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Metal-Free Transfer Hydrogenation of Nitroarenes in Water with Vasicine: Revelation of Organocatalytic Facet of an Abundant Alkaloid

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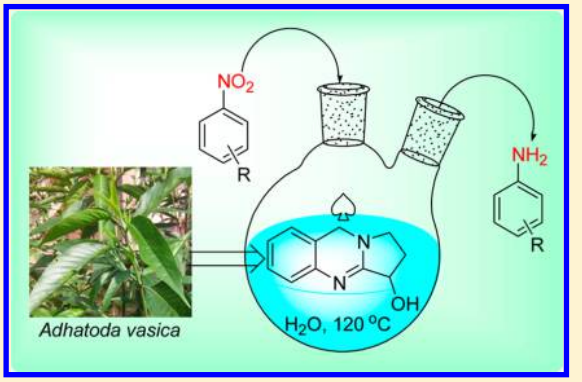
Supporting Information

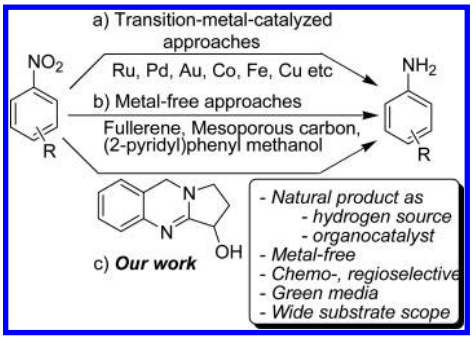
ABSTRACT: Vasicine, an abundantly available quinazoline alkaloid from the leaves of *Adhatoda vasica*, has been successfully employed for metal- and base-free reduction of nitroarenes to the corresponding anilines in water. The method is chemoselective and tolerates a wide range of reducible functional groups, such as ketones, nitriles, esters, halogens, and heterocyclic rings. Dinitroarenes reduced selectively to the corresponding nitroanilines under the present reaction conditions.



Plant-derived natural products are attractive alternatives to metal-based catalysts in terms of sustainability, stability, selectivity, and economy, therefore emerged as promising organocatalysts for various organic transformations.[1] In this regard, vasicine, a quinazoline alkaloid abundantly available in *Adhatoda vasica* leaves, has been developed as an efficient and renewable organocatalyst for C−C bond formation[2] and is still in its infancy. Vasicine is a privileged structure having both Lewis basic and acidic sites and hence is able to activate both a nucleophile and an electrophile, so it has great potential to be explored as an organocatalyst for various organic transformations.

Metal-free approaches for chemoselective hydrogenation of unsaturated compounds has emerged as an environmentally benign and cost-effective alternative to hydrogenation employing H_2 or other reducing agents based on transition-metal catalysts.[3] Reduction of nitroarenes to anilines is an important organic transformation as anilines are important precursors for bioactive natural products, pharmaceuticals, agrochemicals, dyes, and photographic materials.[4] Different strategies for reduction of nitroarenes encompass catalytic hydrogenation, electrocatalytic hydrogenation, and hydrogenation with stoichiometric amounts of reducing agents in the presence of various metal-based catalysts (Scheme 1a).[5−11] Despite the advantages of high yield and high chemo- and regioselectivity, the use of high pressure equipment, flammable hydrogen gas, hazardous reagents, relatively expensive, and the presence of inherent toxicity with these metal complexes demand an alternative approach.

Scheme 1. Strategies for Hydrogenation of Nitroarenes



Concerning metal-free hydrogenation of nitroarenes, very few reports, including 9,10-dihydroanthracene,[12] 1,4-dihydropyridines,[13] fullerenes/H_2,[14] reduced graphene oxide/hydrazine hydrate,[15] mesoporous carbon/hydrazine hydrate,[16] and (2-pyridyl)phenyl methanol,[17] are available (Scheme 1b); however, the chemoselective reduction of a nitro moiety in the presence of other reducible functional groups is a challenging task.

Furthermore, approaches avoiding the use of organic solvents in the sense of toxicity and cost have attracted much attention. Water, which is also known as a universal solvent, is an economic, nontoxic, and environmentally benign alternative to

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organic solvents.[18] Therefore, it is requisite to develop selective and metal-free approaches utilizing environmentally benign reagents and solvents. Recently, our group has reported a transition-metal-free approach for reduction of nitroarenes in DMSO:H_2O employing glucose as a hydrogen source and KOH as base.[19] Use of glucose as reducing agent for transition-metal-free reduction was inspiring, so carrying out the reaction in water without employing any base could make the present method highly attractive.

Herein, we report a metal-free approach for the reduction of nitroarenes to the corresponding anilines in water employing vasicine as an organocatalyst and reducing agent (Scheme 1c). Vasicine is mainly isolated from *Adhatoda vasica* leaves (present up to 1.3%),[20] a renewable source, which is a prime requirement of sustainability. Moreover, easy synthetic protocols for the synthesis of vasicine are also available.[21] To the best of our knowledge, this is the first report on metal-free transfer hydrogenation of nitroarenes with vasicine in water.

In our previous report on vasicine-catalyzed direct arylation of unactivated arenes with aryl halides,[2a] we serendipitously observed the reduction of 1-bromo-4-nitrobenzene to the corresponding aniline in 94% yield. Encouraged by this result, we planned to explore the potential of vasicine and related alkaloids for reduction of nitroarenes. To optimize the reaction conditions, the reduction of 1,3-dinitrobenzene was carried out in the presence of vasicine and related alkaloids (Figure 1, (**L1**−**L5**)) in different solvents under varying temperature conditions (Table 1).

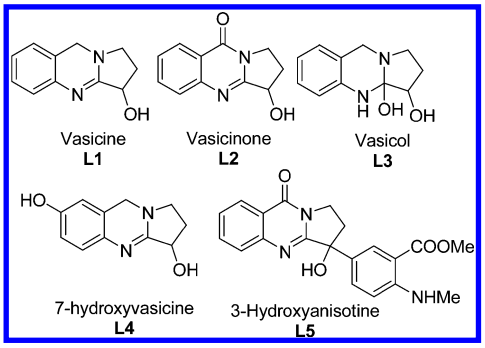
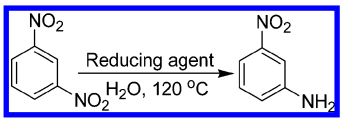


Figure 1. Structures of vasicine and related alkaloids.

Among different alkaloids, vasicine (**L1**) was found to be the most active in water at 120 °C and gave the product 3-nitroaniline chemoselectively in 95% yield (Table 1, entry 1).

Although comparable yields were obtained with other solvents, i.e., ethylene glycol, PEG-400, and DMF (Table 1, entries 2−4), water was chosen as the solvent of choice, considering the cost, availability, and environment. In the case of toluene, although full conversion of the starting substrate was observed, only 50% of the desired product was obtained along with azo and azoxy derivatives as side products, while, in DMSO, a poor yield of product was observed (Table 1, entries 5 and 6). As expected, no reaction occurred in the absence of vasicine (Table 1, entry 7). Vasicinone and other alkaloids provided the desired product in lower yield under the same reaction conditions (Table 1, entries 8−11). While 1 equiv of vasicine gave lower yield, no significant change in the yield of product was observed using 2 equiv of vasicine (Table 1, entries 12 and 13). A decrease in reaction time and temperature gave a lower yield of the product (Table 1, entries 14 and 15).

Table 1. Optimization of Reaction Conditions for Reduction of 1,3-Dinitrobenzene[a]



entry	reducing agent	solvent	conv./yield (%)[b]
1	**L1**	H_2O	>99/95
2	**L1**	ethylene glycol	>99/92
3	**L1**	PEG-400	>99/94
4	**L1**	DMF	>99/90
5	**L1**	toluene	>99/50
6	**L1**	DMSO	50/30
7		H_2O	nr
8	**L2**	H_2O	15/13
9	**L3**	H_2O	50/43
10	**L4**	H_2O	76/70
11	**L5**	H_2O	13/10
12	**L1** (1 equiv)	H_2O	68/62
13	**L1** (2 equiv)	H_2O	>99/95
14	**L1**	H_2O	50/45[c]
15	**L1**	H_2O	85/81[d]

[a]Reaction conditions: 1,3-dinitrobenzene (0.5 mmol), reducing agent (0.75 mmol), H_2O (4 mL) at 120 °C for 24 h. [b]Isolated yield. [c]Reaction carried out at 80 °C. [d]Reaction carried out for 12 h.

Next, the scope of the method was evaluated for reduction of various substituted nitroarenes. Generally, nitroarenes substituted with electron-withdrawing substituents lead to accumulation of *N*-hydroxylamine and azo or azoxy intermediates;[22] however, under the present reaction conditions, reduction of nitroarenes bearing electron-withdrawing substituents proceeded smoothly and the desired products were obtained in good to excellent yield (Table 2) without the accumulation of intermediates.

Nitroarenes substituted with easily reducible functional groups such as ketones and nitriles selectively reduced to the corresponding anilines with excellent yield (Table 2, **2a**−**2b** and **2c**−**2d**). Nitroarenes containing other susceptible functional groups, such as sulphonamide, esters, acid, and amide, were reduced selectively in good to excellent yields (Table 2, **2e**−**2j**). The nitroarene containing the *N*-phenyl moiety provided the corresponding aniline in 93% yield (Table 2, **2k**). In the case of dinitroarenes, only one nitro group reduced selectively, leaving the other nitro group unaffected (Table 2, **2l**−**2n**). Many metal-based approaches failed to show such high chemoselectivity.[23] 4-Nitrochalcone reduced selectively to 4-aminochalcone with 81% yield without affecting the carbonyl and conjugated C═C bond (Table 2, **2o**). In the case of 1-bromo-4-nitrobenzene, though poor reduction was observed in water, a moderate yield corresponding to the desired product was obtained in toluene (Table 2, **2p**). 1-Nitronaphthalene and 3-nitrobiphenyl reduced selectively, providing products in 90% yield (Table 2, **2q** and **2r**).

In the case of nitrobenzene and its derivatives having electron-donating groups such as *p*-methoxy and *p*-methyl (Table 2, **2s**−**2u**), poor yields of the products were observed. Reduction of polysubstituted nitroarenes having labile functionalities such as chloro and ester groups also proceeded smoothly, providing the corresponding aniline in good yield. 2-Chloro-5-nitroaniline provided the corresponding aniline with 85% yield without dehalogenation (Table 2, **2v**). In the case of

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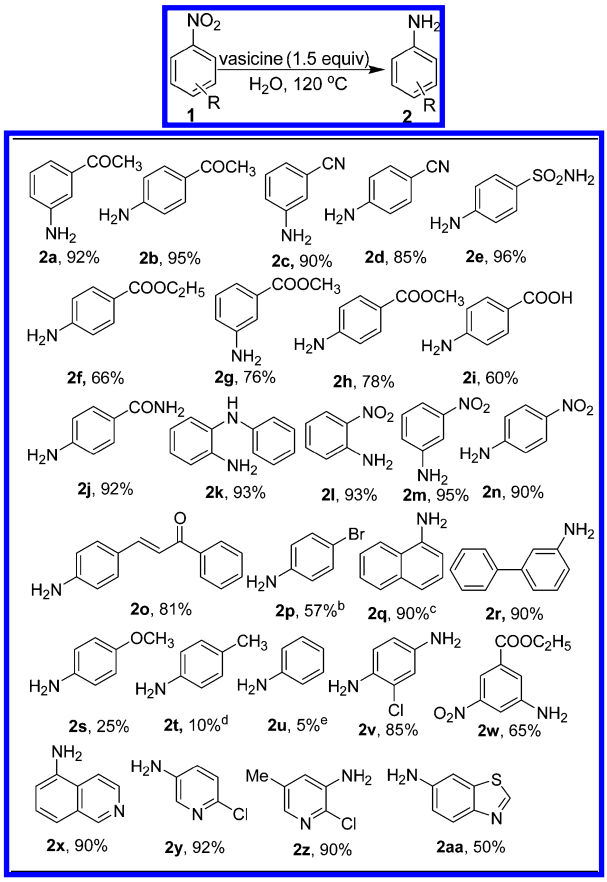
Table 2. Reduction of Nitroarenes to Anilines[a]



[a]Reaction conditions: nitroarene (0.5 mmol), vasicine (0.75 mmol), H_2O (4 mL), 120 °C, 24 h. Isolated yield. [b]Reaction carried out in toluene (4 mL). [c]Reaction carried out in the presence of K_2CO_3 (0.5 mmol), vasicine (0.5 mmol). [d]Mixture of corresponding azo (50%) and azoxy (35%) products was observed. [e]Mixture of corresponding azo (46%) and azoxy (43%) products was observed.

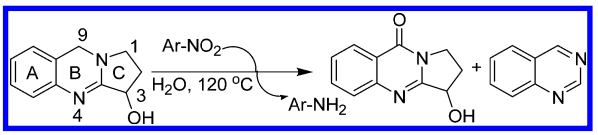
ethyl-3,5-dinitrobenzoate, selective reduction was observed with 65% yield (Table 2, **2w**). Different substituted heterocyclic nitroarenes were reduced to the corresponding anilines in excellent yield without affecting the heterocyclic ring (Table 2, **2x**–**2aa**).

Further, to investigate the reaction mechanism and role of vasicine, different experiments have been carried out. To determine whether the nitro group is reduced via transfer hydrogenation or by molecular hydrogen generated by dehydrogenation of vasicine, reduction of 1,3-dinitrobenzene was carried out under a H_2 atmosphere in the presence of a catalytic amount of vasicine. In this experiment, no reaction occurred, which demonstrates that the nitro moiety is not reduced by molecular hydrogen. Furthermore, to rule out the possibility of a radical mechanism, as proposed by Coellen and Reuchardt,[12] the model reaction was carried out in the presence of TEMPO, a radical scavanger, and no suppression in the yield of product was observed. Therefore, it concludes that this is a case of transfer hydrogenation in which vasicine is working both as a hydrogen source as well as an organocatalyst.

Further, to determine which hydrogen from vasicine was transferred to nitroarene, the byproducts of vasicine from the model reaction were analyzed.

Vasicinone and quinazoline were observed as major by-products, which shows that benzylic hydrogen (C9) and hydrogen evolved via degradation of the ring C of vasicine are responsible for reduction of nitroarenes (Scheme 2). This fact

Scheme 2. Degradation of Vasicine



is supported by the observation that a poor yield of the product was observed when reduction of 1,3-dinitrobenzene was carried out in the presence of vasicinone (Table 1, entry 8).

Further, to investigate the role of vasicine, the model reaction was monitored for different time intervals using a UV–visible spectrophotometer (Figure 2).

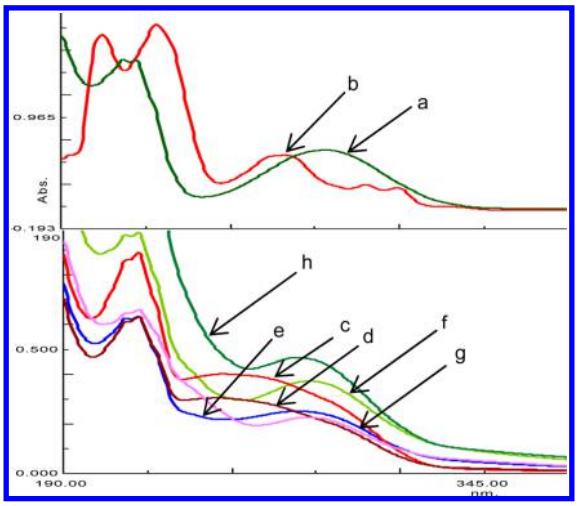
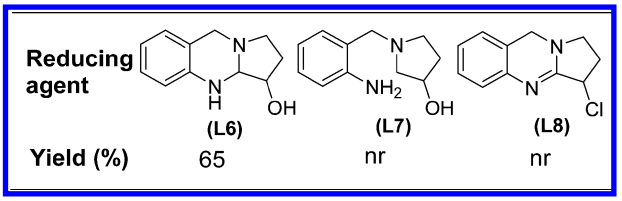


Figure 2. UV–vis absorption spectral change in the course of reaction time of the reaction mixture containing 1,3-dinitrobenzene and vasicine in water: (a) vasicine; (b) vasicinone; (c) reaction after 15 min; (d) reaction after 30 min; (e) reaction after 1 h; (f) reaction after 2 h; (g) reaction after 4 h; (h) reaction after 24 h.

A blue shift in λ_{max} of vasicine was observed from 286 to 249 nm during 30 min of reaction, which indicated some kind of interaction between vasicine and nitroarene. However, the band at λ_{max} 249 nm further returned to 282 nm after 1 h of reaction. At the end of reaction (after 24 h), the λ_{max} was observed at 275 nm, which further confirmed the formation of vasicinone.

To understand the importance of basicity and rigidity of vasicine (**L1**) in the reduction of nitroarenes, reduction of 1,3-dinitrobenzene was carried out with different derivatives of vasicine (Table 3). **L6** was found to be less effective (65%

Table 3. Evaluation of Vasicine Derivatives for the Reduction of Nitroarenes[a,b]



[a]Reaction conditions: 1,3-dinitrobenzene (0.5 mmol), reducing agent (0.75 mmol), H_2O (4 mL), 120 °C, 24 h. [b]Isolated yield

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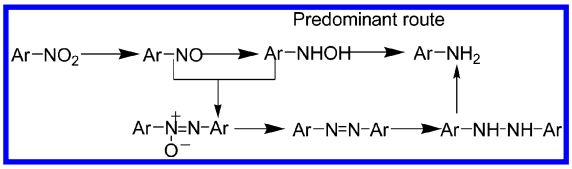
yield) when compared with vasicine, while reduction was not observed with **L7**. Thus, reaction with ligands **L6** and **L7** clearly demonstrated the requirement for basicity and rigidity, which decreases from vasicine > **L6** > **L7**. The importance of the hydroxyl group was proved by the reaction of 1,3-dinitrobenzene with **L8**, which showed no reactivity.

Further, to investigate the reduction pathway of nitroarenes, the reduction of 3-nitroacetophenone was monitored at different time intervals by mass spectroscopy (ESI-MS). The formations of *N*-(3-acetylphenyl)hydroxylamine and 3,3′-diacetylazoxybenzene as intermediates were observed in mass spectra, suggesting both types of routes in the reduction of nitroarenes, i.e., the direct and condensation pathways.

Furthermore, when the reductions of *N*-(3-acetylphenyl)-hydroxylamine and 3,3′-diacetylazobenzene were carried out under the present reaction conditions, no reaction occurred with 3,3′-diacetylazobenzene, but *N*-(3-acetylphenyl)-hydroxylamine provided 3-aminoacetophenone as the major product. Therefore, these results clearly suggested that the direct route is predominant in the present reaction conditions (Scheme 3).

Scheme 3. Possible Pathways for Reduction of Nitroarenes



In conclusion, the dual role of vasicine has been explored, i.e., a hydrogen source as well as an organocatalyst, for efficient chemoselective reduction of nitroarenes to the corresponding anilines under metal-free conditions. In the presence of vasicine, reduction of different substituted nitroarenes to the corresponding anilines occurred in good to excellent yield. Reactions under metal- and base-free conditions and water as a solvent are a few advantages of this method.

EXPERIMENTAL SECTION

General Information. High grade solvents were used for all reactions. Column chromatography was carried out with 60−120 mesh silica gel and monitored with TLC on silica gel 60 F_{254} plates using UV light as visualizing agent. ^{1}H NMR and ^{13}C NMR experiments were recorded on 300 and 600 MHz instruments. Chemical shifts are reported in parts per million (ppm) downfield from an internal standard. Mass spectra were recorded on electrospray ionization quadrupole time-of-flight (ESI-QTOF-MS) mass spectrometry.

Isolation of Vasicine and Related Alkaloids. Dried leaves of *Adhatoda vasica* (5 kg) were powdered and extracted with MeOH:H_2O (80:20). The extracts were collected and concentrated using a rotary evaporator. The extract was then treated with 2 N HCl and stirred at room temperature for a few hours. It was then filtered, and the filtrate was extracted with ethyl acetate. The aqueous acidic layer was basified with ammonium hydroxide to pH 9 and then extracted with $CHCl_3$. The chloroform extract was concentrated using a rotary evaporator to give the crude alkaloid extract. The crude alkaloidal extract was then subjected to column chromatography on basic alumina and eluted with hexane:ethyl acetate:MeOH in increasing polarity. Fractions eluted with hexane:ethyl acetate (1:1) afforded 3-hydroxyanisotine (100 mg). Fractions eluted with ethyl acetate afforded vasicinone (1 g) and vasicol (1 g). Fractions eluted with ethyl acetate:MeOH (9:1) and ethyl acetate:MeOH (7:3) provided vasicine (12.5 g) and 7-hydroxyvasicine (100 mg), respectively. The identification and characterization of compounds were carried out using ^{1}H NMR and ^{13}C NMR.

*Vasicine (**L1**).*[20c] **L1** was obtained by following the general procedure described above and purified by column chromatography (ethyl acetate:MeOH (9:1)) as a white amorphous solid. Yield 12.5 g, 0.25%. mp 196−197 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.13−6.83 (m, 4H), 4.75−4.73 (m, 1H), 4.55−4.50 (m, 2H), 3.35−3.19 (m, 2H), 2.37−2.36 (m, 1H) 2.12−2.09 (m, 1H); ^{13}C NMR (150 MHz, MeOD): δ 163.9, 142.4, 128.4, 125.8, 124.1, 123.7, 119.0, 70.2, 48.1, 47.1, 28.9. MS (ESI-TOF) *m*/*z*: $[M + H]^+$ for $C_{11}H_{13}N_2O$ 189.26.

*Vasicinone (**L2**).*[20c] **L2** was obtained by following the general procedure described above and purified by column chromatography (100% ethyl acetate) as a white amorphous solid. Yield 1 g. mp 198−199 °C; ^{1}H NMR (600 MHz, MeOD): δ 8.32−8.29 (m, 1H), 7.75 (m, 1H), 7.53−7.49 (m, 2H) 5.31−5.26 (m, 1H), 4.40−4.35 (m, 1H), 4.12−4.02 (m, 1H), 2.70−2.66 (m, 1H), 2.37−2.33 (m, 1H); ^{13}C NMR (150 MHz, MeOD): δ 160.6, 130.1, 148.6, 134.4, 126.9, 126.7, 126.6, 121.0, 71.9, 43.4, 29.3. MS (ESI-TOF) *m*/*z*: $[M + H]^+$ for $C_{11}H_{11}N_2O_2$ 203.09.

*Vasicol (**L3**).*[20c] **L3** was obtained by following the general procedure above and purified by column chromatography (ethyl acetate) as a yellow viscous oil. Yield 1 g. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.08 (t, 1H), 7.00 (d, *J* = 6.8 Hz, 1H), 6.63 (t, 2H) 4.42−4.27 (m, 4H), 3.27−3.24 (m, 1H), 3.16−3.13 (m, 1H), 2.34−2.33 (m, 1H) 1.90−1.87 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.3, 145.7, 131.3, 129.5, 118.6, 117.3, 115.7, 69.9, 44.7, 43.1, 27.6, 142.4, 128.4, 125.8, 124.1, 123.7, 119.0, 70.2, 48.1, 47.1, 28.9. MS (ESI-TOF) *m*/*z*: $[M + H]^+$ for $C_{11}H_{15}N_2O_2$ 207.00.

*7-Hydroxyvasicine (**L4**).*[24] **L4** was obtained by following the general procedure described above and purified by column chromatography (ethyl acetate:MeOH (9:1)) as a white amorphous solid. Yield 100 mg. ^{1}H NMR (600 MHz, MeOD): δ 6.96−6.94 (m, 1H), 6.69−6.68 (m, 1H), 6.54 (s, 1H), 4.90 (merged with solvent peak, 1H), 4.72−4.64 (m, 2H), 3.63−3.60 (m, 1H), 3.53−3.49 (m, 1H) 2.53 (m, 1H), 2.06−2.03 (m, 1H); ^{13}C NMR (150 MHz, MeOD): δ 161.0, 156.1, 124.2, 120.0, 118.8, 115.2, 112.8, 70.8, 49.4, 46.2, 29.2. MS (ESI-TOF) *m*/*z*: $[M + H]^+$ for $C_{11}H_{13}N_2O_2$ 205.22.

*3-Hydroxyanisotine (**L5**).*[20c] **L5** was obtained by following the general procedure described above and purified by column chromatography (hexane:ethyl acetate (1:1)) as an off-white amorphous solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.32 (d, *J* = 8.1 Hz, 1H), 7.98 (d, *J* = 1.9 Hz, 1H), 7.75−7.71 (m, 3H), 7.50−7.48 (m, 1H), 7.39 (dd, 1H), 6.62 (d, *J* = 8.8 Hz, 1H), 4.33−4.29 (m, 4H), 3.27−3.24 (m, 1H), 4.01−3.97 (m, 1H), 3.78 (s, 1H), 2.88 (d, *J* = 7.8 Hz, 3H), 2.65−2.61 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.6, 161.0, 160.8, 151.8, 149.0, 134.2, 131.9, 128.5, 127.5, 127.0, 126.8, 126.5, 121.1, 111.1, 109.6, 81.1, 51.5, 42.8, 37.7, 29.5. MS (ESI-TOF) *m*/*z*: $[M + H]^+$ for $C_{17}H_{17}N_3O_4$ 365.96.

Method for Synthesis of Vasicine Derivatives. *(**L6**).*[25] To a solution of vasicine (200 mg, 1.06 mmol) in ethanol (5 mL) was added sodium borohydride (40 mg, 1.06 mmol) at room temperature, and the mixture was stirred for 2 h. Upon completion of reaction (as monitored by TLC), the reaction was quenched with ethyl acetate and concentrated in vacuo, and the residue was chromatographed over basic alumina to afford the desired product (mixture of diastereoisomers). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.10−6.91(m, 2H), 6.78−6.48 (2H), 4.49 (s, 2H), 4.36−4.32 (1H), 4.14−4.01 (m, 1H) 3.97−3.72 (m, 2H), 2.93−2.89 (m, 1H), 2.47−2.30 (m, 1H), 1.85−1.74 (m, 1H) ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.8, 142.7, 127.9, 127.7, 120.3, 119.2, 118.7, 118.6, 117.0, 115.1, 74.4, 71.3, 52.5, 49.9, 49.4, 32.7, 32.2. MS (ESI-TOF) *m*/*z*: $[M + H]^+$ for $C_{11}H_{15}N_2O$ 191.26 $[M + H]^+$.

*(**L7**).*[25] To a solution of vasicine (200 mg, 1.06 mmol) in methanol:water (1:1, 4 mL) was added sodium borohydride (101.7 mg, 3.17 mmol) in small portions at regular intervals at room temperature, and stirring was continued for 10 h. The reaction was quenched with ethyl acetate, and the product was extracted with chloroform. The chloroform layer was evaporated at reduced pressure on a rotary evaporator, and chromatography over basic alumina and elution with hexane−ethyl acetate gave a semisolid light yellow

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compound in 90% (183 mg) yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.18−7.12 (m, 1H), 7.04 (d, J = 6.3 Hz, 1H), 6.71(t, 2H), 5.20 (brs, 2H), 4.45−4.42 (m, 1H), 3.87 (dd, J = 12.9, 14.2 Hz, 2H), 3.25−3.17 (m, 1H), 3.01 (d, J = 11.1 Hz, 1H), 2.82−2.77 (m, 1H), 2.68−2.59 (m, 1H), 2.32−2.22 (m, 1H), 1.97−1.87 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ147.1, 131.7, 130.0, 119.8, 118.5, 116.9, 70.8, 62.0, 57.5, 52.3, 34.7. MS (ESI-TOF) m/z: $[M + H]^+$ for $C_{11}H_{17}N_2O$ 192.95.

*3-Chlorovasicine (**L8**).*[26] To a solution of vasicine (1 mmol) in dichloromethane was added thionyl chloride (216 μL, 3 mmol) and pyridine (8 μL, 0.1 mmol) at 0 °C. The mixture was allowed to stir for 5 h at room temperature. The excess of thionyl chloride was removed in vacuo, and the residue was chromatographed over basic alumina to afford the product as a brown solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.16−7.12 (m, 2H), 7.01(t, 1H), 6.88 (d, J = 7.2 Hz, 1H), 4.75 (d, J = 5.8 Hz, 1H), 4.64 (dd, 2H), 3.58−3.54 (m, 1H), 3.32−3.29 (m, 1H), 2.54−2.48 (m, 1H), 2.29−2.26 (m, 1H) ^{13}C NMR (150 MHz, $CDCl_3$): δ 160.0, 142.2, 128.6, 125.8, 125.0, 124.9, 119.0, 56.9, 48.8, 47.4, 31.1. MS (ESI-TOF) m/z: $[M + H]^+$ for $C_{11}H_{12}ClN$ 207.30.

Representative Experimental Procedure for Reduction of Nitro Compounds. A mixture of the nitro compound (0.5 mmol) and vasicine (0.75 mmol) in H_2O (4 mL) was stirred at 120 °C for 24 h. Time was not optimized separately for all substrates. After completion of reaction, as monitored by TLC, the reaction mixture was cooled to ambient temperature and extracted with ethyl acetate. The ethyl acetate layer was dried under reduced pressure using a rotatory evaporator. The crude was chromatographed over silica gel to afford the desired product.

Characterization of Nitro Reduction Products. All compounds were identified by spectral comparison with literature data.

*3-Aminoacetophenone (**2a**, CAS Number 99-03-6).* **2a** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (17:3)) as a white solid. Yield 62 mg, 92%; mp 94−95 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 (d, J = 7.4 Hz, 1H), 7.25−7.21 (m, 2H), 6.86 (d, J = 7.8 Hz, 1H), 3.83 (s, 2H), 2.54 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 198.5, 146.7, 138.2, 129.4, 119.6, 118.8, 114.0, 26.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_8H_{10}NO$ 136.0762; Found 136.0772.

*4-Aminoacetophenone (**2b**).*[7c] **2b** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (4:1)) as a white solid. Yield 64 mg, 95%; mp 100−101 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83−7.80 (m, 2H), 6.67−6.64 (m, 2H), 4.19 (s, 2H), 2.52 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 196.9, 151.5, 131.2, 128.2, 114.1, 26.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_8H_{10}NO$ 136.0762; Found 136.0772.

*3-Aminobenzonitrile (**2c**).*[7c] **2c** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (9:1)) as a brown solid. Yield 53 mg, 90%; mp 51−52; °C; ^{1}H NMR (300 MHz, CD_3COCD_3): δ 7.26−7.21 (m, 1H), 6.98−6.90 (m, 3H), 5.16 (s, 2H); ^{13}C NMR (75 MHz, CD_3COCD_3): δ 149.1, 130.4, 120.0, 119.4, 118.9, 116.7, 112.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_7H_7N_2$ 119.0609; Found 119.0612.

*4-Aminobenzonitrile (**2d**).*[7c] **2d** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (4:1)) as a brown solid. Yield 50 mg, 85%; mp 82−83 °C; ^{1}H NMR (300 MHz, CD_3COCD_3): δ 7.39 (d, J = 8.4 Hz, 2H), 6.75 (d, J = 8.4 Hz, 2H), 5.61 (s, 2H); ^{13}C NMR (75 MHz, CD_3COCD_3): δ 153.0, 133.7, 120.3, 114.2, 98.2.

*4-Aminobenzenesulphonamide (**2e**).*[7c] **2e** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (3:7)) as a yellow solid. Yield 83 mg, 96%; mp 161−162 °C; ^{1}H NMR (300 MHz, CD_3OD): δ 7.59 (d, J = 8.7 Hz, 2H) 6.70 (d, J = 8.7 Hz, 2H); ^{13}C NMR (75 MHz, CD_3OD): δ 152.5, 130.3, 127.9, 113.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_6H_9N_2O_2S$ 173.0385; Found 173.0389.

*Ethyl-4-aminobenzoate (**2f**).*[7c] **2f** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (4:1)) as a pale yellow solid. Yield 54.4 mg, 66%; mp 90−91 °C; ^{1}H NMR (300 MHz, CD_3COCD_3): δ 7.76−7.72 (m, 2H), 6.71−6.66 (m, 2H), 5.38 (brs, 2H), 4.28−4.21 (q, 2H), 1.31 (t, 3H); ^{13}C NMR (75 MHz, CD_3COCD_3): δ 166.3, 153.4, 131.5, 118.4, 113.3, 59.8, 14.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_9H_{12}NO_2$ 166.0868; Found 166.0884.

*Methyl-3-aminobenzoate (**2g**).*[7c] **2g** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (4:1)) as a white solid. Yield 51.5 mg, 67%; mp 48−49 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39 (d, J = 7.5 Hz, 1H), 7.33 (s, 1H), 7.17 (t, J = 7.7 Hz, 1H), 6.82 (d, J = 7.8 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 167.3, 146.6, 131.0, 129.2, 119.5, 119.4, 115.7, 52.0.

*Methyl-4-aminobenzoate (**2h**).*[7c] **2h** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (4:1)) as a white solid. Yield 58.8 mg, 78%; mp 111−113 °C; ^{1}H NMR (300 MHz, CD_3COCD_3): δ 7.74 (d, J = 8.7 Hz, 2H), 6.69 (d, J = 8.7 Hz, 2H), 5.42 (brs, 2H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, CD_3COCD_3): δ 166.8, 153.5, 131.5, 118.0, 113.3, 50.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_8H_{10}NO_2$ 152.0712; Found 152.0741.

*4-Aminobenzoic Acid (**2i**).*[7c] **2i** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (1:1)) as a white solid. Yield 41 mg, 60%; mp 166−167 °C; ^{1}H NMR (300 MHz, CD_3OD): δ 7.75 (d, J = 8.6 Hz, 2H), 6.64 (d, J = 8.6 Hz, 2H); ^{13}C NMR (75 MHz, CD_3OD): δ 171.2, 155.0, 133.2, 119.6, 114.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_7H_8NO_2$ is 138.0555; Found 138.0576.

*4-Aminobenzamide (**2j**).*[7c] **2j** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (1:4)) as a white solid. Yield 62.5 mg, 92%; mp 178−179 °C; ^{1}H NMR (600 MHz, CD_3OD): δ 7.63 (d, J = 8.3 Hz, 2H), 6.65 (d, J = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, CD_3OD): δ 171.3, 152.1, 129.0, 120.8, 113.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_7H_9N_2O$ 137.0715; Found 137.0722.

*2-Aminodiphenylamine (**2k**).*[7c] **2k** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (19:1)) as a brown solid. Yield 85.5 mg, 93%; mp 66−67 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.21 (t, 2H), 7.13 (d, J = 7.6 Hz, 1H), 7.02 (t, 1H), 6.83−6.80 (m, 2H), 6.77−6.74 (m, 3H), 5.19 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 145.3, 141.8, 129.3, 128.6, 125.7, 124.8, 119.3, 119.2, 116.2, 115.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{12}H_{13}N_2$ 185.1079; Found 185.1068.

*2-Nitroaniline (**2l**).*[7c] **2l** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (9:1)) as a yellow solid. Yield 64.6 mg, 93%; mp 73−74 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.12−8.10 (m, 1H), 7.37−7.3 (m, 1H), 6.81−6.79 (m, 1H), 6.71−6.69 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 144.6, 135.65, 135.62, 126.2, 118.7, 116.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_6H_7N_2O_2$ 139.0508; Found 139.0525.

*3-Nitroaniline (**2m**).*[7c] **2m** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (4:1)) as a yellow solid. Yield 65.5 mg, 95%; mp 111−112 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60−7.57 (m, 1H), 7.51−7.50 (m, 1H), 7.32−7.26 (m, 1H), 6.98−6.94 (m, 1H), 4.02 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.6, 147.8, 130.3, 121.0, 113.5, 109.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_6H_7N_2O_2$ 139.0508; Found 139.0552.

*4-Nitroaniline (**2n**).*[7c] **2n** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (4:1)) as a yellow solid. Yield 65.5 mg, 95%; mp 147−148 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10−8.06 (m, 2H), 6.67−6.62 (m, 2H), 4.43 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.9, 126.7, 113.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_6H_7N_2O_2$ 139.0508; Found 1389.0441.

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*4-Aminochalcone (**2o**).*[19] **2o** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (9:1)) as a yellow solid. Yield 90.7 mg, 81%; mp 140−142 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00−7.98 (m, 2H), 7.75 (d, J = 15.5 Hz, 1H), 7.55−7.54 (m, 1H), 7.49−7.47 (m, 4H), 7.34 (d, J = 15.5 Hz, 1H), 6.68 (d, J = 7.8 Hz, 2H), 4.03 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 190.7, 149.1, 145.5, 138.8, 132.3, 130.5, 128.5, 128.3, 125.1, 118.0, 114.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{14}NO$ 224.1075; Found 224.1089.

*4-Bromoaniline (**2p**).*[7c] **2p** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (9:1)) as a brown solid. Yield 49 mg, 57%; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.23 (d, J = 8.4 Hz 2H), 6.55 (d, J = 8.4 Hz 2H), 3.67 (brs, 2H) ^{13}C NMR (150 MHz, $CDCl_3$): δ 145.5, 132.0, 116.7, 110.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for C_6H_7BrN 171.9762; Found 171.9741.

*1-Aminonaphthalene (**2q**).*[7c] **2q** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (19:1)) as a brown solid. Yield 64 mg, 90%; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.83 (d, J = 7.2 Hz, 2H), 7.48−7.47 (m, 2H), 7.34−7.31 (m, 2H), 6.79 (d, J = 7.02 Hz, 1H), 3.98 (brs, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 142.1, 134.4, 128.5, 126.3, 125.8, 124.9, 123.7, 120.8, 119.0, 109.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{10}H_{10}N$ 144.0813; Found 144.0834.

*3-Aminobiphenyl (**2r**, CAS Number 2243-47-2).* **2r** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (19:1)) as a brown solid. Yield 76 mg, 90%; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.57 (d, J = 7.5 Hz 2H), 7.44−7.41 (m, 2H), 7.35−7.32 (m, 1H), 7.26−7.22 (m, 1H), 7.00 (d, J = 7.5 Hz 1H), 6.91 (s, 1H), 6.68 (d, J = 7.3 Hz 1H), 3.61 (brs, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 146.7, 142.4, 141.4, 129.6, 128.6, 127.2, 127.1, 117.7, 114.1, 113.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{12}H_{12}N$ 170.0970; Found 170.0984.

*2-Chloro-4-aminoaniline (**2v**).* **2v** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (4:1)) as a brown solid. Yield 60.3 mg, 85%; mp 71−73 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.00 (d, J = 8.3 Hz 1H), 6.12−6.06 (m, 2H), 3.67 (brs, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.5, 143.8, 130.2, 109.7, 107.1, 102.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_6H_8ClN_2$ 143.0376; Found 143.0387.

*Ethyl-3-amino-5-nitrobenzoate (**2w**).*[7c] **2w** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (3:1)) as a yellow solid. Yield 68 mg, 65%; mp 155−156 °C; ^{1}H NMR (600 MHz, CD_3OD): δ 8.19 (m, 1H), 7.64−7.61 (m, 2H), 4.39 (q, J = 7.1 Hz 2H), 1.40 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.8, 149.2, 147.5, 132.7, 120.9, 113.9, 112.4, 61.7, 14.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_9H_{11}N_2O_4$ 211.0719; Found 211.0701.

*5-Aminoisoquinoline (**2x**).*[7c] **2x** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (6:4)) as a brown solid. Yield 64 mg, 90%; mp 128−129 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.20 (s, 1H), 8.50 (d, J = 5.8 Hz, 2H), 7.59 (d, J = 5.9 Hz, 1H), 7.42(d, J = 4.0 Hz, 2H), 6.97 (t, 1H), 4.25 (brs, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 153.3, 142.4, 141.6, 126.8, 1281, 126.3, 118.3, 114.4, 113.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_9H_9N_2$ 145.0766; Found 145.0798.

*2-Amino-5-chloropyridine (**2y**, CAS Number 1072-98-6).* **2y** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (7:3)) as a yellow solid. Yield 59 mg, 92%; mp 115−116 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.02−6.91 (m, 2H), 3.89 (brs, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 142.0, 139.8, 136.2, 124.8, 124.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_5H_6ClN_2$ 129.0220; Found 129.0250.

*3-Amino-2-chloro-5-methylpyridine (**2z**, CAS Number 34552-13-1).* **2z** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (7:3)) as a yellow solid. Yield 64 mg, 90%; mp 84−85 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.62 (s, 1H), 6.86 (s, 1H), 4.00 (brs, 2H), 2.22 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 139.0, 138.9, 134.4, 133.3, 123.2, 17.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_6H_8ClN_2$ 143.0376; Found 143.0354.

*6-Aminobenzothiazole (**2aa**).*[7c] **2aa** was obtained by following the general procedure described above and purified by column chromatography (*n*-hexane:ethyl acetate (7:3)) as a brown solid. Yield 45 mg, 50%; mp 105−108 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.68 (s, 1H), 7.88−7.86 (m, 1H), 7.14 (s, 1H), 6.86−6.84 (m, 1H), 3.46 (brs, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 149.8, 146.7, 144.8, 135.4, 123.9, 115.8, 105.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_7H_7N_2S$ 151.0330; Found 151.0314.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra. 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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