4, filtered, and the solvent was concentrated. Purification by flash chromatography yielded 0.43 g of **15** (19% over three steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.35 (s, 1H), 8.57 (d, J = 9.1 Hz, 1H), 7.71 (d, J = 9.1 Hz, 1H), 7.36 (dd, J = 1.8, 0.9 Hz, 1H), 6.34 (dd, J = 3.2, 1.8 Hz, 1H), 6.29 (dd, J = 3.3, 0.9 Hz, 1H), 4.85 (s, 2H), 4.18 (s, 2H), 3.05 (t, J = 6.2 Hz, 2H), 2.70 (m, 2H), 2.12 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.6, 178.2, 168.5, 150.1, 144.1, 142.6, 140.8, 138.7, 120.2, 119.9, 117.9, 110.4, 109.0, 52.0, 46.2, 40.0, 39.2, 31.4, 28.6, 21.7. HRMS (ESI) calcd for $C_{22}H_{26}BrN_2O_4^+$ (MH^+) 461.1070, found 461.1073.

*N-Benzyl-N-(2-(4-bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-ylamino)-2-oxoethyl)furan-2-carboxamide (**16**).* General procedure **B** was followed using 8-amino-5-bromo-3,4-dihydronaphthalen-1(2H)-one (**11**) (0.42 g, 1.7 mmol), DIPEA (0.36 mL, 2.1 mmol) and bromoacetyl bromide (0.18 mL, 2.1 mmol). The work-up yielded 2-bromo-N-(4-bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl)-acetamide (0.70 g) which was used without further purification. ^{1}H NMR (500 MHz, CDCl3) δ 12.80 (s, 1H), 8.56 (d, J = 9.1 Hz, 1H), 7.76 (d, J = 9.1 Hz, 1H), 4.04 (s, 2H), 3.08 (t, J = 6.2 Hz, 2H), 2.76 (m, 2H), 2.16 (m, 2H). To 2-bromo-N-(4-bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl)acetamide (0.70 g) and DIPEA (0.34 mL, 2.0 mmol) in DCM (40 mL) was added benzyl amine (0.29 mL, 2.7 mmol). The mixture was allowed to stir overnight, quenched with water (50 mL), the organic phase was separated, and the aqueous layer was extracted with DCM (3 × 100 mL). The combined organic fractions were dried over Na_2SO_4, filtered, and the solvent was concentrated yielding 2-(benzylamino)-N-(4-bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl)acetamide (0.88 g) ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.92 (s, 1H), 8.67 (d, J = 9.1, 0.7 Hz, 1H), 7.72 (d, J = 9.1 Hz, 1H), 7.47 (m, 2H), 7.37 (m, 3H), 3.93 (s, 2H), 3.50 (s, 2H), 3.07 (t, J = 6.2 Hz, 2H), 2.75 (m, 2H), 2.15 (m, 2H).To 2-(benzylamino)-N-(4-bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl)acetamide (0.88 g) and DIPEA (0.44 mL, 2.5 mmol) in DCM (45 mL) was added 2-furoyl chloride (0.27 mL, 2.7 mmol). The mixture was allowed to stir overnight, quenched with water (50 mL), the organic phase was separated, and the aqueous layer was extracted with DCM (3 × 100 mL). The combined organic fractions were dried over Na_2SO_4, filtered, and the solvent was concentrated. Purification by flash chromatography yielded 0.32 g of **16** (39% over three steps). ^{1}H NMR (500 MHz, $CDCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.68 (m, 1H), 8.63 (d, J = 8.8 Hz, 1H), 7.74 (d, J = 9.1 Hz, 1H), 7.50 (m, 1H), 7.36 (m, 5H), 7.21 (m, 1H), 6.51 (m, 1H), 5.04 (m, 2H), 4.28 (m, 2H), 3.05 (m, 2H), 2.69 (m, 2H), 2.12 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.8, 163.5, 144.6, 144.3, 140.7, 138.8, 136.5, 136.2, 135.0, 129.1, 128.9, 128.9, 128.4, 127.8, 127.8, 120.3, 119.7, 118.1, 111.6, 52.2, 46.6, 40.0, 31.4, 21.7. HRMS (ESI) calcd for $C_{24}H_{22}BrN_2O_4^+$ (MH^+) 481.0757, found 481.0758.

*N-(2-Formyl-4-(pyridin-3-yl)phenyl)-3-(furan-2-yl)propanamide (**3b**).* General procedure for Suzuki coupling **D** with pyridine boronic acid using pyridine-3-boronic acid (0.39 g, 3.2 mmol), $Pd_2(dba)_3$ (0.035 g, 0.038 mmol), PCy_3 (0.027 g, 0.096 mmol), and N-(4-bromo-2-(hydroxymethyl)phenyl)-3-(furan-2-yl)propanamide (**1a**) (0.61 g, 1.9 mmol), dioxane (5.0 mL), and aqueous K_3PO_4 (5.0 mmol, 3.9 mL of a 1.27 M solution) was followed. The crude 3-(furan-2-yl)-N-(2-(hydroxymethyl)-4-(pyridin-3-yl)phenyl)propanamide (**1b**) (0.60 g) was used without further purification ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.63 (s, 1H), 8.56 (dd, J = 4.8, 1.1 Hz, 1H), 8.25 (d, J = 8.4 Hz, 1H), 7.84 (ddd, J = 7.9, 2.4, 1.6 Hz, 1H), 7.52 (dd, J = 8.4, 2.2 Hz, 1H), 7.37 (m, 3H), 6.33 (dd, J = 3.2, 1.9 Hz, 1H), 6.13 (dd, J = 3.1, 0.6 Hz, 1H), 4.75 (s, 2H), 3.14 (t, J = 7.5 Hz, 2H), 2.81 (t, J = 7.5 Hz, 2H), 1.41 (s, 1H) To a stirred solution of 3-(furan-2-yl)-N-(2-(hydroxymethyl)-4-(pyridin-3-yl)phenyl)propanamide (0.60 g, 1.9 mmol) in DCM (45 mL) was added MnO_2 (2.28 g, 26.2 mmol). After 24 h, the solution was filtered through Celite, concentrated, and purified by flash chromatography yielding 0.31 g of **3b** (51% over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.22 (s, 1H), 10.05 (s, 1H), 8.92 (d, J = 8.7 Hz, 1H), 8.90 (dd, J = 2.4, 0.9 Hz, 1H), 8.66 (dd, J = 4.8, 1.6 Hz, 1H), 7.91 (m, 2H), 7.86 (dd, J = 8.7, 2.3 Hz, 1H), 7.43 (ddd, J = 7.9, 4.8, 0.9 Hz, 1H), 7.35 (dd, J = 1.9, 0.9 Hz, 1H), 6.31 (dd, J = 3.2, 1.9 Hz, 1H), 6.11 (m, 1H), 3.14 (m, 2H), 2.88 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.3, 171.3, 153.9, 149.0, 147.9, 141.3, 140.6, 134.6, 134.5, 134.2, 133.9, 132.6, 123.7, 122.0, 120.8, 110.2, 105.6, 36.6, 23.6. HRMS (ESI) calcd for $C_{19}H_{17}N_2O_3^+$ (MH^+) 321.1234, found 321.1241.

General Procedures for the Irradiation and Subsequent Coupling of Bromo-Substituted Aromatic Compounds with Pyridine-3-boronic. *AcidGeneral Procedure for Irradiation (**C**).* Solutions with *ca.* 6 mM of the photoprecursors **3a**, **3d**, **9**−**11**, **14**−**16** in 5% aq. acetonitrile were degassed and irradiated in Pyrex or borosilicate glass reaction vessels in a Rayonet reactor equipped with RPR-3500 UV lamps (broadband 300−400 nm UV source with peak emission at 350 nm) until the reaction was complete, as determined by ^{1}H NMR. The solution was concentrated and the cycloaddition products were used without further purification.

*General Procedure for Suzuki Coupling with Pyridine-3-boronic acid (**D**).* Aqueous K_3PO_4 (1.70 mmol, 1.33 mL of a 1.27 M solution), degassed for 30 min prior to the addition, was added to the reaction

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mixture containing pyridine-3-boronic acid (1.1 mmol), $Pd_2(dba)_3$ (0.01 mmol, 0.9 mol %), PCy_3 (0.024 mmol, 2.2 mol %), and the heteroaryl bromide (1.0 mmol) in dioxane (2.67 mL) under nitrogen atmosphere. The mixture was refluxed for 36 h with vigorous stirring. Then it was cooled to room temperature, filtered through a layer of silica gel (washed with EtOAc), concentrated, diluted with water (40 mL) and extracted with EtOAc (3 × 75 mL). The combined organic fractions were dried over Na_2SO_4, filtered, concentrated, and the product(s) were purified using flash chromatography.

*General Procedure for Suzuki Coupling with Phenylboronic Acid (**E**).* The heteroaryl halide (0.94 mmol), $Pd(PPh_3)_4$ (5.3 mol %, 0.050 mmol), were suspended in dimethoxyethane (4 mL) the mixture was allowed to stir under nitrogen atmosphere for ∼10 min. Phenylboronic acid (1.1 mmol) followed by aq. Na_2CO_3 (1.06 mL, 2 M solution, 2.12 mmol) were added to the mixture, and the resulting solution was refluxed under nitrogen atmosphere for 24 h. The mixture was allowed to cool to room temperature, extracted with Et_2O (6 × 40 mL), and the combined organic fractions were washed with water, dried over Na_2SO_4, concentrated, and subjected to flash chromatography.

*General Procedure for Suzuki Coupling with Thiophene-2-boronic and Furan-2-boronic Acids (**F**).* To a stirred mixture of the heteroaryl iodide (0.20 g, 0.54 mmol) and $Pd(PPh_3)_4$ (5.2−5.8 mol %, 0.032 g, 0.028 mmol) in DME (16 mL) was added thiophene-2- or furan-2-boronic acid (0.077 g, 0.60 mmol). The mixture was placed under nitrogen atmosphere, and $NaHCO_3$ (0.095 g, 1.1 mmol) in H_2O (16 mL) was added. The reaction mixture was heated under reflux with vigorous stirring for 12 h. Subsequently, the organic solvent was removed under reduced pressure, an extraction was performed on the remaining aqueous layer using EtOAc (5 × 25 mL), the organic layer was dried using $MgSO_4$, filtered, concentrated, and subjected to flash chromatography

*8-Hydroxy-5-phenyl-12-oxa-1-azatetracyclo[11.3.0.0^{2,7}.0^{9,13}]-hexadeca-2,4,6,10-tetraen-16-one (**4f**) and 2-Hydroxy-5-phenyl-16-oxa-9-azatetracyclo[11.2.1.0^{3,8}.0^{5,9}]hexadeca-3,5,7,14-tetraen-10-one (**5f**).* General procedure **C** was followed. From N-(4-bromo-2-formylphenyl)-3-(furan-2-yl)propanamide (**3a**) (1.0 g, 3.1 mmol) a mixture of 5-bromo-8-hydroxy-12-oxa-1-azatetracyclo[11.3.0.0^{2,7}.0^{9,13}]-hexadeca-2,4,6,10-tetraen-16-one (**4a**) and 5-bromo-2-hydroxy-16-oxa-9-azatetracyclo[11.2.1.0^{3,8}.0^{5,9}]hexadeca-3,5,7,14-tetraen-10-one (**5a**) in the ratio of 1:1 was formed, which was introduced into Suzuki coupling following the general procedure **E.** From 0.3 g of that mixture (0.94 mmol), phenylboronic acid (0.13 g, 1.1 mmol), $Pd(PPh_3)_4$ (0.058 g, 0.05 mmol) Na_2CO_3 (1.06 mL of a 2 M solution, 2.12 mmol) after chromatographic separation 0.089 g (30%) of **4f** and 0.13 g (44%) of **5f** were isolated.

(4f): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.3 Hz, 1H), 7.64 (dd, J = 8.3, 2.1 Hz, 1H), 7.59 (m, 2H), 7.46 (m, 3H), 7.38 (m, 1H), 6.27 (t, J = 2.8 Hz, 1H), 4.84 (d, J = 2.1 Hz, 1H), 4.70 (dd, J = 3.1, 2.2 Hz, 1H), 3.89 (q, J = 2.3 Hz, 1H), 2.86 (m, 1H), 2.59 (m, 1H), 2.47 (m, 2H), 2.19(s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 146.7, 140.1, 138.8, 133.3, 131.3, 128.9, 128.2, 127.5, 127.4, 126.9, 123.5, 101.4, 99.4, 70.5, 56.1, 35.2, 29.8. HRMS (ESI) calcd for $C_{20}H_{18}NO_3^+$ (MH^+) 320.1281, found 320.1281.

(5f): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (m, 4H), 7.54 (m, 1H), 7.45 (m, 2H), 7.38 (m, 1H), 6.36 (dd, J = 5.9, 1.9 Hz, 1H), 5.70 (dd, J = 5.8, 1.1 Hz, 1H), 5.09 (m, 1H), 4.75 (d, J = 7.0 Hz, 1H), 3.15 (s, 1H), 2.89 (m, 1H), 2.65 (m, 1H), 2.57 (dt, J = 13.8, 9.8, 1H), 2.48 (ddd, J = 13.9, 9.5, 1.7, 1H) . ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 139.9, 139.5, 134.8, 133.5, 131.6, 131.2, 129.3, 128.8, 128.0, 127.5, 127.2, 127.0, 103.6, 83.7, 79.5, 30.0, 28.9. HRMS (ESI) calcd for $C_{20}H_{18}NO_3^+$ (MH^+) 320.1281, found 320.1283.

*8-Hydroxy-5-pyridin-3-yl-12-oxa-1-azatetracyclo-[11.3.0.0^{2,7}.0^{9,13}]hexadeca-2,4,6,10-tetra-en-16-one (**4b**) and 2-Hydroxy-5-pyridin-2-yl-16-oxa-9-azatetracyclo[11.2.1.0^{3,8}.0^{5,9}]-hexadeca-3,5,7,14-tetraen-10-one (**5b**). Pathway A.* General procedure C was followed. From 0.25 g (0.78 mmol) of N-(2-formyl-4-(pyridin-3-yl)phenyl)-3-(furan-2-yl)propanamide (**3b**) after chromatographic separation 0.12 g (47%) of **4b** and 0.10 g (40%) of **5b** was obtained.

Pathway B. General procedure **C** was followed. From 0.34 g (1.1 mmol) of N-(4-bromo-2-formylphenyl)-3-(furan-2-yl)propanamide (**3a**) a mixture of 5-bromo-8-hydroxy-12-oxa-1-azatetracyclo-[11.3.0.0^{2,7}.0^{9,13}]hexadeca-2,4,6,10-tetraen-16-one (**4a**) and 5-bromo-2-hydroxy-16-oxa-9-azatetracyclo[11.2.1.0^{3,8}.0^{5,9}]hexadeca-3,5,7,14-tetraen-10-one (**5a**)in the ratio of 1:1 was formed., which was introduced into the Suzuki coupling following the general procedure **D**. From 0.34 g of that mixture, pyridine-3-boronic acid (0.23 g, 1.9 mmol), $Pd_2(dba)_3$ (0.021 g, 0.023 mmol), PCy_3 (0.016 g, 0.057 mmol), dioxane (3.1 mL), and aqueous K_3PO_4 (2.86 mmol, 2.3 mL of a 1.27 M solution) after chromatographic separation 0.024 g (6.8%) of **4b** and 0.10 g (28%) of **5b** was obtained.

4b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, J = 2.4 Hz, 1H), 8.56 (dd, J = 4.8, 1.6 Hz, 1H), 8.05 (d, J = 8.3 Hz, 1H), 7.83 (ddd, J = 8.0, 2.4, 1.6 Hz, 1H), 7.57 (dd, J = 8.3, 2.1 Hz, 1H), 7.41 (d, J = 2.1 Hz, 1H), 7.36 (ddd, J = 8.0, 4.8, 0.9 Hz, 1H), 6.29 (t, J = 2.8 Hz, 1H), 4.88 (d, J = 2.2 Hz, 1H), 4.71 (dd, J = 3.1, 2.3 Hz, 1H), 3.93 (q, J = 2.3 Hz, 1H), 2.90 (ddd, J = 16.1, 10.3, 8.2 Hz, 1H), 2.56 (m, 3H), 1.64 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 148.4, 148.0, 146.8, 135.7, 135.1,134.4, 134.2, 131.8, 128.2, 127.4, 123.8, 123.6, 101.4, 99.4, 70.3, 56.1, 35.2, 29.8 HRMS (ESI) calcd for $C_{19}H_{17}N_2O_3^+$ (MH^+) 321.1234, found 321.1241.

5b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, J = 2.1 Hz, 1H), 8.61 (dd, J = 4.8, 1.6 Hz, 1H), 7.88 (dt, J = 8.0, 1.9 Hz, 1H), 7.65 (d, J = 8.3 Hz, 1H), 7.58 (dd, J = 8.4, 2.2 Hz, 1H), 7.53 (d, J = 2.2 Hz, 1H), 7.39 (ddd, J = 7.9, 4.8, 0.9 Hz, 1H), 6.38 (dd, J = 5.8, 1.8 Hz, 1H), 5.71 (dd, J = 5.8, 1.2 Hz, 1H), 5.10 (m, 1H), 4.76 (d, J = 3.3 Hz, 1H), 2.91 (dt, J = 17.2, 9.7 Hz, 1H), 2.67 (ddd, J = 17.2, 9.8, 1.8, 1H), 2.58 (dt, J = 13.8, 9.8, 1H), 2.50 (ddd, J = 13.8, 9.5, 1.8, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 148.7, 148.1, 136.0, 135.4, 134.8, 134.2, 133.9, 132.5, 131.2, 129.3, 128.4, 127.2, 123.6, 103.6, 83.6, 79.4, 30.0, 28.9. HRMS (ESI) calcd for $C_{19}H_{17}N_2O_3^+$ (MH^+) 321.1234, found 321.1241.

*8-Hydroxy-6-(pyridin-3-yl)-12-oxa-1-azatetracyclo-[11.3.0.0^{2,7}.0^{9,13}]hexadeca-2,4,6,10-tetra-en-16-one (**17b**) and 2-Hydroxy-6-(pyridin-3-yl)-16-oxa-9-azatetracyclo[11.2.1.0^{3,8}.0^{5,9}]-hexa-deca-3,5,7,14-tetraen-10-one (**18b**).* General procedure **C** was followed. From 0.25 g (0.78 mmol) of N-(5-bromo-2-formylphenyl)-3-(furan-2-yl)propanamide (**9**) a mixture of 6-bromo-8-hydroxy-12-oxa-1-azatetracyclo[11.3.0.0^{2,7}.0^{9,13}]hexadeca-2,4,6,10-tetraen-16-one (**17a**) and 6-bromo-2-hydroxy-16-oxa-9-azatetracyclo[11.2.1.0^{3,8}.0^{5,9}]-hexadeca-3,5,7,14-tetraen-10-one (**18a**) in the ratio of 1:0.8 was formed, which was introduced into the Suzuki coupling following the general procedure general procedure **D** . From 0.25 g of that mixture, pyridine-3-boronic acid (0.14 g, 1.1 mmol), $Pd_2(dba)_3$ (0.014 g, 0.015 mmol), PCy_3 (0.012 g, 0.043 mmol), dioxane (2.25 mL), and aqueous K_3PO_4 (0.73 mmol, 0.97 mL of a 1.27 M solution) after chromatographic separation 0.072 g (28%) of **17b** and 0.059 g (23%) of **18b** was isolated.

17b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, J = 4.8 Hz, 1H), 8.41 (s, 1H), 8.12 (d, J = 1.7 Hz, 1H), 7.89 (ddd, J = 7.9, 2.4, 1.6 Hz, 1H), 7.33 (m, 2H), 6.28 (t, J = 2.8 Hz, 1H), 4.86 (d, J = 2.2 Hz, 1H), 4.71 (dd, J = 3.0, 2.2 Hz, 1H), 3.93 (q, J = 2.4 Hz, 1H), 2.88 (m, 1H), 2.56 (m, 4H), 1.64 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 148.3, 148.0, 146.7, 139.1, 135.0, 134.7, 131.0, 129.5, 124.3, 123.6, 121.9, 101.5, 99.5, 69.8, 56.2, 35.2, 29.9. HRMS (ESI) calcd for $C_{19}H_{17}N_2O_3^+$ (MH^+) 321.1234, found 321.1237.

18b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.61 (s, 1H), 7.91 (dt, J = 8.0, 2.0 Hz, 1H), 7.76 (d, J = 1.8 Hz, 1H), 7.43 (m, 2H), 7.38 (t, J = 7.5, 4.8 Hz, 1H), 6.37 (dd, J = 5.9, 1.9 Hz, 1H), 5.71 (dd, J = 5.9, 1.2 Hz, 1H), 5.08 (m, 1H), 4.73 (s, 1H), 3.17 (s, 1H), 2.94 (m, 1H), 2.68 (ddd, J = 17.3, 9.8, 1.8 Hz, 1H), 2.58 (dt, J = 13.9, 9.8, 1H), 2.50 (ddd, J = 13.9, 9.5, 1.8, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 148.8, 148.2, 138.2, 134.8, 134.5, 133.4, 133.2, 132.8, 129.3, 126.4, 125.1, 123.6, 103.7, 83.6, 79.0, 30.1, 28.9. HRMS (ESI) calcd for $C_{19}H_{17}N_2O_3^+$ (MH^+) 321.1234, found 321.1240.

*8-Hydroxy-8-methyl-5-(pyridin-3-yl)-12-oxa-1-azatetracyclo-[11.3.0.0^{2,7}.0^{9,13}]hexadeca-2,4,6,10-tetraen-16-one (**19b**) and 2-Hydroxy-2-methyl-5-(pyridin-3-yl)-16-oxa-9-azatetracyclo [11.2.1.0^{3,8}.0^{5,9}]hexadeca-3,5,7,14-tetraen-10-one (**20b**).* General procedure **C** was followed. From 0.50 g (1.5 mmol) of N-(2-acetyl-4-bromophenyl)-3-(furan-2-yl)propanamide (**10**) a mixture of 5-bromo-8-hydroxy-8-methyl-12-oxa-1-azatetracyclo[11.3.0.0^{2,7}.0^{9,13}]-

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hexa-deca-2,4,6,10-tetraen-16-one (**19a**) and 5-bromo-2-hydroxy-2-methyl-16-oxa-9-azatetracyclo [11.2.1.0^{3,8}.0^{5,9}]hexadeca-3,5,7,14-tetraen-10-one (**20a**) in the ratio of 1:1 was formed, which was introduced into the Suzuki coupling following the general procedure **D**. From 0.25 g of that mixture, pyridine-3-boronic acid (0.14 g, 1.1 mmol), $Pd_2(dba)_3$ (0.014 g, 0.015 mmol), PCy_3 (0.012 g, 0.043 mmol), dioxane (2.25 mL), and aqueous K_3PO_4 (0.73 mmol, 0.97 mL of a 1.27 M solution) 0.071 g (28%) of **19b** and 0.072 g (30%) of **20b** was obtained.

19b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (dd, J = 4.8, 1.7 Hz, 1H), 8.22 (d, J = 2.4 Hz, 1H), 7.94 (d, J = 8.2 Hz, 1H), 7.73 (ddd, J = 7.9, 2.4, 1.6 Hz, 1H), 7.43 (dd, J = 8.2, 2.0 Hz, 1H), 7.38 (d, J = 2.1 Hz, 1H), 7.28 (dd, J = 7.8, 4.8 Hz, 1H), 6.25 (t, J = 2.8 Hz, 1H), 4.65 (dd, J = 3.1, 2.2 Hz, 1H), 4.18 (s, 1H), 3.74 (t, J = 2.4 Hz, 1H), 2.85 (m, 1H), 2.52 (m, 3H), 1.79 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 147.9, 147.8, 146.9, 136.1, 134.9, 134.5, 134.3, 134.3, 127.4, 124.1, 123.7, 123.5, 101.6, 99.1, 70.5, 61.3, 35.1, 29.8, 25.4. HRMS (ESI) calcd for $C_{20}H_{19}N_2O_3^+$ (MH^+) 335.1390, found 335.1396.

20b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.63 (s, 1H), 7.87 (dt, J = 8.1, 1.8 Hz, 1H), 7.72 (d, J = 1.9 Hz, 1H), 7.56 (m, 2H), 7.40 (dd, J = 8.0, 4.7 Hz, 1H), 6.37 (dd, J = 5.9, 1.9 Hz, 1H), 5.72 (dd, J = 5.8, 1.1 Hz, 1H), 4.78 (t, J = 1.4 Hz, 1H), 3.57 (s, 1H), 2.95 (dt, J = 17.4, 9.8 Hz, 1H), 2.69 (ddd, J = 17.4, 9.7, 1.8 Hz, 1H), 2.57 (dt, J = 13.9, 9.9, 1H), 2.49 (ddd, J = 13.9, 9.5, 1.8, 1H), 1.80 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 148.6, 148.2, 137.1, 136.0, 136.0, 134.8, 134.3, 132.6, 129.3, 129.0, 126.9, 126.4, 123.6, 103.4, 89.2, 78.0, 30.2, 28.5, 24.7. HRMS (ESI) calcd for $C_{20}H_{19}N_2O_3^+$ (MH^+) 335.1390, found 335.1398.

*11-Hydroxy-16-(pyridine-3-yl)-7-oxa-2-azapentacyclo-[9.7.1.0^{2,6}.0^{6,10}.0^{15,19}]nonadeca-1(19),8,15(16),17-tetraen-3-one (**21b**) and 10-Hydroxy-15-(pyridine-3-yl)-9-oxa-2-azapentacyclo [8.7.1.1^{6,9}.0^{2,6}.0^{14,18}] nonadeca-1(18),7,14(15),16(17)tetraen-3-one (**22b**).* General procedure **C** was followed. From 0.36 g (0.99 mmol) of N-(4-bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl)-3-(furan-2-yl)propanamide (**11**) a mixture of 11-hydroxy-16-bromo-7-oxa-2-azapentacyclo[9.7.1.0^{2,6}.0^{6,10}.0^{15,19}]nonadeca-1(19),8,15(16),17-tetraen-3-one (**21a**) and 10-hydroxy-15-bromo-9-oxa-2-azapentacyclo-[8.7.1.1^{6,9}.0^{2,6}.0^{14,18}]nonadeca-(18),7,14(15),16(17) tetraen-3-one (**22a**) in the ratio of 1:1.9 was formed, which was introduced into Suzuki coupling following the general procedure **D**. From 0.36 g of that mixture, pyridine-3-boronic acid (0.14 g, 1.1 mmol), $Pd_2(dba)_3$ (0.011 g, 0.012 mmol), PCy_3 (0.078 g, 0.028 mmol), dioxane (3.1 mL), and aqueous K_3PO_4 (1.70 mmol, 1.34 mL of a 1.27 M solution) after chromatographic separation 0.13 g (36%) **21b** and 0.057 g (16%) **22b** was obtained.

21b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (dd, J = 4.8, 1.6 Hz, 1H), 8.04 (s, 1H), 7.81 (d, J = 8.2 Hz, 1H), 7.62 (ddd, J = 7.8, 2.3, 1.6 Hz, 1H), 7.32 (ddd, J = 7.8, 4.8, 0.9 Hz, 1H), 7.21 (d, J = 8.2 Hz, 1H), 6.33 (t, J = 2.8 Hz, 1H), 4.76 (dd, J = 3.2, 2.2 Hz, 1H), 3.78 (t, J = 2.4 Hz, 1H), 2.90 (m, 1H), 2.58 (m, 6H), 2.05 (m, 1H), 1.92 (td, J = 13.0, 3.4 Hz, 1H), 1.84 (m, 1H), 1.67 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 149.6, 147.9, 146.8, 136.7, 136.6, 135.7, 135.1, 134.2, 130.0, 129.6, 122.9, 121.5, 101.5, 99.4, 69.5, 60.0, 41.0, 35.2, 29.8, 28.7, 18.4. HRMS (ESI) calcd for $C_{22}H_{21}N_2O_3^+$ (MH^+) 361.1547, found 361.1550.

22b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (dd, J = 4.9, 1.7, 1H), 8.55 (dd, J = 2.3, 0.9, 1H), 7.61 (dt, J = 7.8, 2.0, 1H), 7.36 (ddd, J = 7.8, 4.9, 0.9, 1H), 7.28 (m, 1H), 7.15 (d, J = 8.1, 1H), 6.43 (dd, J = 5.8, 1.9, 1H), 5.76 (dd, J = 5.9, 1.1, 1H), 4.62 (m, 1H), 3.51 (s, 1H), 3.03 (ddd, J = 17.4, 10.3, 9.2, 1H), 2.71 (ddd, J = 17.5, 9.6, 1.7, 1H), 2.56 (m, 4H), 2.09 (m, 1H), 1.99 (m, 1H), 1.77 (m, 1H), 1.69 (td, J = 13.5, 3.1, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 149.9, 148.3, 137.5, 137.3, 136.5, 136.2, 135.3, 133.8, 129.6, 129.3, 126.4, 123.1, 103.2, 88.0, 75.4, 35.8, 30.4, 30.3, 29.7, 28.6, 17.8. HRMS (ESI) calcd for $C_{22}H_{21}N_2O_3^+$ (MH^+) 361.1547, found 361.1553.

*8-Hydroxy-5-pyridin-3-yl-15-pivaloyl-12-oxa-1,15-diazatetracyclo[11.3.0.0^{2,7}.0^{9,13}]heptadeca-2,4,6,10-tetraen-17-one (**23b**) and 2-Hydroxy-12-pivaloyl-5-(pyridin-3-yl)-17-oxa-9,12-diazatetracyclo[11.2.1.0^{3,8}.0^{5,9}]heptadeca-3,5,7,15-tetraen-10-one (**24b**).* General procedure **C** was followed. From 0.26 g (0.62 mmol) of N-(2-(4-bromo-2-formylphenylamino)-2-oxoethyl)-N-(furan-2-ylmethyl)pivalamide (**14**) a mixture of 5-bromo-8-hydroxy-15-pivaloyl-12-oxa-1,15-diazatetracyclo[11.3.0.0^{2,7}.0^{9,13}]heptadeca-2,4,6,10-tetraen-17-one (**23a**) and 5-bromo-2-hydroxy-12-pivaloyl-17-oxa-9,12-diazatetracyclo[11.2.1.0^{3,8}.0^{5,9}]heptadeca-3,5,7,15-tetraen-10-one (**24a**) in the ratio of 1:1.4 was formed, which was introduced into the Suzuki coupling following the general procedure **D**. From 0.26 g of that mixture, pyridine-3-boronic acid (0.086 g, 0.70 mmol), $Pd_2(dba)_3$ (0.0063 g, 0.0069 mmol), PCy_3 (0.0046 g, 0.016 mmol), dioxane (2.0 mL), and aqueous K_3PO_4 (1.1 mmol, 0.84 mL of a 1.27 M solution) after chromatographic separation 0.050 g, (19%) of **23b** and 0.030 g (12%) of **24b** was obtained.

23b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, J = 4.3 Hz, 1H), 8.44 (s, 1H), 7.81 (ddd, J = 7.9, 2.4, 1.6 Hz, 1H), 7.75 (d, J = 8.3 Hz, 1H), 7.54 (dd, J = 8.3, 2.2 Hz, 1H), 7.34 (t, J = 7.8, 4.9 Hz, 1H), 7.32 (d, J = 2.2 Hz, 1H), 6.22 (t, J = 2.7 Hz, 1H), 5.09 (d, J = 18.7 Hz, 1H), 4.76 (dd, J = 3.1, 2.3 Hz, 1H), 4.75 (d, J = 2.2 Hz, 1H), 4.67 (dd, J = 13.9, 1.9 Hz, 1H), 4.14 (d, J = 18.7 Hz, 1H), 3.81 (d, J = 13.9 Hz, 1H), 3.70 (q, J = 2.3 Hz, 1H), 1.66 (s, 1H),1.36 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.5, 164.9, 148.4, 147.9, 146.9, 135.9, 135.5, 134.6, 134.3, 133.9, 127.9, 127.8, 127.2, 123.6, 99.8, 94.9, 68.9, 55.1, 51.7, 50.2, 38.9, 28.3. HRMS (ESI) calcd for $C_{24}H_{26}N_3O_4^+$ (MH^+) 420.1918, found 420.1921.

24b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.61 (s, 1H), 7.86 (ddd, J = 8.0, 2.4, 1.5 Hz, 1H), 7.52 (dd, J = 8.3, 2.2 Hz, 1H), 7.43 (d, J = 2.2 Hz, 1H), 7.38 (m, 2H), 6.31 (dd, J = 6.0, 1.8 Hz, 1H), 5.75 (dd, J = 5.9, 1.0 Hz, 1H), 5.16 (m, 1H), 4.92 (dd, J = 18.2, 1.6 Hz, 1H), 4.76 (d, J = 3.6 Hz, 1H), 4.68 (dd, J = 14.0, 1.6 Hz, 1H), 4.26 (d, J = 18.4 Hz, 1H), 3.96 (d, J = 14.0 Hz, 1H), 3.42 (s, 1H), 1.37 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.8, 166.1, 148.8, 148.1, 137.3, 136.3, 135.7, 135.2, 134.3, 134.1, 131.1, 130.3, 128.0, 126.9, 123.6, 96.9, 83.9, 79.1, 49.9, 49.7, 38.9, 28.3. HRMS (ESI) calcd for $C_{24}H_{26}N_3O_4^+$ (MH^+) 420.1918, found 420.1920.

*10-Hydroxy-5-pivaloyl-16-(pyridine-3-yl)-20-oxa-2,5-diazapentacyclo[9.7.1.1^{7,10}.0^{2,7}.0^{15,19}]icosa-1(19),8,15(16),17(18)-tetraene-3,5-dione (**26b**).* General procedure **C** was followed. From 0.43 g (0.93 mmol) of N-(2-(4-bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-ylamino)-2-oxoethyl)-N-(furan-2-ylmethyl)pivalamide (**15**) a mixture of 12-hydroxy-17-bromo-6-pivaloyl-8-oxa-2,5-diazapentacyclo-[10.7.1.0^{2,7}.0^{7,11}.0^{16,20}]icosa-1(20),9,16(17),18-tetraen-3,6-dione (**25a**) and 10-hydroxy-5-pivaloyl-16-bromo-20-oxa-2,5-diazapentacyclo-[9.7.1.1^{7,10}.0^{2,7}.0^{15,19}]icosa-1(19),8, 15(16),17(18)tetraen-3,5-dione (**26a**) in the ratio of 1:1.5 was formed, which was introduced into the Suzuki coupling following the general procedure **D.** From 0.43 g (0.93 mmol) of that mixture, using pyridine-3-boronic acid (0.21 g, 1.7 mmol), $Pd_2(dba)_3$ (0.020 g, 0.022 mmol), PCy_3 (0.015 g, 0.053 mmol), dioxane (3 mL), and aqueous K_3PO_4 (2.7 mmol, 2.1 mL of a 1.27 M solution) after chromatographic separation 0.086 g, (20%) of **26b** was obtained. **26b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, J = 3.8 Hz, 1H), 8.54 (s, 1H), 7.62 (dt, J = 7.9, 1.9 Hz, 1H), 7.37 (dd, J = 7.8, 4.8 Hz, 1H), 7.09 (m, 2H), 6.36 (dd, J = 5.9, 1.8 Hz, 1H), 5.80 (dd, J = 5.9, 0.9 Hz, 1H), 4.97 (d, J = 18.5 Hz, 1H), 4.73 (m, 2H), 4.30 (d, J = 18.3 Hz, 1H), 3.93 (d, J = 13.9 Hz, 1H), 3.48 (s, 1H), 2.59 (m, 1H), 2.47 (ddd, J = 17.4, 12.6, 5.5 Hz, 1H), 2.10 (m, 1H), 1.96 (m, 1H), 1.76 (m, 1H), 1.60 (dt, J = 13.5, 2.9 Hz, 1H), 1.39 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.8, 166.2, 149.8, 148.4, 138.4, 137.1, 136.9, 136.5, 136.2, 135.6, 135.2, 129.2, 128.6, 128.2, 123.2, 96.3, 88.4, 75.3, 49.9, 49.1, 38.9, 36.2, 30.4, 28.3, 17.8. HRMS (ESI) calcd for $C_{27}H_{30}N_3O_4^+$ (MH^+) 460.2231, found 460.2234.

*10-Hydroxy-5-benzyl-16-(pyridin-3-yl)-20-oxa-2,5-diazapentacyclo[9.7.1.1^{7,10}.0^{2,7}.0^{15,19}]icosa-1(19),8,15(16),17(18)-tetraene-3,5-dione (**28b**).* General procedure **C** was followed. From 0.81 g (1.7 mmol) of N-benzyl-N-(2-(4-bromo-8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl- amino)-2-oxoethyl)furan-2-carboxamide (**16**) a mixture of 12-hydroxy-17-bromo-6-benzyl-8-oxa-2,5-diazapentacyclo [10.7.1.0^{2,7}.0^{7,11}.0^{16,20}]icosa-1(20),9,16(17),18-tetraen-3,6-dione (**27a**) and 10-hydroxy-5-benzyl-16-bromo-20-oxa-2,5-diazapentacyclo-[9.7.1.1^{7,10}.0^{2,7}.0^{15,19}]icosa-1(19),8,15(16),17(18)tetraen-3,5-dione (**28a**) in the ratio of 1:16 was formed, which was then introduced into the Suzuki coupling following the general procedure **D** From 0.20 g of that mixture, pyridine-3-boronic acid (0.081 g, 0.66 mmol), $Pd_2(dba)_3$

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(0.0090 g, 0.022 mmol), PCy_3 (0.0066 g, 0.024 mmol), dioxane (1.2 mL), and aqueous K_3PO_4 (0.42 mmol, 0.56 mL of a 1.27 M solution) upon chromatographic separation 0.072 g, (36%) of **28b** was obtained. **28b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (dd, J = 5.0, 1.7 Hz, 1H), 8.51 (m, 1H), 7.62 (dt, J = 7.8, 2.0 Hz, 1H), 7.40 (m, 6H), 7.13 (d, J = 8.0 Hz, 1H), 7.04 (d, J = 7.9 Hz, 1H), 6.40 (dd, J = 6.0, 1.8 Hz, 1H), 6.10 (d, J = 5.9 Hz, 1H), 4.96 (d, J = 14.5 Hz, 1H), 4.87 (m, 1H), 4.57 (d, J = 14.5 Hz, 1H), 4.40 (d, J = 18.2 Hz, 1H), 4.11 (d, J = 18.2 Hz, 1H), 3.16 (s, 1H), 2.59 (m, 1H), 2.47 (ddd, J = 17.5, 12.6, 5.4 Hz, 1H), 2.11 (m, 1H), 1.96 (qdd, J = 13.2, 4.9, 2.5 Hz, 1H), 1.79 (m, 1H), 1.64 (td, J = 13.4, 3.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 162.5, 149.8, 148.6, 139.2, 136.9, 136.8, 136.4, 136.1, 135.8, 135.7, 134.6, 129.8, 129.1, 128.5, 128.5, 128.5, 128.4, 123.1, 96.5, 89.6, 75.8, 49.9, 49.8, 36.3, 30.2, 17.7. HRMS (ESI) calcd for $C_{29}H_{26}N_3O_4^+$ (MH^+) 480.1918, found 480.1927.

*8-Hydroxy-5-(thiophen-2-yl)-12-oxa-1-azatetracyclo-[11.3.0.0^{2,7}.0^{9,13}]hexadeca-2,4,6,10-tetraen-12-one (**4h**) and 2-Hydroxy-5-(thiophen-2-yl)-16-oxa-9-azatetracyclo[11.2.1.0^{3,8}.0^{5,9}]-hexadeca-3,5,7,14-tetraen-10-one (**5h**).* General procedure **C** was followed. From (0.42 g, 1.1 mmol) of N-(2-Formyl-4-iodophenyl)-3-(furan-2-yl)propanamide (**3d**) a mixture of 8-hydroxy-5-iodo-2-yl-12-oxa-1-azatetracyclo[11.3.0.0^{2,7}.0^{9,13}]hexadeca-2,4,6,10-tetraen-12-one (**4d**) and 2-hydroxy-5-iodo-16-oxa-9-azatetracyclo[11.2.1.0^{3,8}.0^{5,9}]-hexadeca-3,5,7,14-tetraen-10-one (**5d**) in the ratio 1:1 was formed, which was introduced into the Suzuki coupling following the general procedure **F**. From 0.20 g (0.54 mmol) of that mixture, $Pd(PPh_3)_4$ (0.032 g, 0.028 mmol), thiophene-2-boronic acid (0.077 g, 0.60 mmol), $NaHCO_3$ (0.095 g, 1.1 mmol) in H_2O (16 mL) upon chromatographic separion 0.030 g (17%) of **4h** and 0.044 g (26%) of **5h**

4h:^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, J = 8.3 Hz, 1H), 7.66 (dd, J = 8.3, 2.2 Hz, 1H), 7.48 (d, J = 2.2 Hz, 1H), 7.31 (s, 1H), 7.30 (m, 1H), 7.10 (dd, J = 5.0, 3.7 Hz, 1H), 6.28 (t, J = 2.8 Hz, 1H), 4.83 (t, J = 2.5 Hz, 1H), 4.70 (dd, J = 3.1, 2.2 Hz, 1H), 3.89 (q, J = 2.3 Hz, 1H), 2.88 (ddd, J = 16.6, 10.6, 8.2 Hz, 1H), 2.60 (m, 1H), 2.54 (dd, J = 16.5, 8.9 Hz, 1H), 2.45 (ddd, J = 12.7, 10.6, 8.9 Hz, 1H), 1.90 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 146.7, 143.3, 133.4, 132.0, 131.3, 128.1, 127.0, 126.2, 125.0, 123.6, 123.3, 101.3, 99.3, 70.4, 55.9, 35.1, 29.8. HRMS (ESI) calcd for $C_{18}H_{15}LiNO_3S^+$ (MLi^+) 332.0927, found 332.0935.

5h: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (dd, J = 8.4, 2.2 Hz, 1H), 7.55 (m, 2H), 7.31 (m, 2H), 7.10 (dd, J = 5.1, 3.6 Hz, 1H), 6.36 (dd, J = 5.8, 1.9 Hz, 1H), 5.70 (dd, J = 5.9, 1.1 Hz, 1H), 5.07 (m, 1H), 4.72 (dd, J = 10.8, 3.3 Hz, 1H), 2.93 (m, 2H), 2.69 (ddd, J = 17.4, 9.8, 1.9 Hz, 1H), 2.58 (m, 1H), 2.49 (ddd, J = 13.9, 9.5, 1.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 143.0, 134.7, 133.6, 132.9, 131.9, 131.6, 129.9, 129.3, 128.1, 126.0, 125.2, 123.4, 103.6, 83.6, 79.3, 30.1, 28.9. HRMS (ESI) calcd for $C_{18}H_{15}LiNO_3S^+$ (MLi^+) 332.0927, found 332.0931.

*5-(Furan-2-yl)-8-hydroxy-12-oxa-1-azatetracyclo-[11.3.0.0^{2,7}.0^{9,13}]hexadeca-2,4,6,10-tetraen-12-one (**4g**) and 4-(Furan-2-yl)-15-hydroxy-16-oxa-8-azatetracyclo[10.3.1.0^{2,7}.0^{8,12}]-hexadeca-2,4,6,13-tetraen-9-one (**29**).* General procedure **C** was followed. From (0.31 g, 0.84 mmol) of N-(2-Formyl-4-iodophenyl)-3-(furan-2-yl)propanamide (**3d**) 0.31 g of a mixture of 8-hydroxy-5-iodo-12-oxa-1-azatetracyclo[11.3.0.0^{2,7}.0^{9,13}]hexadeca-2,4,6,10-tetraen-12-one (**4d**) and 2-hydroxy-5-iodo-16-oxa-9-azatetracyclo-[11.2.1.0^{3,8}.0^{5,9}]hexadeca-3,5,7,14-tetraen-10-one (**5d**) in the ratio of 2.9:1 was formed, which was introduced into the Suzuki coupling following the general procedure **F**. From 0.31 g (0.83 mmol)of that mixture, $Pd(PPh_3)_4$ (0.056 g, 0.048 mmol), furan-2-boronic acid (0.11 g, 0.98 mmol), $NaHCO_3$ (0.16 g, 1.9 mmol) in water (27 mL) upon chromatographic separation 0.068 g (27%) of **4g** and 0.10 g (39%) of an inseparable mixture of 5-(furan-2-yl)-2-hydroxy-16-oxa-9-azatetracyclo[11.2.1.0^{3,8}.0^{5,9}]hexadeca-3,5,7,14-tetraen-10-one (**5g**) and **29** was isolated. The latter mixture of **5g** and **29** (0.093 g, 0.30 mmol) was dissolved in 4 mL of DMSO and heated at 160 °C for 60 min. Upon cooling the solvent was removed under reduced pressure and subjected to chromatographic separation yielding 0.043 g of **29**.

5g: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 8.4 Hz, 1H), 7.70 (dd, J = 8.4, 2.0 Hz, 1H), 7.57 (d, J = 2.0 Hz, 1H), 7.48 (dd, J = 1.8, 0.7 Hz, 1H), 6.66 (dd, J = 3.3, 0.8 Hz, 1H), 6.50 (dd, J = 3.4, 1.8 Hz, 1H), 6.26 (t, J = 2.8 Hz, 1H), 4.83 (d, J = 2.2 Hz, 1H), 4.68 (dd, J = 3.0, 2.2 Hz, 1H), 3.88 (m, 1H), 2.87 (ddd, J = 16.3, 10.4, 8.2 Hz, 1H), 2.52 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 153.1, 146.7, 142.2, 133.2, 131.2, 128.5, 125.0, 124.0, 123.5, 111.8, 105.2, 101.4, 99.3, 70.4, 55.9, 35.1, 29.8. HRMS (ESI) calcd for $C_{18}H_{16}NO_4^+$ (MH^+) 310.1074, found 310.1081.

29: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, J = 8.7 Hz, 1H), 7.63 (dd, J = 8.6, 2.0 Hz, 1H), 7.51 (d, J = 2.0 Hz, 1H), 7.48 (dd, J = 1.9, 0.8 Hz, 1H), 6.64 (dd, J = 3.4, 0.8 Hz, 1H), 6.50 (dd, J = 3.4, 1.8 Hz, 1H), 6.11 (ddd, J = 9.7, 5.3, 1.2 Hz, 1H), 5.86 (m, 1H), 5.23 (s, 1H), 4.03 (d, J = 5.2 Hz, 1H), 2.74 (m, 2H), 2.40 (m, 2H), 2.28 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 153.1, 142.2, 131.6, 129.5, 127.1, 127.0, 124.1, 123.5, 120.6, 120.2, 111.8, 105.0, 86.1, 78.1, 66.8, 30.3, 29.9. HRMS (ESI) calcd for $C_{18}H_{15}LiNO_4^+$ (MLi^+) 316.1156, found 316.1164.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra and XRay 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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