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Novel synthesis and functionalization of *ortho*–*ortho* disubstituted biphenyls and a highly condensed novel heterocycle using radical cyclization reaction

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ABSTRACT

This paper describes a novel synthetic route for the preparation of *ortho*–*ortho* disubstituted biphenyls and compounds possessing highly condensed ring system represented by structures **X** and **Y**, respectively. Several approaches, such as intermolecular Grubb's olefin metathesis, Heck and, Suzuki reactions were incorporated to functionalize the core structures of **X** and **Y** making it suitable for the preparation of a library of compounds.

1. Introduction

ortho–*ortho* Disubstituted biphenyls incorporating a median size (six- to nine-membered) lactam ring are found in several pharmacologically active natural products[1–3] (i.e., Rhazinilam and Steganacin) and synthetic drug candidates (i.e., LY 411575).[4] In recent publications[5,6] we reported a novel route for the synthesis of *ortho*–*ortho* disubstituted biphenyls containing an eight-membered lactam ring represented by structure **X** (Fig. 1). Our approach toward the synthesis of these compounds involved radical cyclization of the compounds represented by structures **3a**–**d**, using tributyltin hydride (TBTH) and 2,2′-azobisisobutyronitrile (AIBN). We speculated that the conversion of **3a**–**d** to biphenyls **7a**–**d** proceeded via intermediates **4**, **5**, and **6**. Radical precursors **3a**–**d** were prepared by C-alkylation of imines **2a**–**d** using indium and allyl bromide. The imines **2a**–**d** were prepared in turn by the reactions of the corresponding isatins and substituted 2-bromoanilines (Scheme 1).

Similarly, the imines **2a**–**c** when reacted with indium and substituted cinnamyl bromides yielded **8a**–**c**. Radical cyclization of **8a**–**c** produced the *ortho*–*ortho* disubstituted biphenyls **10a**–**c** along with the compounds **11a**–**c**, representing a highly condensed novel ring system. Compounds **11a**–**c** were formed presumably through the intermediacy of **9** (Scheme 2).

2. Present study

Structures represented by **7a**, **10a**, and **11a** are novel and have many desirable attributes of drug like molecules, such as molecular weights below 500, several sites of hydrogen bond acceptors and donors. They also represent highly condensed ring systems with rigid conformations, which might provide advantages in binding to receptors and enzymes. Thus we decided to explore our chemistry further and determine whether a library of compounds with different substitutions in rings **A**, **B**, and **C** of **10a** and **11a** could be prepared for biological testing. The chemistry disclosed will also allow synthesis of **7a** with different substitutions in rings **A** and **C**. We have already noted that the substitution in ring **C** could be easily achieved by using different anilines for the preparation of the imines represented, for example, by the structure **2d**. For making different substitutions on ring A of **7a**, **10a**, and **11a** we needed to develop a convenient synthesis of substituted isatins starting with compound **12** and using Suzuki reaction. It should be noted that the method disclosed in the present paper for the preparation of isatins **15a**–**g** is general and the yields are good to excellent. Different approaches were also necessary to bring changes in ring **B** than the one disclosed in our previous publication because preparation of substituted cinnamyl bromides following published procedures[7]

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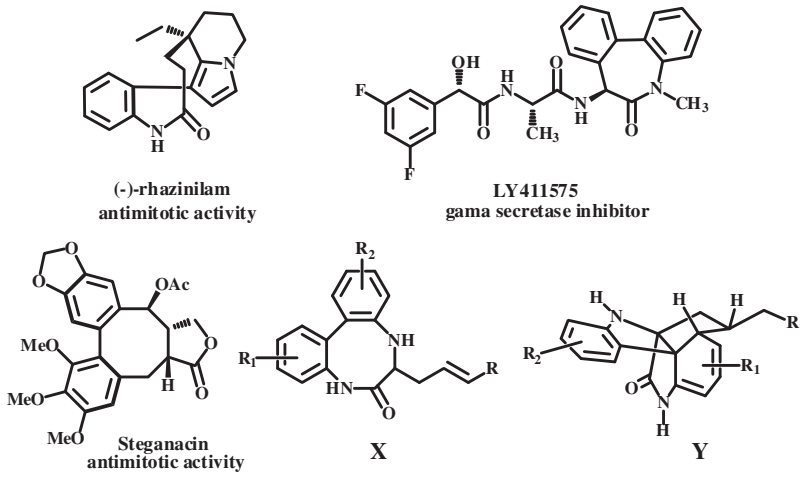
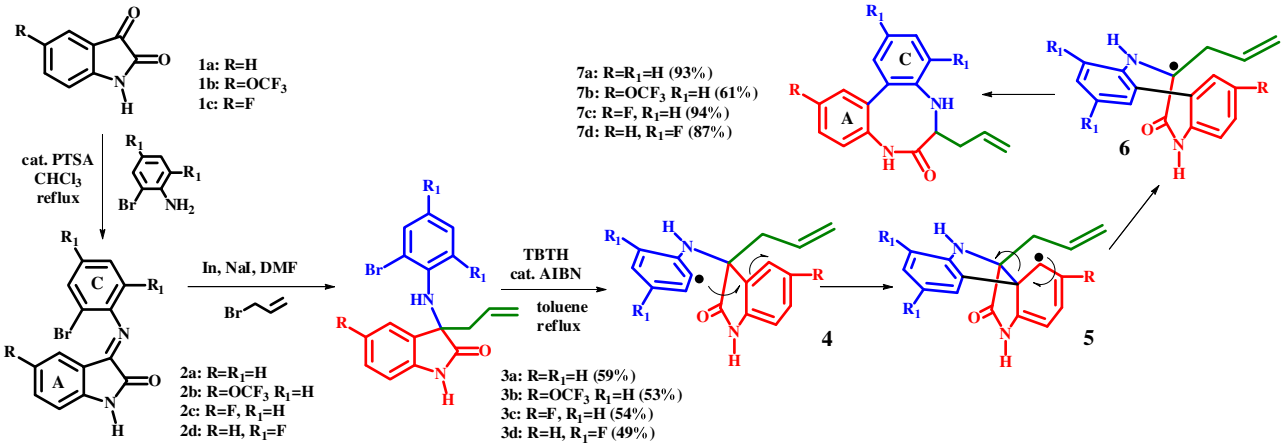
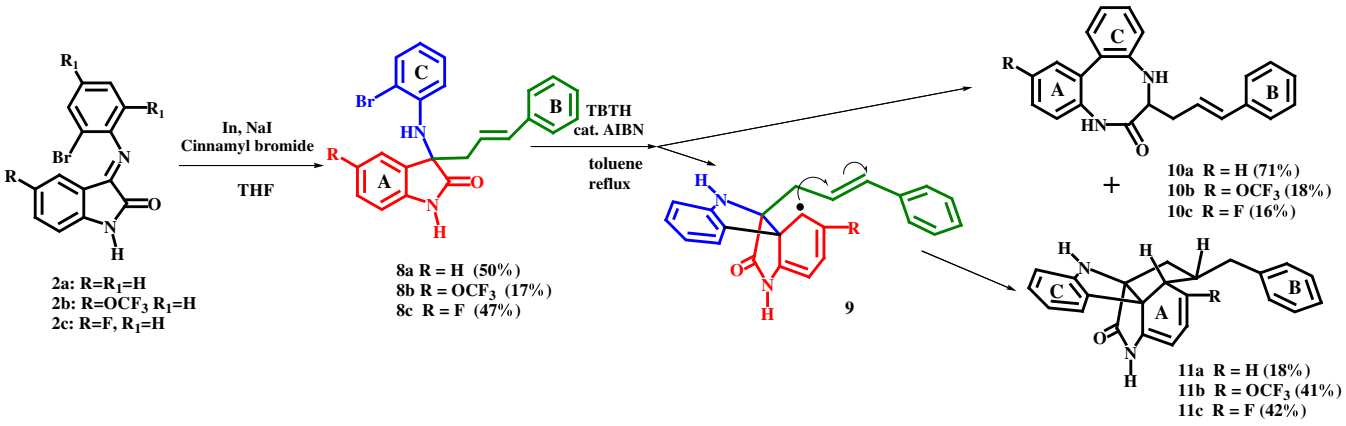


Fig. 1. Examples of *ortho–ortho* disubstituted biphenyls.



Scheme 1. Synthesis of novel *ortho–ortho* disubstituted biphenyls **7a–d**.

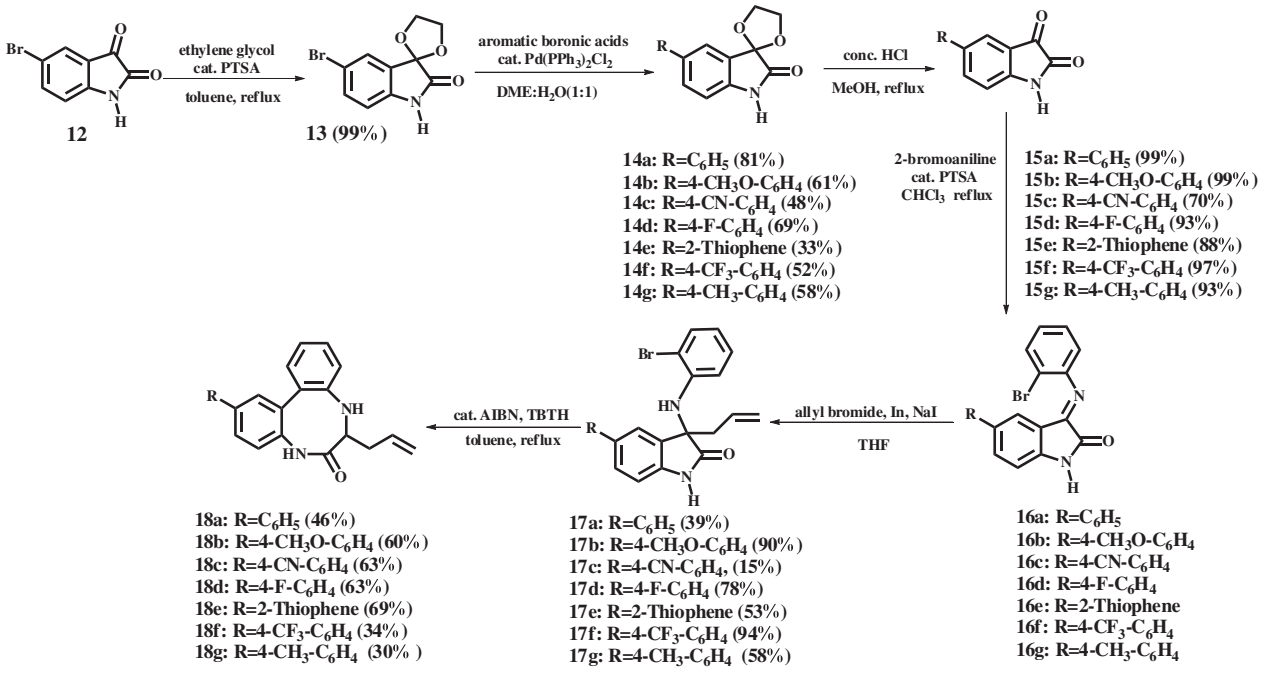


Scheme 2. Synthesis of novel *ortho–ortho* disubstituted biphenyls **10a–c** and highly condensed compounds **11a–c**.

proved difficult because of the inherent instability of the compounds. To overcome this problem we explored the possible use of Heck reaction and Grubbs olefin metathesis of the synthone **3a** to prepare **21a–e**. In the present paper we wish to report the details of our findings and we believe using the chemistry described, a library of compounds represented by **7a**, **10a**, and **11a** could be conveniently prepared for biological testing.

2.1. Modification of ring A

A convenient method of preparation of substituted isatins was necessary for studying the substituent effects in ring **A**. As we could not reproduce the Suzuki reaction on 5-bromoisatin reported in the literature,[8] we reasoned that the free carbonyl (ketone) group presented the problem. Thus 5-bromoisatin **12** was converted to



Scheme 3. Synthesis of novel derivatives with modification of ring **A**.

the ketal[9] **13**, with ethylene glycol in the presence of catalytic amounts of *p*-toluenesulphonic acid, which proved to be a suitable substrate for the Suzuki reactions (Scheme 3).

Compound **13** underwent Suzuki cross-coupling with corresponding arylboronic acids to yield **14a**–**g**, which upon heating under reflux with hydrochloric acid yielded structurally-diverse isatins **15a**–**g** Treatment of **15a**–**g** with 2-bromoaniline yielded the imines **16a**–**g**, which without purification were treated with allyl bromide and indium to yield **17a**–**g**. Radical cyclization of **17a**–**g** afforded substituted *ortho*–*ortho* disubstituted biphenyls **18a**–**g** with different substituents in ring **A**.

2.2. Modification of ring B

In our earlier publication[6] we encountered difficulties preparing, substituted cinnamyl bromides required for the C-alkylation of imines **2a**–**c**, perhaps due to their inherent instabilities. Thus we investigated two alternative approaches to modify the **B** ring of structure **8a**–**c** involving intermolecular Heck Reaction and Grubb's olefin metathesis of **3a**, respectively (Scheme 4).

Under Heck reaction conditions, **3a** underwent intramolecular coupling and yielded spirooxindole **28**. Intermolecular Heck reaction of **3a** with bromobenzene yielded **8a**. Similarly, **21a** and **21b** were prepared from **3a** via intermolecular Heck reaction with the corresponding substituted bromobenzenes. We did not detect the formation of **28** during the intermolecular Heck reaction sequence. This might be due to the fact that in general the yields during the Heck reaction were poor to modest. Radical reaction of **21a** yielded **22a** and **23a**, whereas the radical reaction of **21b** yielded **22b** and **23b**. We would also like to point out that **7a** under Heck reaction conditions with bromobenzene yielded **10a**.

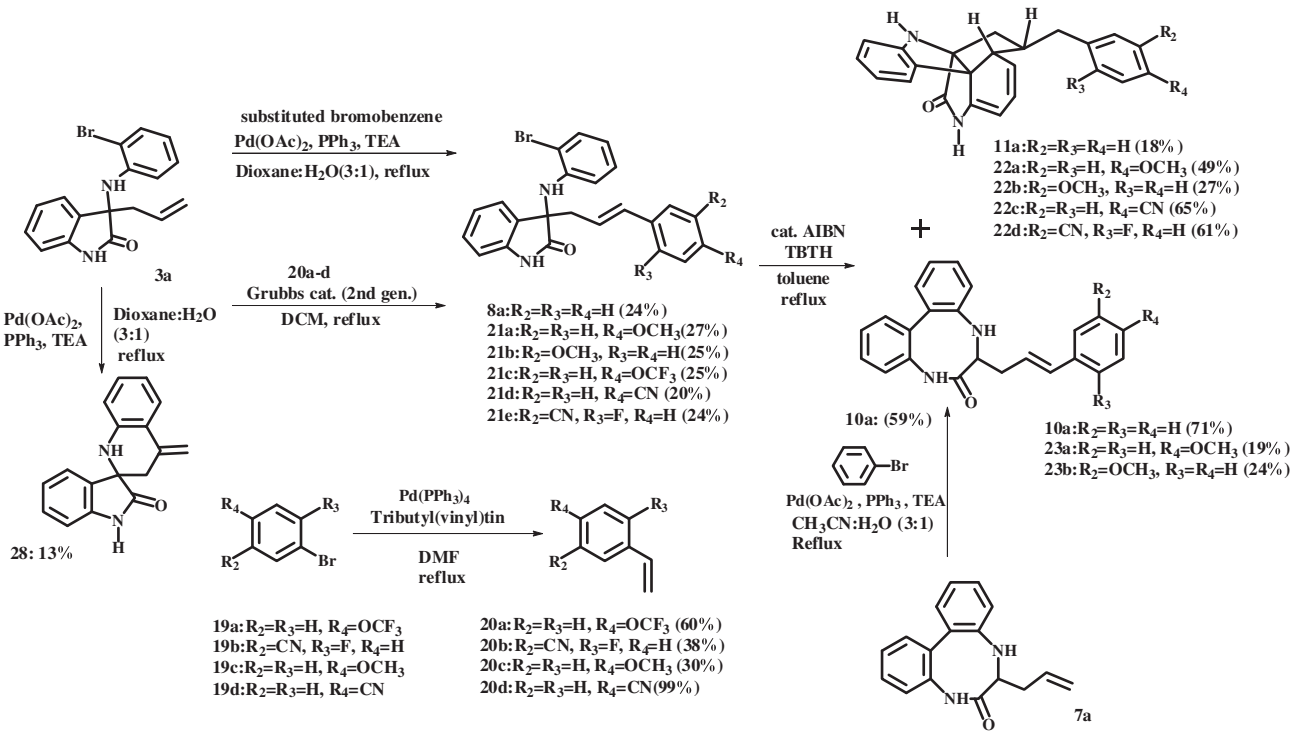
For the Grubb's metathesis sequence we needed substituted styrenes **20a**–**d**, which were synthesized via the Stille reaction of substituted bromobenzenes **19a**–**d**, respectively. Grubb's metathesis of **3a** and **20a** yielded **21c**. Similarly, **3a** with **20d** yielded **21d**, whereas **3a** with **20b** yielded **21e**. Interestingly under radical reaction conditions **21d** yielded only **22c** and **21e** yielded only **22d**.

In our earlier communication[6] we noted that compound **7a** could be converted to **24** by treatment with allyl bromide in DMF solution without the presence of cesium carbonate (Scheme 5). Further alkylation of the lactam –NH– of **24** was then carried out with methyl iodide in the presence of cesium carbonate to yield **25a**. Treatment of **24** with benzylbromide, cesium carbonate, and sodium iodide in DMF solution yielded **25b** and **25c** as atropisomers (Fig. 2). The structures of **25b** and **25c** were deduced by NMR spectroscopy. Briefly, atropisomer **25b** showed long range NOE's between H3 and H15, H12 and H23 and H6 and H25, thus the H3 proton occupied axial geometry relative to the plane of the eight-membered ring. Atropisomer **25c** had the H3 proton in the equatorial configuration with respect to the plane of the eight-membered ring. The rate of interconversion of the atropisomers **25b** and **25c** was very slow at 65 °C. Ring closure metathesis of **25b** yielded **26a** whereas that of **25c** yielded **26b**. NOE experiments were utilized to help assign the conformations of **26a** and **26b** (Fig. 3). We believe the new analogs reported in this paper will also be substrates for the preparation of analogs of atropisomers **25b** and **25c**, which could in turn be converted to analogs of **26a** and **26b**. Thus a rich library of drug like molecules can be prepared using the chemistry disclosed in the present paper.

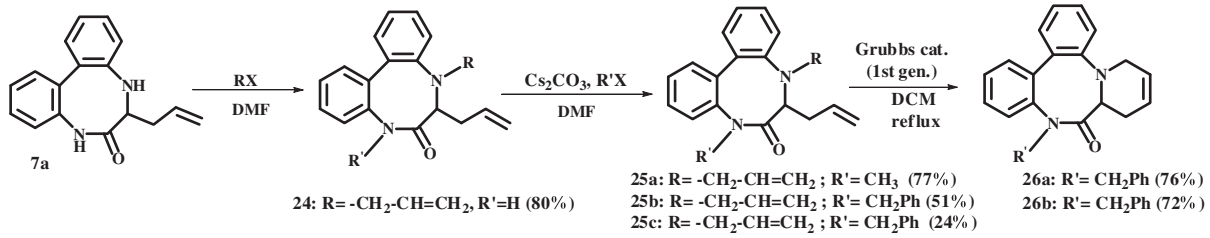
3. Experimental section

3.1. General

All the reactions were performed under nitrogen with magnetic stirring. Air- and moisture-sensitive reagents were transferred using disposable syringes available from Aldrich Chemical Co. Anhydrous solvents were obtained from Aldrich and Pharmco Co. and used without further drying. All commercially-available chemicals were used without further purification. TLC was performed on glass plates coated with Analtech silica gel (250 microns) and compounds were visualized using UV light or exposure to iodine vapors. NMR spectra were recorded with Varian 400 MHz and 600 MHz spectrometers. Chemical shifts are reported in parts per million relative to TMS, and coupling constants (*J*) are reported in Hz. The compositions of all the compounds disclosed in this paper were confirmed using mass spectrometry.



Scheme 4. Synthesis of novel derivatives with modification of ring **B**.



Scheme 5. Synthesis of atropisomers **26a** & **26b**.

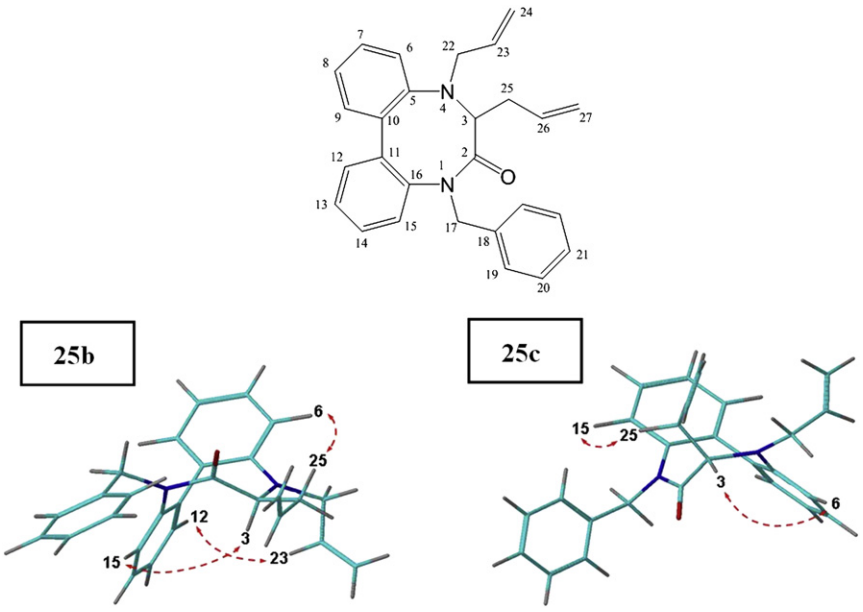


Fig. 2. NOE in atropisomers **25b** & **25c**.

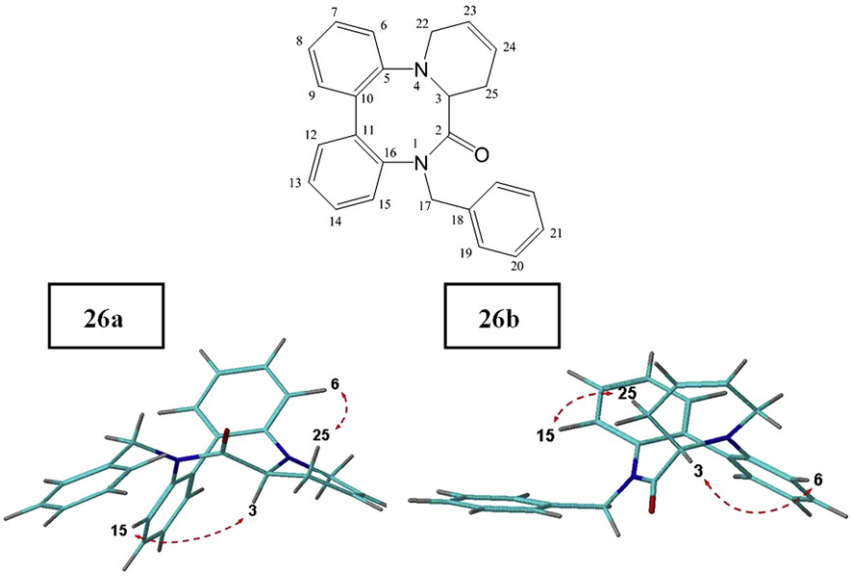


Fig. 3. NOE in atropisomers **26a** & **26b**.

3.2. General procedure for synthesis of Schiff bases (for example 16g)

*3.2.1. 3-((2-Bromophenyl)imino)-5-(p-tolyl)indolin-2-one (**16g**).* To a solution of **15g** (379 mg, 1.60 mmol) and 2-bromoaniline (825 mg, 4.80 mmol) in chloroform (14 mL), *p*-toluenesulphonic acid (5.95 mg, 0.03 mmol) was added. The above mixture was placed under nitrogen atmosphere and allowed to reflux for 48 h. The reaction mixture was evaporated to dryness and used in the next step without further purification.

*3.2.2. 3-((2-Bromophenyl)imino)indolin-2-one (**2a**).* The title compound was prepared from compound **1a** and 2-bromoaniline, following the general procedure for synthesis of Schiff bases. The compound was carried on to the next step without further purification.

*3.2.3. 3-[(2-Bromophenyl)imino]-5-(trifluoromethoxy)-1,3-dihydro-2H-indol-2-one (**2b**).* The title compound was prepared from compound **1b** and 2-bromoaniline, following the general procedure for synthesis of Schiff bases. The compound was carried on to the next step without further purification.

*3.2.4. 3-[(2-Bromophenyl)imino]-5-fluoro-1,3-dihydro-2H-indol-2-one (**2c**).* The title compound was prepared from compound **1c** and 2-bromoaniline, following the general procedure for synthesis of Schiff bases. The compound was carried on to the next step without further purification.

*3.2.5. 3-[(2-Bromo-4,6-difluorophenyl)imino]-1,3-dihydro-2H-indol-2-one (**2d**).* The title compound was prepared from compound **1a** and 2-bromo-4,6-difluoroaniline, following the general procedure for synthesis of Schiff bases. The compound was carried on to the next step without further purification.

*3.2.6. 3-((2-Bromophenyl)imino)-5-phenylindolin-2-one (**16a**).* The title compound was prepared from compound **15a** and 2-bromoaniline, following the general procedure for synthesis of Schiff bases. The compound was carried on to the next step without further purification.

*3.2.7. 3-((2-Bromophenyl)imino)-5-(4-methoxyphenyl)indolin-2-one (**16b**).* The title compound was prepared from compound **15b** and 2-bromoaniline, following the general procedure for synthesis of Schiff bases. The compound was carried on to the next step without further purification.

*3.2.8. 4-(3-((2-Bromophenyl)imino)-2-oxoindolin-5-yl)benzonitrile (**16c**).* The title compound was prepared from compound **15c** and 2-bromoaniline, following the general procedure for synthesis of Schiff bases. The compound was carried on to the next step without further purification.

*3.2.9. 3-((2-Bromophenyl)imino)-5-(4-fluorophenyl)indolin-2-one (**16d**).* The title compound was prepared from compound **15d** and 2-bromoaniline, following the general procedure for synthesis of Schiff bases. The compound was carried on to the next step without further purification.

*3.2.10. 3-((2-Bromophenyl)imino)-5-(thiophen-2-yl)indolin-2-one (**16e**).* The title compound was prepared from compound **15e** and 2-bromoaniline, following the general procedure for synthesis of Schiff bases. The compound was carried on to the next step without further purification.

*3.2.11. 3-((2-Bromophenyl)imino)-5-(4-(trifluoromethyl)phenyl)indolin-2-one (**16f**).* The title compound was prepared from compound **15f** and 2-bromoaniline, following the general procedure for synthesis of Schiff bases. The compound was carried on to the next step without further purification.

3.3. General procedure for C-alkylation using allyl bromide: (for example preparation of 3a)

*3.3.1. 3-Allyl-3-((2-bromophenyl)amino)indolin-2-one (**3a**).* To a solution of compound **2a** (600 mg, 2.00 mmol) in DMF (or THF), indium (229 mg, 2.0 mmol), and sodium iodide (450 mg, 3.00 mmol) were added. To the stirred reaction mixture allyl bromide (362 mg, 3.00 mmol) was added dropwise. After the reaction was complete, the reaction mass was filtered and evaporated to dryness. The residue was diluted with DCM and washed with 30% HCl. The aqueous layer was extracted with DCM three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated to yield the crude compound, which was purified by column chromatography to yield **3a**. Yield: 59%. Crystals were obtained from DCM and hexane. Mp 180–182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 7.38 (dd,

J=7.9, 1.5 Hz, 1H), 7.28–7.24 (m, 1H), 7.19 (dd, J=7.4, 0.6 Hz, 1H), 7.02 (dt, J=7.6, 1.0 Hz, 1H), 6.93 (d, J=7.8 Hz, 1H), 6.79 (dt, J=8.4, 1.4 Hz, 1H), 6.52–6.45 (m, 1H), 5.95–5.82 (m, 2H), 5.42–5.27 (m, 2H), 5.20 (s, 1H), 2.82–2.65 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.48, 141.90, 139.47, 132.48, 130.00, 129.58, 129.11, 128.22, 123.88, 123.06, 121.82, 119.05, 112.65, 110.86, 110.70, 63.70, 44.63; HRMS: calcd for $C_{17}H_{16}{}^{79}BrN_2O$ $[M+H]^+$: 343.0446, found: 343.0430.

*3.3.2. 3-Allyl-3-((2-bromophenyl)amino)-5-(trifluoromethoxy)indolin-2-one (**3b**).* The title compound was obtained from compound **2b**, following the general procedure for C-allylation using allyl bromide. Yield: 53%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.06–8.01 (m, 3H), 7.39–7.17 (m, 2H), 7.12 (d, J=8.21 Hz, 1H), 6.88 (d, J=8.39 Hz, 1H), 5.94–5.47 (m, 1H), 5.22–5.00 (m, 2H), 3.70 (b, 1H), 2.68 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.97, 145.04, 141.61, 138.09, 132.68, 131.30, 129.29, 128.29, 122.47, 122.30, 121.70, 119.50, 119.14, 117.66, 112.42, 111.56, 110.96, 64.16, 44.51; HRMS: calcd for $C_{18}H_{15}{}^{79}BrF_3N_2O_2$ $[M+H]^+$: 427.0269, found: 427.0251.

*3.3.3. 3-Allyl-3-((2-bromophenyl)amino)-5-fluoroindolin-2-one (**3c**).* The title compound was prepared from compound **2c**, following the general procedure for C-alkylation using allyl bromide. Yield: 54%. Crystals were obtained from DCM and hexane. Mp 160–162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (s, 1H), 7.39 (dd, J=7.9, 1.4 Hz, 1H), 6.99–6.89 (m, 2H), 6.89–6.74 (m, 2H), 6.51 (dt, J=7.7, 1.4 Hz, 1H), 6.09–5.72 (m, 2H), 5.41–5.31 (m, 2H), 5.19 (s, 1H), 2.84–2.71 (m, 1H), 2.67–2.59 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.69, 160.58, 158.17, 141.65, 135.36, 135.34, 132.63, 131.49, 131.42, 129.51, 128.28, 122.26, 119.35, 115.79, 115.55, 112.46, 111.91, 111.67, 111.57, 111.50, 110.90, 64.12, 44.53; HRMS: calcd for $C_{17}H_{15}{}^{79}BrFN_2O$ $[M+H]^+$: 361.0352, found: 361.0349.

*3.3.4. 3-Allyl-3-((2-bromo-4,6-difluorophenyl)amino)indolin-2-one (**3d**).* The title compound was prepared from compound **2d**, following the general procedure for C-alkylation using allyl bromide. Yield: 49%. Crystals were obtained from DCM and hexane. Mp 187–189 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 7.17 (ddd, J=7.8, 6.5, 2.4 Hz, 1H), 7.01 (ddd, J=7.7, 2.8, 2.0 Hz, 1H), 6.95–6.80 (m, 3H), 6.45 (ddd, J=11.3, 8.3, 2.9 Hz, 1H), 5.87 (tdd, J=17.2, 10.0, 7.4 Hz, 1H), 5.42–5.25 (m, 2H), 4.56 (s, 1H), 2.82 (dd, J=13.4, 7.8 Hz, 1H), 2.65 (dd, J=13.4, 7.1 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 180.68, 180.65, 157.15, 157.02, 154.71, 154.58, 152.10, 151.98, 140.49, 130.24, 129.16, 128.96, 128.68, 123.83, 123.78, 122.17, 122.10, 122.04, 115.52, 115.45, 115.41, 115.34, 115.20, 115.17, 114.96, 114.92, 110.42, 104.23, 103.97, 103.72, 65.55, 44.85; HRMS: calcd for $C_{17}H_{14}{}^{79}BrF_2N_2O$ $[M+H]^+$: 379.0252, found: 379.0247.

*3.3.5. 3-Allyl-3-((2-bromophenyl)amino)-5-phenylindolin-2-one (**17a**).* The title compound was prepared from compound **16a**, following the general procedure for C-alkylation using allyl bromide. Yield: 39%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.67–7.23 (m, 8H), 7.02 (d, J=8.1 Hz, 1H), 6.83 (t, J=7.8 Hz, 1H), 6.50 (t, J=7.6 Hz, 1H), 6.02–5.85 (m, 2H), 5.43–5.32 (m, 2H), 5.24 (s, 1H), 2.92–2.64 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 178.94, 141.91, 140.41, 138.59, 136.52, 132.54, 130.39, 129.95, 129.25, 128.76, 128.28, 127.94, 127.14, 126.78, 122.65, 121.96, 119.18, 112.72, 110.73, 63.78, 44.79; HRMS: calcd for $C_{23}H_{20}{}^{79}BrN_2O$ $[M+H]^+$: 419.0754, found: 419.0742.

*3.3.6. 3-Allyl-3-((2-bromophenyl)amino)-5-(4-methoxyphenyl)indolin-2-one (**17b**).* The title compound was prepared from compound **16b**, following the general procedure for C-alkylation using allyl bromide. Yield: 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.50–7.35 (m, 5H), 7.11–6.91 (m, 3H), 6.81 (t, J=7.3 Hz, 1H), 6.49 (t, J=7.2 Hz, 1H), 5.98–5.82 (m, 2H), 5.43–5.32 (m, 2H), 5.23 (s, 1H), 3.83 (s, 3H), 2.82 (dd, J=13.3, 7.2 Hz, 1H), 2.69 (dd, J=13.3, 7.9 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 178.88, 158.98, 141.90, 137.99, 136.15, 132.97, 132.48, 130.30, 129.96, 128.24, 127.77, 127.38, 122.20, 121.86, 119.10, 114.15, 112.70, 110.87, 110.65, 63.75, 55.30, 44.76; HRMS: calcd for $C_{24}H_{22}{}^{79}BrN_2O_2$ $[M+H]^+$: 449.0859, found: 449.0847.

*3.3.7. 4-(3-Allyl-3-((2-bromophenyl)amino)-2-oxoindolin-5-yl)benzonitrile (**17c**).* The title compound was prepared from compound **16c**, following the general procedure for C-alkylation using allyl bromide. Yield: 15%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.78 (d, J=8.3 Hz, 2H), 7.70 (d, J=8.3 Hz, 2H), 7.63 (dd, J=8.0, 1.7 Hz, 1H), 7.55 (d, J=1.1 Hz, 1H), 7.50 (dd, J=7.8, 0.8 Hz, 1H), 7.16 (d, J=8.1 Hz, 1H), 6.93 (t, J=7.7 Hz, 1H), 6.62 (t, J=7.42 Hz, 1H), 6.10–6.01 (m, 2H), 5.52–5.47 (m, 2H), 5.33 (s, 1H), 2.93 (dd, J=13.3, 7.0 Hz, 1H), 2.80 (dd, J=13.3, 7.7 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.87, 142.75, 141.94, 140.29, 135.72, 132.48, 132.40, 129.41, 129.37, 128.25, 126.85, 125.51, 124.82, 123.28, 119.42, 118.75, 112.80, 111.36, 110.93, 110.63, 62.88, 45.74; HRMS: calcd for $C_{24}H_{19}{}^{79}BrN_3O$ $[M+H]^+$: 444.0706, found: 444.0692.

*3.3.8. 3-Allyl-3-((2-bromophenyl)amino)-5-(4-fluorophenyl)indolin-2-one (**17d**).* The title compound was prepared from compound **16d**, following the general procedure for C-alkylation using allyl bromide. Yield: 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.35 (s, 1H), 7.52–7.39 (m, 5H), 7.16–7.05 (m, 2H), 6.98 (d, J=8.1 Hz, 1H), 6.81 (t, J=7.61 Hz, 1H), 6.49 (t, J=7.66 Hz, 1H), 6.01–5.85 (m, 2H), 5.43–5.32 (m, 2H), 5.25 (s, 1H), 2.84 (dd, J=13.3, 7.2 Hz, 1H), 2.69 (dd, J=13.3, 7.2 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 178.99, 163.52, 161.07, 141.87, 138.58, 136.56, 136.53, 135.55, 132.56, 130.48, 129.87, 128.38, 128.30, 128.27, 128.18, 127.82, 122.45, 121.99, 119.19, 115.70, 115.48, 112.64, 110.92, 110.80, 63.77, 44.77; HRMS: calcd for $C_{23}H_{19}{}^{79}BrFN_2O$ $[M+H]^+$: 437.0659, found: 437.0648.

*3.3.9. 3-Allyl-3-((2-bromophenyl)amino)-5-(thiophen-2-yl)indolin-2-one (**17e**).* The title compound was prepared from compound **16e**, following the general procedure for C-alkylation using allyl bromide. Yield: 53%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58–8.25 (b, 1H), 7.55 (d, J=8.0, 1H), 7.48 (s, 1H), 7.41 (dd, J=7.9, 1.5 Hz, 1H), 7.27–7.21 (m, 2H), 7.06 (dd, J=5.0, 3.7 Hz, 1H), 6.97 (dd, J=8.1, 1.5 Hz, 1H), 6.85 (t, J=7.8 Hz, 1H), 6.53 (t, J=7.61 Hz, 1H), 6.02–5.84 (m, 2H), 5.49–5.27 (m, 2H), 5.23 (s, 1H), 2.90–2.73 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.90, 144.53, 142.90, 140.95, 135.20, 134.89, 133.96, 133.42, 129.86, 129.17, 128.14, 125.89, 125.60, 125.50, 123.93, 123.52, 119.30, 118.26, 117.35, 65.63, 45.56; HRMS: calcd for $C_{21}H_{18}{}^{79}BrN_2OS$ $[M+H]^+$: 425.0318, found: 425.0301.

*3.3.10. 3-Allyl-3-((2-bromophenyl)amino)-5-(4-(trifluoromethyl)phenyl)indolin-2-one (**17f**).* The title compound was prepared from compound **16f**, following the general procedure for C-alkylation using allyl bromide. Yield: 94%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 7.60–7.52 (m, 4H), 7.50 (dd, J=8.1, 1.6 Hz, 1H), 7.43 (s, 1H), 7.38 (d, J=8.0 Hz, 1H), 7.02 (d, J=8.0 Hz, 1H), 6.81 (t, J=7.7 Hz, 1H), 6.49 (t, J=7.6 Hz, 1H), 5.91–5.84 (m, 2H), 5.42–5.32 (m, 2H), 5.23 (s, 1H), 2.82 (dd, J=13.3, 7.2 Hz, 1H), 2.68 (dd, J=13.3, 7.2 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.09, 149.51, 143.88, 141.85, 139.47, 134.95, 132.62, 130.71, 129.76, 129.01, 128.56, 128.30, 128.26, 127.03, 125.74, 125.71, 125.70, 122.67, 122.14, 119.31, 112.63, 111.03, 108.24, 63.82, 44.75; HRMS: calcd for $C_{24}H_{19}{}^{79}BrF_3N_2O$ $[M+H]^+$: 487.0627, found: 487.0619.

*3.3.11. 3-Allyl-3-((2-bromophenyl)amino)-5-(p-tolyl)indolin-2-one (**17g**).* The title compound was prepared from compound **16g**, following the general procedure for C-alkylation using allyl bromide. Yield: 58%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.51 (dd, J=8.0, 1.6 Hz, 1H), 7.43–7.19 (m, 4H), 7.22 (d, J=8.1 Hz, 2H), 7.00 (d, J=7.8 Hz, 1H), 6.83 (t, J=7.6 Hz, 1H), 6.51 (t, J=7.4 Hz, 1H), 5.94–5.85 (m, 2H), 5.42–5.33 (m, 2H), 5.23 (s, 1H), 2.83 (dd, J=13.2, 7.2 Hz,

1H), 2.70 (dd, *J*=13.6, 7.6 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.21, 141.94, 138.38, 137.54, 136.92, 136.44, 132.52, 130.30, 130.00, 129.45, 128.29, 127.68, 126.60, 122.42, 121.92, 119.14, 112.74, 110.90, 110.80, 63.84, 44.78, 21.03; HRMS: calcd for $C_{24}H_{22}{}^{79}BrN_2O$ $[M+H]^+$: 433.0910, found: 433.0902.

3.4. General procedure for C-alkylation using cinnamyl bromide: (for example preparation of 8a)

*3.4.1. 3-((2-Bromophenyl)-amino)-3-cinnamylindolin-2-one (**8a**).* To a solution of compound **2a** (1.5 g, 4.37 mmol) dissolved in DMF (or THF), indium (502 mg, 4.37 mmol), and sodium iodide (982 mg, 6.55 mmol) were added followed by the addition of cinnamyl bromide (292 mg, 6.55 mmol) dropwise. The mixture was allowed to react for 3 h at room temperature. After the reaction was complete, the reaction mass was filtered and evaporated to dryness. The crude reaction mixture was diluted with DCM and washed with 30% HCl. The aqueous layer was extracted with DCM three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated to yield the crude compound, which was purified by column chromatography to yield **8a**. Yield: 50%. Crystals were obtained from DCM and hexane. Mp 163–165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.31 (s, 1H), 7.47–7.13 (m, 8H), 7.04 (t, *J*=7.5 Hz, 1H), 6.93 (d, *J*=7.7 Hz, 1H), 6.78–6.70 (m, 2H), 6.48 (dt, *J*=7.7, 1.4 Hz, 1H), 6.24 (td, *J*=15.5, 7.6 Hz, 1H), 5.88 (dd, *J*=8.2, 1.3 Hz, 1H), 5.31 (s, 1H), 2.93 (dd, *J*=13.8, 7.0 Hz, 1H), 2.77 (dd, *J*=13.4, 7.8 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.86, 141.99, 139.62, 136.74, 136.67, 132.48, 129.66, 129.21, 128.59, 128.30, 127.81, 126.47, 123.85, 123.11, 121.26, 119.17, 112.81, 110.95, 110.85, 64.14, 43.87; HRMS: calcd for $C_{23}H_{20}{}^{79}BrN_2O$ $[M+H]^+$: 419.0759, found: 419.0769.

*3.4.2. (Z)-3-((2-Bromophenyl)amino)-3-(3-phenylallyl)-5-(trifluoromethoxy)indolin-2-one (**8b**).* The title compound was prepared from compound **2b**, following the general procedure for C-alkylation using cinnamyl bromide. Crystals were obtained from DCM and hexane. Mp 139–141 °C; Yield: 17%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H), 7.42–7.21 (m, 6H), 7.15–7.08 (m, 2H), 6.94–6.87 (m, 1H), 6.84–6.76 (m, 1H), 6.66 (d, *J*=15.8 Hz, 1H), 6.51 (dt, *J*=7.8, 1.3 Hz, 1H), 6.33–6.02 (m, 1H), 5.82 (dd, *J*=8.2, 1.2 Hz, 1H), 5.27 (s, 1H), 3.02–2.68 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.77, 145.07, 145.05, 141.67, 138.09, 137.22, 136.41, 132.66, 131.47, 128.63, 128.31, 128.01, 126.42, 122.39, 120.24, 119.60, 117.68, 112.56, 111.55, 110.97, 64.49, 43.78; HRMS: calcd for $C_{24}H_{19}{}^{79}BrF_3N_2O_2$ $[M+H]^+$: 503.0582, found: 503.0603.

*3.4.3. 3-((2-Bromophenyl)amino)-3-cinnamyl-5-fluoroindolin-2-one (**8c**).* The title compound was prepared from compound **2c**, following the general procedure for C-alkylation using cinnamyl bromide. Crystals were obtained from DCM and hexane. Mp 214–216 °C; Yield: 47%. ^{1}H NMR (400 MHz, DMSO) δ 10.86 (s, 1H), 7.48–7.05 (m, 8H), 7.02–6.87 (m, 2H), 6.62 (d, *J*=15.8 Hz, 1H), 6.58–6.47 (m, 1H), 6.19–6.11 (m, 1H), 5.75 (d, *J*=7.7 Hz, 1H), 5.32 (s, 1H), 2.96–2.84 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 178.70, 160.62, 158.21, 141.70, 136.99, 136.52, 135.19, 135.17, 132.61, 131.69, 131.62, 128.58, 128.25, 127.92, 126.45, 120.47, 119.47, 115.85, 115.61, 112.61, 112.04, 111.79, 111.20, 111.12, 110.94, 64.34, 43.85; HRMS: calcd for $C_{23}H_{19}{}^{79}BrFN_2O$ $[M+H]^+$]: 438.3122, found: 437.0651.

3.5. General procedure for radical cyclization: (for example preparation of 7a)

*3.5.1. 7-Allyl-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**7a**).* Compound **3a** (90 mg, 0.26 mmol) was dissolved in toluene. AIBN (8.61 mg, 0.052 mmol) was added at 80 °C followed by slow addition of TBTH (83.9 mg, 0.28 mmol) at the same temperature. The above mixture was allowed to reflux for 2 h. The mixture was then evaporated to dryness. The residue was diluted with DCM and washed with water. The aqueous layer was extracted with DCM three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated. The crude mixture was purified using column chromatography to yield **7a**. Yield: 93%. Crystals were obtained from DCM and hexane. Mp 179–181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.48–7.32 (m, 3H), 7.18–7.05(m, 2H), 6.89–6.72 (m, 2H), 6.62 (d, *J*=8.1 Hz, 1H), 5.79–5.65 (m, 1H), 5.16–4.86 (m, 2H), 4.33 (dd, *J*=16.4, 7.1 Hz, 1H), 3.82 (d, *J*=9.5 Hz, 1H), 2.61–2.45 (m, 1H), 2.41–2.32 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.62, 145.46, 140.57, 135.74, 134.00, 133.37, 132.66, 129.00, 128.46, 128.37, 125.48, 124.31, 119.38, 118.15, 117.87, 52.72, 35.48; HRMS: calcd for $C_{17}H_{17}{}^{79}N_2O$ $[M+H]^+$: 265.1341, found: 265.1357.

*3.5.2. 7-Allyl-2-(trifluoromethoxy)-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**7b**).* The title compound was prepared from compound **3b**, following the general procedure for radical cyclization. Yield: 61%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.24–7.02 (m, 5H), 6.88–6.75 (m, 2H), 6.62 (d, *J*=7.90 Hz, 1H), 5.76–5.63 (m, 1H), 5.15–4.88 (m, 2H), 4.31 (ddd, *J*=9.36, 7.57, 6.42 Hz, 1H), 3.90 (d, *J*=9.49 Hz, 1H), 2.57–2.48 (m, 1H), 2.46–2.25 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.80, 148.76, 15.74, 148.72, 145.40, 142.44, 134.50, 133.88, 133.11, 129.57, 126.65, 124.87, 122.86, 121.65, 120.49, 119.53, 119.08, 118.32, 118.12, 52.61, 35.37; HRMS: calcd for $C_{18}H_{16}F_3N_2O_2$ $[M+H]^+$: 349.1164, found: 349.1152.

*3.5.3. **7**-Allyl-2-fluoro-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**7c**).* The title compound was prepared from compound **3c**, following the general procedure for radical cyclization. Yield: 94%. Crystals were obtained from DCM and hexane. Mp 191–193 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.18–6.97 (m, 4H), 6.87–6.74 (m, 2H), 6.61 (d, *J*=8.1 Hz, 1H), 5.81–5.54 (m, 1H), 5.11–5.02 (m, 2H), 4.37–4.22 (m, 1H), 3.89 (d, *J*=9.4 Hz, 1H), 2.59–2.45 (m, 1H), 2.43–2.27 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.78, 163.40, 160.94, 145.39, 142.75, 142.67, 133.70, 133.25, 131.90, 131.87, 129.43, 127.08, 126.99, 123.27, 119.44, 119.32, 119.10, 118.35, 118.00, 115.15, 114.93, 52.63, 35.36; HRMS: calcd for $C_{17}H_{16}FN_2O$ $[M+H]^+$: 283.1241, found: 283.1240.

*3.5.4. 7-Allyl-9,11-difluoro-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**7d**).* The title compound was prepared from compound **3d**, following the general procedure for radical cyclization. Yield: 87%. Crystals were obtained from DCM and hexane. Mp 156–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.49–7.29 (m, 3H), 7.17–7.10 (m, 1H), 6.88–6.74 (m, 1H), 6.50–6.39 (m, 1H), 5.81–5.60 (m, 1H), 5.23–4.96 (m, 2H), 4.37–4.19 (m, 1H), 4.03–3.90 (m, 1H), 2.64–2.51 (m, 1H), 2.49–2.37 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.12, 155.73, 155.60, 153.35, 153.22, 152.71, 152.59, 150.30, 150.18, 138.44, 138.43, 135.60, 133.02, 132.31, 129.27, 128.71, 125.89, 118.18, 115.01, 114.98, 114.79, 114.76, 103.63, 103.38, 103.12, 52.34, 35.35; HRMS: calcd for $C_{18}H_{15}F_2N_2O$ $[M+H]^+$: 301.3106, found: 301.1139.

*3.5.5. 7-Cinnamyl-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**10a**) and 5-benzyl-4a,5,6,7-tetrahydro-1,6a-(epiminomethano)-indeno[1,7a-b]indol-12-one (**11a**).* The title compounds were prepared from compound **8a**, following the general procedure for radical cyclization. Yields-**10a**: 71% and **11a**: 18%.

Compound **10a**: Crystals were obtained from DCM and hexane. Mp 195–197 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.53–7.03 (m, 10H), 6.88–6.75 (m, 2H), 6.63 (d, *J*=7.8 Hz, 1H), 6.41 (d, *J*=15.9 Hz, 1H), 6.16–6.06 (m, 1H), 4.40 (dd, *J*=7.5, 7.1 Hz, 1H), 3.86 (d, *J*=8.8 Hz, 1H), 2.72–2.64 (m, 1H), 2.60–2.48 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.51, 145.43, 140.57, 137.01, 135.67, 133.99,

132.99, 132.69, 129.02, 128.52, 128.42, 127.27, 126.12, 125.53, 124.84, 124.29, 119.40, 118.187, 53.09, 34.87; HRMS: calcd for $C_{23}H_{21}N_2O$ $[M+H]^+$: 341.1648, found: 341.1653.

Compound **11a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.32–7.07 (m, 7H), 6.69 (t, J=7.3 Hz, 1H), 6.62 (d, J=8.1 Hz, 1H), 6.12 (dd, J=9.4, 5.3 Hz, 1H), 5.69 (dd, J=8.5, 4.7 Hz, 1H), 5.45 (d, J=5.3 Hz, 1H), 4.90 (s, 1H), 2.89 (dd, J=13.4, 4.5 Hz, 1H), 2.65 (dd, J=13.4, 8.4 Hz, 1H), 2.45–2.30 (m, 2H), 2.28–2.17 (m, 1H), 1.83 (dd, J=13.9, 11.1 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 180.33, 148.91, 140.31, 138.20, 129.41, 128.96, 128.73, 128.32, 126.09, 124.56, 123.85, 123.21, 119.55, 110.42, 97.88, 78.00, 60.96, 49.66, 49.62, 40.72, 40.63; HRMS: calcd for $C_{23}H_{21}N_2O$ $[M+H]^+$: 341.1648, found: 341.1653.

*3.5.6. 7-Cinnamyl-2-(trifluoromethoxy)-7,8-dihydrodibenzo[e,g][1,4] diazocin-6(5H)-one (**10b**) and rac-(4aS,5R,6aS,11bS)-5-benzyl-4-(trifluoromethoxy)-4a,5,6,7-tetrahydro-1,6a-(epiminomethano)indeno[1,7a-b]indol-12-one (**11b**).* The title compound was prepared from compound **8b**, following the general procedure for radical cyclization. Yields-**10b**: 18% and **11b**: 41%.

Compound **10b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.37–7.05 (m, 9H), 6.82–6.71 (m, 2H), 6.62 (d, J=8.1 Hz, 1H), 6.45 (d, J=15.9 Hz, 1H), 6.18–6.6.09 (m, 1H), 4.42–4.37 (m, 1H), 3.85 (d, J=7.5 Hz, 1H), 2.74–2.56 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.77, 145.07, 145.05, 141.67, 138.09, 137.22, 136.41, 132.66, 131.47, 128.63, 128.31, 128.01, 126.42, 122.39, 120.24, 119.60, 117.68, 112.56, 111.55, 110.97, 54.49, 33.78; HRMS: calcd for $C_{24}H_{20}F_3N_2O_2$ $[M+H]^+$: 425.1477, found: 425.1475.

Compound **11b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.32–7.08 (m, 7H), 6.74 (t, J=7.4 Hz, 1H), 6.62 (d, J=8.1 Hz, 1H), 6.06 (d, J=4.9 Hz, 1H), 5.37 (d, J=6.0 Hz, 1H), 4.89 (s, 1H), 3.12 (d, J=10.10 Hz, 1H), 2.71–2.45 (m, 3H), 2.25–2.13 (m, 1H), 1.85 (dd, J=14.0, 10.3 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 180.48, 148.84, 146.71, 139.63, 136.99, 129.96, 128.74, 128.42, 127.78, 126.26, 123.78, 121.70, 120.00, 119.13, 110.60, 109.73, 94.83, 77.89, 62.74, 51.99, 48.62, 40.02, 39.80; HRMS: calcd for $C_{24}H_{20}F_3N_2O_2$ $[M+H]^+$: 425.1477, found: 425.1476.

*3.5.7. 7-Cinnamyl-2-fluoro-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**10c**) and rac-(4aS,5R,6aS,11bS)-5-benzyl-4-fluoro-4a,5,6,7-tetrahydro-1,6a-(epiminomethano)indeno[1,7a-b]indol-12-one (**11c**).* The title compounds were prepared from compound **8c**, following the general procedure for radical cyclization. Yields-**10b**: 16% and **11b**: 42%.

Compound **10c**: Crystals were obtained from THF and hexane. Mp 108–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.35–7.01 (m, 9H), 6.86–6.73 (m, 2H), 6.63 (d, J=8.1 Hz, 1H), 6.42 (d, J=15.9 Hz, 1H), 6.17–6.00 (m, 1H), 4.42–4.35 (m, 1H), 3.88 (d, J=7.5 Hz, 1H), 2.72–2.52 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.54, 163.48, 161.01, 145.37, 142.85, 142.76, 136.98, 133.70, 133.22, 131.80, 131.77, 129.50, 128.50, 127.40, 127.22, 127.13, 126.18, 124.68, 123.29, 119.54, 119.42, 119.19, 118.45, 115.25, 115.03, 53.07, 34.84; HRMS: calcd for $C_{23}H_{20}FN_2O$ $[M+H]^+$: 359.1560, found: 359.1557.

Compound **11c**: Crystals were obtained from THF and hexane. Mp>235 °C; ^{1}H NMR (400 MHz, d_6-DMSO-$CDCl_3$) δ 7.84 (s, 1H), 7.21–6.91 (m, 7H) 6.54–6.48 (m, 2H), 6.11 (s, 1H), 5.71 (dd, J=11.3, 5.9 Hz, 1H), 5.17 (dd, J=5.8, 4.9 Hz, 1H), 2.94 (dd, J=13.5, 3.8 Hz, 1H), 2.58–2.42 (m, 2H), 2.35–2.22 (m, 1H), 1.99 (dd, J=13.8, 7.3 Hz, 1H), 1.74–1.67 (m, 1H); ^{13}C NMR (400 MHz, d_6-DMSO-$CDCl_3$) δ 178.22, 160.34, 157.69, 148.13, 138.04, 135.03, 135.01, 127.97, 127.36, 126.79, 126.64, 124.60, 121.84, 116.70, 108.24, 107.02, 100.27, 100.07, 91.38, 91.31, 77.19, 76.31, 76.29, 61.00, 49.92, 49.69, 46.23, 46.21; HRMS: calcd for $C_{23}H_{20}FN_2O$ $[M+H]^+$: 359.1560, found: 359.1567.

*3.5.8. 7-Allyl-2-phenyl-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**18a**).* The title compound was prepared from compound **17a**, following the general procedure for radical cyclization. Yield: 46%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.70–7.07 (m, 9H), 6.92 (d, J=6.8 Hz, 1H), 6.81 (t, J=7.41 Hz, 1H), 6.66 (d, J=8.0 Hz, 1H), 5.83–5.67 (m, 1H), 5.17–5.00 (m, 2H), 4.44–4.40 (m, 1H), 3.90 (d, J=9.5 Hz, 1H), 2.62–2.39 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.66, 145.48, 141.44, 140.90, 139.72, 134.83, 134.06, 133.35, 131.37, 129.15, 128.89, 127.73, 126.99, 126.91, 125.86, 124.25, 119.48, 118.22, 118.02, 52.77, 35.56; HRMS: calcd for $C_{23}H_{21}N_2O$ $[M+H]^+$: 341.1648, found: 341.1643.

*3.5.9. 7-Allyl-2-(4-methoxyphenyl)-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**18b**).* The title compound was prepared from compound **17b**, following the general procedure for radical cyclization. Yield: 60%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62–7.52 (m, 4H), 7.24 (s, 1H), 7.16–7.10 (m, 2H), 7.00 (d, J=7.8 Hz, 2H), 6.93 (d, J=7.8 Hz, 1H), 6.81 (t, J=7.4 Hz, 1H), 6.65 (d, J=8.2 Hz, 1H), 5.81–5.72 (m, 1H), 5.12–5.05 (m, 2H), 4.42 (dd, J=15.5, 7.8 Hz, 1H), 3.87 (s, 3H), 3.78 (d, J=7.3 Hz, 1H), 2.62–2.53 (m, 1H), 2.43–2.38 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.43, 159.48, 145.45, 141.08, 140.89, 134.13, 133.98, 133.36, 132.20, 130.84, 129.11, 128.03, 126.41, 125.86, 124.37, 119.47, 118.23, 118.00, 114.32, 55.34, 52.75, 35.59; HRMS: calcd for $C_{24}H_{23}N_2O_2$ $[M+H]^+$: 371.1754, found: 371.1744.

*3.5.10. 4-(7-Allyl-6-oxo-5,6,7,8-tetrahydrodibenzo[e,g][1,4]diazocin-2-yl)benzonitrile (**18c**).* The title compound was prepared from compound **17c**, following the general procedure for radical cyclization. Yield: 63%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76–7.70 (m, 3H), 7.60–7.54 (m, 2H), 7.44 (s, 1H), 7.20 (d, J=8.8 Hz, 2H), 7.14 (dt, J=8.1, 1.7 Hz, 1H), 6.87 (dd, J=7.7, 1.5 Hz, 1H), 6.80 (t, J=7.4 Hz, 1H), 6.63 (d, J=7.8 Hz, 1H), 5.79–5.68 (m, 1H), 5.12–5.07 (m, 2H), 4.36 (dd, J=15.2, 7.3 Hz, 1H), 3.75 (d, J=9.7 Hz, 1H), 2.62–2.56 (m, 1H), 2.48–2.40 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.89, 160.23, 147.45, 141.56, 140.23, 134.02, 133.78, 133.38, 131.20, 130.62, 129.10, 127.69, 126.40, 125.56, 124.37, 119.40, 118.02, 117.10, 116.82, 56.34, 36.74; HRMS: calcd for $C_{24}H_{20}N_3O$ $[M+H]^+$: 366.1601, found: 366.1591.

*3.5.11. 7-Allyl-2-(4-fluorophenyl)-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**18d**).* The title compound was prepared from compound **17d**, following the general procedure for radical cyclization. Yield: 63%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95(s, 1H), 7.63–7.53 (m, 4H), 7.21–7.10 (m, 4H), 6.91 (dd, J=7.7, 1.3 Hz, 1H), 6.81 (t, J=7.3 Hz, 1H), 6.64 (d, J=8.1 Hz, 1H), 5.80–5.72 (m, 1H), 5.18–5.04 (m, 2H), 4.45–4.40 (b, 1H), 3.87–3.80 (b, 1H), 2.58 (td, J=14.12, 5.9 Hz, 1H), 2.41 (td, J=13.5, 6.7 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.22, 161.46, 145.44, 141.09, 140.52, 134.74, 133.94, 133.29, 131.23, 129.24, 128.64, 128.56, 126.78, 125.96, 124.11, 119.53, 118.28, 118.07, 115.91, 115.70, 52.76, 35.61; HRMS: calcd for $C_{23}H_{20}FN_2O$ $[M+H]^+$: 359.1554, found: 359.1542.

*3.5.12. 7-Allyl-2-(thiophen-2-yl)-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**18e**).* The title compound was prepared from compound **17e**, following the general procedure for radical cyclization. Yield: 69%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.60–7.50(m, 2H), 7.35–7.25 (m, 2H), 7.17–7.01 (m, 3H), 6.89 (dd, J=7.7, 1.5 Hz, 1H), 6.85–6.75 (m, 1H), 6.64 (d, J=8.1 Hz, 1H), 5.78–5.65 (m, 1H), 5.08–5.00 (m, 2H), 4.46–4.38 (m, 1H), 3.93 (d, J=9.4 Hz, 1H), 2.60–2.35 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.90, 145.53, 142.94, 140.96, 135.00, 134.59, 133.96, 133.32, 129.86, 129.18, 128.15, 125.89, 125.59, 125.37, 123.93, 123.59, 119.40, 118.17, 117.95, 52.80, 35.47; HRMS: calcd for $C_{21}H_{19}N_2OS$ $[M+H]^+$: 347.1213, found: 347.1202.

*3.5.13. 7-Allyl-2-(4-(trifluoromethyl)phenyl)-7,8-dihydrodibenzo [e,g][1,4]diazocin-6(5H)-one (**18f**).* The title compound was prepared from compound **17f**, following the general procedure for

radical cyclization. Yield: 34%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.79–7.68 (m, 4H), 7.62–7.59 (m, 2H), 7.20–7.13 (m, 2H), 6.90 (d, J=7.2 Hz, 1H), 6.81 (t, J=7.4 Hz, 1H), 6.65 (d, J=8.2 Hz, 1H), 5.80–5.70 (m, 1H), 5.10–5.00 (m, 2H), 4.41 (dd, J=16.3, 7.3 Hz, 1H), 3.86 (d, J=9.5 Hz, 1H), 2.63–2.52 (m, 1H), 2.45–2.35 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.58, 145.52, 143.24, 143.23, 141.20, 139.88, 135.86, 134.01, 133.27, 131.55, 129.32, 127.28, 127.07, 126.03, 125.89, 125.86, 125.82, 125.78, 123.90, 119.54, 118.27, 118.08, 52.82, 35.57; HRMS: calcd for $C_{24}H_{20}F_3N_2O$ $[M+H]^+$: 409.1522, found: 409.1508.

*3.5.14. 7-Allyl-2-(p-tolyl)-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**18g**).* The title compound was prepared from compound **17g**, following the general procedure for radical cyclization. Yield: 30%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.59–7.54 (m, 4H), 7.27 (d, J=7.7 Hz, 2H), 7.12 (d, J=7.8 Hz, 2H), 6.91 (d, J=7.3 Hz, 1H), 6.80 (t, J=7.4 Hz, 1H), 6.65 (d, J=8.2 Hz, 1H), 5.79–5.65 (m, 1H), 5.10–5.06 (m, 2H), 4.44 (dd, J=16.2, 7.2 Hz, 1H), 3.92 (d, J=9.5 Hz, 1H), 2.57 (td, J=14.0, 8.8 Hz, 1H), 2.47–2.37 (m, 4H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.87, 145.52, 141.22, 140.77, 137.53, 136.84, 134.66, 134.06, 133.39, 131.07, 129.58, 129.05, 126.77, 126.62, 125.76, 124.34, 119.38, 118.16, 117.91, 52.77, 35.52, 21.08; HRMS: calcd for $C_{24}H_{23}N_2O$ $[M+H]^+$: 355.1805, found: 355.1796.

*3.5.15. rac-(4aR,5R,6aS,11bS)-5-(4-Methoxybenzyl)-4a,5,6,7-tetrahydro-1,6a-(epiminomethano)indeno[1,7a-b]indol-12-one (**22a**) and 7-(3-(4-methoxyphenyl)allyl)-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**23a**).* The title compounds were prepared from compound **21a**, following the general procedure for radical cyclization. Yields-**22a**: 49%. and **23a**: 19%.

Compound (**22a**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.09–7.05 (m, 2H), 7.02 (d, J=8.5 Hz, 2H), 6.78 (d, J=8.5 Hz, 2H), 6.69 (t, J=7.4 Hz, 1H), 6.61 (d, J=8.1 Hz, 1H), 6.11 (dd, J=9.4, 5.3 Hz, 1H), 5.68 (dd, J=9.3, 5.3 Hz, 1H), 5.44 (d, J=5.3 Hz, 1H), 4.90 (s, 1H), 3.77 (s, 3H), 2.82 (dd, J=13.9, 4.3 Hz, 1H), 2.60 (dd, J=13.7, 7.9 Hz, 1H), 2.39–2.30 (m, 2H), 2.22 (dd, J=13.9, 6.5 Hz, 1H), 1.81 (dd, J=13.7, 10.8 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 180.43, 157.95, 148.92, 138.22, 132.39, 129.65, 129.39, 129.02, 124.47, 123.85, 123.32, 119.53, 113.73, 110.40, 97.89, 78.01, 60.95, 55.20, 49.82, 49.57, 40.58, 39.73; HRMS: calcd for $C_{24}H_{23}N_2O_2$ $[M+H]^+$: 371.1760, found: 371.1747.

Compound (**23a**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.55–7.35 (m, 9H), 6.82–6.70 (m, 2H), 6.63 (d, J=8.1 Hz, 1H), 6.42 (d, J=15.9 Hz, 1H), 6.17–6.00 (m, 1H), 4.54 (m, 1H), 3.75 (d, J=7.5 Hz, 1H), 3.20 (s, 3H), 2.69–2.52 (m, 2H); ^{13}C NMR (400 MHz, d_6-DMSO) δ 178.27, 159.62, 142.78, 141.56, 135.66, 133.07, 130.19, 129.96, 129.82, 129.08, 128.11, 124.17, 122.86, 120.02, 119.43, 114.75, 112.94, 111.01, 110.31, 56.99, 55.78, 33.82; HRMS: calcd for $C_{24}H_{23}N_2O_2$ $[M+H]^+$: 371.1760, found: 371.1750.

*3.5.16. rac-(4aR,5R,6aS,11bS)-5-(3-Methoxybenzyl)-4a,5,6,7-tetrahydro-1,6a-(epiminomethano)indeno[1,7a-b]indol-12-one (**22b**) and 7-(3-(3-methoxyphenyl)allyl)-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**23b**).* The title compounds were prepared from compound **21b**, following the general procedure for radical cyclization. Yields-**22b**: 27% and **23b**: 24%.

Compound **22b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17(s, 1H), 7.21–7.13 (m, 1H), 7.12–7.07 (m, 2H), 6.75–6.60 (m, 5H), 6.19 (dd, J=9.4, 5.4 Hz, 1H), 5.74 (dd, J=9.3, 5.9 Hz, 1H), 5.41 (d, J=5.4 Hz, 1H), 4.89 (s, 1H), 3.78 (s, 3H), 2.94–2.82 (m, 1H), 2.61 (dd, J=13.3, 8.9 Hz, 1H), 2.42–2.32 (m, 2H), 2.29–2.20 (m, 1H), 1.90–1.82 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 180.23, 159.55, 148.92, 141.93, 138.18, 129.42, 129.30, 128.96, 124.60, 123.85, 123.19, 121.18, 119.56, 114.66, 111.21, 110.43, 97.86, 77.98, 60.96, 55.12, 49.66, 49.50, 40.74, 40.66; HRMS: calcd for $C_{24}H_{23}N_2O_2$ $[M+H]^+$: 371.1760, found: 371.1762.

Compound **23b**: ^{1}H NMR (400 MHz, d_6-benzene) δ 7.91 (s, 1H), 7.35–7.01 (m, 9H), 6.86–6.73 (m, 2H), 6.63 (d, J=8.1 Hz, 1H), 6.42 (d, J=15.9 Hz, 1H), 6.17–6.00 (m, 1H), 4.37 (m, 1H), 3.88 (d, J=7.5 Hz, 1H), 3.26 (s, 3H), 2.72–2.52 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.55, 159.72, 141.94, 139.52, 138.16, 136.50, 132.45, 129.61, 129.54,129.19,128.25, 123.87, 123.10, 121.57, 119.16, 119.08, 113.22, 112.79, 111.98, 110.85, 110.79, 64.07, 55.19, 33.74; HRMS: calcd for $C_{24}H_{23}N_2O_2$ $[M+H]^+$: 371.1760, found: 371.1767.

*3.5.17. rac-4-(((4aS,5S,6aR,11bR)-12-oxo-4a,5,6,7-Tetrahydro-1,6a-(epiminomethano)indeno[1,7a-b]indol-5-yl)methyl)benzonitrile (**22c**).* The title compound was prepared from compound **21d**, following the general procedure for radical cyclization. Yield: 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 7.52 (d, J=8.3 Hz, 2H), 7.19 (d, J=8.2 Hz, 2H), 7.12–7.02 (m, 2H), 6.68 (dt, J=7.5, 0.8 Hz, 1H), 6.60 (d, J=7.9 Hz, 1H), 6.12 (dd, J=9.4, 5.3 Hz, 1H), 5.62 (dd, J=9.4, 5.6 Hz, 1H), 5.45 (d, J=5.3 Hz, 1H), 4.95 (s, 1H), 2.91 (dd, J=13.5, 4.4 Hz, 1H), 2.68 (dd, J=13.5, 8.6 Hz, 1H), 2.38–2.15(m, 2H), 2.15 (dd, J=13.9, 6.6 Hz, 1H), 1.80–1.72 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 180.73, 149.08, 146.25, 138.60, 132.45, 129.82, 129.76, 128.89, 125.35, 124.12, 122.79, 119.93, 119.14, 110.71, 110.32, 98.31, 78.25, 61.12, 49.83, 49.32, 41.07, 40.70; HRMS: calcd for $C_{24}H_{20}N_3O$ $[M+H]^+$: 366.1601, found: 366.159.

*3.5.18. rac-4-Fluoro-3-(((4aS,5S,6aR,11bR)-12-oxo-4a,5,6,7-tetrahydro-1,6a-(epiminomethano)indeno[1,7a-b]indol-5-yl)methyl) benzonitrile (**22d**).* The title compound was prepared from compound **21e**, following the general procedure for radical cyclization. Yield: 61%. ^{1}H NMR (400 MHz, $CDCl_3$+DMSO) δ 8.89 (s, 1H), 7.55–7.42 (m, 2H), 7.18–7.07 (m, 3H), 6.65 (t, J=7.4 Hz, 1H), 6.59 (d, J=7.8 Hz, 1H), 6.14 (dd, J=9.3, 5.3 Hz, 1H), 5.58 (dd, J=9.4, 5.6 Hz, 1H), 5.43 (d, J=5.3 Hz, 1H), 4.93 (s, 1H), 2.85 (dd, J=13.3, 5.3 Hz, 1H), 2.78 (dd, J=13.7, 8.0 Hz, 1H), 2.42–2.36 (m, 2H), 2.29 (dd, J=13.6, 6.9 Hz, 1H), 1.83 (dd, J=13.2, 11.2 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.82, 164.62, 162.07, 148.97, 138.84, 135.29, 135.23, 132.48, 132.39, 129.53, 129.41, 129.36, 128.75, 125.39, 123.84, 121.79, 119.48, 118.04, 116.82, 116.58, 110.41, 108.35, 108.31, 97.50, 77.78, 60.78, 49.43, 47.83, 40.441, 33.00; HRMS: calcd for $C_{24}H_{19}FN_3O$ $[M+H]^+$: 384.1507, found: 384.1493.

3.6. Preparation of 5′-bromospiro[[1,3]dioxolane-2,3′-indolin]-2′-one (13)

To a solution of 5-bromoisatin (1 g, 4.42 mmol) in toluene (40 mL), ethylene glycol (4.9 mL, 84.48 mmol) and *p*-toluenesulphonic acid (38.1 mg, 0.22 mmol) were added. The reaction mixture was refluxed for 5 h and then evaporated to dryness. The residue was diluted with DCM and washed with saturated sodium bicarbonate solution. The aqueous layer was extracted with DCM three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated. The crude mixture was purified using column chromatography to yield **13**. Yield: 99%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J=6.7 Hz, 1H), 7.46–7.41 (m, 2H), 6.71 (d, J=8.3 Hz, 1H), 4.60–4.52 (m, 2H), 4.38–4.30 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 176.24, 140.64, 134.36, 128.54, 126.37, 115.82, 112.11, 112.05, 65.96; HRMS: calcd for $C_{10}H_9{}^{79}BrNO_3$ $[M+H]^+$: 269.9760, found: 269.9749.

3.7. General procedure for Suzuki reaction: (for example preparation of 14a)

*3.7.1. 5′-Phenylspiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**14a**).* To a solution of **13** (500 mg, 1.85 mmol) in ethylene glycol dimethyl ether (5 mL), dichlorobis(triphenylphosphine)palladium (II) (39 mg, 0.0555 mmol) was added. The reaction mixture was

stirred at room temperature for 15 min. Phenylboronic acid (338 mg, 2.775 mmol), sodium bicarbonate (466.6 mg, 5.55 mmol), and water (5 mL) were added. The reaction mixture was refluxed for 2 h and then evaporated to dryness. The residue was diluted with DCM and washed with 10% sodium hydroxide solution. The aqueous layer was extracted with DCM three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated. The crude mixture was purified using column chromatography to yield **14a**. Yield: 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.59 (s, 1H), 7.55–7.48 (m, 3H), 7.41 (t, J=7.6 Hz, 2H), 7.32 (t, J=7.3 Hz, 1H), 6.89 (d, J=8.1 Hz, 1H), 4.59 (dt, J=6.1, 4.2 Hz, 2H), 4.35 (dt, J=6.3, 4.2 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.13, 140.86, 140.32, 136.93, 130.36, 128.75, 127.16, 126.746, 124.91, 124.16, 110.77, 102.21, 65.87; HRMS: calcd for $C_{16}H_{14}NO_3$ $[M+H]^+$: 268.0968, found: 268.0959.

*3.7.2. 5′-(4-Methoxyphenyl)spiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**14b**).* The title compound was prepared from compound **13** and 4-methoxyphenylboronic acid, following the general procedure for Suzuki reaction. Yield: 61%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.44 (s, 1H), 7.32 (s, 1H), 7.30–7.25 (m, 3H), 6.76 (d, J=8.7 Hz, 2H), 6.69 (d, J=8.1 Hz, 1H), 4.39 (dd, J=8.2, 5.2 Hz, 2H), 4.15 (dd, J=7.9, 5.6 Hz, 2H), 3.65 (s, 3H); ^{13}C NMR (400 MHz, d_6-acetone) δ 175.54, 160.17, 142.76, 136.45, 133.74, 130.41, 128.45, 126.66, 124.10, 115.18, 111.65, 103.07, 66.56, 55.67; HRMS: calcd for $C_{17}H_{16}NO_4$ $[M+H]^+$: 298.1074, found: 298.1062.

*3.7.3. 4-(2′-Oxospiro[[1,3]dioxolane-2,3′-indolin]-5′-yl)benzonitrile (**14c**).* The title compound was prepared from compound **13** and 4-cyanophenylboronic acid, following the general procedure for Suzuki reaction. Yield: 48%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78–7.58 (m,7H), 6.93 (d, J=8.1 Hz, 1H), 4.60 (dt, J=6.0, 4.1 Hz, 2H), 4.36 (dt, J=6.3, 4.2 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.43, 144.68, 142.10, 134.67, 132.63, 130.65, 127.24, 125.93, 125.32, 124.30, 118.81, 110.99, 110.81, 65.90; HRMS: calcd for $C_{17}H_{13}N_2O_3$ $[M+H]^+$: 293.0921, found: 293.0922.

*3.7.4. 5′-(4-Fluorophenyl)spiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**14d**).* The title compound was prepared from compound **13** and 4-fluorophenylboronic acid, following the general procedure for Suzuki reaction. Yield: 69%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.53–7.45 (m, 4H), 7.13–7.05 (m, 2H), 6.89 (d, J=8.1 Hz, 1H), 4.60 (dd, J=8.3, 5.1 Hz, 2H), 4.36 (dd, J=7.9, 5.5 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.12, 163.55, 161.10, 140.88, 136.48, 136.45, 135.95, 130.24, 128.35, 128.27, 124.96, 124.03, 115.72, 115.51, 110.82, 65.86; HRMS: calcd for $C_{16}H_{13}FNO_3$ $[M+H]^+$: 286.0874, found: 286.0862.

*3.7.5. 5′-(Thiophen-2-yl)spiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**14e**).* The title compound was prepared from compound **13** and 2-thiopheneboronic acid, following the general procedure for Suzuki reaction. Yield: 33%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82–7.65 (m, 3H), 7.28–7.20 (m, 2H), 7.05 (dd, J=4.9, 3.8 Hz, 1H), 6.83 (d, J=8.0 Hz, 1H), 4.59 (dt, J=6.3, 4.9 Hz, 2H), 4.37 (dt, J=7.6, 4.4, 1.8 Hz, 2H); ^{13}C NMR (400 MHz, d_6-acetone) δ 175.42, 144.48, 143.39, 132.38, 130.25, 129.84, 129.13, 126.85, 125.98, 125.36, 123.70, 123.39, 111.89, 66.63; HRMS: calcd for $C_{14}H_{12}NO_3S$ $[M+H]^+$: 274.0532, found: 274.052.

*3.7.6. 5′-(4-(Trifluoromethyl)phenyl)spiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**14f**).* The title compound was prepared from compound **13** and 4-trifluoromethlyphenylboronic acid, following the general procedure for Suzuki reaction. Yield: 52%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.80–7.68 (m, 6H), 7.02 (d, J=8.1 Hz, 1H), 4.75–4.63 (m, 2H), 4.51–4.41 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.15, 143.76, 141.76, 135.31, 130.63, 129.40, 129.08, 126.97, 125.75, 125.71, 125.56, 125.20, 124.25, 122.85, 111.03, 102.08, 65.92; HRMS: calcd for $C_{17}H_{13}F_3NO_3$ $[M+H]^+$: 336.0842, found: 336.0828.

*3.7.7. 5′-(p-Tolyl)spiro[[1,3]dioxolane-2,3′-indolin]-2′-one (**14g**).* The title compound was prepared from compound **13** and 4-methylphenylboronic acid, following the general procedure for Suzuki reaction. Yield: 58%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.56 (s, 1H), 7.50 (dd, J=8.1, 1.7 Hz, 1H), 7.41 (d, J=8.0 Hz, 2H), 7.21 (d, J=8.0 Hz, 2H), 6.86 (d, J=8.1 Hz, 1H), 4.58 (t, J=6.7 Hz, 2H), 4.34 (t, J=6.7 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (400 MHz, d_6-acetone) δ 175.35, 159.04, 140.18, 136.64, 132.90, 129.87, 127.77, 124.80, 123.82, 114.18, 110.56, 65.85, 55.30, 22.25; HRMS: calcd for $C_{17}H_{16}NO_3$ $[M+H]^+$: 282.1125, found: 282.1116.

3.8. General procedure for ketal deprotection: (for example preparation of 15a)

*3.8.1. 5-Phenylindoline-2,3-dione (**15a**).* To a solution of **14a** (630 mg, 2.36 mmol) in methanol (12 mL), concd HCl (5 mL) was added and the mixture was allowed to reflux for 4 h. The reaction mixture was evaporated to dryness. The residue was diluted with DCM and washed with saturated sodium bicarbonate solution. The aqueous layer was extracted with DCM three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated. The crude mixture was purified using column chromatography to yield **15a**. Yield: 99%. ^{1}H NMR (400 MHz, DMSO) δ 7.90 (d, J=8.2 Hz, 1H), 7.75 (s, 1H), 7.69–7.61 (m, 2H), 7.52–7.40 (m, 2H), 7.40–7.36 (m, 1H), 7.03–6.97 (m, 1H); ^{13}C NMR (400 MHz, d_6-acetone) δ 183.91, 159.09, 149.88, 139.28, 136.65, 136.10, 128.93, 127.48, 126.37, 122.61, 118.66, 112.69; HRMS: calcd for $C_{14}H_{10}NO_2$ $[M+H]^+$: 224.0706, found: 224.0698.

*3.8.2. 5-(4-Methoxyphenyl)indoline-2,3-dione (**15b**).* The title compound was prepared from compound **14b**, following the general procedure for ketal deprotection. Yield: 99%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 7.70 (d, J=1.3 Hz, 1H), 7.66 (dd, J=8.1, 2.0 Hz, 1H), 7.41 (d, J=8.8 Hz, 2H), 6.93 (dd, J=8.4, 6.9 Hz, 3H), 3.81 (s, 3H); ^{13}C NMR (400 MHz, d_6-acetone) δ 184.09, 142.89, 140.56, 137.42, 136.93, 136.881, 135.66, 130.11, 129.45, 128.72, 126.56, 124.83, 123.93, 110.71, 58.85; HRMS: calcd for $C_{15}H_{12}NO_3$ $[M+H]^+$: 254.0812, found: 254.0801.

*3.8.3. 4-(2,3-Dioxoindolin-5-yl)benzonitrile (**15c**).* The title compound was prepared from compound **14c**, following the general procedure for ketal deprotection. Yield: 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.79 (s, 1H), 7.76 (dd, J=8.3, 1.8 Hz, 1H), 7.70 (d, J=8.4 Hz, 2H), 7.64 (d, J=8.2 Hz, 2H), 7.03 (d, J=8.1 Hz, 1H); ^{13}C NMR (400 MHz, d_6-acetone) δ 183.96, 159.10, 149.65, 137.20, 136.41, 136.09, 134.15, 131.79, 129.56, 126.22, 122.34, 118.63, 112.62; HRMS: calcd for $C_{15}H_9N_2O_2$ $[M+H]^+$: 249.0659, found: 249.0655.

*3.8.4. 5-(4-Fluorophenyl)indoline-2,3-dione (**15d**).* The title compound was prepared from compound **14d**, following the general procedure for ketal deprotection. Yield: 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.75 (s, 1H), 7.70 (dd, J=8.0, 2.0 Hz, 1H), 7.50–7.42 (m, 2H), 7.13 (t, J=8.6 Hz, 2H), 6.98 (d, J=8.1 Hz, 1H); ^{13}C NMR (400 MHz, d_6-acetone) δ 185.81, 165.61, 163.17, 160.98, 151.81, 138.50, 137.64, 136.99, 130.36, 130.28, 126.42, 124.90, 124.51, 120.58, 117.64, 117.43, 114.63; HRMS: calcd for $C_{14}H_9FNO_2$ $[M+H]^+$: 242.0612, found: 242.0601.

*3.8.5. 5-(Thiophen-2-yl)indoline-2,3-dione (**15e**).* The title compound was prepared from compound **14e**, following the general procedure for ketal deprotection. Yield: 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.16 (s, 1H), 7.81 (s, 1H), 7.76 (dd, J=8.2, 1.9 Hz, 1H), 7.32–7.22 (m, 2H), 7.07 (dd, J=4.8, 3.8 Hz, 1H), 6.92 (d, J=7.8 Hz,

1H); ^{13}C NMR (400 MHz, d_6-acetone) δ 184.76, 159.94, 150.69, 143.30, 139.27, 136.20, 129.30, 126.00, 124.42, 122.17, 119.61, 113.82; HRMS: calcd for $C_{12}H_8NO_2S$ $[M+H]^+$: 230.0270, found: 230.0269.

*3.8.6. 5-(4-(Trifluoromethyl)phenyl)indoline-2,3-dione (**15f**).* The title compound was prepared from compound **14f**, following the general procedure for ketal deprotection. Yield: 97%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.73 (s, 1H), 7.79 (s, 1H), 7.76 (dd, J=8.3, 1.8 Hz, 1H), 7.70 (d, J=8.4 Hz, 2H), 7.64 (d, J=8.2 Hz, 2H), 6.95 (d, J=8.1 Hz, 1H); ^{13}C NMR (400 MHz, d_6-acetone) δ 183.88, 163.68, 161.25, 149.88, 136.57, 136.54, 135.72, 135.06, 128.43, 128.35, 122.97, 122.58, 118.65, 115.71, 115.50, 112.70; HRMS: calcd for $C_{15}H_9F_3NO_2$ $[M+H]^+$: 292.0580, found: 292.0578.

*3.8.7. 5-(p-Tolyl)indoline-2,3-dione (**15g**).* The title compound was prepared from compound **14g**, following the general procedure for ketal deprotection. Yield: 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.42 (s, 1H), 7.82 (s, 1H), 7.76 (d, J=8.3 Hz, 1H), 7.41 (d, J=8.4 Hz, 2H), 7.28 (d, J=8.2 Hz, 2H), 6.95 (d, J=8.1 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (400 MHz, d_6-acetone) δ 183.95, 159.10, 149.65, 137.21, 136.42, 136.09, 134.15, 129.57, 126.23, 122.35, 118.64, 112.63, 20.11; HRMS: calcd for $C_{15}H_{12}NO_2$ $[M+H]^+$: 238.0863, found: 238.0863.

3.9. Intramolecular Heck reaction: (preparation of 28)

*3.9.1. 4′-Methylene-3′,4′-dihydro-1′H-spiro[indoline-3,2′-quinolin]-2-one (**28**).* To a solution of **3a** (200 mg, 0.58 mmol) in CH_3CN (9 mL) and water (3 mL), $Pd(OAc)_2$ (6.54 mg, 0.03 mmol), PPh_3(15.3 mg, 0.06 mmol), and triethylamine (0.10 mL, 2.56 mmol) were added. The reaction mixture was refluxed for 24 h and then evaporated to dryness. The residue was diluted with DCM and washed with water. The aqueous layer was extracted with DCM three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated. The crude compound was purified by column chromatography to yield **28**. Yield: 13%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.56 (d, J=7.9 Hz, 1H), 7.22 (t, J=7.8 Hz, 1H), 7.17–7.07 (m, 2H), 6.96 (t, J=7.6 Hz, 1H), 6.88 (d, J=7.7 Hz, 1H), 6.78 (t, J=7.6 Hz, 1H), 6.57 (d, J=8.1 Hz, 1H), 5.64 (s, 1H), 4.87 (s, 1H), 4.24 (s, 1H), 3.01 (d, J=14.0 Hz, 1H), 2.60 (d, J=13.5 Hz, 1H); ^{13}C NMR (400 MHz, d_6-acetone) δ 177.82, 143.73, 140.99, 137.41, 133.60, 129.46, 128.93, 124.42, 124.15, 122.10, 119.33, 117.28, 115.32, 109.73, 108.41, 60.40, 39.52; HRMS: calcd for $C_{17}H_{15}N_2O$ $[M+H]^+$: 263.1179, found: 263.1168.

3.10. General procedure for intermolecular Heck reaction: (for example preparation of 8a)

To a solution of **3a** (300 mg, 0.87 mmol) in CH_3CN (24 mL) and water (8 mL), $Pd(OAc)_2$ (9.8 mg, 0.05 mmol) and PPh_3(25.2 mg, 0.09 mmol) were added. The reaction mixture was stirred under nitrogen to which triethylamine (0.14 mL, 0.96 mmol) and bromobenzene (0.33 mL, 2.56 mmol) were added dropwise. The mixture was refluxed for 2 days and then evaporated to dryness. The residue was diluted with DCM and washed with water. The aqueous layer was extracted with DCM three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated. The crude compound was purified by column chromatography to yield **8a**. Yield 24%.

*3.10.1. (E)-3-((2-Bromophenyl)amino)-3-(3-(4-methoxyphenyl)allyl) indolin-2-one (**21a**).* The title compound was prepared from compound **3a** and 4-bromoanisole, following the general procedure for intermolecular Heck reaction. Yield: 27%. Crystals were obtained from DCM and hexane. Mp 199–200 °C; ^{1}H NMR (400 MHz, d_6-DMSO) δ 10.84 (s, 1H), 7.38 (dd, J=7.9, 1.3 Hz, 1H), 7.32–7.17 (m, 4H), 7.03–6.80 (m, 5H), 6.58 (d, J=15.8 Hz, 1H), 6.48 (dt, J=7.8, 7.8, 1.3 Hz, 1H), 6.00 (td, J=15.5, 7.6, 7.6 Hz, 1H), 5.77 (dd, J=8.2, 1.2 Hz, 1H), 5.30 (s, 1H), 3.72 (s, 3H), 2.76–2.70 (m, 2H); ^{13}C NMR (400 MHz, d_6-DMSO) δ 178.27, 159.62, 142.78, 141.56, 135.66, 133.07, 130.19, 129.96, 129.82, 129.08, 128.11, 124.17, 122.86, 120.02, 119.43, 114.75, 112.94, 111.01, 110.31, 63.99, 55.78, 43.82; HRMS: calcd for $C_{24}H_{22}{}^{79}BrN_2O_2$ $[M+H]^+$: 449.0865, found: 449.0854.

*3.10.2. (E)-3-((2-Bromophenyl)amino)-3-(3-(3-methoxyphenyl)allyl) indolin-2-one (**21b**).* The title compound was prepared from compound **3a** and 3-bromoanisole, following the general procedure for intermolecular Heck reaction. Yield: 25%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 7.36 (d, J=7.9 Hz, 1H), 7.30–7.18 (m, 3H), 7.04 (t, J=7.5 Hz, 1H), 6.94–6.70 (m, 5H), 6.63 (d, J=15.9 Hz, 1H), 6.48 (t, J=7.64 Hz, 1H), 6.19 (td, J=15.4, 7.7, 7.7 Hz, 1H), 5.86 (d, J=8.1 Hz, 1H), 5.25 (s, 1H), 3.80 (s, 3H), 2.92 (dd, J=13.4, 7.3 Hz, 1H), 2.77 (dd, J=13.5, 8.1 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.55, 159.72, 141.94, 139.52, 138.16, 136.50, 132.45, 129.61, 129.54, 129.19, 128.25, 123.87, 123.10, 121.57, 119.16, 119.08, 113.22, 112.79, 111.98, 110.85, 110.79, 64.07, 55.19, 43.74; HRMS: calcd for $C_{24}H_{22}{}^{79}BrN_2O_2$ $[M+H]^+$: 449.0865, found: 449.0852.

3.11. General procedure for Stille reaction: (for example preparation of 20a)

*3.11.1. 1-(Trifluoromethoxy)-4-vinylbenzene (**20a**).* To a solution of 1-bromo-4-trifluoromethoxybenzene **19a** (345.5 mg, 1.43 mmol) in DMF (3 mL), tributyl(vinyl)tin (500 mg, 1.58 mmol) and tetrakis(triphenylphosphine)palladium(0) (82.8 mg, 0.072 mmol) were added. The reaction mixture was then refluxed for 2 days and then evaporated to dryness. The residue was diluted with DCM and washed with saturated aqueous sodium chloride. The aqueous layer was extracted with DCM three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated. The crude compound was purified by column chromatography to give **20a**. Yield 60%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J=8.8 Hz, 2H), 7.12 (d, J=8.8 Hz, 2H), 6.65 (dd, J=17.6, 10.9 Hz, 1H), 5.68 (d, J=17.6 Hz, 1H), 5.24 (d, J=10.4 Hz, 1H).

*3.11.2. 4-Fluoro-3-vinylbenzonitrile (**20b**).* The title compound was prepared from compound **19b**, following the general procedure for Stille reaction. Yield: 38%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, J=6.9, 1.8 Hz, 1H), 7.53 (ddd, J=8.3, 4.6, 2.1 Hz, 1H), 7.15 (dd, J=9.6, 8.8 Hz, 1H), 6.82 (dd, J=17.7, 11.0 Hz, 1H), 5.89 (d, J=17.8 Hz, 1H), 5.52 (d, J=11.2 Hz, 1H).

*3.11.3. 1-Methoxy-4-vinylbenzene (**20c**).* The title compound was prepared from compound **19c**, following the general procedure for Stille reaction. Yield: 30%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J=9.1 Hz, 2H), 6.78 (d, J=9.1 Hz, 2H), 6.66 (dd, J=17.6, 10.9 Hz, 1H), 5.61 (dd, J=17.6, 0.9 Hz, 1H), 5.12 (dd, J=10.9, 0.9 Hz, 1H), 3.81 (s, 3H).

*3.11.4. 4-Vinylbenzonitrile (**20d**).* The title compound was prepared from compound **19d**, following the general procedure for Stille reaction. Yield: 99%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63–7.59 (m, 2H), 7.55–7.48 (m, 2H), 6.72 (dd, J=17.6, 10.9 Hz, 1H), 5.87 (d, J=17.6 Hz, 1H), 5.44 (d, J=10.9 Hz, 1H).

3.12. General procedure for intermolecular Grubb's metathesis: (for example preparation of 21d)

*3.12.1. (E)-4-(3-(3-((2-Bromophenyl)-amino)-2-oxoindolin-3-yl) prop-1-en-1-yl)benzonitrile (**21d**).* To a solution of **3a** (201.6 mg, 1.56 mmol) in DCM (20 mL), **20d** (535.7 mg, 1.56 mmol) and second generation Grubb's catalyst (66.2 mg, 0.08 mmol) were

added. The solution was then refluxed for 1 day. The reaction mass was diluted with DCM and washed with water. The aqueous layer was extracted with DCM three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated. The crude compound was purified by column chromatography to give **21d**. Yield: 20%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.58 (d, J=8.4 Hz, 2H), 7.41 (d, J=8.3 Hz, 2H), 7.36 (dd, J=7.9, 1.5 Hz, 1H), 7.31–7.21 (m,2H), 7.07 (dt, J=7.5, 0.9 Hz, 1H), 6.94 (d, J=7.8 Hz, 1H), 6.79 (dt, J=8.3, 1.4 Hz, 1H), 6.66 (d, J=15.8 Hz, 1H), 6.50 (dt, J=7.7 1.4 Hz, 1H), 6.36 (ddd, J=15.5, 8.1, 7.1 Hz, 1H), 5.87 (dd, J=8.2, 1.4 Hz, 1H), 5.18 (s, 1H), 2.93 (ddd, J=13.4, 6.9, 1.2 Hz, 1H), 2.83 (ddd, J=13.4, 8.3, 0.8 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 178.67, 141.75, 140.94, 139.29, 134.72, 132.48, 132.40, 129.41, 129.37, 128.23, 126.85, 125.51, 123.82, 123.28, 119.42, 118.75, 112.80, 111.06, 110.93, 110.63, 63.88, 43.74; HRMS: calcd for $C_{24}H_{19}{}^{79}BrN_3O$ $[M+H]^+$: 444.0706, found: 444.0694.

*3.12.2. (E)-3-((2-Bromophenyl)amino)-3-(3-(4-(trifluoromethoxy) phenyl)allyl)indolin-2-one (**21c**).* The title compound was prepared from compound **3a** and **20a**, following the general procedure for intermolecular Grubbs Metathesis. Yield: 25%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.40–7.00 (m, 8H), 6.94 (d, J=7.8 Hz, 1H), 6.79 (dt, J=8.3, 1.4 Hz, 1H), 6.66 (d, J=15.8 Hz, 1H), 6.50 (dt, J=7.7, 1.4 Hz, 1H), 6.36 (ddd, J=15.5, 8.1, 7.1 Hz, 1H), 5.87 (dd, J=8.2, 1.4 Hz, 1H), 5.18 (s, 1H), 2.93–2.83 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 179.76, 141.89, 139.58, 135.40, 135.03, 132.47, 130.01, 129.54, 129.11, 128.63, 128.31, 128.01, 126.42, 122.39, 120.24, 119.60, 117.68, 112.80, 112.56, 111.55, 110.97, 110.84, 64.10, 43.75; HRMS: calcd for $C_{24}H_{19}{}^{79}BrF_3N_2O_2$ $[M+H]^+$: 503.0577, found: 503.0568.

*3.12.3. (E)-3-(3-(3-((2-Bromophenyl)amino)-2-oxoindolin-3-yl) prop-1-en-1-yl)-4-fluorobenzonitrile (**21e**).* The title compound was prepared from compound **3a** and **20b**, following the general procedure for intermolecular Grubbs Metathesis. Yield: 24%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H), 7.37 (dd, J=7.8, 1.0 Hz, 1H), 7.24–7.17 (m, 3H), 7.18 (d, J=7.3 Hz, 1H), 7.01 (t, J=7.5 Hz, 1H), 6.92 (d, J=7.7 Hz, 1H), 6.78 (t, J=7.4 Hz, 1H), 6.48 (dt, J=7.9, 0.9 Hz, 1H), 5.92–5.82 (m, 2H), 5.42–5.30 (m, 2H), 5.20 (s, 1H), 2.78 (dd, J=13.3, 7.4 Hz, 1H), 2.64 (dd, J=13.2, 7.5 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 180.70, 160.52, 158.21, 142.70, 137.99, 136.32, 134.19, 134.17, 132.41, 131.39, 131.60, 128.78, 128.45, 127.95, 127.45, 120.48, 119.47, 115.85, 115.61, 112.61, 111.79, 111.20, 111.12, 110.94, 63.34, 42.85; HRMS: calcd for $C_{24}H_{18}{}^{79}BrFN_3O$ $[M+H]^+$: 462.0612, found: 462.0598.

3.13. Preparation of 24

*3.13.1. 7,8-Diallyl-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**24**).* To a solution of **7a** (25 mg, 0.09 mmol) in DMF, allyl bromide (0.01 mL, 0.11 mmol) and sodium iodide (21.2 mg, 0.14 mmol) were added. The resulting mixture was stirred at room temperature for 16 h. The reaction mixture was then evaporated to dryness, diluted with DCM and the organic layer was washed with water. The aqueous layer was extracted with DCM three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated. The crude mixture was purified by column chromatography to yield **24**. Yield: 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–6.97 (m, 8H), 5.90–5.68 (m, 1H), 5.58–5.24 (m, 1H), 5.18–4.93 (m, 2H), 4.92–4.73 (m, 2H), 3.95–3.75 (m, 1H), 3.57 (d, J=4.4 Hz, 1H), 3.34 (d, J=5.9 Hz, 1H), 2.81–2.28 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 172.54, 147.17, 141.17, 139.10, 136.25, 136.36, 135.26, 131.90, 131.59, 130.86, 129.45, 127.97, 125.95, 125.28, 117.77, 116.94, 63.19, 57.35, 36.25; HRMS: calcd for $C_{20}H_{21}N_2O$ $[M+H]^+$: 305.1648, found: 305.1644.

3.14. General procedures for alkylation of amide nitrogen: (for example preparation of 25a)

*3.14.1. 7,8-Diallyl-5-methyl-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one (**25a**).* To a solution of **24** (100 mg, 0.33 mmol) in DMF, cesium carbonate (214 mg, 0.65 mmol) and methyl iodide (0.04 mL, 0.65 mmol) were added. The reaction mixture was stirred for 18 h. The mixture was then evaporated to dryness, diluted with DCM and the organic layer was washed with water. The aqueous layer was extracted with DCM three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated. The crude mixture was purified using column chromatography to give **25a**. Yield: 77%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52–7.33 (m, 3H), 7.29–7.23 (m, 2H), 7.16–7.08 (m, 2H), 7.02 (dd, J=7.7, 1.5 Hz, 1H), 5.80–5.67 (m, 1H), 5.65–5.50 (m, 1H), 5.11–4.79 (m, 4H), 3.83 (dd, J=9.6, 3.6 Hz, 1H), 3.48–3.24 (m, 2H), 2.98 (s, 3H), 2.87–2.67 (m, 1H), 2.49–2.33 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 170.63, 148.17, 142.17, 140.10, 136.15, 135.36, 135.06, 130.90, 130.59, 130.36, 129.15, 127.77, 125.55, 125.08, 116.77, 116.54, 63.84, 57.47, 36.51, 36.11; HRMS: calcd for $C_{21}H_{23}N_2O$ $[M+H]^+$: 319.1805, found: 319.1802.

*3.14.2. 7,8-Diallyl-5-benzyl-7,8-dihydrodibenzo[e,g][1,4]diazocin-6(5H)-one atropisomers of (**25b**) and (**25c**).* The title compound was prepared from compound **24** and benzylbromide, following the general procedure for alkylation of amide nitrogen. (**25b**: 51% and **25c**: 24%).

Compound **25b**: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.40 (1H, td, J=7.5, 1.8 Hz), 7.36 (1H, td, J=7.5, 1.7 Hz), 7.26 (1H, dd, J=1.8, 7.4 Hz), 7.18 (1H, td, J=7.6, 1.8 Hz), 7.17 (1H, dd, J=7.7, 1.5 Hz), 7.12 (1H, tt, J=1.8, 7.3 Hz), 7.07 (1H, dd, J=1.6, 8.0 Hz), 7.02 (2H, t, J=7.8 Hz), 6.85 (1H, td, J=7.5, 1.7 Hz), 6.81 (2H, d, J=7.8 Hz), 6.35 (1H, dd, J=1.8, 7.5 Hz), 5.79 (1H, m), 5.55 (1H, m), 5.07 (1H, dq, J=17.3, 1.8 Hz), 5.04 (1H, bd, J=10.3 Hz), 4.97 (1H, d, J=14.3 Hz), 4.87 (1H, dq, J=17.0, 1.7 Hz), 4.84 (1H, bd, J=9.9 Hz), 4.44 (1H, d, J=14.3 Hz), 3.83 (1H, dd, J=3.5, 9.7 Hz), 3.38 (1H, ddt, J=5.1, 14.9, 1.6 Hz), 3.28 (1H, dd, J=7.9, 14.9 Hz), 2.82 (1H, m), 2.45 (1H, m); ^{13}C NMR (400 MHz, $CDCl_3$) δ 170.31, 147.66, 140.86, 140.25, 136.45, 136.32, 135.23, 135.02, 130.77, 130.08, 128.81, 128.51, 128.10, 127.70, 126.96, 125.74, 125.02, 116.89, 116.51, 63.87, 57.71, 52.23, 36.67; HRMS: calcd for $C_{27}H_{27}N_2O$ $[M+H]^+$: 395.2118, found: 395.2111.

Compound **25c**: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.40 (1H, td, J=7.5, 1.6 Hz), 7.35 (1H, td, J=7.5, 1.4 Hz), 7.26 (1H, td, J=1.6, 7.3 Hz), 7.23 (1H, dd, J=7.8, 1.4 Hz), 7.19 (1H, dd, J=8.1, 1.3 Hz), 7.17 (1H, tt, J=1.4, 7.5 Hz), 7.12 (1H, dd, J=1.8, 7.5 Hz), 7.08 (2H, t, J=7.6 Hz), 6.87 (1H, td, J=7.4, 1.3 Hz), 6.81 (2H, d, J=7.9 Hz), 6.47 (1H, dd, J=1.6, 7.4 Hz), 5.80 (1H, m), 5.45 (1H, m), 5.10–5.15 (2H, m), 4.91 (1H, d, J=14.2 Hz), 4.87–4.93 (2H, m), 4.38 (1H, d, J=14.2 Hz), 3.97 (1H, dd, J=5.1, 10.5 Hz), 3.78 (1H, ddt, J=6.7, 15.6, 1.4 Hz), 3.59 (1H, ddt, J=4.2, 15.6, 2.0 Hz), 2.40 (1H, m), 2.05 (1H, m); ^{13}C NMR (400 MHz, $CDCl_3$) δ 169.78, 147.66, 140.74, 140.23, 136.66, 136.44, 135.36, 133.96, 129.23, 128.92, 128.64, 128.59, 128.04, 128.00, 127.48, 127.05, 125.88, 123.91, 122.52, 117.34, 116.61, 73.59, 54.67, 54.49, 35.84; HRMS: calcd for $C_{27}H_{27}N_2O$ $[M+H]^+$: 395.2118, found: 395.2111.

3.15. General procedure for ring closing metathesis: (for example preparation of 26a)

*3.15.1. 11-Benzyl-9,9a-dihydro-6H-dibenzo[e,g]pyrido[1,2-a][1,4]diazocin-10(11H)-one (**26a**).* To a solution of **25b** (127.9 mg, 0.32 mmol) in DCM (10 mL), first generation Grubb's catalyst (13.3 mg, 0.02 mmol) was added. The reaction mass was refluxed for 2 h. The mixture was then diluted with DCM and washed with water. The aqueous layer was extracted with DCM three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated. The crude mixture was purified using column chromatography to give **26a**. Yield: 76%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 (1H, td, J=7.6, 1.8 Hz), 7.19–7.27 (4H, m),

7.15 (1H, tt, J=1.4, 7.3 Hz), 7.10 (1H, t, J=7.4 Hz), 6.99 (2H, t, J=7.8 Hz), 6.85 (1H, td, J=7.4, 1.8 Hz), 6.79 (2H, d, J=7.8 Hz), 6.25 (1H, dd, J=1.6, 7.6 Hz), 5.78 (1H, m), 5.58 (1H, m), 5.33 (1H, d, J=14.3 Hz), 4.39 (1H, d, J=14.3 Hz), 3.86 (1H, dd, J=3.2, 9.7 Hz), 3.52 (1H, m), 3.28 (1H, m), 2.93 (1H, m), 1.96 (1H, m); ^{13}C NMR (400 MHz, $CDCl_3$) δ 170.84, 148.53, 140.31, 140.05, 136.30, 134.99, 132.01, 130.93, 129.61, 128.87, 128.83, 128.60, 128.10, 127.76, 126.97, 125.26, 125.08, 124.87, 124.86, 58.04, 55.90, 51.70, 30.36; HRMS: calcd for $C_{25}H_{23}N_2O$ $[M+H]^+$: 367.1805, found: 367.1798.

*3.15.2. 11-Benzyl-9,9a-dihydro-6H-dibenzo[e,g]pyrido[1,2-a][1,4]diazocin-10(11H)-one (**26b**).* The title compound was prepared from compound **25c**, following the general procedure for ring closing metathesis. Yield: 72%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (1H, td, J=7.6, 1.7 Hz), 7.29–7.34 (3H, m), 7.25 (1H, dd, J=7.9, 1.4 Hz), 7.17 (1H, tt, J=1.4, 7.3 Hz), 7.11 (1H, dd, J=1.5, 7.1 Hz), 7.07 (2H, t, J=7.6 Hz), 6.98 (1H, td, J=7.6, 1.6 Hz), 6.76 (2H, d, J=7.8 Hz), 6.58 (1H, dd, J=1.7, 7.5 Hz), 5.63 (1H, m), 5.59 (1H, m), 5.13 (1H, d, J=14.2 Hz), 4.28 (1H, d, J=14.2 Hz), 3.91 (1H, dd, J=3.4, 11.2 Hz), 3.83 (1H, m), 2.99 (1H, m), 2.46 (1H, m), 2.31 (1H, m); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.03, 148.30, 140.41, 140.17, 137.42, 136.40, 128.95, 128.87, 128.26, 128.19, 128.04, 127.34, 127.04, 125.73, 125.61, 124.91, 123.77, 121.47, 69.37, 55.24, 50.66, 30.05; HRMS: calcd for $C_{25}H_{23}N_2O$ $[M+H]^+$: 367.1805, found: 367.1799.

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