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Note

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Copper-Catalyzed Selective *N*-Vinylation of 3-(Hydroxyimino)indolin-2-ones with Alkenyl Boronic Acids: Synthesis of *N*-Vinyl Nitrones and Spirooxindoles

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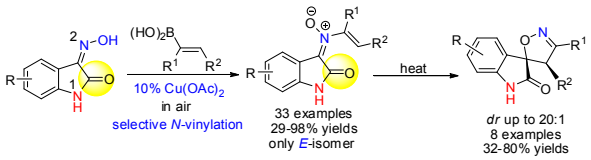


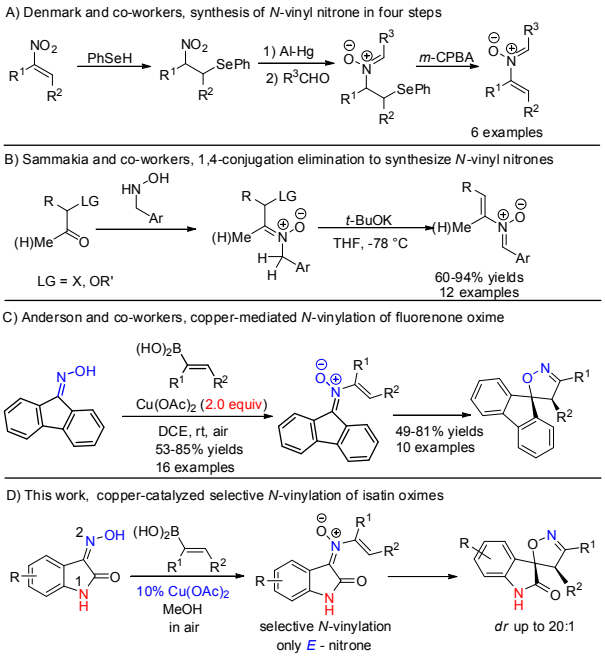
ABSTRACT: A copper-catalyzed selective cross-coupling reaction of 3-(hydroxyimino)indolin-2-ones with alkenyl boronic acids to access (*E*)-*N*-vinyl oxindole nitrones has been achieved under mild conditions. The studies showed that catalytic copper salt selectively gave mono *N*-vinylation products while 2.0 equiv of copper salt provided double *N*-vinylation products. The control experiments revealed that the carbonyl group in 3-(hydroxyimino)indolin-2-one played important roles on *N*-vinylation. Furthermore, the prepared *N*-vinyl oxindole nitrones could be converted to spirooxindoles in good yields under thermal conditions.

Nitrones are a versatile and important type of compounds and can undergo a variety of reactions.[1] Recently, *N*-vinyl nitrones have attracted much attentions as useful

synthetic intermediates and showed distinctive characteristics because of the rich chemistry of the double bond.[2] Despite many strategies have been developed to synthesize *N*-aryl or *N*-alkyl nitrones, methods to access *N*-vinyl nitrones are sparsely reported.[3] In 2006, Denmark and Montgomery reported the first general and practical method to prepare *N*-vinyl nitrones from nitroalkenes and aldehydes in four steps involving 1,4-addition, reduction, condensation and oxidation (Scheme 1-A).[4] In 2015, Sammakia and co-workers developed an efficient condensation of an α-chloroaldhyde or an α-acetoxy ketone with a substituted benzyl hydroxylamine and sequence of 1,4-conjugation elimination in the presence of a base to provide various *N*-vinyl nitrones in two steps (Scheme 1-B).[5] Although Denmark and Sammakia independently developed an efficient and general method to afford *N*-vinyl nitrones, their methods suffered from some drawbacks, such as multi-step synthesis, non-commercial starting materials, and functional groups tolerance. To develop a more facile method from readily available starting materials, Anderson's group recently reported a copper-mediated *N*-vinylation of 9-fluorenone oximes with alkenyl boronic acids to prepare *N*-vinyl nitrones in good yields (Scheme 1-C).[6] The prepared *N*-vinyl nitrones underwent a rearrangement to provide spiroisoxazoles under thermal conditions. In 2015, Anderson and co-workers continued to report a similar *N*-vinylation of chalcone oximes to access corresponding *N*-vinyl nitrones.[7] Anderson's *N*-vinylation route is indeed short and efficient. Despite only fluorenone oximes and chalcone oximes are used, it is the most direct strategy to prepare *N*-vinyl nitrones up to now. Therefore, *N*-vinylation of oximes *via* the Chan–Lam reaction is

still desirable.[8] In particular, it is more challenging for the controllable selectivity of coupling reaction of oxime substrates with additional N-H or O-H groups to synthesize *N*-vinyl nitrones. This could improve the efficiency in synthesis of complex molecules and avoid protection and deprotection procedures.[9]

During studies on synthesis of nitrones in our group,[10] we hypothesized that a selective N^2-vinylation of 3-(hydroxyimino)indolin-2-one containing both N-H and O-H groups with alkenyl boronic acids would directly afford *N*-vinyl oxindole nitrones *via* the Chan-Lam reaction (Scheme 1-D). Oxindole nitrones have been extensively utilized in cycloaddition reactions because of its facile access to privileged spirooxindoles.[11] Herein, we reported a copper-catalyzed selective *N*-vinylation of 3-(hydroxyimino)indolin-2-one with alkenyl boronic acids to synthesize various (*Z*)-*N*-vinyl nitrones and sequence of rearragement to afford spirooxindole-isoxazolines.

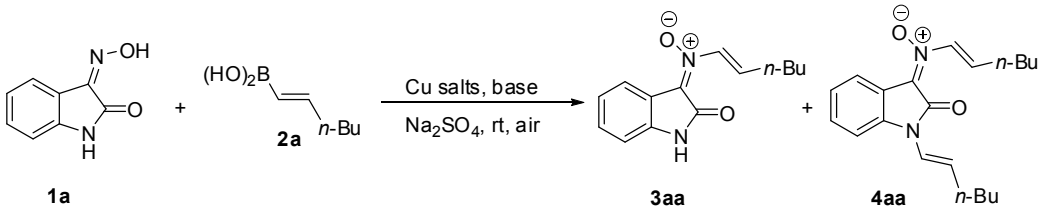


Scheme 1 An Overview of Synthesis of *N*-Vinyl Nitrones

Initially, the *N*-vinylation was screened by using 3-(hydroxyimino)indolin-2-one **1a** and alkenyl boronic acid **2a**. No reaction occurred for 24 h in 1,2-dichloroethane (DCE) when $CuCl_2$ or $Cu(OTf)_2$ was used as catalyst in the presence of pyridine (pyr) with Na_2SO_4 as an additive (Table 1, entries 1-2). To our delight, *N*-vinyl nitrone **3aa** was isolated in good yield as a major isomer accompanied with nitrone **4aa** as a minor isomer when CuCl or $Cu(OAc)_2$ was used (Table 1, entries 3-4). Compounds **3aa** and **4aa** were easily separated by flash chromatography. The structure of nitrone **3** was further confirmed by the X-ray diffraction analysis of nitrone **3ca** in Table 2, which indicates the C=N bond of nitrone **3** is a *E*–configuration.[12] Actually, the yield of **3aa** was a little bit lower without addition of Na_2SO_4 (Table 1, entry 5). A screen of solvents revealed that MeOH sharply promoted the formation of **3aa** and gave the best result (Table 1, entries 6-10). The MeOH perhaps affected the pKa value of N-H group and the nucleophilicity of nitrogen in oxindole so that mono *N*-vinylation product was observed as a major isomer. Product **3aa** was obtained in 93% yield when alkenyl boronic acid **2a** was decreased to 2.0 equiv (Table 1, entry 11). The base affected the reaction obviously (Table 1, entries 12-15). The yield of **3aa** was only afforded in 8% using NEt_3 while 57% yield of **3aa** was obtained by using Cs_2CO_3. The addition of t-BuOK or without base inhibited the reaction competely. The yield of **3aa** was improved to 95% when the reaction ran at 40 °C, however, decreased yield of **3aa** was observed by higher temperature (Table 1, entries 16-17). The amount of copper salt played important roles on the yield of **3aa** and **4aa** (Table 1, entries 18-19). Increasing the amount of $Cu(OAc)_2$ decreased the yield of **3aa** but improved the yield

of **4aa** (Table 1, entries 11 *vs* 18-19). The similar result was also observed in DCE (Table 1, entries 21-22). In particular, nitrone **4aa** was afforded in 77% yield accompanied with **3aa** in 17% yield in DCE under 2.0 equiv of $Cu(OAc)_2$ with 4.0 equiv of **2a** (Table 1, entry 22). But the yield of **4aa** was reduced with increasing temperature (Table 1, entry 23). These results disclosed that *N*-vinylation process was controlled by the amount of copper catalyst.

Table 1. Optimization of the reaction conditions[a,b]



entry	Cu salt	amount of Cu	solvent	base	**3aa**%	**4aa**%
1	$CuCl_2$	10%	DCE	pyr	-	-
2	$Cu(OTf)_2$	10%	DCE	pyr	-	-
3	CuCl	10%	DCE	pyr	73	15
4	$Cu(OAc)_2$	10%	DCE	pyr	74	11
5[c]	$Cu(OAc)_2$	10%	DCE	pyr	65	6
6	$Cu(OAc)_2$	10%	toluene	pyr	75	6
7	$Cu(OAc)_2$	10%	MeCN	pyr	73	3
8	$Cu(OAc)_2$	10%	DMF	pyr	68	6
9	$Cu(OAc)_2$	10%	DMSO	pyr	65	8

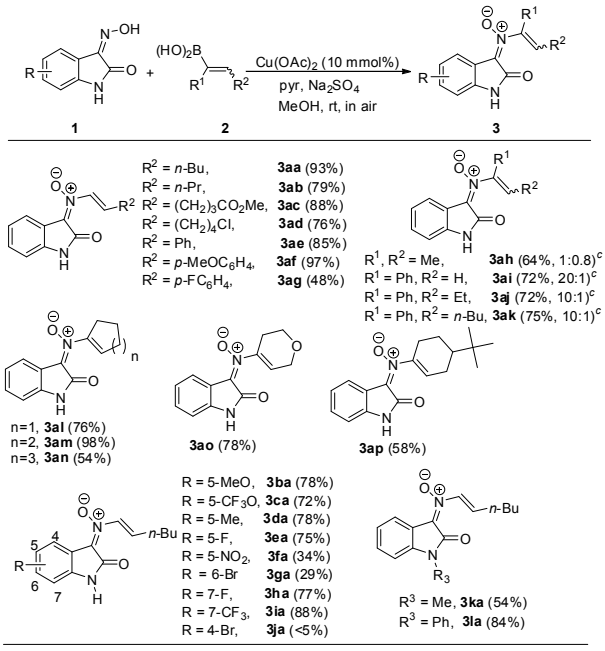
10	$Cu(OAc)_2$	10%	MeOH	pyr	89	4
11[d]	$Cu(OAc)_2$	10%	MeOH	pyr	93	4
12[d]	$Cu(OAc)_2$	10%	MeOH	NEt_3	8	-
13[d]	$Cu(OAc)_2$	10%	MeOH	t-BuOK	-	-
14[d]	$Cu(OAc)_2$	10%	MeOH	Cs_2CO_3	57	-
15[d]	$Cu(OAc)_2$	10%	MeOH	-	-	-
16[d,e]	$Cu(OAc)_2$	10%	MeOH	pyr	95	2
17[d,f]	$Cu(OAc)_2$	10%	MeOH	pyr	77	8
18[d]	$Cu(OAc)_2$	50%	MeOH	pyr	72	26
19[d]	$Cu(OAc)_2$	200%	MeOH	pyr	44	54
20[d]	$Cu(OAc)_2$	200%	DCE	pyr	23	62
21[g]	$Cu(OAc)_2$	200%	DCE	pyr	17	77
22[g]	$Cu(OAc)_2$	50%	DCE	pyr	47	43
23[e,g]	$Cu(OAc)_2$	200%	DCE	pyr	46	52

[a]Reaction conditions: **1a** (0.3 mmol), **2a** (0.9 mmol, 3.0 equiv), Cu salts (10 % mmol), base (3.0 equiv), Na_2SO_4 (6.0 equiv), solvent (3 mL), 25 °C, 2−24 h; [b]Isolated yield; [c]without Na_2SO_4; [d]**2a** (0.6 mmol, 2.0 equiv) was used; [e]ran at 40 °C; [f]ran at 80 °C; [g]**2a** (1.2 mmol, 4.0 equiv) was used.

To test the scope of formation of *N*-vinyl nitrone **3**, several 3-(hydroxyimino)indolin-2-ones (**1a-l)** and alkenyl boronic acids (**2a-p**) were screened under copper-catalyzed conditions identified in Table 1, entry 11. As shown in Table 2, various linear and cyclic alkenyl boronic acids were efficiently converted

into the corresponding *N*-vinyl oxindole nitrones **3** in good to excellent yields. Monosubstituted alkenyl boronic acids provided better yields than linear disubstituted alkenyl boronic acids (**3aa-ag** *vs* **3ah-ak**). However, linear disubstituted alkenyl boronic acids afforded both isomers of nitrone **3** (**3ah-ak**).[13] The isomers of nitrone **3ah-ak** were the *E*/*Z* configuration of the C=C bond, which were derived from the alkenyl boronic acids. This showed that both *E* and *Z* configuration of alkenyl boronic acids could be coupled to provide *N*-vinyl nitrones. Cyclic alkenyl boronic acids gave moderate yields and tolerated five, six, and seven-membered rings while cyclohexenyl boronic acid **2m** afforded nitrone **3am** in 98% yield (**3al-ap**). The substituted groups on the aryl ring of 3-(hydroxyimino)indolin-2-ones were also examined under the copper-catalyzed conditions. The coupling reaction was compatible with the 5, 6, 7-positions in the aryl ring of the oximes (**3ba-ia**). Electron-donating and electron-withdrawing groups at the 5-position did not affect the yields of *N*-vinyl oxindole nitrones except for 5-NO_2 group giving 34% yield (**3ba-fa**). When 6-Br substituted oxime **1g** was used, nitrone **3ga** was obtained in 29% yield perhaps owing to the solubility of the oxime in MeOH.[14] The coupling reaction did not occur when the oxime **1j** with a 4-bromo group because of the steric hindrance (**3ja**). When methyl- and phenyl-protected oximes **1k** and **1l** were used, nitrone **3ka** and **3la** were afforded in 54% and 84% yields, respectively. In all cases, the *N*-vinyl nitrone **3** was obtained as a major isomer while *N*-vinyl nitrone **4** was always observed in less than 8% yield. Some sensitive functional groups such as halides, ester, and nitro groups were compatible, which enables further transformations.

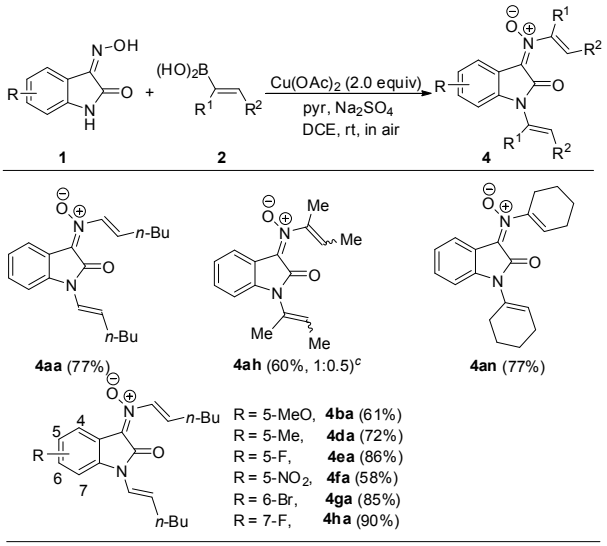
Table 2. The Scope of Preparing *N*-Vinyl Nitrone **3**[a,b]



[a]Reaction conditions: **1** (0.3 mmol), alkenyl boronic acid **2** (0.6 mmol, 2.0 equiv), $Cu(OAc)_2$ (0.03 mmol, 10 %), pyr (0.9 mmol, 3.0 equiv), Na_2SO_4 (6.0 equiv), MeOH (3 mL), 25 °C, 2−24 h; [b]Isolated yield; [c]*E*/*Z* ratio for C=C bond in nitrone.

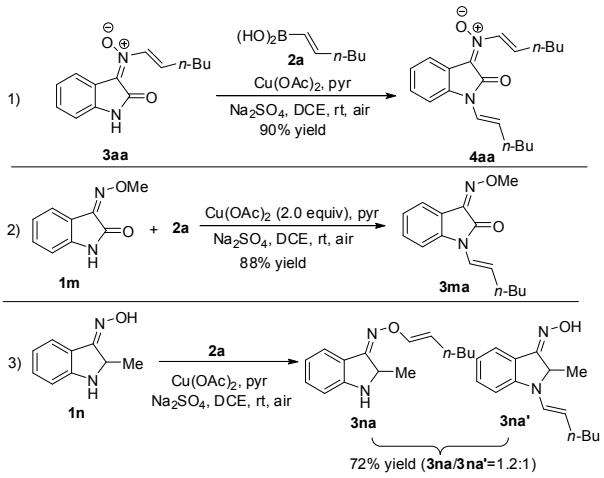
The scope of double *N*-vinylation of oxime **1** to prepare *N*-vinyl nitrone **4** was further evaluated under the copper-mediated conditions identified in Table 1, entry 21. The reaction tolerated a variety of alkenyl boronic acids **2** and 3-(hydroxyimino)indolin-2-ones **1** (Table 3). Linear and cyclic alkenyl boronic acids gave the corresponding nitrone **4** in good to excellent yields. Compared to formation of nitrone **3ah**, when 2-butenyl boronic acid **2h** with a 2:1 *E*/*Z* ratio was used, nitrone **4ah** was afforded with a 1:0.5 *E*/*Z* ratio at the C=C bond. Most of 3-(hydroxyimino)indolin-2-ones bearing either electron-donating or electron-withdrawing groups in the 5, 6, 7–positions could provide corresponding nitrone **4** in good to excellent yields.

Table 3. The Scope of Preparing *N*-Vinyl Nitrone **4**[a,b]



[a]Reaction conditions: **1** (0.3 mmol), alkenyl boronic acid **2** (1.2 mmol, 4.0 equiv), $Cu(OAc)_2$ (0.6 mmol, 2.0 equiv), pyr (0.9 mmol, 3.0 equiv), Na_2SO_4 (6.0 equiv), DCE (3 mL), 25 °C, 2−24 h; [b]Isolated yield; [c]*E*/*Z* ratio of C=C bond in nitrone.

Treatment of nitrone **3aa** with alkenyl boronic acid **2a** under copper-mediated conditions, nitrone **4aa** was isolated in 90% yield (Scheme 2-1). To study the effect on formation of *N*-vinyl nitrones from oxime structure, we performed the control experiments. While methyl protected oxime **1m** reacted with **2a**, N^1-vinylation product **3ma** was afforded in 88% yield (Scheme 2-2). To our surprise, the oxime **1m** and alkenyl boronic acid **2a** were subjected to the optimal conditions, *O*- or N^1-vinylation product **3na** and **3na'** were observed in 72% yield (Scheme 2-3). These results suggested that the carbonyl group in oxime **1** mainly controlled the formation of nitrones **3** or **4** because it decreased the nucleophilicity of the *N*-atom.

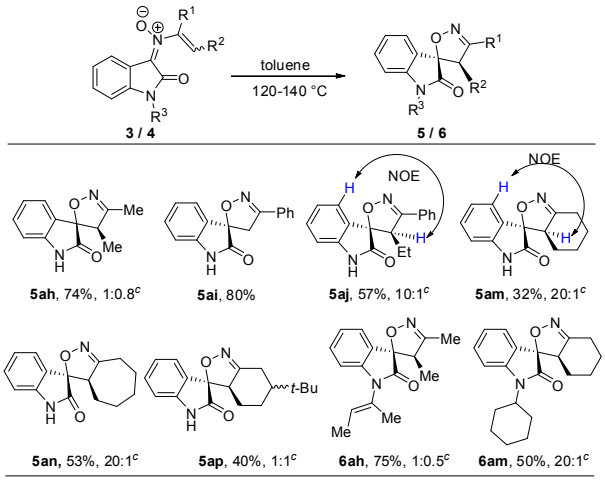


Scheme 2. The Structural Effect on *N*-Vinylation of Oximes

With the two types of *N*-vinyl nitrones **3** and **4** in hand, we explored their thermal rearrangements. As shown in Table 4, both nitrones **3** and **4** could be smoothly converted to corresponding spirooxindole product **5** and **6** in moderate to good yields in toluene at 120−140 °C. Both disubstituted linear and cyclic *N*-vinyl nitrones were compatible for this thermal transformation, while monosubstituted *N*-vinyl nitrone such as **3aa-ag** in Table 2 decomposed. The disubstituted linear *N*-vinyl nitrones required shorter reaction time and provided better yields than cyclic *N*-vinyl nitrones (**5ah**, **5ai**, **5aj** *vs* **5am**, **5an**, **5ap**). As expected based on Anderson's mechanism,[6] the diastereoselectivity of spirooxindoles correlates with the *E*/*Z*-isomer ratio at C=C bond in the *N*-vinyl nitrones. When nitrone **3ah** with a 1:0.8 *E*/*Z* ratio was heated at 120 °C, a 1:0.8 *dr* value of spirooxindole **5ah** was obtained. Spirooxindole **5aj** was afforded in 10:1 *dr* by heating nitrone **3aj** with 10:1 *E*/*Z* ratio at C=C bond. When nitrone **3am** and **3an** with a 20:1 *E*/*Z* ratio were subjected to the optimal condtions, the spirooxindole **5am** and **5an** were furnished with 20:1 *dr* value. The relative configuration of the spirooxindole was determined by NOESY spectra of **5aj** and **5am**,

which revealed that the proton connected with ethyl group in **5aj** or with six-membered ring in **5am** both had correlation with the proton of the aryl ring.[15] Since spirooxindoles and isoxazoles have been identified as bioactive compounds, this strategy to access these compounds might lead to expand more applications in pharmaceuticals.[16]

Table 4. Thermal Reaction to Form Spirooxindole **5** or **6**[a,b]



[a]Reaction conditions: **3** or **4** (0.2 mmol), toluene (2 mL), 120−140 °C, 10−48 h; [b]Isolated yield; [c]*dr* value.

In summary, We have developed a copper-catalyzed *N*-vinylation of 3-(hydroxyimino)indolin-2-ones with alkenyl boronic acids to prepare (*E*)-*N*-vinyl oxindole nitrones in good to excellent yields. The reaction tolerated linear and cyclic alkenyl boronic acids with various functional groups. The *N*-vinyl nitrones could undergo a thermal rearrangement to access various spirooxindoles in good yields and high diastereoselectivity. This coupling strategy provided not only a facile method to prepare *N*-vinyl nitrones but also a good entry for spirooxindoles to be further studied in pharmaceuticals.

EXPERIMENTAL SECTION

General Methods. All reactions were performed under an air atmosphere. Commercially available reagents were used without further purification. The NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on 400, or 500 MHz instrument with TMS as the internal standard. NMR data are represented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in hertz (Hz), and integration. IR spectra were recorded on FT-IR spectrometer, and only major peaks are reported in cm^{-1}. HRMS were measured in ESI mode and the mass analyzer of the HRMS was TOF. Flash column chromatography was performed on silica gel (300-400 mesh). The oxime **1a**[17], **1b**[18], **1c**[10b], **1d**[17], **1e**[17], **1f**,[19] **1g**[17], **1h**[20], **1i**[21], **1j**[22], **1k**[23], **1l**[24], **1m**[25], and **1n**[26], the alkenyl boronic acid **2a-p**[6,7] were prepared according to literature methods and their spectral data matched literature values.

General procedure for preparing *N*-vinyl nitrone 3: In a 25 mL flask was charged with 3-(hydroxyimino)indolin-2-one **1** (0.3 mmol), alkenyl boronic acid **2** (0.6 mmol, 2.0 equiv), $Cu(OAc)_2$ (0.03 mmol, 10%) and anhydrous Na_2SO_4 (6.0 equiv) under air atmosphere. Then, MeOH (3.0 mL) and pyridine (0.9 mmol, 3.0 equiv) was added *via* syringe. The reaction flask was then capped with a septum pierced with a ventilation needle and stirred vigorously at 25 °C for 2−24 h until the oxime **1** disappeared (monitored by TLC). At this time, the reaction was quenched by H_2O (10 mL) and extracted with DCM (3 × 10 mL). Then, dried over with Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the crude product

was purified by flash chromatography (the crude residue was dry loaded on silica gel, 1/10 to 1/6, ethyl acetate/petroleum ether) to provide *N*-vinyl nitrone **3**.

(1*E*,*NE*)-*N*-(2-Oxoindolin-3-ylidene)hex-1-en-1-amine oxide (3aa), 0.068 g, 93% yield, orange solid. mp: 170−171 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 10.94 (s, 1H), 8.79 (d, J = 13.2 Hz, 1H), 8.23 (d, J = 7.6 Hz, 1H), 7.36 (t, J = 7.6 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 6.96−6.86 (m, 2H), 2.30 (q, J = 7.2 Hz, 2H), 1.47−1.41 (m, 2H), 1.37−1.30 (m, 2H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 161.8, 140.9, 134.7, 132.8, 132.6, 132.5, 125.3, 122.6, 119.0, 110.4, 30.7, 29.0, 22.3, 14.2; IR (thin film) 3452, 3174, 2926, 1683, 1525, 1459, 1213, 771 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{17}N_2O_2$ $(M+H)^+$ 245.1290, found 245.1312.

(1*E*,*NE*)-*N*-(2-Oxoindolin-3-ylidene)pent-1-en-1-amine oxide (3ab), 0.055 g, 79% yield, orange solid. mp: 173−174 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 10.95 (s, 1H), 8.82 (d, J = 13.2 Hz, 1H), 8.25 (d, J = 13.2 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.98−6.88 (m, 2H), 2.30 (q, J = 7.6 Hz, 2H), 1.55−1.46 (m, 2 H), 0.96 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 161.7, 140.8, 134.4, 132.8, 132.6, 132.4, 125.2, 122.5, 118.9, 110.3, 31.2, 21.8, 14.0; IR (thin film) 3396, 3178, 2960, 1714, 1532, 1460, 1205, 657 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{13}H_{15}N_2O_2$ $(M+H)^+$ 231.1134, found 231.1128.

(1*E*,*NE*)-6-Methoxy-6-oxo-*N*-(2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (3ac), 0.076 g, 88% yield, orange solid. mp: 145−146 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 10.94 (s, 1H), 8.79 (d, J = 13.2 Hz, 1H), 8.23 (d, J = 7.2 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 6.93−6.87 (m, 2H), 3.59 (s, 3H), 2.39 (t, J

= 7.6 Hz, 2H), 2.33−2.28 (m, 2 H), 1.75 (t, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 173.5, 161.7, 140.9, 133.7, 133.1, 132.7, 132.6, 125.2, 122.5, 118.9, 110.4, 51.7, 33.1, 28.5, 23.9; IR (thin film) 3459, 3179, 2952, 1712, 1530, 1461, 1207, 655 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{17}N_2O_4$ $(M+H)^+$ 289.1188, found 289.1181.

(1*E*,*NE*)-6-Chloro-*N*-(2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (3ad), 0.063 g, 76% yield, orange solid. mp: 157−158 °C; ^{1}H NMR (500 MHz, DMSO–d_6): δ 10.94 (s, 1H), 8.80 (d, J = 13.0 Hz, 1H), 8.23 (d, J = 8.5 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.04 (t, J = 7.5 Hz, 1H), 6.96−6.87 (m, 2H), 3.68 (t, J = 7.0 Hz, 2H), 2.34 (t, J = 7.0 Hz, 2H), 1.80 (q, J = 6.5 Hz, 2 H), 1.63 (q, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, DMSO–d_6): δ 161.7, 140.9, 134.2, 133.0, 132.7, 132.5, 125.2, 122.5, 118.9, 110.4, 45.5, 32.0, 28.4, 25.8; IR (thin film) 3398, 3161, 2929, 1713, 1533, 1460, 1208, 657 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{16}ClN_2O_2$ $(M+H)^+$ 279.0900, found 279.0898.

(1*E*,*NE*)-*N*-(2-Oxoindolin-3-ylidene)-2-phenylethenamine oxide (3ae), 0.067 g, 85% yield, orange solid. mp: 212−213 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 11.0 (s, 1H), 9.54 (d, J = 13.6 Hz, 1H), 8.28 (d, J = 7.6 Hz, 1H), 7.80 (d, J = 13.6 Hz, 1H), 7.65 (d, J = 6.8 Hz, 2H), 7.48−7.42 (m, 3H), 7.38 (t, J = 7.6 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.91 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 161.9, 141.0, 133.6, 133.4, 132.9, 131.8, 131.2, 130.8, 129.7, 128.7, 125.4, 122.6, 119.1, 110.5; IR (thin film) 3453, 3175, 2927, 1710, 1525, 1459, 1253, 657 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{13}N_2O_2$$(M+H)^+$ 265.0977, found 265.0971.

(1*E*,*NE*)-2-(4-Methoxyphenyl)-*N*-(2-oxoindolin-3-ylidene)ethenamine oxide (3af), 0.085 g, 97% yield, orange solid. mp: 207−208 °C; ^{1}H NMR (500 MHz,

DMSO–d_6): δ 10.99 (s, 1H), 9.47 (d, J = 13.0 Hz, 1H), 8.28 (d, J = 7.5 Hz, 1H), 7.78 (d, J = 13.0 Hz, 2H), 7.62 (d, J = 8.5 Hz, 2H), 7.06 (t, J = 6.5 Hz, 3H), 6.90 (d, J = 6.5 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (125 MHz, DMSO–d_6): δ 161.9, 161.5, 140.7, 132.7, 132.5, 131.2, 130.5, 129.9, 125.8, 125.2, 122.5, 119.2, 115.3, 110.4, 55.9; IR (thin film) 3398, 3161, 2929, 1713, 1533, 1460, 1208, 657 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{15}N_2O_3$ $(M+H)^+$ 295.1083, found 295.1082.

(1*E*,*NE*)-2-(4-Methoxyphenyl)-*N*-(2-oxoindolin-3-ylidene)ethenamine oxide (3ag), 0.040 g, 48% yield, orange solid. mp: 131−132 °C; ^{1}H NMR (500 MHz, DMSO–d_6): δ 11.04 (s, 1H), 9.50 (d, J = 13.5 Hz, 1H), 8.29 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 13.5 Hz, 1H), 7.75−7.72 (m, 2H), 7.40 (t, J = 7.5 Hz, 1H), 7.35 (t, J = 8.5 Hz, 2H), 7.08 (t, J = 8.0 Hz, 1H), 6.9 (d, J = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 164.9 (d, J = 247.1 Hz), 161.9, 141.0, 133.5, 133.0, 131.7, 131.1 (d, J = 60.5 Hz), 130.1, 130.0 (d, J = 29.0 Hz), 125.4, 122.7, 119.0, 116.9 (d, J = 21.9 Hz), 110.5; IR (thin film) 3430, 3200, 2926, 1705, 1508, 1457, 1231, 655 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{12}FN_2O_2$ $(M+H)^+$ 283.0883, found 283.0873.

***N*-(2-Oxoindolin-3-ylidene)but-2-en-2-amine oxide (3ah)**, *E*/*Z* = 1:0.8, 0.041 g, 64% yield, orange solid. mp: 128−129 °C; *E-isomer*: ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.77 (s, 1H), 8.20 (d, J = 7.6 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.06 (t, J = 8.0 Hz, 1H), 6.91 (d, J = 7.6 Hz, 1H), 5.75 (t, J = 6.4 Hz, 1H), 2.02 (s, 3H), 1.71 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.6, 143.0, 141.2, 134.0, 132.6, 124.5, 122.6, 122.4, 118.9, 110.4, 19.5, 13.0; *Z-isomer*: ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.71 (s, 1H), 8.15 (d, J = 7.6 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 6.91 (t, J = 7.6 Hz, 1H),

6.88 (d, J = 8.0 Hz, 1H), 5.50 (t, J = 6.4 Hz, 1H), 1.99 (s, 3H), 1.43 (d, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.1, 142.5, 141.0, 133.5, 132.3, 124.4, 122.2, 119.4, 118.2, 110.2, 14.3, 12.5; IR (thin film) 3453, 3074, 2927, 1697, 1518, 1461, 1217, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{13}N_2O_2$ $(M+H)^+$ 217.0977, found 217.0977.

(2*E*,*NE*)-*N*-(2-Oxoindolin-3-ylidene)but-2-en-2-amine oxide (3ai), 0.057 g, 72% yield, orange solid. mp: 143−144 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 10.77 (s, 1H), 8.27 (d, J = 7.2 Hz, 1H), 7.46−7.38 (m, 6H), 7.09 (t, J = 7.6 Hz, 1H), 6.91 (d, J = 8.0 Hz, 1H), 6.04 (s, 1H), 5.60 (s, 1H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 160.4, 151.6, 141.6, 135.3, 133.0, 132.8, 129.7, 129.4, 125.8, 124.9, 122.5, 118.5, 111.6, 110.6; IR (thin film) 3454, 3084, 2925, 1708, 1546, 1346, 1197, 696 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{13}N_2O_2$ $(M+H)^+$ 265.0977, found 265.0976.

(1*E*,*NE*)-*N*-(2-Oxoindolin-3-ylidene)-1-phenylbut-1-en-1-amine oxide (3aj), 0.063 g, 72% yield, orange oil. ^{1}H NMR (500 MHz, DMSO–d_6): δ 10.76 (s, 1H), 8.31 (d, J = 7.5 Hz, 1H), 7.43−7.30 (m, 6H), 7.10 (t, J = 7.5 Hz, 1H), 6.92 (d, J = 8.0 Hz, 1H), 6.33 (t, J = 7.5 Hz, 1H), 2.10−2.00 (m, 2H), 1.01 (t, J = 3.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO–d_6): δ 159.9, 144.9, 141.5, 135.5, 133.5, 133.0, 129.1, 128.7, 126.6, 125.0, 124.8, 122.5, 118.0, 110.5, 21.3, 13.5; IR (thin film) 3435, 3196, 2930, 1713, 1547, 1461, 1192, 697 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{17}N_2O_2$ $(M+H)^+$ 293.1290, found 293.1282.

(1*E*,*NE*)-*N*-(2-Oxoindolin-3-ylidene)-1-phenylhex-1-en-1-amine oxide (3ak), 0.072 g, 75% yield, orange oil. ^{1}H NMR (400 MHz, DMSO–d_6): δ 10.74 (s, 1H), 8.30

(d, J = 7.2 Hz, 1H), 7.43−7.29 (m, 6H), 7.10 (t, J = 7.6 Hz, 1H), 6.92 (d, J = 7.6 Hz, 1H), 6.33 (t, J = 7.6 Hz, 1H), 2.06−2.00 (m, 2H), 1.42−1.36 (m, 2H), 1.29−1.24 (m, 2H), 0.82 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 159.9, 145.4, 141.5, 135.5, 133.6, 133.0, 129.2, 128.7, 125.4, 125.1, 124.8, 122.5, 118.0, 110.5, 30.6, 27.3, 22.2, 14.1; IR (thin film) 3252, 2928, 1716, 1617, 1546, 1459, 1196, 747 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{21}N_2O_2$ $(M+H)^+$ 321.1603, found 321.1595.

(*E*)-*N*-(2-Oxoindolin-3-ylidene)cyclopent-1-enamine oxide (3al), 0.052 g, 76% yield, orange solid. mp: 144−145 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 10.76 (s, 1H), 8.19 (d, J = 7.6 Hz, 1H), 7.38 (t, J = 7.2 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 6.12−6.11 (m, 1H), 2.70−2.69 (m, 2H), 2.51−2.50 (m, 2H), 2.08−2.01 (m, 2H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 160.4, 146.7, 141.0, 134.8, 132.6, 128.4, 124.5, 122.2, 118.8, 110.2, 31.8, 31.1, 22.4; IR (thin film) 3411, 3176, 2950, 1717, 1549, 1337, 1243, 688 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{13}H_{13}N_2O_2$ $(M+H)^+$ 229.0977, found 229.0972.

(*E*)-*N*-(2-Oxoindolin-3-ylidene)cyclohex-1-enamine oxide (3am), 0.071 g, 98% yield, orange solid. mp: 186−187 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 10.69 (s, 1H), 8.15 (d, J = 7.6 Hz, 1H), 7.36 (t, J = 7.6 Hz, 1H), 7.02 (t, J = 7.2 Hz, 1H), 6.88 (d, J = 7.6 Hz, 1H), 5.95−5.91 (m, 1H), 2.35−2.28 (m, 2H), 2.14−2.13 (m, 2H), 1.77−1.74 (m, 2H), 1.62−1.59 (m, 2H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 160.6, 144.9, 141.0, 133.7, 132.3, 124.5, 124.3, 122.1, 118.8, 110.2, 25.9, 24.1, 22.2, 21.2; IR (thin film) 3452, 3174, 2927, 1683, 1526, 1459, 1214, 771 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{15}N_2O_2$ $(M+H)^+$ 243.1134, found 243.1131.

(1*E*,*NE*)-*N*-(2-Oxoindolin-3-ylidene)cyclohept-1-enamine oxide (3an), 0.042 g, 54% yield, orange solid. mp: 170−171 °C; ^{1}H NMR (500 MHz, DMSO–d_6): δ 10.67 (s, 1H), 8.13 (d, J = 7.5 Hz, 1H), 7.35 (d, J = 7.5 Hz, 1H), 7.01 (t, J = 7.5 Hz, 1H), 6.87 (d, J = 7.5 Hz, 1H), 6.04 (t, J = 6.0 Hz, 1H), 2.48−2.45 (m, 2H), 2.21−2.19 (m, 2H), 1.73−1.71 (m, 4H), 1.64−1.63 (m, 2H); ^{13}C NMR (125 MHz, DMSO–d_6): δ 160.7, 148.8, 140.9, 133.3, 132.3, 129.0, 124.3, 122.2, 118.9, 110.2, 31.5, 30.7, 26.8, 26.2, 26.1; IR (thin film) 3456, 3194, 2926, 1621, 1463, 1341, 1193, 752 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{17}N_2O_2$ $(M+H)^+$ 257.1290, found 257.1285.

(*E*)-*N*-(2-Oxoindolin-3-ylidene)-3,6-dihydro-2H-pyran-4-amine oxide (3ao), 0.057 g, 78% yield, orange solid. mp: 178−179 °C; ^{1}H NMR (500 MHz, DMSO–d_6): δ 10.76 (s, 1H), 8.16 (d, J = 7.5 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.03 (t, J = 7.0 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H), 6.14−6.12 (m, 1H), 4.21−4.20 (m, 2H), 3.86 (t, J = 5.5 Hz, 2H), 2.44−2.43 (m, 2H); ^{13}C NMR (125 MHz, DMSO–d_6): δ 160.6, 141.5, 141.2, 134.1, 132.6, 124.4, 123.6, 122.2, 118.7, 110.2, 63.9, 63.7, 26.2; IR (thin film) 3450, 3194, 2923, 1705, 1539, 1459, 1121, 659 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{13}H_{13}N_2O_3$ $(M+H)^+$ 245.0926, found 245.0920.

(*E*)-4-tert-Butyl-*N*-(2-oxoindolin-3-ylidene)cyclohex-1-enamine oxide (3ap), 0.052 g, 58% yield, orange solid. mp: 175−176 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 10.70 (s, 1H), 8.15 (d, J = 7.5 Hz, 1H), 7.36 (t, J = 7.5 Hz, 1H), 7.02 (t, J = 7.5 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H), 5.95−5.93 (m, 1H), 2.36−2.33 (m, 2H), 2.19−2.15 (m, 1H), 1.93−1.88 (m, 2H), 1.36−1.31 (m, 2H), 0.89 (s, 9H); ^{13}C NMR (125 MHz, DMSO–d_6): δ 160.5, 144.7, 141.0, 133.8, 132.3, 124.7, 124.3, 122.2, 118.8, 110.2,

42.9, 32.4, 30.3, 29.5, 27.5, 27.2, 25.8, 23.8; IR (thin film) 3433, 3194, 2964, 1650, 1463, 1341, 1193, 763 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{23}N_2O_2$ $(M+H)^+$ 299.1760, found 299.1759.

(1*E*,*NE*)-*N*-(5-Methoxy-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (3ba), 0.064 g, 78% yield, orange solid. mp: 170−171 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.84 (d, J = 13.2 Hz, 1H), 8.49 (s, 1H), 8.06 (d, J = 2.0 Hz, 1H), 7.13−7.06 (m, 1H), 6.92 (t, J = 8.4 Hz, 1H), 6.79 (d, J = 2.0 Hz, 1H), 3.83 (s, 3H), 2.37 (q, J = 7.2 Hz, 2H), 1.57−1.49 (m, 2H), 1.45−1.34 (m, 2H), 0.96 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 155.9, 135.5, 132.8, 132.7, 132.6, 119.7, 118.8, 110.5, 110.3, 55.9, 30.7, 29.2, 22.2, 13.8; IR (thin film) 3453, 3193, 2927, 1713, 1526, 1488, 1247, 653 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{19}N_2O_3$ $(M+H)^+$ 275.1396, found 275.1393.

(1*E*,*NE*)-*N*-(2-Oxo-5-(trifluoromethoxy)indolin-3-ylidene)hex-1-en-1-amine oxide (3ca), 0.071 g, 72% yield, orange solid. mp: 171−172 °C; ^1H NMR (400 MHz, DMSO–d_6): δ 11.12 (s, 1H), 8.76 (d, J = 13.2 Hz, 1H), 8.12 (s, 1H), 7.37(d, J = 8.4 Hz, 1H), 7.00−6.94 (m, 2H), 2.32 (q, J = 7.2 Hz, 2H), 1.49−1.42 (m, 2H), 1.38−1.29 (m, 2H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 161.6, 143.4, 139.8, 135.7, 132.7, 132.1, 125.4, 122.0 (d, J = 253.8 Hz), 119.8, 117.6, 112.2, 55.9, 30.5, 28.9, 22.1, 14.1; IR (thin film) 3452, 3174, 2933, 1701, 1517, 1466, 1164, 661 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{16}F_3N_2O_3$ $(M+H)^+$ 329.1113, found 329.1097.

(1*E*,*NE*)-*N*-(5-Methyl-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (3da). 0.060 g, 78%, orange solid. mp: 179−180 °C; ^1H NMR (400 MHz, DMSO–d_6): δ 10.82 (s, 1H), 8.79 (d, J = 13.2 Hz, 1H), 8.06−8.05 (m, 1H), 7.16 (d, J = 8.0 Hz, 1H),

6.95−6.88 (m, 1H), 6.77 (d, J = 7.6 Hz, 1H), 2.30−2.27 (m, 5H), 1.49−1.41 (m, 2H), 1.38−1.31 (m, 2H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 161.8, 138.6, 134.4, 133.0, 132.7, 132.5, 131.3, 125.6, 119.0, 110.1, 30.6, 28.9, 22.2, 21.2, 14.1; IR (thin film) 3453, 3170, 2927, 1698, 1516, 1481, 1259, 658 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{19}N_2O_2$ $(M+H)^+$ 259.1447, found 259.1445.

(1*E*,*NE*)-*N*-(5-Fluoro-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (3ea), 0.059 g, 75% yield, orange solid. mp: 178−179 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.82 (d, J = 13.0 Hz, 1H), 8.25 (s, 1H), 8.17 (dd, J = 8.5, 2.0 Hz, 1H), 7.13−7.03 (m, 2H), 6.82 (t, J = 8.0 Hz, 1H), 2.37 (q, J = 7.0 Hz, 2H), 1.56−1.50 (m, 2H), 1.44−1.37 (m, 2H), 0.96 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.8, 160.0 (d, J = 238.8 Hz), 136.4, 134.7, 132.8, 131.9, 120.1 (d, J = 40 Hz), 118.2 (d, J = 98.5 Hz), 113.0 (d, J = 109 Hz), 110.1 (d, J = 33 Hz), 30.6, 29.2, 22.3, 13.8; IR (thin film) 3454, 3175, 2930, 1699, 1517, 1477, 1247, 658 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{16}FN_2O_2$ $(M+H)^+$ 263.1196, found 263.1198.

(1*E*,*NE*)-*N*-(5-Nitro-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (3fa), 0.030 g, 34% yield, yellow solid. mp: 64−65 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 11.60 (s, 1H), 8.92 (s, 1H), 8.70 (d, J = 13.2 Hz, 1H), 7.27 (t, J = 7.2 Hz, 1H), 7.05−6.99 (m, 2H), 2.34 (q, J = 6.8 Hz, 2H), 1.49−1.44 (m, 2H), 1.38−1.32 (m, 2H), 0.93 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 161.9, 146.0, 142.6, 136.6, 132.8, 131.5, 128.5, 119.7, 119.2, 110.5, 30.4, 29.0, 22.2, 14.2; IR (thin film) 3434, 2927, 1635, 1528, 1462, 1344, 1122, 747 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{16}N_3O_4$ $(M+H)^+$ 290.1141, found 290.1165.

(1*E*,*NE*)-*N*-(6-Bromo-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (3ga), 0.028 g, 29% yield, yellow solid. mp: 184−185 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 11.07 (s, 1H), 8.73 (d, J = 13.2 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 7.23 (d, J = 8.0 Hz, 1H), 7.02 (s, 1H), 6.98−6.91 (m, 1H), 2.30 (q, J = 6.8 Hz, 2H), 1.49−1.42 (m, 2H), 1.38−1.31 (m, 2H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 161.5, 142.0, 135.2, 132.8, 131.9, 126.3, 125.2, 124.9, 118.2, 113.1, 30.5, 28.9, 22.2, 14.1; IR (thin film) 3453, 3172, 2927, 1692, 1521, 1443, 1213, 661 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{14}BrN_2O_2$ $(M-H)^-$ 321.0239, found 321.0234.

(1*E*,*NE*)-*N*-(7-Fluoro-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (3ha), 0.060 g, 77% yield, orange solid. mp: 183−184 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 11.47 (s, 1H), 8.79 (d, J = 13.2 Hz, 1H), 8.07 (d, J = 7.6 Hz, 1H), 7.31 (t, J = 9.6 Hz, 1H), 7.07 (t, J = 8.0 Hz, 1H), 6.98−6.94 (m, 1H), 2.32 (q, J = 7.2 Hz, 2H), 1.48−1.43 (m, 2H), 1.37−1.31 (m, 2H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 161.5, 147.7 (d, J = 240.7 Hz), 135.5, 132.7, 132.2 (d, J = 5.1 Hz), 127.6 (d, J = 13.2 Hz), 123.4 (d, J = 5.7 Hz), 121.8 (d, J = 15.1 Hz), 121.2 (d, J = 2.9 Hz), 119.4 (d, J = 16.8 Hz), 30.6, 28.9, 22.2, 14.2; IR (thin film) 3454, 3219, 2928, 1716, 1525, 1354, 1190, 672 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{16}FN_2O_2$ $(M+H)^+$ 263.1196, found 263.1193

(1*E*,*NE*)-*N*-(2-Oxo-7-(trifluoromethyl)indolin-3-ylidene)hex-1-en-1-amine oxide (3ia), 0.083 g, 88% yield, orange solid. mp: 157−158 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 11.39 (s, 1H), 8.79 (d, J = 13.2 Hz, 1H), 8.52 (d, J = 7.2 Hz, 1H), 7.64 (d, J = 7.2 Hz, 1H), 7.23 (t, J = 7.2 Hz, 1H), 6.96−6.95 (m, 1H), 2.32 (q, J = 6.8 Hz,

2H), 1.49−1.46 (m, 2H), 1.38−1.34 (m, 2H), 0.92 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 162.1, 137.6, 135.9, 132.9, 131.1, 128.3, 128.1 (d, J = 14.4 Hz), 125.1, 122.6, 120.7, 111.5 (d, J = 131.2 Hz), 30.5, 29.0, 22.2, 14.1; IR (thin film) 3454, 3170, 2927, 1695, 1528, 1435, 1120, 687 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{16}F_3N_2O_2$ $(M+H)^+$ 313.1164, found 313.1186.

(1*E*,*NE*)-*N*-(1-Methyl-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (3ka), 0.042 g, 54% yield, orange solid. mp: 55−56 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 8.80 (d, J = 13.2 Hz, 1H), 8.22 (d, J = 7.2 Hz, 1H), 7.42 (t, J = 7.2 Hz, 1H), 7.08−7.02 (m, 2H), 6.96−6.90 (m, 1H), 3.17 (s, 3H), 2.30 (q, J = 6.8 Hz, 2H), 1.49−1.42 (m, 2H), 1.38−1.29 (m, 2H), 0.92 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 160.2, 142.0, 134.9, 132.8, 132.4, 131.9, 124.8, 123.0, 118.1, 109.2, 30.5, 29.0, 26.5, 22.2, 14.2; IR (thin film) 3107, 2955, 2925, 1688, 1529, 1465, 1195, 750 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{19}N_2O_2$ $(M+H)^+$ 259.1447, found 259.1446.

(1*E*,*NE*)-*N*-(2-Oxo-1-phenylindolin-3-ylidene)hex-1-en-1-amine oxide (3la), 0.081 g, 84% yield, orange solid. mp: 120−121 °C; ^{1}H NMR (400 MHz, DMSO–d_6): δ 8.84 (d, J = 13.2 Hz, 1H), 8.40 (d, J = 7.6 Hz, 1H), 7.61−7.57 (m, 2H), 7.51−7.48 (m, 3H), 7.41 (t, J = 7.6 Hz, 1H), 7.18 (t, J = 7.6 Hz, 1H), 7.04−6.97 (m, 1H), 6.77 (d, J = 7.6 Hz, 1H), 2.33 (q, J = 6.8 Hz, 2H), 1.51−1.43 (m, 2H), 1.39−1.32 (m, 2H), 0.92 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 159.9, 141.9, 135.3, 134.0, 132.9, 132.6, 131.8, 130.1, 128.9, 127.7, 125.1, 123.6, 118.4, 109.5, 30.5, 28.9, 22.1, 14.2; IR (thin film) 3454, 3097, 2926, 1692, 1496, 1457, 1189, 745 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{21}N_2O_2$ $(M+H)^+$ 321.1603, found 321.1596.

General procedure for preparing *N*-vinyl nitrone 4，3m and 3n: In a 25 mL flask was charged with indoline-2,3-dione oxime **1** (0.3 mmol), alkenyl boronic acid **2** (1.2 mmol, 4.0 equiv), $Cu(OAc)_2$ (0.6 mmol, 2.0 equiv) and anhydrous Na_2SO_4 (6.0 equiv) under air atmosphere. Then, DCE (3.0 mL) and pyridine (0.9 mmol, 3.0 equiv) was added *via* syringe. The reaction flask was then capped with a septum pierced with a ventilation needle and stirred vigorously at 25 °C for 2−24 h until the oxime **1** disappeared (monitored by TLC). At this time, the reaction was quenched by H_2O (10 mL) and extracted with DCM (3 × 10 mL). Then, dried over with Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (the crude residue was dry loaded on silica gel, 1/50 to 1/20, ethyl acetate/petroleum ether) to provide nitrone **4**.

(1*E*,*NE*)-*N*-(1-((*E*)-Hex-1-enyl)-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (4aa), 0.075 g, 77% yield, brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.82 (d, J = 7.2 Hz, 1H), 8.40 (d, J = 6.0 Hz, 1H), 7.30 (t, J = 6.4 Hz, 1H), 7.06−6.97 (m, 3H), 6.37 (d, J = 7.6 Hz, 1H), 6.19−6.13 (m, 1H), 2.28 (q, J = 5.6 Hz, 2H), 2.18 (q, J = 5.6 Hz, 2H), 1.48−1.36 (m, 4H), 1.35−1.28 (m, 4H), 0.88−0.80 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 140.0, 135.5, 132.8, 131.6, 131.5, 125.6, 125.2, 123.5, 119.6, 118.6, 109.0, 31.6, 30.6, 30.5, 29.2, 22.2, 22.1, 13.9, 13.8; IR (thin film) 3091, 2953, 1695, 1602, 1527, 1462, 1183, 743 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{27}N_2O_2$ $(M+H)^+$ 327.2073, found 327.2095.

(2*E*,*NE*)-*N*-(1-((*E*)-But-2-en-2-yl)-2-oxoindolin-3-ylidene)but-2-en-2-amine oxide (4ah), *E* / *Z* = 1:0.5, 0.049 g, 60% yield, brown liquid. *E-isomer*: ^{1}H NMR (400

MHz, $CDCl_3$): δ 8.36 (d, J = 7.0 Hz, 1H), 7.30 (d, J = 11.0 Hz, 1H), 7.04 (d, J = 8.0 Hz, 1H), 6.77 (d, J = 8.0 Hz, 1H), 5.71 (q, J = 6.5 Hz, 1H), 5.62−5.61 (m, 1H), 2.08 (s, 3H), 1.90 (s, 3H), 1.77 (d, J = 6.0 Hz, 5H), 1.51 (d, J = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.8, 143.2, 141.7, 133.6, 131.7, 128.9, 126.5, 125.0, 123.1, 122.8, 118.1, 109.0, 29.6, 14.6, 13.0, 12.7; *Z-isomer:* ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (d, J = 8.0 Hz, 1H), 7.26 (t, J = 8.0 Hz, 1H), 7.04 (q, J = 7.2 Hz, 1H), 6.77 (d, J = 6.4 Hz, 1H), 5.62−5.61 (m, 1H), 5.43−5.41 (m, 1H), 2.05 (s, 3H), 1.89 (s, 3H), 1.73 (d, J = 4.8 Hz, 5H), 1.51 (d, J = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.2, 142.7, 141.5, 133.1, 131.6, 128.9, 126.2, 124.9, 122.8, 119.9, 117.6, 108.9, 19.4, 14.1, 13.0, 12.3; IR (thin film) 2922, 2859, 1710, 1604, 1541, 1460, 1185, 748 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{19}N_2O_2$ $(M+H)^+$ 271.1447, found 271.1445.

(*E*)-*N*-(1-Cyclohexenyl-2-oxoindolin-3-ylidene)cyclohex-1-enamine oxide (4an), 0.074 g, 77% yield, brown liquid. ^{1}H NMR (500 MHz, DMSO–d_6): δ 8.22 (d, J = 7.5 Hz, 1H), 7.40 (t, J = 7.5 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H), 5.94−5.93 (m, 1H), 5.86−5.85 (m, 1H), 2.31−2.30 (m, 2H), 2.20−2.14 (m, 6H), 1.75−1.74 (m, 4H), 1.64−1.61 (m, 4H); ^{13}C NMR (125 MHz, DMSO–d_6): δ 158.3, 145.0, 141.7, 132.9, 132.2, 131.8, 128.6, 124.6, 124.2, 122.8, 118.1, 109.4, 26.5, 25.9, 24.7, 24.1, 22.6, 22.2, 21.7, 21.2; IR (thin film) 3055, 2933, 1709, 1603, 1460, 1375, 1189, 747 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{23}N_2O_2$ $(M+H)^+$ 323.1760, found 323.1760.

(1*E*,*NE*)-*N*-(1-((*E*)-Hex-1-enyl)-5-methoxy-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (4ba), 0.066 g, 61% yield, brown liquid. ^{1}H NMR (400 MHz, DMSO–d_6):

δ 8.83 (d, J = 13.2 Hz, 1H), 8.05 (d, J = 2.4 Hz, 1H), 7.04−6.97 (m, 1H), 6.91−6.82 (m, 2H), 6.40−6.36 (m, 1H), 6.14−6.07 (m, 1H), 3.75 (s, 3H), 2.28 (q, J = 6.8 Hz, 2H), 2.17 (q, J = 6.8 Hz, 2H), 1.47−1.27 (m, 8H), 0.88 (dt, J = 6.8 Hz, 1.2 Hz, 6H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 159.4, 156.2, 135.5, 134.0, 132.9, 131.9, 124.0, 119.8, 119.3, 118.1, 110.4, 109.9, 55.8, 31.7, 30.6, 30.5, 29.2, 22.2, 22.1, 13.8, 13.7; IR (thin film) 3095, 2958, 1694, 1648, 1529, 1482, 1272, 717 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{29}N_2O_3$ $(M+H)^+$ 357.2178, found 357.2179.

(1*E*,*NE*)-*N*-(1-((*E*)-Hex-1-enyl)-5-methyl-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (4da), 0.074 g, 72% yield, brown liquid. ^{1}H NMR (400 MHz, DMSO–d_6): δ 8.81 (d, J = 13.2 Hz, 1H), 8.23 (s, 1H), 7.08 (d, J = 8.0 Hz, 1H), 7.02−6.97 (m, 1H), 6.86 (d, J = 7.5 Hz, 1H), 6.38 (d, J = 14.5 Hz, 1H), 6.15−6.09 (m, 1H), 2.27−2.23 (m, 5H), 2.16−2.12 (q, J = 5.6 Hz, 2H), 1.48−1.35 (m, 4H), 1.34−1.28 (m, 4H), 0.88 (dt, J = 7.5 Hz, 2.5 Hz, 6H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 159.5, 137.9, 135.2, 133.1, 132.8, 132.0, 131.7, 126.1, 124.3, 119.7, 118.6, 108.8, 31.6, 30.6, 30.5, 29.2, 22.2, 22.1, 21.0, 13.8, 13.7; IR (thin film) 3094, 2957, 1696, 1646, 1528, 1461, 1185, 727 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{29}N_2O_2$ $(M+H)^+$ 341.2229, found 341.2229.

(1*E*,*NE*)-*N*-(5-Fluoro-1-((*E*)-hex-1-enyl)-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (4ea), 0.088 g, 86% yield, brown liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.86 (d, J = 8.5 Hz, 1H), 8.18−8.16 (m, 1H), 7.10−7.01 (m, 2H), 6.96−6.95 (m, 1H), 6.42 (d, J = 14.5 Hz, 1H), 6.20−6.16 (m, 1H), 2.34 (q, J = 7.5 Hz, 2H), 2.23 (q, J = 6.0 Hz, 2H), 1.54−1.44 (m, 4H), 1.40−1.35 (m, 4H), 0.94 (dt, J = 7.5 Hz, 2.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.1 (d, J = 239.5 Hz), 159.3, 136.3, 136.0, 132.9, 131.1,

125.1, 119.6 (d, J = 6.4 Hz), 117.7 (d, J = 24.6 Hz), 112.8, 112.5, 109.6 (d, J = 8.3 Hz), 31.5, 30.5, 30.4, 29.2, 22.2, 22.1, 13.8, 13.7; IR (thin film) 3091, 2956, 1695, 1644, 1530, 1476, 1264, 805 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{26}FN_2O_2$ $(M+H)^+$ 345.1978, found 345.1980.

(1*E*,*NE*)-*N*-(1-((*E*)-Hex-1-enyl)-5-nitro-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (4fa), 0.065 g, 58% yield, brown liquid. ^1H NMR (500 MHz, $CDCl_3$): δ 9.17 (s, 1H), 8.77 (d, J = 13.0 Hz, 1H), 8.22 (d, J = 8.5 Hz, 1H), 7.11−7.04 (m, 2H), 6.36 (d, J = 14.5 Hz, 1H), 6.23−6.19 (m, 1H), 2.31 (q, J = 7.0 Hz, 2H), 2.22 (q, J = 7.0 Hz, 2H), 1.50−1.41 (m, 4H), 1.38−1.31 (m, 4H), 0.88 (dt, J = 6.5 Hz, 5.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.5, 143.8, 137.9, 132.9, 129.8, 128.2, 127.2, 120.3, 118.9, 118.8, 108.6, 31.3, 30.4, 30.3, 29.6, 29.3, 22.2, 22.1, 13.8, 13.7; IR (thin film) 3089, 2956, 1708, 1520, 1459, 1343, 1178, 745 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{26}N_3O_4$ $(M+H)^+$ 372.1923, found 372.1926.

(1*E*,*NE*)-*N*-(6-Bromo-1-((*E*)-hex-1-enyl)-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (4ga), 0.104 g, 85% yield, brown liquid. ^1H NMR (500 MHz, $CDCl_3$): δ 8.83 (d, J = 13.0 Hz, 1H), 8.31 (t, J = 5.5 Hz, 1H), 7.27 (t, J = 8.0 Hz, 1H), 7.18 (s, 1H), 7.11−7.06 (m, 1H), 6.38 (d, J = 13.0 Hz, 1H), 6.24−6.18 (m, 1H), 2.34 (q, J = 7.0 Hz, 2H), 2.26 (q, J = 7.0 Hz, 2H), 1.55−1.47 (m, 4H), 1.44−1.36 (m, 4H), 0.97 (dt, J = 16.0 Hz, 7.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.3, 140.8, 136.1, 132.9, 130.8, 126.4, 126.3, 126.2, 125.4, 119.2, 117.4, 112.5, 31.5, 30.5, 30.4, 29.4, 22.2, 22.1, 13.8, 13.7; IR (thin film) 3096, 2956, 1698, 1594, 1465, 1375, 1185, 818 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{26}BrN_2O_2$ $(M+H)^+$ 405.1178, found 405.1181.

(1*E*,*NE*)-*N*-(7-Fluoro-1-((*E*)-hex-1-enyl)-2-oxoindolin-3-ylidene)hex-1-en-1-amine oxide (4ha), 0.093 g, 90% yield, brown liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.91 (d, J = 13.0 Hz, 1H), 8.29 (d, J = 4.5 Hz, 1H), 7.12−7.03 (m, 3H), 6.58 (d, J = 14.0 Hz, 1H), 6.40−6.35 (m, 1H), 2.35−2.31 (q, J = 7.0 Hz, 2H), 2.22−2.18 (q, J = 7.0 Hz, 2H), 1.56−1.45 (m, 4H), 1.42−1.36 (m, 4H), 0.95 (dt, J = 14.5 Hz, 7.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.4, 148.2 (d, J = 244.1 Hz), 136.2, 132.9, 131.3, 126.6, 126.4 (d, J = 8.3 Hz), 124.2 (d, J = 6.4 Hz), 121.3, 121.0, 120.9 (d, J = 3.6 Hz), 119.9 (d, J = 21 Hz), 31.4, 30.6, 30.4, 29.2, 22.2, 22.1, 13.8, 13.7; IR (thin film) 3092, 2955, 1696, 1527, 1446, 1374, 1190, 785 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{26}FN_2O_2$ $(M+H)^+$ 345.1978, found 345.1981.

1-((*E*)-Hex-1-enyl)-3-(methoxyimino)indolin-2-one (3ma), 0.084 g, 88% yield, brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 4.4 Hz, 1H), 7.33 (d, J = 7.2 Hz, 1H), 7.01−7.00 (m, 2H), 6.40−6.36 (m, 1H), 6.19−6.12 (m, 1H),4.22 (s, 3H), 2.15 (q, J = 6.8 Hz, 2H), 1.42−1.36 (m, 2H), 1.34−1.27 (m, 2H), 0.88−0.84 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3, 143.0, 132.3, 127.9, 124.6, 123.3, 120.9, 119.5, 116.0, 109.6, 64.8, 31.6, 30.5, 22.2, 13.9; IR (thin film) 3053, 2961, 1728, 1606, 1461, 1381, 1003, 748 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{19}N_2O_2$ $(M+H)^+$ 259.1447, found 259.1440.

Mixture of 3na and 3na', 0.053 g, 72% yield, yellow liquid. **3na**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 4.4 Hz, 1H), 7.55 (d, J = 8.8 Hz, 1H), 7.19−7.15 (m, 1H), 7.10−7.06 (m, 1H), 6.98 (d, J = 14.0 Hz, 1H), 6.56 −6.49 (m, 1H), 5.34 (q, J = 6.8 Hz, 1H), 2.61 (brs, 1H), 1.65 (d, J = 6.8 Hz, 3H), 1.45−1.39 (m, 2H), 1.38−1.29 (m, 2H),

0.89 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 136.2, 126.9, 124.8, 121.5, 121.1, 120.3, 117.0, 109.5, 62.7, 31.2, 29.7, 22.9, 22.1, 13.8; **3na'**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.35−7.31 (m, 1H), 7.10−7.06 (m, 1H), 6.93 (d, J = 14.0 Hz, 1H), 6.17 −6.10 (m, 1H), 5.27 (q, J = 6.8 Hz, 1H), 2.61 (brs, 1H), 1.63 (d, J = 6.8 Hz, 3H), 1.45−1.39 (m, 2H), 1.38−1.29 (m, 2H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.7, 139.6, 127.1, 125.6, 123.8, 121.4, 121.2, 119.7, 117.2, 65.5, 31.9, 29.8, 23.4, 22.2, 13.9; IR (thin film) 2959, 2857, 1672, 1627, 1464, 1383, 1083, 767 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{21}N_2O$ $(M+H)^+$ 245.1654, found 245.1641.

General procedure for synthesis of spirooxindole 5 or 6: In a 25 mL seal tube was charged with *N*-vinyl nitrone **3** or **4** (0.2 mmol). Then, toluene (2.0 mL) was added *via* syringe. The reaction mixture was stirred vigorously at 120−140 °C for 8−65 h until nitrone **3** or **4** disappeared (monitored by TLC). At this time, the solvent was removed under reduced pressure and the crude product was purified by flash chromatography (the crude residue was dry loaded on silica gel, 1/4 to 1/1, ethyl acetate/petroleum ether) to provide spirooxindole **5** or **6.**

3',4'-Dimethyl-4'H-spiro[indoline-3,5'-isoxazol]-2-one (5ah), *dr* = 1:0.8, 0.032 g, 74% yield, light yellow liquid. *major isomer*: ^{1}H NMR (500 MHz, DMSO–d_6): δ 10.54 (s, 1H), 7.39 (d, J = 7.5 Hz, 1H), 7.30 (t, J = 7.5 Hz, 1H), 7.04 (t, J = 7.5 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H), 3.75 (q, J = 7.0 Hz, 1H), 1.93 (s, 3H), 1.10 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO–d_6): δ 176.9, 159.7, 143.2, 130.9, 128.2, 125.7, 122.9, 110.9, 87.7, 53.6, 12.7, 11.5; *minor isomer:* ^{1}H NMR (500 MHz, DMSO–d_6): δ

10.43 (s, 1H), 7.25 (d, J = 7.0 Hz, 1H), 7.29 (t, J = 7.5 Hz, 1H), 7.00 (t, J = 7.5 Hz, 1H), 6.85 (d, J = 7.5 Hz, 1H), 3.59 (q, J = 7.5 Hz, 1H), 1.93 (s, 3H), 0.97 (d, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, DMSO–d_6): δ 174.6, 159.5, 142.8, 130.9, 126.8, 124.9, 122.4, 110.5, 87.6, 51.6, 11.3, 10.8; IR (thin film) 3431, 2926, 1728, 1621, 1471, 1189, 1010, 757 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{13}N_2O_2$ $(M+H)^+$ 217.0977, found 217.0976.

3'-Phenyl-4'H-spiro[indoline-3,5'-isoxazol]-2-one (5ai), 0.043 g, 80% yield, light yellow liquid. ^{1}H NMR (500 MHz, DMSO–d_6): δ 10.66 (s, 1H), 7.75 (d, J = 4.5 Hz, 2H), 7.50−7.49 (m, 3H), 7.41 (d, J = 7.0 Hz, 1H), 7.33 (t, J = 8.0 Hz, 1H), 7.04 (t, J = 7.5 Hz, 1H), 6.92 (d, J = 7.5 Hz, 1H), 3.83 (s, 2H); ^{13}C NMR (125 MHz, DMSO–d_6): δ 176.2, 157.0, 143.0, 131.4, 131.1, 129.5, 129.1, 128.6, 127.5, 125.3, 123.3, 110.9, 85.5, 43.7; IR (thin film) 3456, 3199, 2929, 1636, 1472, 1336, 1117, 748 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{13}N_2O_2$ $(M+H)^+$ 265.0977, found 265.0966.

4'-Ethyl-3'-phenyl-4'H-spiro[indoline-3,5'-isoxazol]-2-one (5aj), *dr* = 10:1, 0.034 g, 57% yield, light yellow liquid. ^{1}H NMR (400 MHz, DMSO–d_6): δ 10.67 (s, 1H), 7.74−7.73 (m, 2H), 7.50 (t, J = 6.8 Hz, 3H), 7.43 (d, J = 7.2 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 6.94 (d, J = 7.6 Hz, 1H), 4.12 (dd, J = 10.0 Hz, 3.2 Hz, 1H), 1.73−1.60 (m, 2H), 0.53 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 176.9, 160.6, 143.2, 131.3, 130.8, 129.4, 129.1, 127.9, 126.8, 124.6, 122.7, 110.9, 88.4, 55.2, 21.5, 12.1; IR (thin film) 3436, 3197, 2938, 1720, 1621, 1469, 1203, 749 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{17}N_2O_2$ $(M+H)^+$ 293.1290, found 293.1282.

4,5,6,7-Tetrahydro-3aH-spiro[benzo[c]isoxazole-3,3'-indolin]-2'-one (5am), 0.016 g, 32% yield, light yellow liquid. ^{1}H NMR (400 MHz, DMSO–d_6): δ 10.45 (s, 1H), 7.36 (d, J = 7.6 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 3.60−3.56 (m, 1H), 2.68−2.64 (m, 1H), 2.28−2.20 (m, 1H), 1.93−1.90 (m, 1H), 1.79−1.70 (m, 2H), 1.66−1.65 (m, 1H), 1.35−1.27 (m, 2H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 174.7, 159.8, 142.8, 130.7, 129.3, 124.7, 122.9, 110.4, 86.1, 56.8, 26.1, 25.2, 24.9, 23.9; IR (thin film) 3454, 3198, 2955, 1711, 1621, 1471, 1194, 749 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{15}N_2O_2$ $(M+H)^+$ 243.1133, found 243.1134.

3,4,5,6,7,8-Hexahydrospiro[cyclohepta[c]isoxazole-3,3'-indolin]-2'-one (5an), 0.027 g, 53% yield, light yellow liquid. ^{1}H NMR (400 MHz, DMSO–d_6): δ 10.41 (s, 1H), 7.48 (d, J = 7.2 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 3.84−3.81 (m, 1H), 2.76−2.70 (m, 1H), 2.39−2.32 (m, 1H), 1.85−1.73 (m, 3H), 1.69−1.50 (m, 2H), 1.39−1.30 (m, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 174.7, 163.9, 143.5, 131.0, 127.5, 125.2, 122.8, 110.5, 88.3, 60.0, 30.9, 28.9, 27.5, 25.8, 24.9; IR (thin film) 3430, 3179, 2925, 1725, 1622, 1471, 1193, 752 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{17}N_2O_2$ $(M+H)^+$ 257.1290, found 257.1289.

6-tert-Butyl-4,5,6,7-tetrahydro-3aH-spiro[benzo[c]isoxazole-3,3'-indol]-2'-one (5ap), *dr* = 1:1, 0.024 g, 40% yield, light yellow liquid. *isomer 1*: ^{1}H NMR (400 MHz, DMSO–d_6): δ 10.44 (s, 1H), 7.42 (d, J = 7.6 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.04 (t, J = 7.2 Hz, 1H), 6.85 (d, J = 7.6 Hz, 7.2 Hz, 1H), 3.99 (q, J = 7.0 Hz, 1H), 2.72−2.63 (m, 1H), 1.98−1.96 (m, 1H), 1.76−1.63 (m, 2H), 1.41−1.33 (m, 2H), 0.81(s, 9H); ^{13}C

NMR (100 MHz, DMSO–d_6): δ 174.9, 161.5, 143.2, 130.9, 129.2, 125.0, 122.9, 110.5, 88.2, 57.3, 53.4, 45.76, 43.6, 32.9, 27.9, 27.2, 24.6, 25.3; *isomer 2*: ^{1}H NMR (400 MHz, DMSO–d_6): δ 10.43 (s, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.03 (t, J = 7.2 Hz, 1H), 6.83 (dd, J = 7.6, 7.2 Hz, 1H), 3.68 (q, J = 7.0 Hz, 1H), 2.29−2.23 (m, 1H), 1.75−1.71 (m, 1H), 1.56−1.47 (m, 2H), 1.26−1.22 (m, 2H), 0.78 (s, 9H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 174.7, 160.0, 142.9, 130.7, 128.1, 124.8, 122.9, 110.5, 86.4, 57.3, 53.6, 45.8, 43.6, 32.6, 28.9, 27.6, 23.9, 22.2; IR (thin film) 3435, 3180, 2930, 1714, 1618, 1461, 1192, 753 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{22}N_2O_2$ $(M+H)^+$ 299.1759, found 299.1758.

1-((*E*)-But-2-en-2-yl)-3',4'-dimethyl-4'H-spiro[indoline-3,5'-isoxazol]-2-one (6ah), *dr* = 1:0.5, 0.041 g, 75% yield, light yellow liquid. *major isomer*: ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.47 (s, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.13 (t, J = 7.2 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 5.67−5.63 (m, 1H), 3.81 (q, J = 7.2 Hz, 1H), 1.99 (s, 3H), 1.87 (d, J = 6.8 Hz, 6H), 1.10 (d, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 174.2, 159.8, 144.1, 131.0, 129.1, 127.6, 126.2, 125.1, 123.6, 110.2, 87.2, 54.1, 14.6, 13.2, 11.5, 10.6; *minor isomer*: ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.45 (s, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.09 (t, J = 7.2 Hz, 1H), 6.86 (d, J = 8.0 Hz, 1H), 5.61−5.58 (m, 1H), 3.64 (q, J = 7.2 Hz, 1H), 1.94 (s, 3H), 1.78 (d, J = 6.8 Hz, 6H), 1.01 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 171.8, 159.6, 143.9, 130.9, 129.0, 126.7, 126.1, 124.9, 123.1, 109.9, 87.1, 51.9, 14.6, 12.7, 11.2, 10.6; IR (thin film) 3057, 2925, 1728, 1611, 1464, 1201, 1100, 757 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{19}N_2O_2$ $(M+H)^+$ 271.1446, found 271.1445.

1'-Cyclohexenyl-4,5,6,7-tetrahydro-3aH-spiro[benzo[c]isoxazole-3,3'-indolin]-2'-one (6am), 0.032 g, 50% yield, light yellow liquid. ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.44 (d, J = 7.6 Hz, 1H), 7.37−7.34 (m, 1H), 7.12 (t, J = 7.6 Hz, 1H), 6.96−6.86 (m, 1H), 5.83−5.82 (m, 1H), 3.65−3.60 (m, 1H), 2.69−2.66 (m, 1H), 2.20−2.12 (m, 5H), 1.93−1.91 (m, 1H), 1.73−1.63 (m, 9H); ^{13}C NMR (100 MHz, DMSO–d_6): δ 171.9, 159.8, 143.7, 131.7, 130.8, 128.6, 128.2, 124.7, 123.6, 109.8, 85.8, 57.3, 26.2, 26.0, 25.2, 24.9, 24.6, 23.8, 22.5, 21.6; IR (thin film) 3060, 2930, 1724, 1610, 1465, 1377, 1191, 765 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{23}N_2O_2$ $(M+H)^+$ 323.1759, found 323.1759.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge *via* the Internet at http://pubs.acs.org.

Spectra of compounds **3**, **4**, **5** and **6** (PDF)

X-ray structure of compound **3ca** (CIF)

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Notes

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(12) CCDC: 1537304 (**3ca**) contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

(13) The ratio of *E*/*Z* isomer of **3ah** was determined by its ^{1}H NMR spectrum. The *E*/*Z* configuration was determined by NOESY sepectra of **3ah**, see more details in Supporting Information.

(14) We found the solubility of oxime **1g** in MeOH was bad. After the reaction ran 24 h, the oxime **1g** was still a solid in the solvent.

(15) Please see the NOESY spectra of compounds **5aj** and **5am** in Supporting Information.

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