Regiospecific Synthesis of Novel Cyclic Nitrostyrenes and 3-Substituted 2-Nitronaphthalenes

Craig Keene, László Kürti*

Division of Chemistry, Department of Biochemistry, UT Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas TX 75390, USA
Fax +1(214)6488856; E-mail: laszlo.kurti@utsouthwestern.edu

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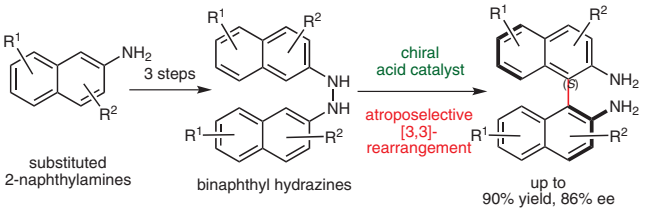
Abstract: A two-step, practical, regiospecific, and readily scalable benzannulation protocol for the preparation of novel 3-alkyl- and 3-aryl-substituted 2-nitronaphthalenes is disclosed. Addition of a β-nitrostyrene or nitroalkene to a solution of freshly prepared lithiated *o*-tolualdehyde *tert*-butyl imine first leads to the formation of a nitronate, via rapid 1,4-addition, then an intramolecular aza-Henry reaction takes place to afford a six-membered carbocycle. Subsequent treatment of the reaction mixture with aqueous acid affords novel substituted cyclic nitrostyrenes that can be conveniently aromatized via a one-pot radical-induced bromination and elimination sequence to furnish the corresponding 3-alkyl- or 3-aryl-2-nitronaphthalenes in excellent yields. The straightforward syntheses of 2-aminonaphthalenes, substituted BINAMs, 2-naphthols as well as tricyclic fused 1,2,3-triazoles are also described.

Key words: cyclic nitrostyrene, 2-nitronaphthalene, 2-aminonaphthalene, BINAM, fused triazole

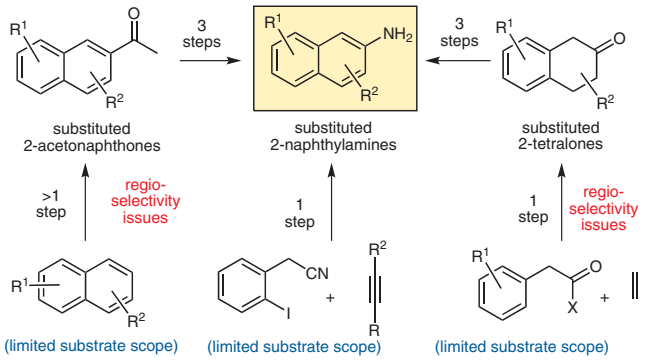
Our group is pursuing the development of powerful and practical new methods for the synthesis of highly functionalized symmetrical and unsymmetrical biaryls. Given the remarkable track record of axially chiral biaryls as highly efficient ligands in asymmetric synthesis, it is clear that convenient synthetic access to many structurally diverse and uniquely functionalized biaryls will have a profound impact on the discovery of new chemical reactivity.

The first scalable organocatalytic atroposelective synthesis of BINAM derivatives was recently demonstrated in our laboratory utilizing a remarkably efficient [3,3]-sigmatropic rearrangement of binaphthyl hydrazines in the presence of 5–20 mol% chiral acid catalysts (Scheme 1).[1] The required binaphthyl hydrazine substrates were prepared from the corresponding substituted 2-naphthylamines via a three-step procedure[2] that involved: (a) diazotization, (b) reduction of the diazonium salt to the corresponding symmetrical azo compound, and (c) reduction of the azo group with Zn/NH_4Cl. However, a convenient and readily scalable synthetic access to a wide variety of substituted 2-naphthylamines, especially to 3-alkyl- and 3-aryl-2-naphthylamines, remains a significant challenge.



Scheme 1 The first scalable organocatalytic atroposelective synthesis of BINAM derivatives

Traditional routes to substituted 2-naphthylamines begin from a limited selection of 2-acetonaphthones or 2-tetralones and require three or more steps to prepare the target molecules (Scheme 2); the overall yields are generally low to moderate to (25–50%).[1,3] A more recent route to substituted 2-naphthylamines involves the transition-metal-catalyzed cross-coupling of internal alkynes with (2-iodophenyl)acetonitrile; while the isolated yield and the regioselectivity are both good, the structural diversity of the products is narrow, which limits the usefulness of this approach.[4]



Scheme 2 Traditional and more recent routes for the preparation of substituted 2-naphthylamines

After we have prepared several 2-naphthylamine substrates using both the traditional and newer routes, it became clear that a new synthetic approach had to be developed that addresses the shortcomings of existing methods. In particular we had difficulties with the preparation of multi-gram quantities of substituted 2-naphthylamines since several steps failed to work efficiently on larger scale (>10 mmol). Therefore, we decided to develop a convergent route to achieve the rapid and practical synthesis of a variety of 3-substituted 2-naphthylamines.

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Three de novo synthetic approaches to substituted naphthalenes **I**–**III** that rely on tandem 1,4-addition/intramolecular cyclization steps are highlighted in Scheme 3.[5] These methods deliver useful functionalized naphthalene derivatives, however, the aromatic starting materials are highly specialized, the reaction conditions are often harsh, and the isolated yields range from moderate to low. Notwithstanding the above mentioned drawbacks, we were inspired by these tandem approaches when our two-step regiospecific benzannulation protocol was designed (Scheme 3).

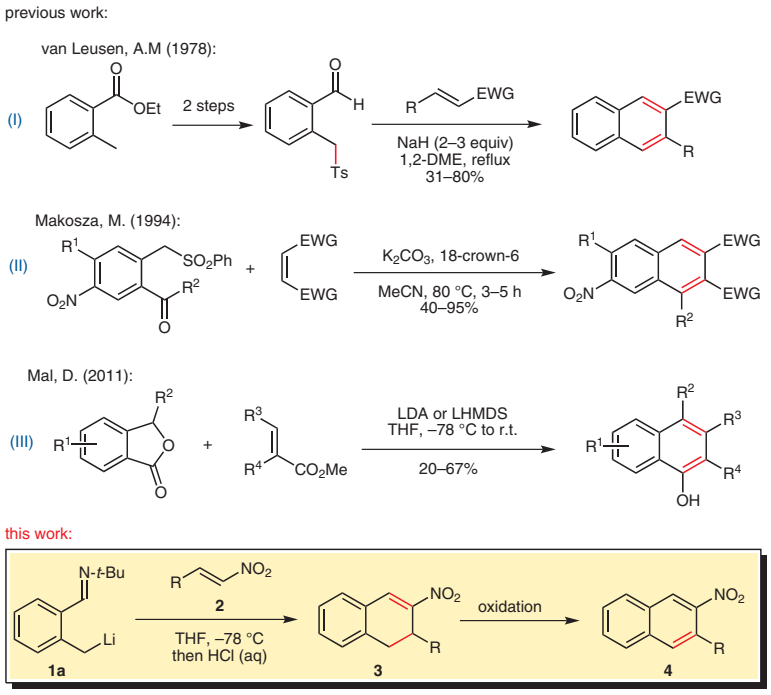
We decided to use the readily available lithiated *o*-tolualdehyde *tert*-butyl imine[6] **1a** as our starting material. This benzylic lithium species has been shown recently by Myers to be an excellent nucleophile that easily adds across the carbon–nitrogen triple bond in aromatic nitriles to afford substituted isoquinolines.[7] Our hypothesis was that β-nitrostyrenes/nitroalkenes **2** should also readily react with **1a** and, upon acidic workup, should yield novel cyclic nitrostyrenes **3**, even though these electrophiles have not been previously reported to undergo this cyclization. Likewise, it appeared reasonable that upon oxidation, cyclic nitrostyrenes **3** would furnish the corresponding 3-substituted 2-nitronaphthalenes **4**. β-Nitrostyrenes and nitroalkenes were selected as coupling partners for three important reasons: (a) they may be readily prepared from inexpensive precursors in decagram to kilogram quantities; (b) the nitro group will occupy the 2-position in the new bicyclic system and thus it perfectly maps on the structure of 2-aminonaphthalenes; and (c) the nitro group is often referred to as a chemical chameleon due to its extraordinary versatility as a functional group, therefore, it will allow the introduction of many other useful functionalities on the naphthalene nucleus.[8]

Benzylic lithium species **1a** was prepared from *o*-tolualdehyde *tert*-butyl imine (**1**) based on conditions described earlier:[6] stoichiometric *n*-butyllithium is added over 30–40 minutes to a solution of **1** and catalytic amounts (15 mol%) of 2,2,6,6-tetramethylpiperidine (TMP) in THF at 0 °C (Table 1). The resulting lateral-lithiated species **1a** forms a deep-purple solution, which is then aged for 45 minutes before cooling to –78 °C. Next, the solution of a particular nitroalkene **2a**–**l** in THF is added over 10 minutes and the reaction mixture is stirred for an additional 30 to 60 minutes. Water is then added into the mixture followed by excess (4 equiv) of concentrated aqueous HCl solution.

Biographical Sketches

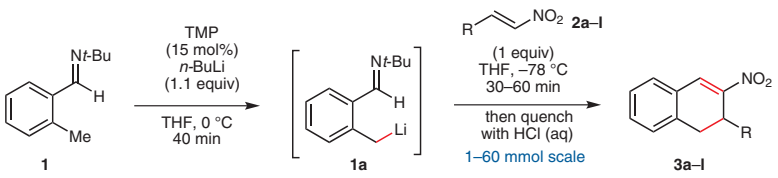
László Kürti was born and raised in Hungary and received his Diploma from the University of Debrecen, Hungary where he conducted research in the laboratory of Professor Sándor Antus. Subsequently, he received his MS degree at the University of Missouri-Columbia working with Professor Michael Harmata, and his Ph.D. degree (2006) in synthetic organic chemistry under the supervision of Professor Amos B. Smith III (University of Pennsylvania). After completing his postdoctoral training (2006–2010) as a Damon Runyon Cancer Fellow in the group of Professor E. J. Corey at Harvard University, he began his independent career at UT Southwestern Medical Center in Dallas in September 2010. László's current research interests include the development of new strategies for the atroposelective synthesis of structurally divserse biaryls that will serve as novel ligands and catalysts as well as transition-metal-free C–C and C–N bond-forming processes for the rapid assembly of heterocyclic compounds to aid drug discovery. He is the co-author of three widely used textbooks/reference books. In 2005 he published with Barbara Czakó the textbook *Strategic Applications of Named Reactions in Organic Synthesis*, in 2007 with Professor Corey the textbook *Molecules and Medicine*, and in 2010 the textbook/reference book *Enantioselective Chemical Synthesis: Methods, Logic and Practice*.

Craig Keene was born in 1988 in Dallas, Texas. He began his studies in Biology at Texas Tech University (Lubbock, Texas) in 2006 and obtained his Bachelor's degree in 2010. In 2011 he joined the graduate program at UT Southwestern Medical Center and since 2012, has been a Ph.D. student in the Kürti Laboratory. His research interests are centered around the development of new synthetic methods for the construction of novel functionalized biaryls, heterocycles, and biomolecules.



Scheme 3 Representative de novo synthetic approaches **I**–**III** to substituted naphthalenes, including our two-step, regiospecific, and scalable benzannulation protocol

Table 1 Synthesis of Novel Cyclic Nitrostyrenes



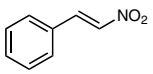
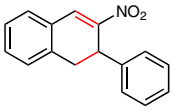
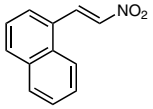
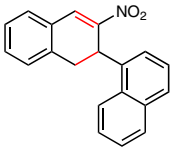
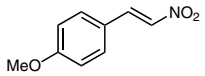
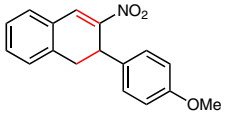
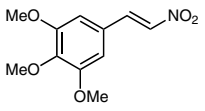
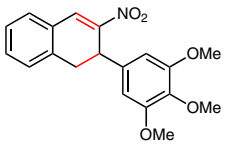
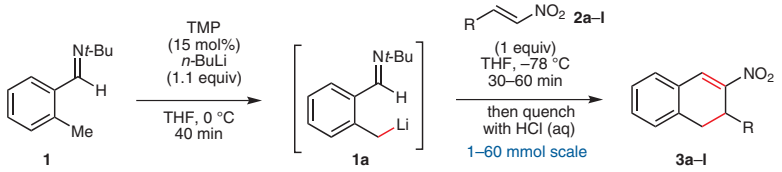
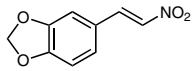
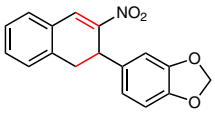
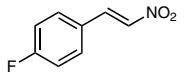
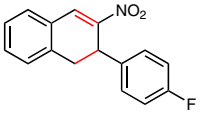
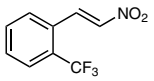
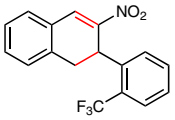
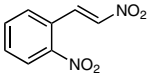
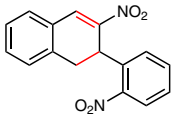
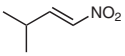
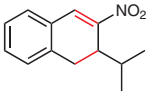
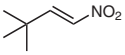
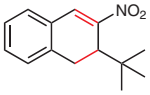
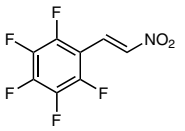
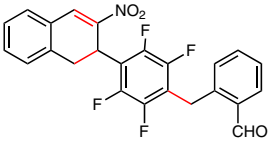
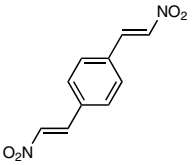
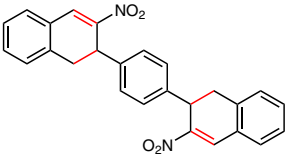
Entry	Nitroalkene		Product		Yield (%)[a]
1[b]	**2a**		**3a**		76
2[c]	**2b**		**3b**		42
3[c]	**2c**		**3c**		67
4[d]	**2d**		**3d**		84

Table 1 Synthesis of Novel Cyclic Nitrostyrenes (continued)



Entry	Nitroalkene		Product		Yield (%)[a]
5[c]	**2e**		**3e**		82
6[c]	**2f**		**3f**		62
7[e]	**2g**		**3g**		52
8[c,f]	**2h**		**3h**		56
9[c]	**2i**		**3i**		54
10[c]	**2j**		**3j**		53
11[e,g]	**2k**		**3k**		57
12[e,g]	**2l**		**3l**		42

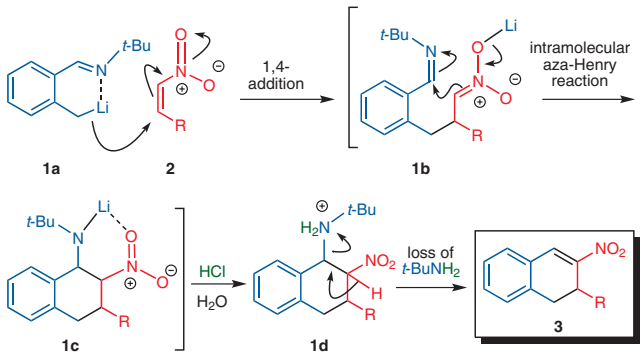
[a] Isolated yield.
[b] Reaction carried out on a 60 mmol scale.
[c] Reaction carried out on a 20–25 mmol scale.
[d] Reaction carried out on a 30 mmol scale.
[e] Reaction carried out on a 9–10 mmol scale.
[f] Substrate **1a** was transmetalated with CuBr before the addition of **2h**.
[g] Two equivalents of **1** were used.

The acidified reaction mixture is then warmed to room temperature and subsequently neutralized with aqueous sodium carbonate solution. Following extraction and chromatographic purification, cyclic nitrostyrenes **3a**–**l** are isolated as yellow crystalline solids (Table 1).

The highest yields of cyclic nitrostyrenes **3** were achieved when employing electron-rich β-nitrostyrenes **2c**–**e** as coupling partners (Table 1, entries 4 and 5), while electron-poor β-nitrostyrenes **2f**–**h** furnished the cyclized products in somewhat lower yields (entries 6–8). It is noteworthy that *o*-nitro-substituted β-nitrostyrene **2h** did not undergo the parent transformation, the reaction instead led to a complex mixture of inseparable products. Presumably, the presence of two nitro groups leads to

many side-reactions that usually take place via complex electron-transfer processes. However, by transmetalating **1a** with 1 equivalent of CuBr, the 1,4-addition step proceeded more cleanly; apparently fewer side reactions took place. We were pleased to observe that nitroalkenes **2i** and **2j** worked well as substrates demonstrating that besides substituted aromatic rings, alkyl substituents may also be introduced. When pentafluoronitrostyrene **2k** (entry 11) was used as the coupling partner, in addition to the expected 1,4-addition/cyclization, a nucleophilic aromatic substitution reaction (S_NAr) also took place to furnish **3k**. We presume that the S_NAr reaction is faster than the tandem 1,4-addition/intramolecular aza-Henry reaction of **1a** with **2k**. Indeed, we were unable to isolate even trace amounts of the expected C_6F_5-substituted cyclic nitrostyrene product; this compound, however, does not undergo S_NAr reaction as it is no longer activated for this transformation.

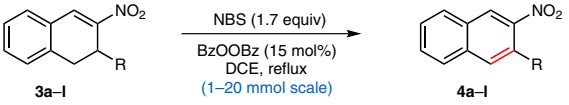
The formation of cyclic nitrostyrenes **3** from **1a** and **2** is rationalized by a mechanism proposed in Scheme 4. At low temperature, benzylic lithium species **1a** rapidly adds to **2** in a 1,4-fashion to generate a nitronate intermediate **1b**, which in turn undergoes an intramolecular aza-Henry reaction to form a six-membered carbocycle **1c**. When the reaction mixture is treated with aqueous acid, the strongly basic nitrogen atom in **1c** is protonated and a facile elimination of *tert*-butylamine takes place to afford the cyclic nitrostyrene **3**.



Scheme 4 Proposed mechanism for the formation of **3** from **1a** and **2** via a tandem 1,4-addition/intramolecular aza-Henry reaction process

By securing multi-gram quantities of cyclic nitrostyrenes **3a–l** (Table 1), the stage was set for their conversion into the corresponding 3-substituted 2-nitronaphthalenes **4**. We were surprised to find that these compounds were remarkably stable towards aromatization via oxidative methods; traditional methods of aromatization (e.g., dehydrogenation involving Pd/C and DDQ) were largely unsuccessful.[9] Only minimal conversion into the corresponding 2-nitronaphthalenes **4** was observed even after 48 hours at reflux temperatures in high-boiling solvents (i.e., chlorobenzene, xylenes). We hypothesized that the introduction of a bromine atom at the benzylic position of compounds **3a–l** would lead to derivatives in which HBr elimination would be facile. We were delighted to find that bromination of cyclic nitrostyrenes **3a–l** under radical conditions using catalytic amounts (15 mol%) of dibenzoyl peroxide and excess *N*-bromosuccinamide (1.7 equiv) at elevated temperatures (>80 °C) in DCE furnished the corresponding 3-substituted 2-nitronaphthalenes **4a–l** in excellent isolated yields (Table 2). It should be noted that compounds **3e** and **3l** did not undergo aromatization under these conditions; complex mixtures of products were obtained instead.

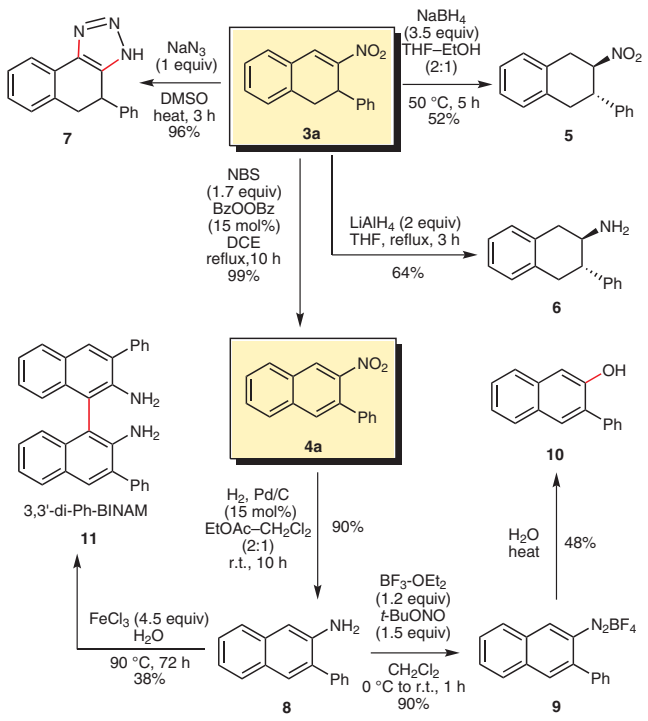
Table 2 Aromatization of Cyclic Nitrostyrenes to the Corresponding 3-Substituted 2-Nitronaphthalenes



Entry[a,b]	Substrate **3**	Time (h)	Yield of **4** (%)
1[c]	**3a**	10	99
2[d]	**3b**	11	99
3	**3c**	14	74
4	**3d**	15	98
5	**3e**	12	0
6[e]	**3f**	16	96
7	**3g**	13	95
8[e]	**3h**	1	95
9[f]	**3i**	10	96
10[f]	**3j**	18	85
11	**3k**	14	32
12	**3l**	6	0

[a] Reactions were performed on a 1 mmol scale unless indicated otherwise.
[b] Reaction times exceeding 12 h lead to the formation of some denitrated product.
[c] Reaction carried out on a 20 mmol scale.
[d] Reaction carried out on a 6.5–7 mmol scale.
[e] Reaction carried out on a 3–4.5 mmol scale.
[f] Reaction carried out on a 9–10 mmol scale.

The synthetic utility of the novel cyclic nitrostyrene **3** and 3-substituted 2-nitronaphthalene **4** products was explored next. For this purpose compounds **3a** and **4a** were selected as representative substrates (Scheme 5, isolated yields are shown). The 1,4-reduction[10] of compound **3a** with $NaBH_4$ cleanly gave the corresponding cyclic nitroalkane **5**, while reduction with $LiAlH_4$ furnished an interesting cyclic amphetamine analogue **6**. Heating **3a** with NaN_3 in DMSO afforded a previously unknown fused 1,2,3-triazole **7** in nearly quantitative yield.[11]



Scheme 5 Synthetic utility of cyclic nitrostyrenes and 3-substituted 2-nitronaphthalenes

The nitro group is stable towards a variety of oxidizing reagents and conditions, whereas the amino group tends to undergo facile oxidation even when exposed to air. For this reason, 2-nitronaphthalenes are excellent surrogates to 2-aminonaphthalenes, which are known to undergo air oxidation. A mild Pd/C-catalyzed hydrogenation of **4a** in a mixture of dichloromethane and ethyl acetate gave 3-phenyl-2-naphthylamine (**8**) in high yield (Scheme 5); this approach to **8** is significantly more effective than those reported in the past.[12] Preparation of 3-phenyl-2-naphthol[13] (**10**) could also be achieved via a highly stable diazonium tetrafluoroborate salt **9**.[14] Finally, we were excited to find that treatment of **8** with iron(III) chloride afforded 3,3′-diphenyl-BINAM (**11**).[15] This transformation proceeds very cleanly; however, liberation of **11** from its various Fe(III) complexes is nontrivial and has not yet been optimized. It is anticipated that other 3-aryl- and 3-alkyl-substituted 2-aminonaphthalenes will undergo similar oxidative dimerization to afford 3,3′-disubstituted 2,2′-diaminonaphthalenes.

In summary, we have developed a two-step, practical, regiospecific, and readily scalable benzannulation method for the preparation of 3-substituted 2-nitronaphthalenes **4** via novel cyclic nitrostyrenes **3**. These products are synthetically versatile as they can be converted into many other valuable compounds such as substituted 2-aminonaphthalenes, BINAMs, 2-naphthols, and fused 1,2,3-triazoles. In the past, the preparation of substituted 2-aminonaphthalenes was a significant synthetic challenge as the various routes often required several steps, suffered from regioselectivity issues, limited scope of substrates, and poor material throughput (i.e., due to the generally low overall yields). The novel synthetic approach that is presented in this manuscript addresses all of these issues effectively. The homo-and heterocoupling of 3-substituted 2-aminonaphthalenes to the corresponding enantiomerically enriched BINAM derivatives as well as the efficient conversion of **3** and **4** into a number of structurally diverse functionalized biaryls are currently underway in our laboratory.

All reactions were carried out in oven-dried glassware under an atmosphere of argon with magnetic stirring. All reagents, including the aromatic aldehydes, TMP, and nitromethane were purchased from Sigma-Aldrich Co. and used without further purification. Solvents were dried by passage through an activated alumina column under argon. Liquids and solutions were transferred via syringe. All reactions were monitored by TLC with E. Merck silica gel 60 F254 precoated plates (0.25 mm). Silica gel (particle size 0.032–0.063 mm) purchased from SiliCycle was used for flash chromatography.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV-400 spectrometer operating at 400 MHz for proton and 100 MHz for carbon nuclei using $CDCl_3$ as solvent, respectively. Chemical shifts are expressed as parts per million (δ, ppm) and are referenced to 7.26 ($CDCl_3$) for ^{1}H NMR and 77.00 ($CDCl_3$) for ^{13}C NMR. Standard abbreviations are used to denote signal multiplicities. High-resolution mass spectrometry was performed on a Shimadzu LCMS-IT-TOF under the conditions of electrospray ionization (ESI) in both positive and negative mode. IR spectra were recorded on a Shimadzu IRPrestige-21 (FT-IR Spectrophotometer).

o-Tolualdehyde *tert*-Butyl Imine (1)

A 500 mL round-bottom flask was charged with *o*-tolualdehyde (5.96 mL, 50 mmol, 1 equiv), *tert*-butylamine (11.56 mL, 110 mmol, 2.2 equiv), and toluene (50 mL). The resulting solution was heated at reflux for 6 h. The solution was then allowed to cool to r.t. and the solvent was removed in vacuo. Purification was performed by vacuum distillation (70–73 °C/0.6 mmHg), which afforded **1** as a colorless oil; yield: 8.41 g (96%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.61 (s, 1 H), 7.89 (dd, J_1 = 7.4 Hz, J_2 = 1.7 Hz, 1 H), 7.32–7.22 (m, 2 H), 7.20–7.16 (m, 1 H), 2.52 (s, 3 H), 1.35 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.7, 137.0, 135.1, 130.5, 129.6, 127.0, 126.1, 57.5, 29.7, 19.1.

NMR spectra are in agreement with the published values.[16]

β-Nitrostyrenes 2a–l; *trans*-β-Nitrostyrene (2a); Typical Procedure

β-Nitrostyrenes **2a–l** were prepared according to the typical procedure detailed below for compound **2a**.

A 500 mL round-bottom flask, equipped with a mechanical stirrer and an internal thermocouple, was charged with benzaldehyde (50.5 mL, 500 mmol, 1 equiv), nitromethane (28.3 mL, 500 mmol, 1 equiv), and reagent grade MeOH (100 mL). The resulting solution was then cooled to 0 °C in an ice bath. Next, a solution of NaOH (20 g, 500 mmol, 1 equiv) in H_2O (20 mL) was then added dropwise at a rate so that the internal temperature does not rise above 15 °C. After the addition of the NaOH solution was complete, the resulting thick white paste was stirred for an additional 15 min before ice water (200 mL) was added; most of the white solid dissolved as a result. The reaction mixture was then transferred to a 500 mL separatory funnel and slowly added to a 2 L Erlenmeyer equipped with a stir bar and containing a solution of aq HCl [prepared from concd HCl (37%, 150 mL) and H_2O (150 mL)]. After the transfer was complete, stirring was continued for an additional 15–30 min during which time a precipitate was formed. The precipitate was then filtered, washed with H_2O (75 mL), and air dried in vacuo. Recrystallization from EtOH afforded 46.2 g of *trans*-β-nitrostyrene

(**2a**) as yellow needles; yield: 46.2 g (62%); mp 55–58 °C (Lit.[17] mp 55–58 °C).

Cyclic Nitrostyrenes 3a–l; General Procedure

o-Tolualdehyde imine **1** (3.51 g, 20 mmol, 1 equiv) was mixed with of 2,2,6,6-tetramethylpiperidine (0.5 mL, 15 mol%) and anhyd THF (20 mL). The solution was then transferred to a flame-dried 100 mL round-bottom flask equipped with a magnetic stir bar and an internal thermocouple, and cooled to 0 °C in an ice bath. Next a solution of 1.6 M *n*-BuLi in hexanes (13.13 mL, 21 mmol, 1.05 equiv) was added dropwise via syringe pump so that the internal temperature was never allowed to rise above 0 °C. When the addition was complete, the resulting deep-purple solution was allowed to stir at 0 °C for an additional 40 min and then cooled to –70 °C in a dry ice/acetone bath. Next, a solution of a particular nitroalkene **2** (20 mmol, 1 equiv) in THF (20 mL) was added at –70 °C over 5 min. The reaction mixture was stirred for an additional 30 to 60 min until the starting materials had all been consumed (as shown by TLC analysis, eluent: EtOAc–hexanes). H_2O (10 mL, 0.5 mL/mmol of substrate) was then injected rapidly into the flask (over 30 sec), followed by concd HCl (37%, 6.5 mL) causing a rapid increase in temperature to about –10 °C. The quenched reaction mixture was allowed to warm to r.t. by placing the flask into a Dewar filled with H_2O, and an additional 30 min of stirring was performed at r.t. Excess HCl was neutralized with a solution of sat. aq Na_2CO_3 (100 mL) and the biphasic reaction mixture was extracted with CH_2Cl_2 (4 × 100 mL). The combined organic layers were dried ($MgSO_4$), filtered, and the solvent was removed in vacuo. The crude product was purified via column chromatography (EtOAc–hexanes).

3a

Reaction was carried out on a 60 mmol scale; yield: 11.3 g (76%); yellow crystalline needles; mp 132.6–134.6 °C; R_f = 0.2 (5% EtOAc–hexanes).

IR (ATR): 1641, 1504, 1492, 1454, 1315 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.13 (s, 1 H), 7.44 (dd, J_1 = 7.1 Hz, J_2 = 1.8 Hz, 2 H), 7.36–7.31 (m, 2 H), 7.22–7.19 (m, 3 H), 7.14–7.11 (m, 3 H), 4.56 (dd, J_1 = 8.7 Hz, J_2 = 1.7 Hz, 1 H), 3.65 (dd, J_1 = 16.4 Hz, J_2 = 8.7 Hz, 2 H), 3.16 (dd, J_1 = 16.4 Hz, J_2 = 1.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.77, 139.96, 134.65, 132.28, 131.75, 130.10, 129.72, 128.66, 128.58, 127.44, 127.31, 126.67, 38.20, 37.04.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{13}NO_2$ $(M + H)^+$: 252.1019; found: 252.1027.

3b

Reaction was carried out on a 20 mmol scale; yield: 2.53 g (42%); yellow solid; mp 183.2–186.5 °C; R_f = 0.2 (5% EtOAc–hexanes).

IR (ATR): 1634, 1568, 1495, 1308, 1227 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.33 (s, 1 H), 8.29 (d, J_1 = 8.55 Hz, 1 H), 7.90 (d, J_1 = 12 Hz, 1 H), 7.71–7.64 (m, 2 H), 7.56 (ddd, J_1 = 8.0 Hz, J_2 = 6.8 Hz, J_3 = 1.1 Hz, 1 H), 7.48 (dd, J_1 = 7.20 Hz, J_2 = 1.70 Hz, 1 H), 7.30–7.24 (m, 2 H), 7.18 (dd, J_1 = 8.20 Hz, J_2 = 7.20 Hz, 1 H), 7.01 (dd, J_1 = 7.20 Hz, J_2 = 1.20 Hz, 1 H), 6.94 (d, J_1 = 8 Hz, 1 H), 5.45 (d, J_1 = 9.0 Hz, 1 H), 3.73 (dd, J_1 = 8 Hz, J_2 = 8 Hz, 1 H), 3.25 (dd, J_1 = 16.3 Hz, J_2 = 1.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.30, 134.71, 134.50, 133.91, 133.60, 131.73, 130.24, 130.21, 129.60, 129.25, 128.87, 127.98, 127.47, 126.49, 125.67, 125.16, 122.96, 122.78, 36.06, 33.61.

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{15}NO_2$ + Na $(M + Na)^+$: 324.0995; found: 324.0981.

3c

Reaction was carried out on a 20 mmol scale; yield: 3.77 g (67%); yellow oil; R_f = 0.15 (5% EtOAc–hexanes).

IR (thin film): 1549, 1508, 1454, 1329, 1306, 1248, 1179, 1032 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.08 (s, 1 H), 7.42 (dd, J_1 = 7.0 Hz, J_2 = 1.9 Hz, 1 H), 7.37–7.29 (m, 2 H), 7.13 (d, J_1 = 8 Hz, 1 H), 7.04–7.01 (m, 2 H), 6.74–6.71 (m, 2 H), 4.50 (dd, J_1 = 8.7 Hz, J_2 = 1.7 Hz, 1 H), 3.71 (s, 3 H), 3.65–3.58 (m, 1 H), 3.12 (dd, J_1 = 16.4 Hz, J_2 = 1.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.76, 150.15, 134.77, 132.07, 131.89, 131.70, 130.05, 129.76, 128.61, 127.76, 127.40, 113.99, 55.06, 37.38, 37.1.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{13}NO_2$ + Na $(M + Na^+)$: 304.0944; found: 304.0932.

3d

Reaction was carried out on a 30 mmol scale; yield: 8.6 g (84%); yellow crystalline solid; mp 115.0–115.8 °C; R_f = 0.1 (10% EtOAc–hexanes).

IR (ATR): 1530, 1472, 1441, 1408, 1348 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.05 (s, 1 H), 7.39 (dd, J_1 = 7.3 Hz, J_2 = 1.5 Hz, 1 H), 7.33–7.24 (m, 2 H), 7.12 (d, J_1 = 4 Hz, 1 H), 6.29 (s, 1 H), 4.44 (d, J_1 = 8.5 Hz, 1 H), 3.73 (s, 3 H), 3.62 (s, 6 H), 3.62–3.56 (m, 1 H), 3.12 (dd, J_1 = 16.4 Hz, J_2 = 1.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.97, 149.86, 136.97, 135.56, 134.82, 132.01, 131.71, 129.82, 129.55, 128.52, 127.38, 103.50, 60.51, 55.66, 38.22, 36.93.

3e

Reaction was carried out on a 20 mmol scale; yield: 4.84 g (82%); red/yellow oil; R_f = 0.22 (10% EtOAc–hexanes).

IR (thin film): 1263, 731 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.08 (s, 1 H), 7.41 (dd, J_1 = 7.1 Hz, J_2 = 1.9 Hz, 1 H), 7.37–7.27 (m, 2 H), 7.13 (d, J_1 = 7.2 Hz, 1 H), 6.65–6.54 (m, 3 H), 5.85 (q, J_1 = 1.4 Hz, 2 H), 4.47 (dd, J_1 = 8.7 Hz, J_2 = 1.6 Hz, 1 H), 3.60 (ddt, J_1 = 16.5 Hz, J_2 = 8.7 Hz, J_3 = 1.3 Hz, 1 H), 3.11 (dd, J_1 = 16.4 Hz, J_2 = 1.7 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.82, 147.66, 146.75, 134.61, 133.78, 132.14, 131.81, 130.15, 129.60, 128.60, 127.48, 119.90, 108.34, 107.18, 100.92, 37.86, 37.21.

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{13}NO_4$ + Na $[M + Na]^+$: 318.0737; found: 318.0733.

3f

Reaction was carried out on a 20 mmol scale; yield: 5.35 g (62%); yellow crystalline solid; mp 118.4–119.4 °C; R_f = 0.25 (10% EtOAc–hexanes).

IR (ATR): 1639, 1504, 1450, 1331, 1308, 1223, 1155 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.43 (dd, J_1 = 7.2 Hz, J_1 = 1.7 Hz, 1 H), 7.34 (ddd, J_1 = 9.5 Hz, J_2 = 7.0 Hz, J_3 = 1.4 Hz, 2 H), 7.15–7.11 (m, 1 H), 7.10–7.03 (m, 2 H), 6.91–6.83 (m, 2 H), 4.53 (dd, J_1 = 8.7 Hz, J_2 = 1.7 Hz, 1 H), 3.67–3.57 (m, 1 H), 3.11 (dd, J_1 = 16.4 Hz, J_2 = 1.7 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.99 (d, J_1 = 245.7 Hz), 149.72, 135.76 (d, J_4 = 3.3 Hz), 134.44, 132.31, 131.92, 130.20, 129.61, 128.64, 128.30 (d, J_3 = 8.1 Hz), 127.59, 115.62 (d, J_2 = 21.4 Hz), 37.51, 37.08.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{12}FNO_2$ + Na $(M + Na^+)$: 292.0744; found: 292.0750.

3g

Reaction was carried out on a 10 mmol scale; yield: 1.65 g (52%); yellow crystalline solid; mp 123.7–124.7 °C; R_f = 0.2 (5% EtOAc–hexanes).

IR (ATR): 1641, 1499, 1454, 1323, 1267 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.24 (s, 1 H), 7.72 (d, J_1 = 7.7 Hz, 1 H), 7.51–7.46 (m, 1 H), 7.38–7.33 (m, 2 H), 7.27 (dt, J_1 = 21.0 Hz, J_2 = 7.6 Hz, 3 H), 7.08 (dd, J_1 = 5.4 Hz, J_2 = 3.3 Hz, 1 H), 6.98 (d,

J_1 = 7.7 Hz, 1 H), 5.0 (d, J_1 = 8 Hz, 1 H), 3.66 (dd, J_1 = 16.7 Hz, J_2 = 9.3 Hz, 1 H), 3.12 (d, J_1 = 16 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.09, 138.11, 133.97, 133.60, 133.58, 132.06, 131.97, 130.17, 129.50, 128.85, 127.66, 127.33, 127.19, 126.88 (q, J_1 = 5.9 Hz), 36.71, 34.20, 29.64.

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{12}F_3NO_2$ + Na (M + Na)$^+$: 342.0712; found: 342.0697.

3h

Reaction was carried out on a 25 mmol scale; yield: 2.06 g (56%); yellow crystalline solid; mp 91.0–93.5 °C; R_f = 0.2 (5% EtOAc–hexanes).

IR (ATR): 1692, 1643, 1599, 1523, 1495, 1355, 1312, 1186 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (s, 1 H), 8.00–7.88 (m, 1 H), 7.47 (dd, J_1 = 7.2 Hz, J_2 = 1.9 Hz, 1 H), 7.41–7.28 (m, 4 H), 7.14 (d, J_1 = 7.0 Hz, 1 H), 7.01–6.96 (m, 1 H), 5.17 (d, J_1 = 9.5 Hz, 1 H), 3.74 (dd, J_1 = 16.9 Hz, J_2 = 9.4 Hz, 1 H), 3.30 (d, J_1 = 17.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.47, 134.28, 134.23, 134.02, 134.00, 133.16, 132.33, 130.43, 129.37, 128.93, 128.27, 127.86, 127.80, 125.39, 36.02, 33.25.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{12}N_2O_4$ + Na (M + Na$^+$): 319.0689: found: 319.0677.

3i

Reaction was carried out on a 20 mmol scale; yield: 2.33 g (54%); yellow oil; R_f = 0.35 (5% EtOAc–hexanes).

IR (thin film): 1547, 1514, 1454, 1366, 1302 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (s, 1 H), 7.35–7.28 (m, 3 H), 7.26–7.19 (m, 2 H), 3.23–3.15 (m, 2 H), 3.11–3.03 (m, 1 H), 1.85 (td, J_1 = 6.9 Hz, J_2 = 5.9 Hz, 1 H), 0.92 (d, J_1 = 6.9 Hz, 3 H), 0.76 (d, J_1 = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.17, 136.47, 131.33, 131.30, 129.86, 129.80, 127.92, 127.06, 37.78, 30.63, 30.13, 20.24, 19.17.

3j

Reaction was carried out on a 20 mmol scale; yield: 2.45 g (57%); yellow crystalline solid; mp 57.9–59.3 °C; R_f = 0.35 (5% EtOAc–hexanes).

IR (ATR): 1638, 1501, 1468, 1454, 1308, 1204 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (s, 1 H), 7.33–7.25 (m, 2 H), 7.20 (dd, J_1 = 13.2 Hz, J_2 = 7.3 Hz, 2 H), 3.31–3.22 (m, 2 H), 3.15 (d, J = 15.5 Hz, 1 H), 0.78 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.40, 137.41, 131.84, 131.27, 129.87, 129.45, 127.32, 126.88, 39.85, 36.84, 30.76, 27.37.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{17}NO_2$ + Na (M + Na)$^+$: 254.1152; found: 254.1138.

3k

Reaction was carried out with **1** (9 mmol) and pentafluoronitrostyrene **2k** (6.83 mmol); yield: 1.13 g (57%); yellow crystalline solid; mp 179.8–188.1 °C; R_f = 0.3 (15% EtOAc–hexanes).

IR (ATR): 1688, 1506, 1479, 1452, 1319, 1198, 1001 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.27 (s, 1 H), 8.08 (s, 1 H), 7.83 (dd, J_1 = 7.6 Hz, J_2 = 1.7 Hz, 1 H), 7.52–7.38 (m, 4 H), 7.33 (t, J_1 = 7.4 Hz, 1 H), 7.18 (d, J_1 = 7.5 Hz, 1 H), 7.06 (d, J_1 = 7.6 Hz, 1 H), 4.99 (dd, J_1 = 9.7 Hz, J_2 = 5.0 Hz, 1 H), 4.55 (s, 2 H), 3.60 (dd, J_1 = 16.8 Hz, J_2 = 9.6 Hz, 1 H), 3.20 (dd, J_1 = 16.8 Hz, J_2 = 4.9 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.80, 145.85, 138.89, 134.18, 134.13, 134.12, 133.95, 133.93, 133.53, 132.08, 130.60, 129.65, 129.40, 127.75, 127.34, 34.94, 29.48, 25.10.

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{15}F_4NO_3$ + Na (M + Na)$^+$: 464.0880; found: 464.0880.

3l

Reaction was carried out with **1** (10 mmol) and nitrostyrene **2l** (5 mmol); yield: 891 mg (42%); yellow solid; mp 225–245 °C; R_f = 0.25 (10% EtOAc–hexanes).

IR (ATR): 1508, 1314, 758 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13–7.97 (m, 1 H), 7.50–7.19 [m, 5 (7) H], 7.17–7.03 (m, 4 H), 6.91 (d, J_1 = 3.4 Hz, 1 H), 4.81 (dd, J_1 = 8.8 Hz, J_2 = 6.4 Hz, 1 H), 4.56–4.35 (m, 2 H), 3.70–3.50 (m, 1 H), 3.19–2.99 (m, 2 H), 1.31–0.95 [m, 6 (8) H].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.67, 140.72, 140.65, 139.21, 139.15, 138.40, 136.04, 134.64, 134.61, 132.21, 132.14, 132.11, 131.85, 131.82, 131.79, 130.13, 130.10, 130.05, 129.63, 129.60, 129.57, 128.69, 128.02, 128.00, 127.73, 127.71, 127.59, 127.46, 127.43, 127.40, 127.27, 127.24, 127.17, 127.12, 127.04, 57.01, 51.00, 45.14, 37.78, 37.71, 37.64, 36.77, 36.68, 30.07, 30.04, 29.98.

HRMS (ESI): *m*/*z* calcd for $C_{26}H_{20}N_2O_4$ + Na (M + Na)$^+$: 447.1315; found: 447.1326.

Radical Bromination of Cyclic Nitrostyrenes 3 To Form 3-Substituted 2-Nitronaphthalenes 4a–l; General Procedure

A 100 mL round-bottom flask, equipped with a magnetic stir bar, was charged with the respective cyclic nitrostyrene **3** (10 mmol, 1 equiv), benzoyl peroxide (370 mg, 15 mol%), NBS (3.03 g, 17 mmol, 1.7 equiv), and 1,2-dichloroethane (67 mL). The resulting solution was then kept at reflux for the indicated amount of time (Table 2). Once the starting material was consumed, the reaction mixture was cooled to r.t., diluted with CH_2Cl_2 (60 mL), and poured into a separatory funnel. Next, 20% aq $Na_2S_2O_3$ (100 mL) was added to neutralize the Br_2 generated during the reaction. The aqueous phase was then extracted with CH_2Cl_2 (3 × 100 mL) and the combined organic layers were dried ($MgSO_4$). The solvent was removed in vacuo and the crude product was purified by column chromatography with EtOAc–hexanes as eluent.

4a

Reaction was carried out on a 20 mmol scale; yield: 4.98 g (99%); yellow solid; mp 90.0–93.5 °C; R_f = 0.22 (5% EtOAc–hexanes).

IR (ATR): 1595, 1522, 1501, 1450, 1348, 1315, 895 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42 (s, 1 H), 7.98 (dd, J_1 = 8.2 Hz, J_2 = 1.4 Hz, 1 H), 7.91 (dd, J_1 = 8.2 Hz, J_2 = 1.4 Hz, 1 H), 7.88 (s, 1 H), 7.70–7.61 (m, 2 H), 7.51–7.40 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.35, 137.68, 134.26, 132.77, 131.25, 131.03, 129.32, 128.77, 128.55, 127.97, 127.89, 127.86, 127.80, 124.51.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{11}NO_2$ + Na (M + Na)$^+$: 272.0682; found: 272.0654.

4b

Reaction was carried out on a 7 mmol scale; yield: 2.07 g (99%); yellow solid; mp 144.5–155.4 °C; R_f = 0.22 (5% EtOAc–hexanes).

IR (ATR): 1528, 1501, 1423, 1366, 1333 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.68 (d, J_1 = 11.1 Hz, 1 H), 8.37 (d, J_1 = 8.5 Hz, 1 H), 8.08 (d, J_1 = 7.4 Hz, 1 H), 7.96–7.85 (m, 3 H), 7.75–7.67 (m, 2 H), 7.64–7.37 (m, 4 H), 7.30 (d, J_1 = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.74, 147.32, 136.46, 136.14, 135.86, 134.50, 134.47, 133.05, 132.48, 131.82, 131.78, 131.54, 131.46, 131.44, 130.59, 130.10, 129.82, 129.60, 129.33, 129.16, 129.08, 128.40, 128.38, 128.22, 127.99, 127.89, 127.87, 127.63, 127.36, 127.27, 126.67, 126.48, 126.46, 125.93, 125.49, 125.22, 125.07, 124.85, 124.78, 123.15.

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{13}NO_2$ + Na (M + Na)$^+$: 322.0839; found: 322.0822.

4c

Reaction was carried out on a 10 mmol scale; yield: 2.07 g (74%); yellow solid; mp 115.0–116.0 °C; R_f = 0.2 (5% EtOAc–hexanes).

IR (ATR): 1520, 1495, 1452, 1437, 1356, 1283, 1254, 1055 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.76 (s, 1 H), 8.13 (d, J_1 = 2.3 Hz, 1 H), 8.09–8.04 (m, 1 H), 7.97–7.93 (m, 1 H), 7.69–7.62 (m, 3 H), 7.40 (dd, J_1 = 8.4, J_2 = 2.2 Hz, 1 H), 7.06 (d, J_1 = 8.4 Hz, 1 H), 4.00 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.85, 144.70, 140.47, 134.38, 134.15, 132.50, 132.19, 130.47, 129.94, 127.81, 126.09, 123.91, 119.82, 111.79, 56.35.

4d

Reaction was carried out on a 6.5 mmol scale; yield: 2.16 g (98%); yellow crystalline solid; mp 120.6–125.4 °C; R_f = 0.15 (10% EtOAc–hexanes).

IR (ATR): 1530, 1472, 1441, 1408, 1372, 1352, 1086, 1005 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.80 (s, 1 H), 8.06 (d, J_1 = 7.9 Hz, 1 H), 7.92 (d, J_1 = 8.0 Hz, 1 H), 7.73–7.63 (m, 3 H), 4.01 (s, 3 H), 3.95 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.76, 147.10, 145.24, 135.98, 134.84, 131.98, 131.95, 131.63, 129.76, 129.39, 128.29, 128.01, 125.62, 113.93, 61.31, 61.04.

4f

Reaction was carried out on a 3 mmol scale; yield: 770 mg (96%); yellow solid; mp 118.8–120.0 °C; R_f = 0.27 (10% EtOAc–hexanes).

IR (ATR): 1638, 1504, 1450, 1331, 1308, 1223 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.41 (s, 1 H), 7.97 (d, J_1 = 8.0 Hz, 1 H), 7.91 (d, J_1 = 8.0 Hz, 1 H), 7.83 (s, 1 H), 7.72–7.61 (m, 2 H), 7.37 (dd, J_1 = 8.5 Hz, J_2 = 5.4 Hz, 2 H), 7.14 (t, J_1 = 8.6 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.56 (d, J_1 = 247.6 Hz), 147.23, 134.27, 133.75 (d, J_3 = 3.5 Hz), 131.77, 131.32, 131.15, 129.77 (d, J_3 = 8.2 Hz), 129.51, 128.85, 127.97, 127.88, 124.68 (d, J_4 = 2.0 Hz), 115.59 (d, J_2 = 21.7 Hz).

4g

Reaction was carried out on a 1 mmol scale; yield: 301 mg (95%); yellow crystalline solid; mp 78.0–80.0 °C; R_f = 0.25 (5% EtOAc–hexanes).

IR (ATR): 1759, 1601, 1526, 1504, 1337, 1313, 1167 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.73 (s, 1 H), 8.12–8.03 (m, 2 H), 7.91 (d, J_1 = 8.1 Hz, 1 H), 7.82–7.77 (m, 2 H), 7.74–7.59 (m, 4 H), 7.53 (dt, J_1 = 11.7 Hz, J_2 = 7.7 Hz, 2 H), 7.39–7.36 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.02, 145.94, 137.23 (q, J_1 = 2.0 Hz), 134.26, 134.15, 131.83, 131.54, 131.41, 130.91, 130.23, 129.93, 129.73, 129.28, 128.82, 128.23, 127.98, 127.93, 126.01 (q, J_2 = 5.1 Hz), 125.36.

HRMS (ESI): *m*/*z* calcd for for $C_{17}H_{10}F_3NO_2$ + Na (M + Na)$^+$: 340.0556; found: 340.0531.

4h

Reaction was carried out on a 4.5 mmol scale; yield: 1.27 g (95%); yellow crystalline solid; mp 136.3–137.9 °C; R_f = 0.22 (5% EtOAc–hexanes).

IR (ATR): 1599, 1517, 1500, 1487, 1346, 1308 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.82 (s, 1 H), 8.23 (d, J_1 = 8.2 Hz, 1 H), 8.07 (d, J_1 = 7.8 Hz, 1 H), 7.88 (d, J_1 = 7.9 Hz, 1 H), 7.74–7.66 (m, 4 H), 7.61 (t, J_1 = 7.8 Hz, 1 H), 7.43 (d, J_1 = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.26, 145.42, 134.79, 134.65, 133.44, 131.63, 131.53, 130.41, 130.26, 130.13, 129.52, 128.96, 128.32, 127.82, 125.81, 124.74.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{10}N_2O_4$ + Na (M + Na)$^+$: 317.0533; found: 317.0510.

4i

Reaction was carried out on a 10 mmol scale; yield: 2.06 g (96%); yellow solid; mp 68.3–73.4 °C; R_f = 0.35 (5% EtOAc–hexanes).

IR (ATR): 1524 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.26 (s, 1 H), 7.93–7.83 (m, 3 H), 7.66–7.50 (m, 2 H), 3.55 (td, J_1 = 6.8 Hz, J_2 = 0.6 Hz, 1 H), 1.39 (d, J_1 = 6.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.52, 138.84, 134.76, 130.45, 128.82, 128.57, 127.53, 127.10, 126.63, 124.04, 28.52, 23.87.

4j

Reaction was carried out on a 9 mmol scale; yield: 1.75 g, 85%; yellow solid; mp 73.8–75.0 °C; R_f = 0.35 (5% EtOAc–hexanes).

IR (ATR): 1630, 1603, 1526, 1499, 1329 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.81 (s, 1 H), 8.24 (d, J_1 = 9.1 Hz, 1 H), 8.04 (d, J_1 = 8.1 Hz, 1 H), 7.96 (t, J_1 = 8.0 Hz, 2 H), 7.67 (dddd, J_1 = 26.5 Hz, J_2 = 8.3 Hz, J_3 = 7.0 Hz, J_4 = 1.4 Hz, 2 H), 1.50 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.35, 135.70, 131.79, 129.87, 129.64, 129.41, 127.89, 127.82, 124.50, 119.12, 35.68, 30.89.

4k

Reaction was carried out on a 0.6 mmol scale; yield: 87 mg (32%); yellow solid; mp 178.3–192.5 °C; R_f = 0.35 (15% EtOAc–hexanes).

IR (ATR): 1688, 1528, 1479, 1325, 1290, 995 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 10.32 (s, 1 H), 8.78 (s, 1 H), 8.15–8.04 (m, 3 H), 7.95 (d, J_1 = 6.9 Hz, 3 H), 7.88 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1 H), 7.78–7.69 (m, 3 H), 7.64–7.35 (m, 6 H), 7.18 (d, J_1 = 7.4 Hz, 1 H), 4.70 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.93, 171.92, 145.58, 138.90, 134.43, 134.12, 134.03, 133.73, 133.54, 133.40, 132.00, 130.28, 130.11, 129.52, 129.45, 129.21, 129.01, 128.41, 128.12, 127.70, 127.37, 126.35, 25.40.

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{13}F_4NO_3$ + Na (M + Na)$^+$: 462.0727; found: 462.0724.

Cyclic Nitroalkane 5

To a 50 mL round-bottom flask, equipped with a magnetic stir bar and an internal thermocouple, were added $NaBH_4$ (645 mg, 4.42 equiv), EtOH (4 mL), and THF (5 mL). Next a solution of **3a** (970 mg, 3.86 mmol, 1 equiv) in THF (8 mL) was added dropwise over a period of 15 min. During the addition, an internal temperature of 35 °C was maintained. After the addition was complete, the reaction was heated to 50 °C for 5 h. The reaction mixture was then diluted with ice water (10 mL) and quenched with 50% AcOH–H_2O (2.3 mL). Next CH_2Cl_2 (70 mL) was added, the layers separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the solvent was removed in vacuo. The crude product was purified by column chromatography using 3% EtOAc–hexanes as eluent; yield: 505 mg (52%); white solid; mp 94.6–96.7 °C; R_f = 0.2 (5% EtOAc–hexanes).

IR (ATR): 3028, 2917, 2360, 1543, 1374 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.24 (m, 6 H), 7.22–7.19 (m, 1 H), 7.14–7.10 (m, 2 H), 5.09 (ddd, J_1 = 8.3 Hz, J_2 = 5.5 Hz, J_3 = 3.9 Hz, 1 H), 3.93 (td, J_1 = 5.9, J_2 = 3.9 Hz, 1 H), 3.43 (d, J_1 = 6.0 Hz, 2 H), 3.32 (qd, J_1 = 17.1 Hz, J_2 = 6.9 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.45, 134.21, 131.65, 128.97, 128.59, 128.52, 127.76, 127.65, 126.86, 126.49, 84.75, 77.32, 77.00, 76.68, 42.18, 32.71, 29.82.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{15}NO_2$ + Na (M + Na)$^+$: 276.0995; found: 276.0985.

Cyclic Amphetamine Analogue 6

A flame-dried 50 mL round-bottom flask, equipped with magnetic stir bar, was charged with $LiAlH_4$ (244 mg, 6.42 mmol, 2 equiv) and anhyd THF (8 mL). The resulting suspension was then cooled to 0 °C. Next, a solution of **3a** (0.807 g, 3.21 mmol, 1 equiv) in anhyd THF (8 mL) was added dropwise. After the addition was complete, the reaction mixture was heated at reflux for 12 h after which it was allowed to cool first to r.t., then to 0 °C in an ice bath. Careful quenching was performed by first adding H_2O (0.244 mL) dropwise, followed by 15% aq NaOH (0.244 mL), and more H_2O (0.73 mL). The resulting slurry was allowed to warm to r.t. and stirred for an additional 30 min. The pasty-white mixture was then filtered over Celite to give a yellow-tinted organic phase. The Celite was then washed sequentially with EtOAc (120 mL) and CH_2Cl_2 (120 mL). The combined organic layers were then evaporated and reagent-grade *i*-PrOH (5 mL) was added to the residue. Next, a slight excess of concd HCl (37%, 0.27 mL) was also added, causing heat evolution. Upon cooling, the HCl salt of **6** begins to precipitate out of solution. Upon dilution with Et_2O (10 mL) more solid precipitated. The solid was filtered, washed with Et_2O (50 mL), dried in vacuo to afford the HCl salt of **6**; yield: 534 mg (64%); white solid; R_f = 0.2 (40% EtOAc–hexanes).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.34 (s, 3 H), 7.51–7.14 (m, 9 H), 3.84 (br s, 1 H), 3.67 (br s, 1 H), 3.41–3.30 (m, 1 H), 3.18 (ddd, J_1 = 21.8 Hz, J_2 = 17.1 Hz, J_3 = 5.3 Hz, 2 H), 2.88–2.77 (m, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 140.28, 135.60, 133.35, 129.92, 129.62, 129.52, 129.30, 128.17, 127.56, 127.01, 50.21, 32.67, 31.29, 26.44.

Fused 1,2,3-Triazole 7

A 10 mL round-bottom flask, equipped with magnetic stir bar, was sequentially charged with **3a** (439 mg, 1.75 mmol, 1 equiv), DMSO (3.5 mL), and NaN_3 (227 mg, 3.5 mmol, 2 equiv). The reaction mixture was then heated at 90 °C for 2 h until all the starting material was consumed (progress was followed by TLC analysis). The flask was allowed to cool to r.t. before adding H_2O (3 mL) dropwise. The biphasic mixture was then extracted in a separatory funnel with CH_2Cl_2 (3 × 30 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the solvent was removed in vacuo. The crude product was purified by column chromatography. Elution with 30% EtOAc–hexanes afforded **7**; yield: 415 mg (96%); crystalline white solid; mp 200–205 °C; R_f = 0.4 (30% EtOAc–hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.78 (br s, 1 H, NH), 7.91 (d, J_1 = 7.4 Hz, 1 H), 7.35–7.17 (m, 8 H), 4.40 (dd, J_1 = 9.0 Hz, J_2 = 6.7 Hz, 1 H), 3.40–3.20 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.55, 135.06, 128.55, 128.48, 128.41, 127.57, 127.31, 127.04, 126.95, 122.95, 38.20, 37.95.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{13}N_3$ + Na (M + H)$^+$: 248.1182; found: 248.1182.

3-Phenyl-2-Aminonaphthalene (8)

A flame-dried 100 mL round-bottom flask, equipped with a magnetic stir bar, was charged with 10% Pd/C (1.3 g, 0.987 mmol, 15 mol%) and EtOAc (10 mL) that was injected slowly along the inner wall of the flask. Next, the solution of 3-phenyl-2-nitronaphthalene (**4a**; 1.64 g, 6.58 mmol, 1 equiv) in CH_2Cl_2 (10 mL) was added. The reaction mixture was then purged with H_2 gas by means of bubbling it through the solution from a balloon for 15 min. Next, a fresh balloon of H_2 gas was placed atop the flask. The reaction mixture was allowed to stir for 10 h at which point the starting material was no longer detected by TLC analysis (eluent: 10% EtOAc–hexanes). The reaction mixture was then filtered through Celite and washed with EtOAc (100 mL) and CH_2Cl_2 (100 mL). The combined organic solvents were removed in vacuo and the residue was purified by column chromatography. Elution with 10% EtOAc–hexanes afforded **8** as a pink oil, which solidified upon standing overnight; yield: 1.3 g (90%); R_f = 0.27 (10% EtOAc–hexanes).

IR (thin film): 1638, 1609, 1504, 1493, 466, 905, 727 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, J_1 = 8.2 Hz, 1 H), 7.67–7.65 (m, 2 H), 7.60–7.51 (m, 4 H), 7.47–7.41 (m, 2 H), 7.31–7.25 (m, 1 H), 7.10 (s, 1 H), 3.92 (br s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.09, 138.97, 134.34, 130.68, 129.42, 129.19, 128.76, 127.93, 127.68, 127.52, 126.24, 125.31, 122.55, 108.87.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{13}N$ (M + H)$^+$: 220.1121; found: 220.1111.

Diazonium Tetrafluoroborate 9

A 100 mL round-bottom flask, equipped with magnetic stir bar, was charged with 3-phenyl-2-aminonaphthalene (**7**; 856 mg, 1 equiv) and CH_2Cl_2 (39 mL). The solution was then cooled to 0 °C in an ice bath and stirred for 10 min. Next, $Et_2O{\cdot}BF_3$ (0.578 mL, 4.68 mmol, 1.2 equiv) was added dropwise, followed by the dropwise addition of neat *tert*-butyl nitrite (0.774 mL, 1.5 equiv) upon which the color of the reaction mixture became brown. The mixture was then allowed to warm to r.t., the diazonium tetrafluoroborate salt was filtered through a frit funnel, and washed with CH_2Cl_2 (5 mL) to afford of **9**; yield: 1.12 g (90%); yellow solid.

3-Phenyl-2-naphthol (10)

A 10 mL round-bottom flask, equipped with magnetic stir bar and gas outlet, was charged with the diazonium salt **9** (318 mg, 1 mmol, 1 equiv), THF (1.6 mL), and H_2O (1.6 mL). The reaction mixture was then heated at 60 °C for 1 h until gas evolution ceased. The resulting red solution was diluted with $CHCl_3$ (5 mL) and transferred into a separatory funnel with H_2O (30 mL). The aqueous phase was then extracted with $CHCl_3$ (3 × 15 mL), the combined organic layers were dried ($MgSO_4$), filtered, and the solvent was removed in vacuo. Elution with 10% EtOAc–hexanes gave **9**; yield: 102 mg (46%); white solid; mp 114.3–115.0 °C; R_f = 0.2 (10% EtOAc–hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, J_1 = 8.3 Hz, 1 H), 7.79–7.74 (m, 2 H), 7.62–7.59 (m, 2 H), 7.55 (t, J_1 = 8.5 Hz, 2 H), 7.48 (ddd, J_1 = 8.3 Hz, J_2 = 6.9 Hz, J_3 = 1.4 Hz, 2 H), 7.40–7.35 (m, 2 H), 5.40 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.69, 136.80, 134.22, 130.39, 129.52, 129.27, 129.16, 128.84, 128.09, 127.72, 126.45, 126.18, 123.84, 110.17.

3,3′-Diphenyl-BINAM (11)

A 50 mL round-bottom flask was charged with a finely ground paste of **8** (219 mg, 1 mmol, 1 equiv) and $FeCl_3{\cdot}6H_2O$ (730 mg, 4.5 mmol, 4.5 equiv) that was prepared with a mortar and pestle. Next, H_2O (0.5 mL) was added, the flask was sealed with a septum, and heated at 90 °C for 72 h, after which time it was cooled to r.t. and then $CHCl_3$ (30 mL) was added. The contents of the flask were then transferred into a separatory funnel along with H_2O (30 mL) and the aqueous phase was washed with $CHCl_3$ (3 × 40 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed in vacuo. The crude material was purified by column chromatography using 4% EtOAc–hexanes to afford **11**; yield: 82 mg (38%); yellow solid; R_f = 0.2 (10% EtOAc–hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, J_1 = 8.1 Hz, 1 H), 7.65 (t, J_1 = 4.2 Hz, 2 H), 7.60–7.49 (m, 3 H), 7.47–7.38 (m, 2 H), 7.30–7.24 (m, 1 H), 7.09 (s, 1 H), 3.92 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.10, 138.99, 134.36, 130.71, 129.44, 129.21, 128.78, 127.95, 127.70, 127.54, 126.25, 125.32, 122.57, 108.89.

HRMS (ESI): *m*/*z* calcd for $C_{32}H_{24}N_2$ + Na (M + Na)$^+$: 459.1832; found: 459.1815.

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