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Synthesis of Functionalized 3-Spiro[cyclopropa[*a*]pyrrolizine]- and 3-Spiro[3-azabicyclo[3.1.0]hexane]oxindoles from Cyclopropenes and Azomethine Ylides via [3 + 2]-Cycloaddition

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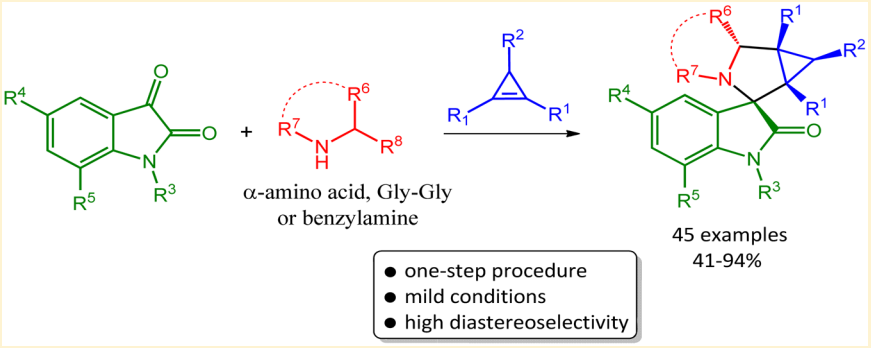
Supporting Information



ABSTRACT: 3-Spiro[cyclopropa[*a*]pyrrolizine]- and 3-spiro[3-azabicyclo[3.1.0]hexane]oxindoles were prepared in moderate to high yields via one-pot three-component reactions using substituted isatins, α-amino acids, and cyclopropenes. The key step is an intramolecular [3 + 2]-cycloaddition reaction of an *in situ* generated azomethine ylide onto a cyclopropene. Both *N*-substituted and *N*-unsubstituted α-amino acids, dipeptide Gly-Gly, and also benzylamine were used as the amine component for the azomethine ylide generation. The anticancer activity of some of the obtained compounds against human leukemia K562 cell line was evaluated by flow cytometry *in vitro*.

INTRODUCTION

1,3-Dipolar cycloaddition reactions have long been recognized as being important for the synthesis of heterocyclic rings.[1] Azomethine ylides are remarkably versatile building blocks in organic synthesis and are known to take part in 1,3-dipolar cycloaddition reactions with a wide range of dipolarophiles.[2] Cycloadditions of azomethine ylides to alkenes are well established reactions in which pyrrolidines and pyrrolizidines are formed, often with a high degree of stereochemical control.[3] These cycloadducts have attracted considerable attention due to the potential biological activities of pyrrolidines and pyrrolizidines.[4] The synthesis of 3-spiropyrrolidine and 3-spiropyrrolizidine oxindoles via 1,3-dipolar cycloaddition reaction of azomethine ylides derived from isatins and α-amino acids has been reported.[5] Natural products that contain the 3-spiropyrrolidine oxindole framework (Figure 1) display a variety of pharmacological effects. For example, coerulescine (**I**), horsfiline (**II**), and elacomine (**III**) are inhibitors of the mammalian cell cycle at the G2/M interphase,[6] and spirotryprostatin A (**IV**) also showed anticancer activity.[7] Various biological activities have been found for synthetic spiropyrrolidinyl oxindoles, e.g., anti-inflammatory,[8] antidiabetic,[9] antitumoric,[10] antiviral,[11] antimalarial,[12] antifungal,[13] antitubercular,[14] and acetylcholinesterase (AChE) inhibitory properties.[15]

Cyclopropenes, the smallest carbocyclic molecules that, due to their high strain, possess unique reactivity in organic synthesis.[16] These compounds are capable of entering into the ring-opening reactions,[17] cycloaddition reactions,[18] and nucleophilic addition to the strained C=C bond.[19] Some cycloaddition-based tandem ring-opening reactions of cyclopropenes were also recently reported.[20] We previously reported the first examples of the reactions of cyclopropenes with carbonyl ylides

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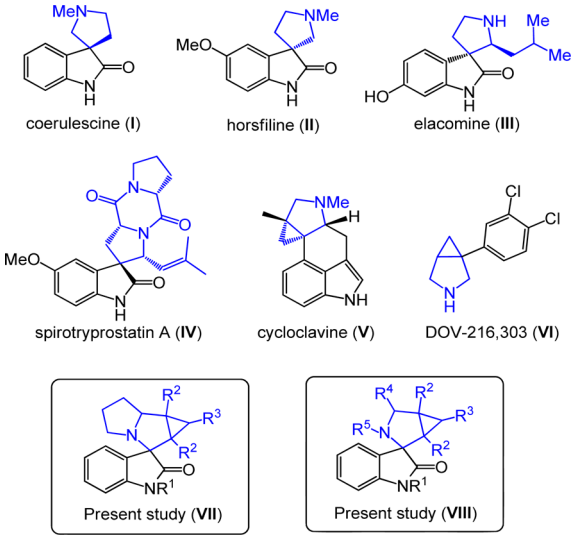


Figure 1. Naturally occurring bioactive spirocyclic oxindoles **I**–**IV**, 3-azabicyclo[3.1.0]hexane containing bioactive compounds **V**, **VI**, and spirocyclic oxindoles **VII**, **VIII** from this work.

and nitrones.[21] Although the scope of 1,3-dipolar cycloadditions in the synthesis of spiro compounds has been broadened by the use of different dipolarophiles, to the best of our knowledge, the utilization of substituted cyclopropenes as dipolarophiles in cycloadditions of azomethine ylides from isatins and α-amino acids has not been studied as yet.

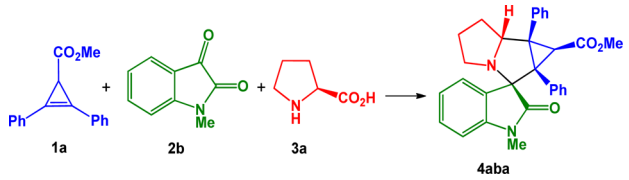
Earlier, Lown and Uchida described reactions between 2,3-diphenylcycloprop-2-en-1-one and 1,2,3-triphenylcycloprop-1-ene with azomethine ylides generated from aziridines.[22] Rath et al. studied cycloadditions between azomethine ylides generated by the decarboxylative condensation of sarcosine with isatins, and 3,4-diphenylcyclobut-3-ene-1,2-dione, but the initially formed product of the 1,3-dipolar cycloaddition of the azomethine ylide and cyclobutenedione was not observed due to its smooth rearrangement into a 3-spiro[3-azabicyclo[3.1.0]-hexane]oxindole derivative under the reaction conditions.[23] Matsumoto and Doyle reported the [3 + 2]-cycloaddition reactions of pyridinium and isoquinolinium dicyanomethylides with 1,2,3-triphenylcycloprop-1-ene.[24]

In this work, we first synthesized 3-spiro[cyclopropa[*a*]-pyrrolizine]- (**VII**) and 3-spiro[3-azabicyclo[3.1.0]hexane]-oxindoles (**VIII**) via one-pot three-component 1,3-dipolar cycloaddition reactions of *in situ* generated azomethine ylides using substituted isatins and α-amino acids to different cyclopropenes under mild conditions. It is also worth to emphasize that the 3-azabicyclo[3.1.0]hexane fragment is present in natural compounds, including duocarmycins, yatakemycin, and cycloclavine (**V**), and is also contained in pharmacologically important compounds such as boceprevir, DOV-216,303 (**VI**), and trovafloxacin.[25]

RESULTS AND DISCUSSION

First, the three-component reaction of methyl 2,3-diphenylcycloprop-2-enecarboxylate (**1a**) (0.4 mmol), *N*-methyl-substituted isatin **2b** (0.4 mmol), and *L*-proline (**3a**) (0.5 mmol), as a simple model substrate (Table 1), was investigated to establish the feasibility of the strategy and optimize the reaction conditions. The reaction was examined in different solvents such as methanol, ethanol, acetonitrile, and acetone under reflux, and DMF at 60 °C. As depicted in Table 1, the

Table 1. Optimization of the Reaction Conditions[a]



entry	solvent	T [°C]	time [h]	yield [%][b]
1	ethanol	reflux	4	77
2	methanol	reflux	4	85
3	acetone	reflux	12	trace
4	acetonitrile	reflux	4	48
5	DMF	60	6	65
6	methanol	rt	12	75

[a]Reaction conditions: **1a** (1 equiv), **2b** (1 equiv), **3a** (1.2 equiv), solvent. [b]Isolated yield.

employed solvent had a significant influence on the reaction outcome. The reaction did not take place in acetone (Table 1, entry 3). When DMF or acetonitrile was used as the solvent, the yield of desired product **4aba** decreased to 65% or 48%, respectively (Table 1, entries 5 and 4). When ethanol was used as the solvent, the yield of **4aba** increased to 77% (Table 1, entry 1). As seen from Table 1, the best results were obtained by refluxing the reaction mixture in methanol for 4 h, providing 3-spiro[cyclopropa[*a*]pyrrolizine]oxindole **4aba** in high yield (85%) along with excellent diastereoselectivities (Table 1, entry 2). The reaction was monitored by TLC analysis, and the starting materials were consumed after 4 h. Lowering the reaction temperature to 20 °C, the reaction proceeded smoothly, and the yield of **4aba** diminished to 75% (Table 1, entry 6). Therefore, refluxing methanol was the most suitable condition for this reaction.

With the suitable reaction conditions (Table 1, entry 2), the generality of this one-pot three-component 1,3-dipolar cycloaddition reaction was examined using a variety of cyclopropenes **1** (Figure 2) and isatins **2** (Figure 3). The results are

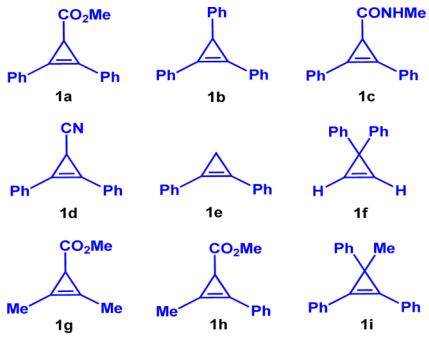


Figure 2. Cyclopropenes **1a**–**i** used in the synthesis of spirocyclic-3,3′-oxindoles.

summarized in Table 2. It should be noted that, when cyclopropenes **1g** and **1h** bearing methyl substituents at the double bond and tetrasubstituted cyclopropene **1i** were used, the three-component 1,3-dipolar cycloaddition did not give the corresponding products. The reactions with cyclopropenes **1a**–**f** proceeded smoothly to give the corresponding spirocyclic-3,3′-oxindoles **4** in moderate to high yields with moderate to excellent stereoselectivities under the optimal conditions (Table 2).

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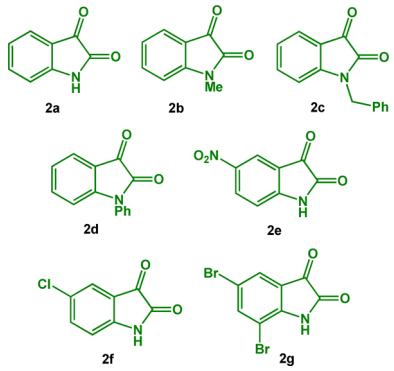

Figure 3. Isatins **2a–g** used in the synthesis of spirocyclic-3,3′-oxindoles.

Experiments with different substituents at the nitrogen atom of **2** were conducted. The corresponding spirooxindole products **4aaa–4bca** were obtained in yields ranging from 48% up to 85% (Table 2) by using the unsubstituted isatin (**2a**), *N*-alkylisatins **2b**, **2c**, and cyclopropenes **1a–d** as substrates. From the ^{1}H NMR spectrum of the crude reaction mixtures, it was concluded that the reactions produced only single diastereomers **4**. The relative configuration of the formed stereocenters of 3-spiro[cyclopropa[*a*]pyrrolizine]oxindoles **4** was determined by single-crystal X-ray diffraction (for compounds **4aaa** and **4bca**) and supported the relative configuration deduced from the NMR spectra (see the Supporting Information, Figures S110 and S111).

A similar three-component 1,3-dipolar cycloaddition reaction occurred on treatment of cyclopropenes **1a**, **1b** with *N*-phenylisatin (**2d**) and *L*-proline (**3a**), giving adducts **4ada** and **4bda** as inseparable mixtures of two diastereomers in 65% and 62% overall yields, respectively [Table 2; the diastereomeric ratios were determined from ^{1}H NMR spectra by integration of the *H*-C(1) and *H*-C(6a) signals]. Cycloadducts **4aea**, **4bea**, **4afa**, and **4bfa** were obtained using 5-nitro- (**2e**) and 5-chloroisatin (**2f**) with moderate chemical yields (56–63%) and diastereoselectivities (5:1–10:1 dr). It is also worth noting that the utilization of 5,7-dibromoisatin (**2g**) afforded the corresponding cycloadducts with a poor diastereoselectivity [**4aga** (3:1 dr) and **4bga** (5:2 dr)] in moderate yields (52% and 61%).

The diastereomeric products **4bga** (44%) and **5bga** (17%) were isolated by preparative thin layer chromatography on silica. The ^{1}H NMR spectra of adducts **4bga** and **5bga** exhibit signals for the cyclopropane proton at δ 3.09 ppm (s) for compound **4bga** and δ 4.23 ppm (s) for compound **5bga**, and signals for *H*-C(6a) at δ 4.70 ppm (t, J = 7.3 Hz) for compound **4bga** and δ 4.21 ppm (dd, J = 11.1, 5.9 Hz) for compound **5bga**. The shift of the signal of the cyclopropane proton in diastereomer **5bga** to a low field [δ 3.09 ppm (**4bga**) and δ 4.23 ppm (**5bga**)] is due to the deshielding effect induced by the carbonyl group of the indole fragment. We also examined the one-pot three-component 1,3-dipolar cycloaddition reactions of cyclopropenes **1e**, **1f**, isatins **2a**, **2b**, and *L*-proline (**3a**). As results, the corresponding cyclopropa[*a*]pyrrolizines **4eaa**, **4eba**, **4faa**, and **4fba** were obtained in 47–93% yields as single diastereomers.

The relative configuration of the product **4faa** was determined on the basis of the H–H NOESY spectrum. For example, the ^{1}H NMR spectrum of compound **4faa** displayed a doublet of doublets at δ 2.30 ppm for the cyclopropane *H*-C(6b) proton, which showed a NOESY correlation with a multiplet at δ 4.56 ppm [methine *H*-C(6a) proton]. This fact indicated that cyclopropane *H*-C(6b) and methine *H*-C(6a) protons are *cis*-oriented relative to each other (see the Supporting Information, Figure S47). Additionally, the absence of a NOE cross-peak of methine *H*-C(6a) and 4-CH of the isatin nucleus was indicative for the assigned relative configuration. The shift of the signal of the other cyclopropane proton *H*-C(1a) to a lower field (δ 2.67 ppm) can be attributed to the influence of the anisotropy of the carbonyl group of the indole fragment, which confirms the relative configuration of the spiro carbon atom.

Next, we extended the study to [3 + 2]-cycloadditions of cyclopropenes **1a**, **1b** with the azomethine ylide derived from sarcosine (**3b**) and *N*-benzylisatin (**2c**) (Table 3). Carrying out the reaction in refluxing methanol or ethanol led to the products in lower yields. Then, the three-component reaction of sarcosine (**3b**), isatin **2c**, and cyclopropene **1a** was carried out in refluxing 1-propanol. After workup, the major diastereomeric spiroadduct **6acb** was isolated in 61% yield and the minor isomer was obtained in much lower yield (3%). Using sarcosine (**3b**) and 1,2,3-triphenylcycloprop-1-ene (**1b**) led to the formation of the major isomer -3-spiro[3-azabicyclo-[3.1.0]hexane]oxindole **6bcb** in 53% yield, while the minor diastereomer **7bcb** was isolated in about 15% yield. The structures of diastereomeric **6bcb** and **7bcb** were established by NMR spectroscopy and X-ray diffraction of single crystals for adduct **6bcb** (see the Supporting Information, Figure S112).

Under similar conditions, the three-component reaction of *L*-4-thiazolidine carboxylic acid (**3c**) with isatins **2b**, **2c** and cyclopropenes **1a**, **1b** resulted in the expected spiro[cyclopropa[3,4]pyrrolo[1,2-*c*][1,3]thiazole-5,3′-indoles] **6acc** and **6bbc** as main products in moderate yields (Table 3). The spectroscopic data confirmed that the obtained spiro compounds **6acc** and **6bbc** have the same configuration as that of the above-mentioned compounds **4**. In the ^{1}H NMR spectrum of compound **6bbc**, the methine protons of the cyclopropane ring and the pyrrolo[1,2-*c*]thiazole fragment appear as a singlet (δ 3.90 ppm) and a doublet of doublets (δ 4.83 ppm, J = 8.9 and 5.3 Hz), respectively. Comparison of the ^{1}H NMR spectra of **6bbc** and **7bbc** reveals a difference concerning the chemical shift of the signal of the cyclopropane proton. The cyclopropane *H*-C(6) signal in **6bbc** (δ 3.90 ppm) is upfield-shifted with respect to the cyclopropane *H*-C(6) signal in **7bbc** (δ 4.36 ppm). This effect can be attributed to the relative orientation of the carbonyl oxindole group attached to C-2 (*vide supra*). It should be emphasized that, when *DL*-pipecolinic acid (**3d**) was used, the three-component 1,3-dipolar cycloaddition reaction produced the cyclopropa[*a*]-indolizine **6abd** only in trace amounts, probably due to the steric effect.

We also attempted to use some primary α-amino acids to examine the feasibility of this reaction. Gratefully, we found that the reactions proceeded smoothly in methanol–water medium to give the 3-spiro[3-azabicyclo[3.1.0]hexane]oxindoles **8** in 41–69% yields with high diastereoselectivity. The results are summarized in Table 4. Initially, the reaction of azomethine ylides *in situ* generated from isatin (**2a**) and α-amino acids **3e–g** with cyclopropenes **1a**, **1b** in methanol–water (3:1) under reflux led to the formation of racemic spirocyclic derivatives **8aae**, **8baf**, and **8bag** in 41–69% yields with good diastereoselectivity (**8aae** and **8baf** – single diastereomers, **8bag** – 6:1 *dr*) (Table 4). In all cases, the cyclopropenes were

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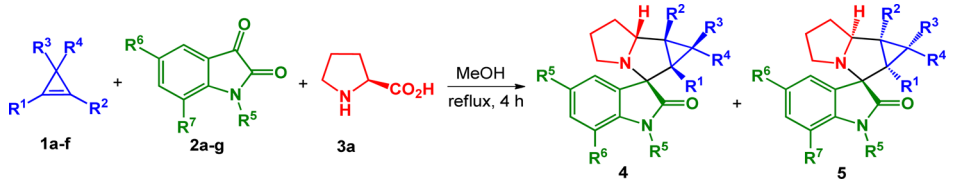
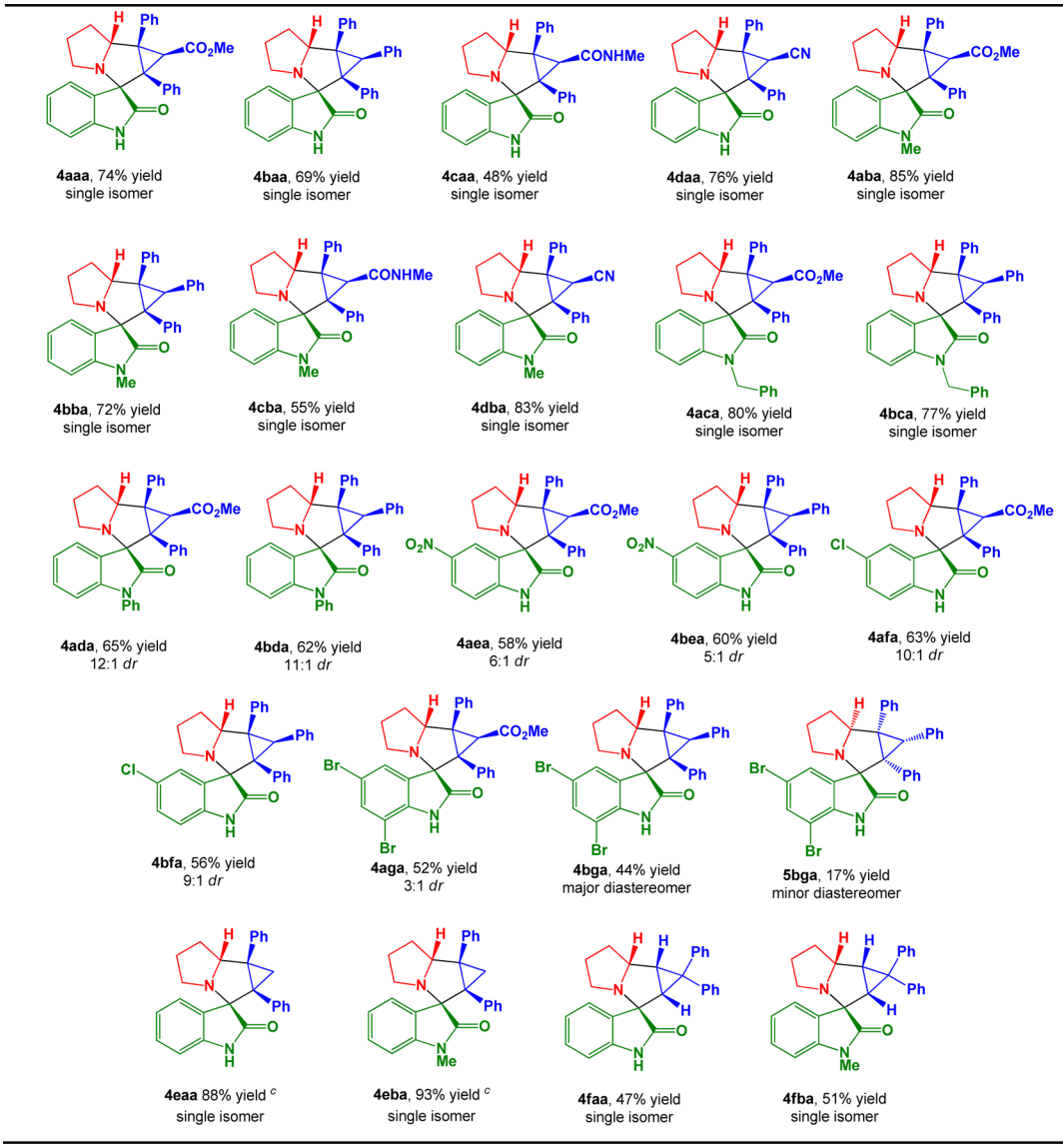
Table 2. Synthesis of Racemic 3-Spiro[cyclopropa[*a*]pyrrolizines] 4 and 5 *via* One-Pot Three-Component Reactions of Isatins 2a–g, *L*-Proline (3a), and Cyclopropenes 1a–f[a,b]





[a]All reactions were carried out with **1** (0.4 mmol), **2** (0.4 mmol), *L*-proline (**3a**) (0.5 mmol) in methanol at reflux. [b]Isolated yield. [c]The reaction was carried out at room temperature for 12 h.

not completely consumed during the reactions. The structures of the cycloadducts **8aae**, **8baf**, and **8bag** were established by spectroscopic analysis. The ^{1}H NMR spectrum of **8aae** shows a doublet of doublets at δ 4.35 ppm (J = 9.4 and 3.4 Hz) for the pyrrolidine CH proton and two peaks at δ 3.18 and 2.12 ppm corresponding to the cyclopropane and the pyrrolidine NH protons, respectively. In a similar way, the azomethine ylides generated from isatin (**2a**) and *L*-phenylalanine (**3h**), *L*-tyrosine (**3i**), 3,5-diiodo-*L*-tyrosine (**3j**), or *DL*-phenylglycine (**3k**), when reacted with **1a**, **1b**, afforded the racemic 3-azabicyclo[3.1.0]hexanes **8bah**, **8aai**, **8baj**, and **8bak** in 42–69% yields as single diastereomers. A gram-scale one-pot three-component reaction of cyclopropene **1b** with isatin **2a** and α-amino acid **3k** was performed under optimized reaction conditions that led to spiroazabicyclohexane **8bak** in 76% yield (even higher than the small-scale reaction; 69%). Analogous spirocycles **8** were synthesized using *L*-tryptophan (**3l**), *L*-methionine (**3m**), and *L*-asparagine (**3n**). The reactions of these amino acids were stereoselective, affording racemic products **8aal**, **8bam**, and **8ban** in moderate yields (Table 4). It should be noted that we did not observe or isolate other diastereomers of the 3-spiro[3-azabicyclo[3.1.0]hexane]-oxindoles **8aae**, **8baf**, **8bah**–**8ban**. Surprisingly, using glycine and *DL*-alanine led to a complex mixture and only trace

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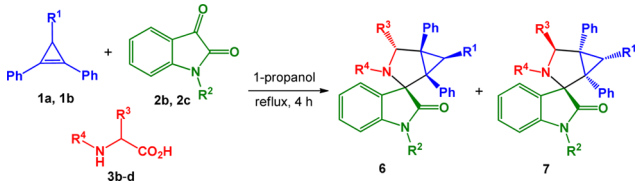
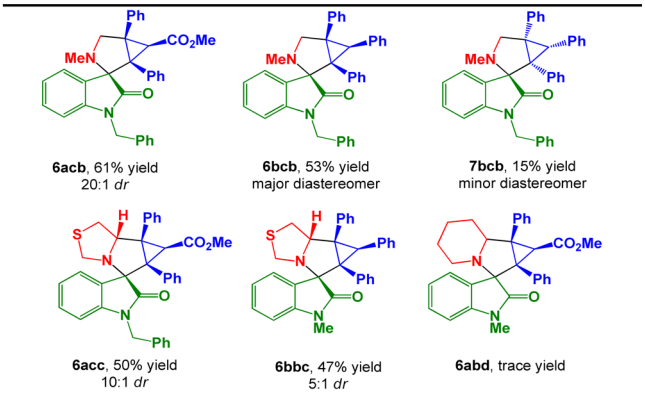
Table 3. Synthesis of Racemic Spirooxindole Products 6 and 7 *via* Three-Component Reaction of Isatins 2b, 2c, α-Amino Acids 3b–d, and Cyclopropenes 1a, 1b[a,b,c]





[a]All reactions were carried out with **1** (0.4 mmol), **2** (0.4 mmol), **3** (0.5 mmol) in 1-propanol at reflux. [b]Isolated yield. [c]In all cases, the unreacted starting material **1** was recovered in 5–20% yields.

amounts of products were obtained. In both cases, the starting cyclopropenes were recovered almost quantitatively. Perhaps, in this case, the side reactions of azomethine ylides from isatin and glycine (or *DL*-alanine) are largely preferred over [3 + 2]-cycloadditions with a dipolarophile such as cyclopropene **1**. It was found that the three-component condensation of isatin (**2a**), *L*-isoleucine (**3o**), and cyclopropenes **1a**, **1b** in boiling aqueous methanol afforded the spirooxindoles **8aao** and **8bao** as chromatographically inseparable 2:1 mixtures of two diastereomers (Table 4). Unfortunately, individual diastereomers could not be isolated by recrystallization.

On the basis of the experimental results and X-ray analysis, plausible reaction pathways are proposed as illustrated in Scheme 1. Condensation of α-amino acid **3** with isatin **2**, followed by decarboxylation, furnishes a nitrogen ylide **D**, which reacts as a 1,3-dipole. This intermediate could in principle react with the dipolarophile along two possible pathways **A** and **B**. Path **A** leads to the formation of the major cycloadducts **4**, **6**, and **8**, whereas path **B** affords the minor products **5** and **7**. The observed diastereoselectivity might be explained by steric hindrance between the bulky phenyl substituent of cyclopropene and the core of isatin in path **B** (TS-*exo*). Indeed, this steric effect could be significantly relieved by the *endo*-approach in path **A**. The phenyl moiety is sufficiently separated from the isatin core in the *endo*-approach **A** (TS-*endo*), and this more stabilized transition state will require less free energy for its activation. Thus, the formation of the cycloadducts will be more favored through the *endo*-approach, and the diastereomers **4**, **6**, and **8** were, therefore, obtained as the major products.

As an amino acid derivative, peptide can also be successfully used in this one-pot three-component reaction. Using peptide as the amine component in this process appeared particularly interesting in order to expand the synthetic utility of this methodology. It was found that the cycloaddition of dipolarophiles **1a**, **1b** with nonstabilized azomethine ylides generated from isatin (**2a**) and the simplest peptide Gly-Gly (**9**) led to spiroazabicyclohexanes **10a** and **10b** in 57% and 70% yield, respectively (Scheme 2). Compound **10a** was obtained as a 10:1 mixture of diastereomers from which the major diastereomer was isolated by preparative thin layer chromatography and subsequent crystallization from chloroform in 57% yield. Spirooxindole **10b** was obtained as a single diastereomer, and the signals of the other possible diastereomer were not found in the ^{1}H NMR spectrum of the crude reaction mixture. The cycloadducts **10a**, **10b** were characterized by IR, ^{1}H NMR, ^{13}C NMR, and mass spectral analysis. For example, in the ^{1}H NMR spectrum of compound **10a**, the NH-proton of the oxindole moiety, COOH and NH protons of the peptide fragment, and the NH-proton of the pyrrolidine ring gave signals at δ 10.04, 12.47, 8.02, and 3.92 ppm, respectively. Four carbonyl groups of compound **10a** gave peaks at δ 179.4, 171.4, 169.9, and 169.4 ppm in the ^{13}C NMR spectrum.

In order to further expand the usability of this reaction, we tried to apply benzylamine as one more amine component for the *in situ* azomethine ylide generation.[26] Initially, a three-component reaction of isatin derivative **2b**, benzylamine (**11A**), and cyclopropene **1b** was conducted in dichloromethane at room temperature. As a result, the spiroazabicyclohexane oxindole **8bbA** was obtained as a single diastereomer in a moderate 46% yield. Subsequently, we attempted to optimize the reaction conditions by solvent screening, and the best results were obtained by refluxing the reaction mixture in methanol–benzene (3:1) mixture for 3 h, providing spirooxindoles **8abA**–**8dbB** in excellent yields (79–94%) (Table 5). The structures and the relative configuration of compounds **8abA**–**8dbB** were deduced from their NMR data and are similar to those of **8aae**–**8ban**.

To show the synthetic utility of the formed spirooxindoles, their oxidation, chlorination, and reduction reactions were studied (Scheme 3). For instance, treatment of **8bak** and **8bbA** with DDQ (2,3-dichloro-5,6-dicyano-*p*-benzoquinone) in *p*-xylene at 110 °C produced spiroazabicyclo[3.1.0]hex-3-eneoxindoles **12a** and **12b** in 48% and 61% yields, respectively. Chlorination on the pyrrolidine nitrogen of **8bak** with *N*-chlorosuccinimide (NCS) led to the formation of *N*-chloroamine **13** in 52% yield. The reduction of **4bba** with $LiAlH_4$ in diethyl ether at ambient temperature produced 2-hydroxyindoline **14** as a single diastereomer in 71% yield. The relative configuration of the compound **14** was unambiguously determined by means of X-ray single-crystal structure analysis (see the Supporting Information, Figure S113). At the same time, reduction of **4bba** with $LiAlH_4$ in Et_2O at reflux for 24 h leads to indoline **15** in 86% yield.

CYTOTOXIC ACTIVITY

The anticancer activity of some of the obtained compounds against the human leukemia K562 cell line was evaluated *in vitro* by flow cytometry, using the commercially available standard drug Imatinib as a positive control. The results of these investigations are shown in Figure 4 (for details, see the Supporting Information, Table S1).

As can be seen, the most potent compounds are **8bag**, **8bam**, and **8bao** with an alkyl or mercaptoalkyl substituent on the azabicyclohexane moiety. The cytotoxicities of **8bag**, **8bam**, and **8bao** are in the micromolar range, in the same order as for Imatinib. A loss of activity is observed when replacing the alkyl by an amidocarboxylic group and phenyl by a carboxymethyl

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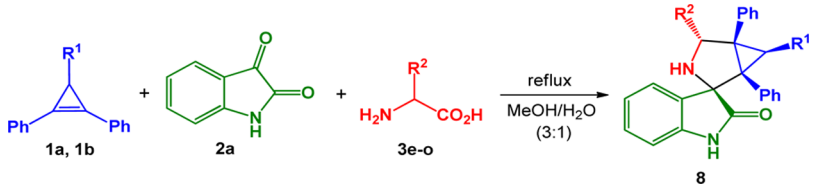
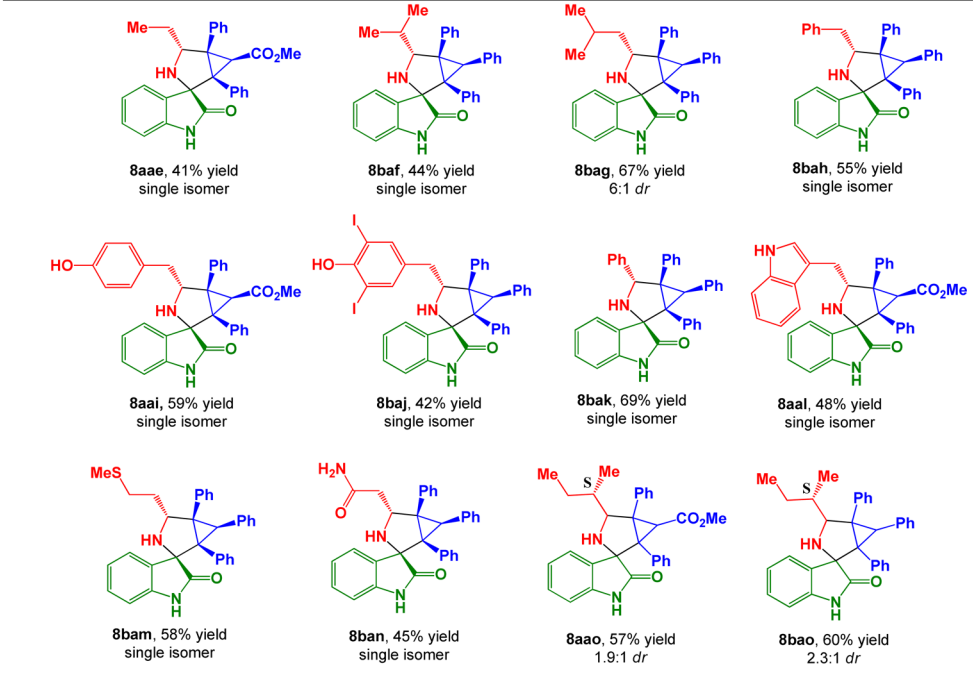
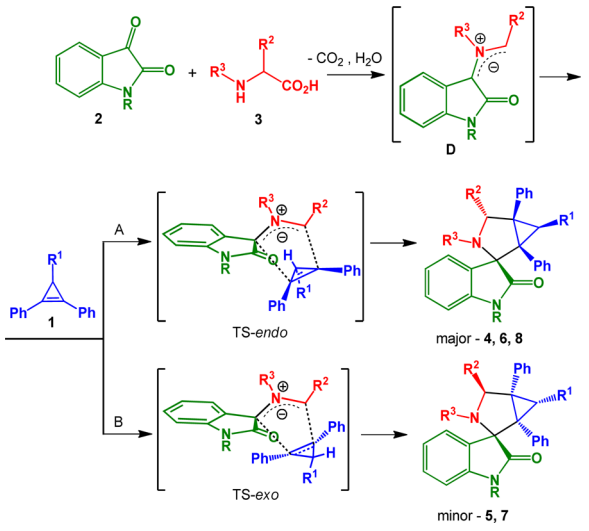
Table 4. Synthesis of 3-Spiro[3-azabicyclo[3.1.0]hexane]oxindoles 8 by Three-Component Reactions of Isatin 2a, α-Amino Acids 3e−o, and Cyclopropenes 1a, 1b[a,b,c]



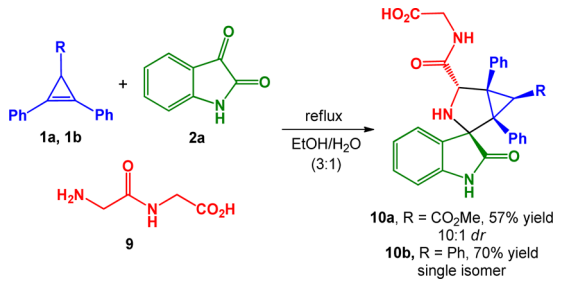


[a]All reactions were carried out with **1** (0.4 mmol), **2a** (0.4 mmol), **3** (0.8 mmol) in MeOH−H_2O (3:1) at reflux. [b]Isolated yield. [c]In all cases, the unreacted starting material **1** was recovered in 10−30% yields.

Scheme 1. Proposed Mechanism for 1,3-Dipolar Cycloaddition of Azomethine Ylides with Cyclopropene Derivatives



Scheme 2. Three-Component 1,3-Dipolar Cycloaddition Reaction of Isatin (2a), Gly-Gly (9), and Cyclopropenes 1a, 1b



group (compare compound **8bao** with **10a** and **10b**), as well as by inserting a pyrrolizine moiety (compare **8bao** with **4cba**). Compounds **8bag**, **8bam**, and **8bao** were also tested as their hydrochloric salts, and they showed the same activity (see the Supporting Information, Table S2, Figure S109). The results indicated that 3-spiro[3-azabicyclo[3.1.0]hexane]oxindole analogues may be useful leads for further biological screenings.

CONCLUSIONS

In this study, we have developed a highly efficient stereoselective synthesis of a novel class of substituted 3-spiro[cyclopropa[*a*]pyrrolizine]- and 3-spiro[3-azabicyclo[3.1.0]hexane]-oxindoles via a 1,3-dipolar cycloaddition of cyclopropenes with azomethine ylides generated from isatins and α-amino acids and also with azomethine ylides generated from isatins and peptide Gly-Gly or benzylamine. It is also worth emphasizing that the use of the peptide as an amine component for the generation of azomethine ylide is the first ever described

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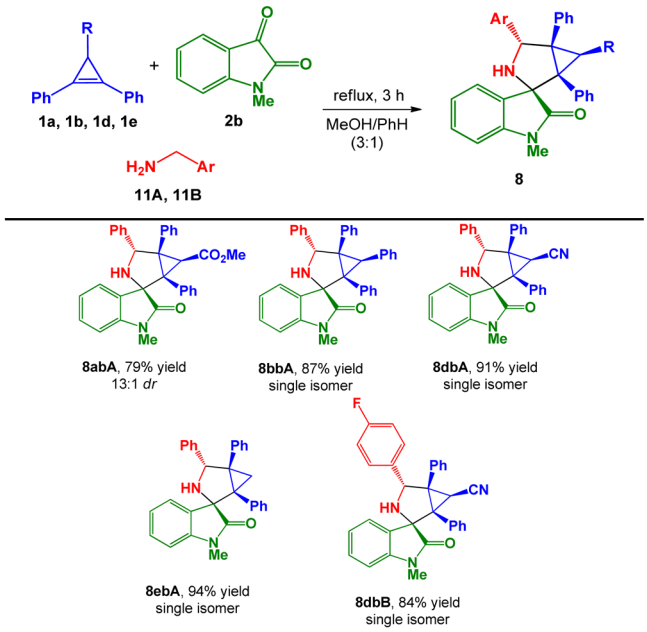
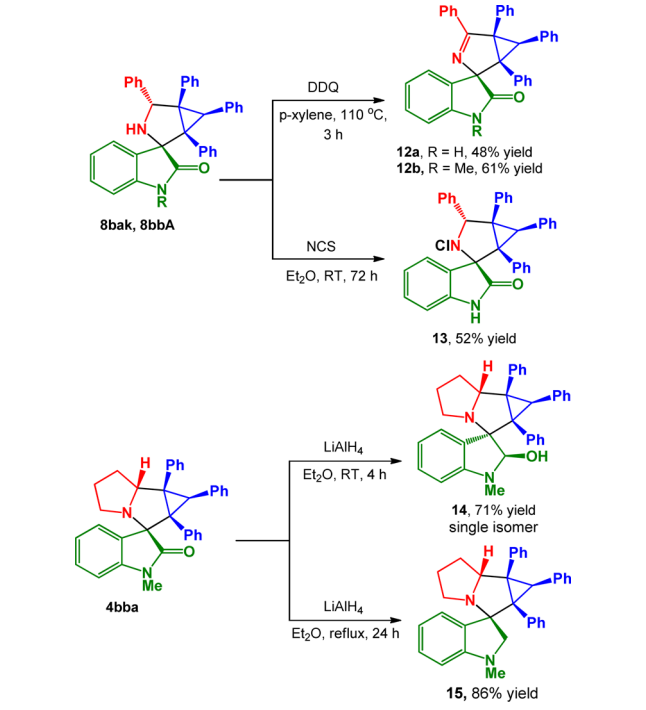
Table 5. Three-Component 1,3-Dipolar Cycloaddition Reaction of Isatin 2b, Benzylamine 11A, 11B, and Cyclopropenes 1a, 1b, 1d, 1e[a,b]



[a]All reactions were carried out with **1** (0.4 mmol), **2** (0.4 mmol), **11** (0.8 mmol) in methanol–benzene (3:1) at reflux. [b]Isolated yield.

Scheme 3. Further Transformations of the Obtained Spirooxindoles 4bba, 8bak, and 8bbA



example. The synthetic potential of the resulting spirocyclic compounds was exemplified in the reduction, oxidation, and chlorination reactions. Furthermore, the biological activity of some of the obtained compounds has been preliminarily demonstrated by *in vitro* evaluation against human leukemia K562 cell line.

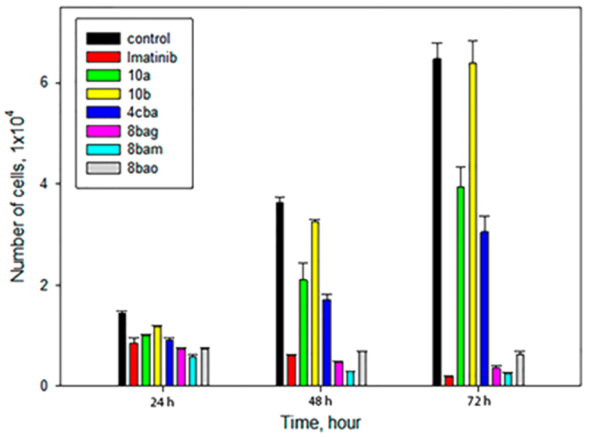


Figure 4. Cytotoxicity of selected compounds against human leukemia K562 cell line (at 25 μM for the tested compounds and 10 μM for Imatinib).

EXPERIMENTAL SECTION

General Remarks. All reagents were used as purchased from commercial suppliers without further purification. Starting materials that were not commercially available were synthesized by the previously reported methods.[27,28] All solvents were dried by standard procedures and freshly distilled prior to use. The progress of reactions was monitored by TLC on Silufol UV-254 plates using UV light and iodine for detection. Preparative thin-layer chromatography (PTLC) was perfomed on silica gel (5–40 mesh). Melting points were determined on a Boetius instrument. ^{1}H NMR spectra were recorded on a 400 MHz spectrometer, while ^{13}C and ^{19}F NMR spectra were recorded on 100 and 376 MHz instruments, respectively. Chemical shifts (δ) in ppm are reported with the use of the residual chloroform (7.26 ppm for ^{1}H and 77.2 ppm for ^{13}C) and dimethyl sulfoxide (2.50 ppm for ^{1}H and 39.5 ppm for ^{13}C) as internal references and the signal of $CFCl_3$ δ 0.0 ppm (^{19}F). Integrals are in accordance with assignments; coupling constants are given in Hz. All ^{13}C and ^{19}F NMR spectra were proton-decoupled. DEPT spectra were used for the assignment of carbon signals. IR spectra were measured in KBr, and wavelengths are reported in cm^{-1}. High resolution mass spectra (HRMS) were recorded for ESI-QTOF mode. Single-crystal X-ray diffraction experiments were performed on a diffractometer at 100 K using monochromated Mo Kα and Cu Kα radiation. Melting points were determined on a melting point apparatus and are uncorrected.

General Procedure A for Three-Component Reaction of Cyclopropenes, Isatins, and *L*-Proline. A mixture of the corresponding cyclopropene **1** (0.4 mmol), isatin **2** (0.4 mmol), and *L*-proline (**3a**) (0.5 mmol) was refluxed in methanol (8 mL) for 4 h. After completion of the reaction as monitored by TLC, the solvent was removed under reduced pressure. The residue was recrystallized or chromatographed on silica gel to obtain the pure products **4** and **5**.

*Methyl (±)-(1R,1aR,2R,6aR,6bS)-2′-Oxo-1a,6b-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carboxylate (**4aaa**).* Prepared according to the general procedure **A** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by recrystallization from methanol furnished **4aaa** as a single diastereomer. Colorless solid; yield: 133 mg (74%); mp 248–251 °C (MeOH); R_f 0.51 (SiO_2, hexane–EtOAc, 3:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, J = 7.4 Hz, 1H), 7.60–7.56 (m, 2H), 7.35 (t, J = 7.5 Hz, 2H), 7.27–7.22 (m, 2H), 7.20 (s, 1H), 7.15 (dt, J = 7.5, 3.8 Hz, 1H), 7.01–6.89 (m, 5H), 6.64 (d, J = 7.7 Hz, 1H), 4.70 (t, J = 6.9 Hz, 1H), 3.39–3.34 (m, 1H), 3.37 (s, 3H), 2.82 (s, 1H), 2.73–2.67 (m, 1H), 2.11–2.03 (m, 1H), 2.00–1.80 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.7, 169.8, 141.9, 134.6, 132.2, 130.8 (4C), 129.6, 127.9 (2C), 127.1 (2C), 127.0, 126.9, 126.2, 125.8, 122.1, 110.0, 75.9, 75.8, 57.4, 51.2, 51.0, 48.9, 29.0, 26.9, 26.8. IR(KBr): 3162, 3052, 3033, 2954, 2842, 1702, 1618, 1417, 1293, 1186,

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1051, 912, 750, 706 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{29}H_{27}N_2O_3$: 451.2016; found: 451.2032.

*(±)-(1R,1aR,2R,6aR,6bS)-1,1a,6b-Triphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indolin]-2′-one (**4baa**).* Prepared according to the general procedure **A** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by recrystallization from methanol furnished **4baa** as a single diastereomer. Colorless solid; yield: 129 mg (69%); mp 227−228 °C (MeOH); R_f 0.60 (SiO_2, hexane−EtOAc, 3:2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, J = 7.3 Hz, 1H), 7.46 (d, J = 7.2 Hz, 2H), 7.27−7.17 (m, 5H), 7.08 (t, J = 7.5 Hz, 1H), 7.04−6.79 (m, 8H), 6.62 (d, J = 7.6 Hz, 1H), 6.41 (d, J = 7.5 Hz, 2H), 4.79 (t, J = 7.0 Hz, 1H), 3.59−3.54 (m, 1H), 3.10 (s, 1H), 2.85−2.78 (m, 1H), 2.20−2.11 (m, 1H), 2.09−1.87 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.5, 141.9, 136.9, 134.8, 132.6, 132.4 (4C), 131.7, 130.7 (2C), 129.3, 127.7 (2C), 127.1, 126.7, 126.6 (4C), 126.1, 125.2, 121.9, 109.8, 76.8, 76.2, 56.8, 49.3, 49.0, 31.9, 27.1, 26.9. IR (KBr): 3193, 3061, 3013, 2962, 2857, 2822, 1702, 1616, 1470, 1326, 1214, 1080, 747, 704 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$calcd for $C_{33}H_{29}N_2O$: 469.2274; found: 469.2299.

*(±)-(1R,1aR,2R,6aR,6bS)-N-Methyl-2′-oxo-1a,6b-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carboxamide (**4caa**).* Prepared according to general procedure **A** using cyclopropene **1c** (100 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by PTLC (EtOAc−hexane, 3:1) furnished **4caa** as a single diastereomer. Colorless solid; yield: 86 mg (48%); mp 168−170 °C (MeOH); R_f 0.33 (SiO_2, EtOAc−hexane, 3:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, J = 7.5 Hz, 1H), 7.71 (d, J = 7.5 Hz, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.32−7.24 (m, 2H), 7.15−7.05 (m, 5H), 7.02−6.98 (m, 2H), 6.65 (d, J = 7.7 Hz, 1H), 4.67 (t, J = 6.6 Hz, 1H), 3.66 (d, J = 4.3 Hz, 1H), 3.47−3.41 (m, 1H), 2.81 (s, 1H), 2.73−2.67 (m, 1H), 2.22 (d, J = 4.7 Hz, 3H), 2.10−2.03 (m, 1H), 1.95−1.88 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.7, 170.0, 141.6, 134.0, 131.8 (2C), 131.6 (2C), 131.2, 129.7, 128.4 (2C), 127.9, 127.8 (2C), 127.6, 126.6, 125.5, 122.4, 109.8, 77.2, 76.6, 55.4, 49.6, 49.5, 31.9, 27.0, 26.9, 25.9. IR (KBr): 3293, 3207, 3061, 2931, 2873, 1721, 1658, 1620, 1545, 1471, 1206, 745, 703 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{29}H_{28}N_3O_2$: 450.2176; found: 450.2178.

*(±)-(1R,1aR,2R,6aR,6bS)-2′-Oxo-1a,6b-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carbonitrile (**4daa**).* Prepared according to general procedure **A** using cyclopropene **1d** (87 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by recrystallization from methanol furnished **4daa** as a single diastereomer. Colorless solid; yield: 127 mg (76%); mp > 260 °C (MeOH); R_f 0.47 (SiO_2, hexane−EtOAc, 3:2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, J = 7.4 Hz, 2H), 7.58 (d, J = 7.4 Hz, 1H), 7.44−7.35 (m, 3H), 7.33−7.26 (m, 2H), 7.16 (t, J = 7.4 Hz, 1H), 7.13−7.00 (m, 5H), 6.67 (d, J = 7.7 Hz, 1H), 4.79 (dd, J = 8.4, 5.9 Hz, 1H), 3.17−3.10 (m, 1H), 2.85 (s, 1H), 2.66 (td, J = 8.0, 3.5 Hz, 1H), 2.20−1.95 (m, 3H), 1.76−1.63 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.0, 141.6, 133.2, 131.5 (2C), 130.0, 129.9 (2C), 129.7, 128.4 (2C), 128.2, 127.8 (2C), 127.7, 125.3, 125.0, 122.5, 118.2, 110.2, 73.4, 72.4, 55.9, 47.0, 46.1, 26.7, 26.3, 14.3. IR (KBr): 3210, 3041, 2971, 2828, 2234, 1736, 1619, 1469, 1318, 1178, 760, 703 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{28}H_{24}N_3O$: 418.1914; found: 418.1929.

*Methyl (±)-(1R,1aR,2R,6aR,6bS)-1′-Methyl-2′-oxo-1a,6b-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carboxylate (**4aba**).* Prepared according to general procedure **A** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin **2b** (65 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by recrystallization from methanol furnished **4aba** as a single diastereomer. Colorless solid; yield: 158 mg (85%); mp 211−216 °C (MeOH); R_f 0.46 (SiO_2, hexane−EtOAc, 2:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, J = 7.3 Hz, 1H), 7.60 (d, J = 7.2 Hz, 2H), 7.38−7.30 (m, 3H), 7.25 (t, J = 7.4 Hz, 1H), 7.17 (t, J = 7.3 Hz, 1H), 6.97−6.88 (m, 5H), 6.60 (d, J = 7.7 Hz, 1H), 4.76 (t, J = 6.9 Hz, 1H), 3.43−3.41 (m, 1H), 3.36 (s, 3H), 2.84 (s, 3H), 2.80 (s, 1H), 2.73−2.69 (m, 1H), 2.12−2.04 (m, 1H), 2.00−1.84 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.5, 169.8, 144.8, 134.6, 132.1, 130.8 (2C), 130.6 (2C), 129.7, 127.9, 127.0 (2C), 126.9 (3C), 125.8, 125.3, 122.1, 108.2, 76.3, 75.5, 57.9, 51.5, 51.2, 49.4, 29.0, 27.1, 26.9, 25.5. IR (KBr): 3057, 2953, 2837, 1747, 1708, 1611, 1469, 1353, 1168, 754, 706 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{30}H_{29}N_2O_3$: 465.2173; found: 465.2171.

*(±)-(1R,1aR,2R,6aR,6bS)-1′-Methyl-1,1a,6b-triphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indolin]-2′-one (**4bba**).* Prepared according to general procedure **A** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin **2b** (65 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by recrystallization from methanol furnished **4bba** as a single diastereomer. Colorless solid; yield: 139 mg (72%); mp 216−217 °C (MeOH); R_f 0.57 (SiO_2, hexane−EtOAc, 2:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, J = 7.3 Hz, 1H), 7.48 (d, J = 6.9 Hz, 2H), 7.27−7.20 (m, 5H), 7.09 (t, J = 7.5 Hz, 1H), 7.00 (t, J = 7.3 Hz, 1H), 6.92 (t, J = 7.5 Hz, 3H), 6.86−6.78 (m, 3H), 6.56 (d, J = 7.7 Hz, 1H), 6.42 (d, J = 7.4 Hz, 2H), 4.84 (t, J = 7.0 Hz, 1H), 3.62 (dt, J = 15.1, 7.4 Hz, 1H), 3.08 (s, 1H), 2.85−2.80 (m, 1H), 2.84 (s, 3H), 2.20−2.11 (m, 1H), 2.06−1.91 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.2, 144.9, 137.0, 134.8, 132.4 (4C), 131.6, 130.7 (4C), 129.3, 127.8 (2C), 126.9, 126.7, 126.6, 126.5, 126.1, 125.6, 125.1, 121.9, 108.0, 77.1, 76.2, 57.3, 49.7, 49.4, 31.9, 27.1 (2C), 25.4. IR (KBr): 3031, 2939, 2790, 1716, 1611, 1495, 1470, 1372, 1349, 1245, 1129, 746, 702 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{34}H_{31}N_2O$: 483.2431; found: 483.2436.

*(±)-(1R,1aR,2R,6aR,6bS)-N,1′-Dimethyl-2′-oxo-1a,6b-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carboxamide (**4cba**).* Prepared according to general procedure **A** using cyclopropene **1c** (100 mg, 0.4 mmol), isatin **2b** (65 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by PTLC (EtOAc−hexane, 3:1) furnished **4cba** as a single diastereomer. Colorless amorphous powder; yield: 102 mg (55%); R_f 0.39 (SiO_2, EtOAc−hexane, 3:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, J = 7.3 Hz, 1H), 7.73 (d, J = 7.4 Hz, 2H), 7.39 (t, J = 7.4 Hz, 2H), 7.33−7.29 (m, 2H), 7.15 (t, J = 7.5 Hz, 1H), 7.10−6.92 (m, 5H), 6.59 (d, J = 7.7 Hz, 1H), 4.72 (t, J = 6.4 Hz, 1H), 3.67 (d, J = 3.9 Hz, 1H), 3.52−3.44 (m, 1H), 2.83 (s, 3H), 2.80 (s, 1H), 2.73−2.67 (m, 1H), 2.24 (d, J = 4.7 Hz, 3H), 2.10−2.04 (m, 1H), 1.97−1.89 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.6, 170.0, 144.7, 134.0, 131.6 (4C), 131.1, 129.7, 128.4 (2C), 127.8, 127.6 (2C), 127.6, 126.1, 125.0, 122.4, 108.1, 76.9, 76.2, 55.8, 49.9, 49.8, 31.9, 27.2, 26.9, 25.9, 25.5. IR (KBr): 3310, 3055, 2935, 2840, 1719, 1651, 1611, 1541, 1469, 1372, 1246, 1130, 928, 743, 704 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{30}H_{30}N_3O_2$: 464.2333; found: 464.2326.

*(±)-(1R,1aR,2R,6aR,6bS)-1′-Methyl-2′-oxo-1a,6b-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carbonitrile (**4dba**).* Prepared according to general procedure **A** using cyclopropene **1d** (87 mg, 0.4 mmol), isatin **2b** (65 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by recrystallization from methanol furnished **4dba** as a single diastereomer. Colorless solid; yield: 143 mg (83%); mp 243−245 °C (MeOH); R_f 0.43 (SiO_2, hexane−EtOAc, 2:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, J = 7.3 Hz, 2H), 7.59 (d, J = 7.3 Hz, 1H), 7.42−7.27 (m, 4H), 7.18 (t, J = 7.3 Hz, 1H), 7.10−6.98 (m, 5H), 6.63 (d, J = 7.8 Hz, 1H), 4.85 (dd, J = 8.2, 6.1 Hz, 1H), 3.21−3.16 (m, 1H), 2.85 (s, 3H), 2.80 (s, 1H), 2.67 (td, J = 7.8, 3.2 Hz, 1H), 2.17−1.97 (m, 3H), 1.79−1.66 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.6, 144.5, 133.2, 131.3 (2C), 130.1, 130.0 (2C), 129.7, 128.5 (2C), 128.1, 127.7 (3C), 124.9, 124.5, 122.5, 118.3, 108.5, 73.6, 72.9, 56.3, 47.6, 46.7, 26.8, 26.5, 25.6, 14.1. IR (KBr): 3071, 2961, 2816, 2233, 1713, 1611, 1490, 1446, 1342, 1246, 1127, 1025, 756, 698 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{29}H_{26}N_3O$: 432.2070; found: 432.2085.

*Methyl (±)-(1R,1aR,2R,6aR,6bS)-1′-Benzyl-2′-oxo-1a,6b-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carboxylate (**4aca**).* Prepared according to general procedure **A** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin **2c** (95 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by recrystallization from methanol furnished **4aca** (173 mg, 80%) as a single diastereomer. Colorless solid; yield: 173 mg (80%);

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mp 209−210 °C (MeOH); R_f 0.52 (SiO_2, hexane−EtOAc, 5:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, J = 7.0 Hz, 1H), 7.65 (d, J = 7.2 Hz, 2H), 7.37 (t, J = 7.6 Hz, 2H), 7.27−7.05 (m, 9H), 6.98 (t, J = 7.8 Hz, 2H), 6.43−6.38 (m, 3H), 5.16 (d, J = 16.2 Hz, 1H), 4.79 (t, J = 6.9 Hz, 1H), 4.29 (d, J = 16.2 Hz, 1H), 3.41−3.37 (m, 1H), 3.38 (s, 3H), 2.87 (s, 1H), 2.74−2.69 (m, 1H), 2.13−2.05 (m, 1H), 2.01−1.85 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.5, 169.8, 144.1, 134.9, 134.6, 132.6, 130.9 (4C), 129.7, 128.6 (2C), 127.9 (2C), 127.5 (2C), 127.1, 127.0, 126.2 (3C), 125.9, 125.3, 122.2, 109.7, 76.1, 75.5, 57.2, 51.3, 51.2, 49.4, 43.4, 29.1, 27.0, 26.9. IR (KBr): 3047, 2943, 2819, 1746, 1721, 1614, 1492, 1435, 1357, 1166, 744, 696 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{36}H_{33}N_2O_3$: 541.2486; found: 541.2498.

*(±)-(1R,1aR,2R,6aR,6bS)-1′-Benzyl-1,1a,6b-triphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indolin]-2′-one (**4bca**).* Prepared according to general procedure **A** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin **2c** (95 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by recrystallization from methanol furnished **4bca** as a single diastereomer. Colorless solid; yield: 172 mg (77%); mp 197−198 °C (MeOH); R_f 0.65 (SiO_2, hexane−EtOAc, 5:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, J = 7.0 Hz, 1H), 7.54 (d, J = 7.0 Hz, 2H), 7.27−7.12 (m, 4H), 7.11−7.03 (m, 10H), 6.95 (t, J = 7.5 Hz, 2H), 6.44 (d, J = 7.4 Hz, 2H), 6.40 (d, J = 7.4 Hz, 2H), 6.36 (d, J = 7.6 Hz, 1H), 5.19 (d, J = 16.2 Hz, 1H), 4.88 (t, J = 7.0 Hz, 1H), 4.30 (d, J = 16.2 Hz, 1H), 3.64−3.58 (m, 1H), 3.15 (s, 1H), 2.84−2.78 (m, 1H), 2.20−2.12 (m, 1H), 2.08−1.93 (m, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.2, 144.1, 136.9, 135.1, 134.8, 132.5 (4C), 132.1, 130.7 (2C), 129.4, 128.5 (4C), 127.8 (2C), 126.9 (2C), 126.7 (2C), 126.6, 126.2 (2C), 126.0, 125.8, 125.2, 122.0, 109.6, 77.0, 76.1, 56.6, 49.8, 49.2, 43.4, 32.1, 27.1 (2C). IR (KBr): 3021, 2962, 2825, 1712, 1610, 1466, 1346, 1176, 1081, 742, 699 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{40}H_{34}N_2NaO$: 581.2563; found: 581.2562.

*Methyl (±)-(1R,1aR,2R,6aR,6bS)-2′-Oxo-1a,1′,6b-triphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carboxylate (**4ada**) and Methyl (±)-(1S,1aS,2R,6aS,6bR)-2′-Oxo-1a,1′,6b-triphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carboxylate (**5ada**).* Prepared according to general procedure **A** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin **2d** (89 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished **4ada** and **5ada** as an inseparable mixture in ratio 12:1, respectively. Data for mixture of diastereomers **4ada** and **5ada**: colorless amorphous powder; yield: 137 mg (65%). IR (KBr): 3021, 2962, 2825, 1712, 1610, 1466, 1346, 1176, 1081, 742, 699 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{35}H_{31}N_2O_3$: 527.2329; found: 527.2331. NMR data for major diastereomer **4ada**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, J = 7.0 Hz, 1H), 7.60 (d, J = 7.2 Hz, 2H), 7.40−7.05 (m, 8H), 7.08−7.04 (m, 1H), 7.00−6.92 (m, 4H), 6.80 (d, J = 7.3 Hz, 2H), 6.50 (d, J = 7.3 Hz, 1H), 4.80 (t, J = 7.0 Hz, 1H), 3.56−3.50 (m, 1H), 3.39 (s, 3H), 2.89−2.86 (m, 1H), 2.87 (s, 1H), 2.16−2.08 (m, 1H), 2.03−1.86 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.1, 169.8, 145.0, 134.5, 133.9, 132.2, 130.8 (2C), 130.7 (2C), 129.6, 129.5 (2C), 128.1, 127.9 (2C), 127.2 (2C), 127.1, 126.9, 126.7 (2C), 126.0, 125.1, 122.6, 109.6, 76.6, 75.8, 58.7, 51.3, 51.2, 49.1, 29.0, 27.1, 27.0.

*(±)-(1R,1aR,2R,6aR,6bS)-1,1a,1′,6b-Tetraphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indolin]-2′-one (**4bda**) and (±)-(1S,1aS,2R,6aS,6bR)-1,1a,1′,6b-Tetraphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indolin]-2′-one (**5bda**).* Prepared according to general procedure **A** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin **2d** (95 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished **4bda** and **5bda** as an inseparable mixture in ratio 11:1, respectively. Data for mixture of diastereomers **4bda** and **5bda**: colorless amorphous powder; yield: 135 mg (62%). IR (KBr): 3076, 3031, 2942, 2801, 1727, 1611, 1498, 1465, 1370, 1298, 1177, 751, 697 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{39}H_{33}N_2O$: 545.2587; found: 545.2590. NMR data for major diastereomer **4bda**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (dd, J = 7.3, 1.0 Hz, 1H), 7.49 (dd, J = 8.0, 1.5 Hz, 2H), 7.40−7.31 (m, 3H), 7.26−7.11 (m, 6H), 7.02 (t, J = 7.3 Hz, 2H), 6.96−6.86 (m, 5H), 6.80 (d, J = 7.3 Hz, 2H), 6.50−6.45 (m, 3H), 4.89 (t, J = 7.1 Hz, 1H), 3.73 (td, J = 8.4, 6.2 Hz, 1H), 3.16 (s, 1H), 3.00−2.96 (m, 1H), 2.26−2.17 (m, 1H), 2.13−1.93 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.8, 145.0, 136.9, 134.8, 134.1, 132.5, 132.4 (2C), 131.8, 130.7 (3C), 129.4 (3C), 129.2, 128.0, 127.7 (2C), 127.2, 126.9, 126.8 (3C), 126.6 (3C), 125.8, 125.2, 122.4, 109.4, 77.4, 76.3, 58.1, 49.4, 49.2, 32.0, 27.2, 27.1.

*Methyl (±)-(1R,1aR,2R,6aR,6bS)-5′-Nitro-2′-oxo-1a,6b-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carboxylate (**4aea**) and Methyl (±)-(1S,1aS,2R,6aS,6bR)-5′-Nitro-2′-oxo-1a,6b-diphenyl-1a,40,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carboxylate (**5aea**).* Prepared according to general procedure **A** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin **2e** (77 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by PTLC (hexane−EtOAc, 1:1) furnished **4aea** and **5aea** as an inseparable mixture in ratio 6:1, respectively. Data for mixture of diastereomers **4aea** and **5aea**: yellow amorphous powder; yield: 115 mg (58%). IR (KBr): 3284, 3047, 2920, 2851, 1743, 1724, 1626, 1602, 1523, 1446, 1338, 1199, 1082, 906, 734, 699 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{29}H_{26}N_3O_5$: 496.1867; found: 496.1873. NMR data for major diastereomer **4aea**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.58 (d, J = 2.0 Hz, 1H), 8.23 (dd, J = 8.6, 2.1 Hz, 1H), 7.71 (s, 1H), 7.54 (d, J = 7.3 Hz, 2H), 7.39−7.23 (m, 3H), 7.03−7.00 (m, 1H), 6.98−6.92 (m, 4H), 6.65 (d, J = 8.6 Hz, 1H), 4.67 (t, J = 7.0 Hz, 1H), 3.48 (s, 3H), 3.33−3.27 (m, 1H), 2.91 (s, 1H), 2.70−2.65 (m, 1H), 2.18−2.10 (m, 1H), 1.99−1.81 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.7, 169.2, 147.7, 143.2, 133.8, 131.3, 130.8 (2C), 130.7 (2C), 128.0 (2C), 127.5 (2C), 127.5, 127.2, 126.7 (2C), 121.5, 109.8, 75.7, 74.9, 57.2, 51.7, 50.4, 48.3, 28.5, 26.8, 26.6.

*(±)-(1R,1aR,2R,6aR,6bS)-5′-Nitro-1,1a,6b-triphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indolin]-2′-one (**4bea**) and (±)-(1S,1aS,2R,6aS,6bR)-5′-Nitro-1,1a,6b-triphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa-[a]pyrrolizine-2,3′-indolin]-2′-one (**5bea**).* Prepared according to general procedure **A** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin **2e** (77 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by PTLC (hexane−EtOAc, 1:1) furnished **4bea** and **5bea** as an inseparable mixture in ratio 5:1, respectively. Data for mixture of diastereomers **4bea** and **5bea**: yellow amorphous powder; yield: 123 mg (60%). IR (KBr): 3233, 3049, 2965, 2877, 1725, 1626, 1602, 1524, 1445, 1337, 1198, 1075, 907, 699 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{33}H_{28}N_3O_3$: 514.2125; found: 514.2121. NMR data for major diastereomer **4bea**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.67 (d, J = 1.7 Hz, 1H), 8.45 (s, 1H), 8.24 (dd, J = 8.6, 2.0 Hz, 1H), 7.44 (d, J = 6.9 Hz, 2H), 7.34−7.23 (m, 3H), 7.04−6.75 (m, 9H), 6.44 (d, J = 7.6 Hz, 2H), 4.75 (t, J = 7.0 Hz, 1H), 3.53−3.48 (m, 1H), 3.20 (s, 1H), 2.81−2.77 (m, 1H), 2.26−2.20 (m, 1H), 2.02−1.84 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.4, 147.9, 143.1, 136.0, 134.2, 132.5, 132.2 (2C), 131.0, 130.7 (3C), 127.9 (2C), 127.5 (2C), 127.3, 126.9, 126.8 (3C), 126.5, 125.6, 121.5, 109.8, 76.9, 75.7, 56.9, 48.8, 48.8, 31.7, 27.1, 26.6.

*Methyl (±)-(1R,1aR,2R,6aR,6bS)-5′-Chloro-2′-oxo-1a,6b-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carboxylate (**4afa**) and Methyl (±)-(1S,1aS,2R,6aS,6bR)-5′-Chloro-2′-oxo-1a,6b-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carboxylate (**5afa**).* Prepared according to general procedure **A** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin **2f** (73 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished **4afa** and **5afa** (122 mg, 63%) as an inseparable mixture in ratio 10:1, respectively. Data for mixture of diastereomers **4afa** and **5afa**: yellow amorphous powder; yield: 122 mg (63%). IR (KBr): 3285, 3041, 2950, 2881, 1735, 1719, 1619, 1478, 1437, 1290, 1199, 818, 749, 699 cm^{-1}. HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{29}H_{25}{}^{35}ClN_2NaO_3$: 507.1446; found: 507.1444. NMR data for major diastereomer **4afa**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, J = 2.0 Hz, 1H), 7.59 (s, 1H), 7.55 (d, J = 7.1 Hz, 2H), 7.34 (t, J = 7.8 Hz, 2H), 7.24 (dd, J = 8.2, 2.1 Hz, 2H), 7.04−6.99 (m, 3H), 6.97−6.92 (m, 2H), 6.54 (d, J = 8.3 Hz, 1H), 4.66 (t, J = 7.1 Hz, 1H), 3.41

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(s, 3H), 3.32−3.25 (m, 1H), 2.80 (s, 1H), 2.71−2.65 (m, 1H), 2.12−2.05 (m, 1H), 1.96−1.77 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.6, 169.6, 140.5, 134.3, 131.8, 130.8 (2C), 130.7 (2C), 129.7, 127.9 (2C), 127.5, 127.4, 127.3 (2C), 127.2, 127.0, 126.1, 110.1, 75.7, 75.5, 57.2, 51.4, 50.6, 48.4, 28.7, 26.8, 26.7.

*(±)-(1R,1aR,2R,6aR,6bS)-5′-Chloro-1,1a,6b-triphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indolin]-2′-one (**4bfa**) and (±)-(1S,1aS,2R,6aS,6bR)-5′-Chloro-1,1a,6b-triphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa-[a]pyrrolizine-2,3′-indolin]-2′-one (**5bfa**).* Prepared according to general procedure **A** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin **2f** (73 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.4 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished **4bfa** and **5bfa** as an inseparable mixture in ratio 9:1, respectively. Data for mixture of diastereomers **4bfa** and **5bfa**: colorless amorphous powder; yield: 113 mg (56%). IR (KBr): 3221, 3043, 2965, 2875, 1717, 1618, 1476, 1201, 815, 763, 700 cm^{-1}. HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{33}H_{27}{}^{35}ClN_2NaO$: 525.1704; found: 525.1699. NMR data for major diastereomer **4bfa**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (s, 1H), 7.47−7.39 (m, 3H), 7.28−7.17 (m, 4H), 7.07−6.80 (m, 8H), 6.58 (d, J = 8.3 Hz, 1H), 6.42 (d, J = 7.6 Hz, 2H), 4.74 (t, J = 7.2 Hz, 1H), 3.52−3.45 (m, 1H), 3.09 (s, 1H), 2.82−2.77 (m, 1H), 2.22−2.13 (m, 1H), 1.95−1.87 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.5, 140.5, 136.6, 134.6, 132.5, 132.5, 132.3 (2C), 131.4, 130.7 (2C), 129.3, 127.8 (2C), 127.3, 127.2, 127.0, 126.7 (5C), 126.1, 125.3, 110.9, 76.7, 76.1, 56.8, 48.8, 48.7, 31.7, 27.1, 26.1.

*Methyl (±)-(1R,1aR,2R,6aR,6bS)-5′,7′-Dibromo-2′-oxo-1a,6b-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]-pyrrolizine-2,3′-indoline]-1-carboxylate (**4aga**) and Methyl (±)-(1S,1aS,2R,6aS,6bR)-5′,7′-Dibromo-2′-oxo-1a,6b-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline]-1-carboxylate (**5aga**).* Prepared according to general procedure **A** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin **2g** (122 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by PTLC (hexane−EtOAc, 3:1) furnished **4aga** and an inseparable mixture of **4aga** and **5aga** in ratio 1.4:1, respectively. Data for major diastereomer **4aga**: beige solid; yield: 54 mg (22%); mp > 260 °C (MeOH−H_2O); R_f 0.51 (SiO_2, hexane−EtOAc, 5:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, J = 0.9 Hz, 1H), 7.59 (d, J = 1.4 Hz, 1H), 7.55 (d, J = 7.3 Hz, 2H), 7.48 (s, 1H), 7.34 (t, J = 7.5 Hz, 2H), 7.26 (t, J = 7.3 Hz, 1H), 7.09−6.95 (m, 5H), 4.63 (t, J = 7.1 Hz, 1H), 3.40 (s, 3H), 3.22−3.18 (m, 1H), 2.80 (s, 1H), 2.69−2.64 (m, 1H), 2.15−2.05 (m, 1H), 2.00−1.83 (m, 2H), 1.80−1.72 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.2, 169.5, 140.5, 134.6, 134.1, 131.5, 130.7 (5C), 128.8, 128.0 (2C), 127.7, 127.5 (2C), 127.1, 114.8, 103.6, 76.4, 75.5, 57.1, 51.4, 50.1, 47.9, 28.6, 26.8, 26.4. IR (KBr): 3155, 3062, 2952, 2891, 1743, 1714, 1610, 1576, 1458, 1291, 1174, 908, 732, 698 cm^{-1}. HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{29}H_{24}{}^{79}Br_2N_2NaO_3$: 629.0046; found: 629.0042; m/z [M + Na]$^+$ calcd for $C_{29}H_{24}{}^{79}Br^{81}BrN_2NaO_3$: 631.0025; found: 631.0026; m/z [M + Na]$^+$ calcd for $C_{29}H_{24}{}^{81}Br_2N_2NaO_3$: 633.0005; found: 633.0009. Data for minor diastereomer **5aga**: yield: 73 mg (30%) for inseparable mixture of **4aga** and **5aga** in ratio 1.4:1. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01−6.94 (m, 13H), 4.49 (t, J = 6.5 Hz, 1H), 3.68 (dt, J = 14.5, 7.2 Hz, 1H), 3.47 (s, 3H), 3.29 (s, 1H), 2.77−2.72 (m, 1H), 2.15−2.05 (m, 1H), 2.00−1.83 (m, 2H), 1.80−1.72 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.0, 169.3, 140.7, 137.7−126.4 (15C), 115.2, 103.1, 76.9, 75.7, 58.7, 51.5, 50.9, 47.2, 28.6, 27.6, 27.3.

*(±)-(1R,1aR,2R,6aR,6bS)-5′,7′-Dibromo-1,1a,6b-triphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indolin]-2′-one (**4bga**) and (±)-(1S,1aS,2R,6aS,6bR)-5′,7′-Dibromo-1,1a,6b-triphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa-[a]pyrrolizine-2,3′-indolin]-2′-one (**5bga**).* Prepared according to general procedure **A** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin **2g** (122 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by PTLC (hexane−EtOAc, 3:1) furnished **4bga** and **5bga** as separated diastereomers. Data for major diastereomer **4bga**: beige solid; yield: 110 mg (44%); mp > 260 °C (MeOH−H_2O); R_f 0.62 (SiO_2, hexane−EtOAc, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, J = 1.5 Hz, 1H), 7.56 (s, 1H), 7.53 (d, J = 1.7 Hz, 1H), 7.43 (dd, J = 7.9, 1.4 Hz, 2H), 7.27−7.19 (m, 3H), 7.07−6.82 (m, 8H), 6.41 (d, J = 7.4 Hz, 2H), 4.70 (t, J = 7.3 Hz, 1H), 3.38−3.34 (m, 1H), 3.09 (s, 1H), 2.75 (td, J = 7.6, 2.4 Hz, 1H), 2.21−2.14 (m, 1H), 2.04−1.94 (m, 2H), 1.87−1.79 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.3, 140.7, 136.4, 134.4, 134.3, 132.5, 132.3 (2C), 131.0, 130.7 (2C), 129.7, 127.8 (2C), 127.6, 127.5 (2C), 127.2, 126.8 (2C), 126.7 (2C), 125.4, 114.6, 103.5, 76.9, 76.4, 56.6, 48.1, 48.0, 31.5, 27.0, 26.2. IR (KBr): 3167, 3058, 2996, 2873, 2821, 1720, 1609, 1496, 1457, 1174, 908, 698 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{33}H_{27}{}^{79}Br_2N_2O$: 625.0485; found: 625.0433; m/z [M + H]$^+$calcd for $C_{33}H_{27}{}^{79}Br^{81}BrN_2O$: 627.0464; found: 627.0462; m/z [M + H]$^+$ calcd for $C_{33}H_{27}{}^{81}Br_2N_2O$: 629.0444; found: 629.0445. Data for minor diastereomer **5bga**: beige solid; yield: 43 mg (17%); mp > 260 °C (MeOH−H_2O); R_f 0.42 (SiO_2, hexane−EtOAc, 5:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04 (s, 1H), 7.49 (d, J = 1.4 Hz, 1H), 7.38 (d, J = 1.6 Hz, 1H), 7.37−7.32 (m, 2H), 7.30−7.25 (m, 4H), 6.99−6.71 (m, 7H), 6.30 (d, J = 7.3 Hz, 2H),4.23 (s, 1H), 4.21 (dd, J = 11.1, 5.9 Hz, 1H), 3.13−3.05 (m, 1H), 2.64 (dt, J = 11.1, 7.7 Hz, 1H), 2.07−1.95 (m, 1H), 1.92−1.76 (m, 2H), 1.61−1.54 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.6, 139.3, 137.0, 133.5, 133.4, 132.6, 132.4 (2C), 132.2, 131.5, 130.7 (3C), 128.2, 128.0 (2C), 127.2, 127.1, 126.9, 126.4 (3C), 124.9, 114.5, 104.0, 81.6, 77.9, 55.6, 48.2, 47.9, 35.2, 32.1, 27.0. IR (KBr): 3169, 3072, 2963, 2821, 1727, 1606, 1497, 1456, 1156, 909, 763, 733, 699 cm^{-1}. HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{33}H_{26}{}^{79}Br_2N_2NaO$: 647.0304; found: 647.0311; m/z [M + H]$^+$ calcd for $C_{33}H_{26}{}^{79}Br^{81}BrN_2NaO$: 649.0284; found: 649.0287; m/z [M + H]$^+$ calcd for $C_{33}H_{26}{}^{81}Br_2N_2NaO$: 651.0263; found: 651.0271.

*(±)-(1aR,2R,6aR,6bS)-1a,6b-Diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indolin]-2′-one (**4eaa**).* The best yield has been found upon carrying out the reaction at room temperature for 12 h using cyclopropene **1e** (77 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by recrystallization from a mixture of hexane−CH_2Cl_2 furnished **4eaa** as a single diastereomer. Colorless solid; yield: 139 mg (88%); mp 216−218 °C (hexane−CH_2Cl_2); R_f 0.63 (SiO_2, hexane−EtOAc, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, J = 7.4 Hz, 1H), 7.60 (s, 1H), 7.44 (d, J = 7.4 Hz, 2H), 7.30−7.06 (m, 5H), 7.00−6.84 (m, 5H), 6.67 (d, J = 7.7 Hz, 1H), 5.01−4.95 (m, 1H), 3.32−3.24 (m, 1H), 2.71−2.64 (m, 1H), 2.12−1.94 (m, 3H), 1.88 (d, J = 5.2 Hz, 1H), 1.80−1.68 (m, 1H), 1.49 (d, J = 5.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.8, 141.7, 138.4, 135.6, 131.5 (3C), 129.1 (2C), 128.0 (2C), 127.3 (2C), 127.0, 126.7, 126.3, 125.9, 121.8, 109.9, 74.5, 71.2, 52.2, 48.4, 42.6, 27.22, 27.15, 17.4. IR (KBr): 3208, 3074, 3057, 3030, 2958, 2833, 1709, 1620, 1472, 1327, 1215, 1196, 1027, 741, 700 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{27}H_{25}N_2O$: 393.1961; found: 393.1959.

*(±)-(1aR,2R,6aR,6bS)-1′-Methyl-1a,6b-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indolin]-2′-one (**4eba**).* The best yield has been found upon carrying out the reaction at room temperature for 12 h using cyclopropene **1e** (77 mg, 0.4 mmol), isatin **2b** (65 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by recrystallization from a mixture of hexane−CH_2Cl_2 furnished **4eba** as a single diastereomer. Colorless solid; yield: 151 mg (93%); mp 165−166 °C (hexane−CH_2Cl_2); R_f 0.68 (SiO_2, hexane−EtOAc, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, J = 7.3 Hz, 1H), 7.49 (d, J = 7.3 Hz, 2H), 7.32−7.23 (m, 3H), 7.19−7.08 (m, 2H), 6.98−6.85 (m, 5H), 6.60 (d, J = 7.7 Hz, 1H), 5.06−5.00 (m, 1H), 3.37−3.29 (m, 1H), 2.91 (s, 1H), 2.72−2.64 (m, 1H), 2.10−1.93 (m, 3H), 1.84 (d, J = 5.2 Hz, 1H), 1.82−1.73 (m, 1H), 1.49 (d, J = 5.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.1, 144.6, 138.3, 135.5, 131.4 (2C), 129.3 (3C), 129.2, 128.1 (2C), 127.2 (2C), 126.6, 126.3, 125.4, 121.9, 108.1, 74.6, 71.8, 52.2, 49.0, 43.2, 27.3, 27.2, 25.6, 17.1. IR (KBr): 3053, 2964, 2932, 2872, 1711, 1611, 1493, 1468, 1373, 1350, 1246, 1161, 1119, 988, 743, 697 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{28}H_{27}N_2O$: 407.2118; found: 407.2127.

*(±)-(1aR,2R,6aR,6bS)-1,1-Diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indolin]-2′-one (**4faa**).* Prepared according to general procedure **A** using cyclopropene **1f** (77 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1)

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furnished **4faa** as a single diastereomer. Colorless solid; yield: 74 mg (47%); mp 258−259 °C (MeOH); R_f 0.55 (SiO_2, hexane−EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (s, 1H, CONH), 7.57 (d, J = 7.0 Hz, 1H, $H_{arom.}$), 7.31−7.14 (m, 9H, $H_{arom.}$), 7.05 (t, J = 7.2 Hz, 1H, $H_{arom.}$), 6.88−6.83 (m, 2H, $H_{arom.}$), 6.68 (d, J = 7.5 Hz, 1H, $H_{arom.}$), 4.58−4.54 (m, 1H, CH), 2.67 (d, J = 7.3 Hz, 1H, $CH_{cycloprop.}$), 2.30 (dd, J = 7.2, 4.2 Hz, 1H, $CH_{cycloprop.}$), 2.24−2.11 (m, 3H, $2CH_2$), 1.98−1.84 (m, 3H, $2CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.0 (CO), 148.8 ($C_{arom.}$), 148.2 ($C_{arom.}$), 141.6 ($C_{arom.}$), 139.8 ($C_{arom.}$), 131.9 ($2CH_{arom.}$), 128.7 ($2CH_{arom.}$), 128.3 ($2CH_{arom.}$), 127.7 ($2CH_{arom.}$), 127.3 ($2CH_{arom.}$), 126.5 ($CH_{arom.}$), 125.9 ($CH_{arom.}$), 121.4 ($CH_{arom.}$), 109.4 ($CH_{arom.}$), 67.9 (C_{spiro}), 65.0 (CH), 45.3 ($C_{cycloprop.}$), 43.7 ($CH_{cycloprop.}$), 41.2 (CH_2), 30.1 ($CH_{cycloprop.}$), 27.3 (CH_2), 23.7 (CH_2). IR (KBr): 3186, 3082, 2925, 2823, 1717, 1691, 1616, 1470, 1408, 1320, 1293, 1208, 750, 699 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{27}H_{25}N_2O$: 393.1961; found: 393.1962.

*(±)-(1aR,2R,6aR,6bS)-1′-Methyl-1,1-diphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indolin]-2′-one (**4fba**).* Prepared according to general procedure **A** using cyclopropene **1f** (77 mg, 0.4 mmol), isatin **2b** (59 mg, 0.4 mmol), and *L*-proline (**3a**) (58 mg, 0.5 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished **4fba** as a single diastereomer. Colorless solid; yield: 83 mg (51%); mp 188−192 °C (MeOH); R_f 0.52 (SiO_2, hexane−EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57 (d, J = 7.0 Hz, 2H), 7.33−7.18 (m, 6H), 7.15 (t, J = 7.6 Hz, 2H), 7.04 (t, J = 7.1 Hz, 1H), 6.89 (t, J = 7.5 Hz, 1H), 6.82 (d, J = 7.7 Hz, 1H), 6.70 (d, J = 7.4 Hz, 1H), 4.63−4.55 (m, 1H), 3.20 (s, 3H), 2.59 (d, J = 7.4 Hz, 1H), 2.29 (dd, J = 7.3, 4.2 Hz, 1H), 2.22−2.12 (m, 2H), 2.08−2.04 (m, 1H), 2.00−1.80 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.1, 148.9, 144.6, 139.9, 131.9 (2C), 128.7, 128.2 (4C), 127.7 (2C), 127.3, 127.0, 126.5, 125.8, 121.4, 107.6, 67.7, 65.0, 45.2, 44.0, 41.2, 30.3, 27.4, 25.7, 23.7. IR (KBr): 3055, 2939, 2814, 1705, 1608, 1489, 1370, 1343, 1234, 1127, 753, 708 cm^{-1}. HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{28}H_{26}N_2NaO$: 429.1937; found: 429.1953.

General Procedure B for Three-Component Reaction of Cyclopropenes, Isatins, and Secondary α-Amino Acids - Sacrosine and *L*-4-Thiazolidinecarboxylic Acid. A mixture of the corresponding cyclopropene **1** (0.4 mmol), isatin **2b** or **2c** (0.4 mmol), and sarcosine (**3b**) or *L*-4-thiazolidinecarboxylic acid (**3c**) (0.5 mmol) was refluxed in 1-propanol (8 mL) for 4 h. After completion of the reaction as monitored by TLC, the solvent was removed under reduced pressure. The residue was recrystallized or chromatographed on silica gel to give the pure products **6** and **7**.

*Methyl (±)-(1R,2R,5S,6R)-1′-Benzyl-3-methyl-2′-oxo-1,5-diphenyl-3-azaspiro[bicyclo[3.1.0]hexane-2,3′-indoline]-6-carboxylate (**6acb**).* Prepared according to general procedure **B** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin **2c** (95 mg, 0.4 mmol), and sarcosine (**3b**) (45 mg, 0.5 mmol). Purification of the crude by PTLC (hexane−EtOAc, 4:1) and subsequent recrystallization from methanol furnished **6acb** as a single diastereomer. Colorless solid; yield: 126 mg (61%); mp 231−233 °C (MeOH); R_f 0.50 (SiO_2, hexane−EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70−7.67 (m, 3H), 7.36 (t, J = 7.5 Hz, 2H), 7.29−7.24 (m, 1H), 7.18−6.96 (m, 10H), 6.50 (d, J = 7.2 Hz, 2H), 6.39−6.34 (m, 1H), 4.97 (d, J = 16.0 Hz, 1H), 4.37 (d, J = 16.1 Hz, 1H), 3.97 (d, J = 9.1 Hz, 1H), 3.60 (s, 1H), 3.46 (d, J = 9.1 Hz, 1H), 3.37 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.0, 170.2, 143.7, 135.1, 134.7, 132.4, 131.2 (2C), 131.0 (2C), 129.5, 128.6 (2C), 127.8 (2C), 127.4 (2C), 127.1 (2C), 127.0, 126.8, 126.3 (2C), 124.6, 123.0, 109.2, 77.2, 65.1, 52.6, 51.2, 44.2, 43.0, 34.2, 29.7. IR (KBr): 3042, 3009, 2941, 2866, 1745, 1710, 1600, 1454, 1333, 1241, 1183, 1100, 972, 760, 697 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{34}H_{31}N_2O_3$: 515.2329; found: 515.2341.

*(±)-(1R,2R,5S,6R)-1′-Benzyl-3-methyl-1,5,6-triphenyl-3-azaspiro-[bicyclo[3.1.0]hexane-2,3′-indolin]-2′-one (**6bcb**) and (±)-(1S,2R,5R,6S)-1′-Benzyl-3-methyl-1,5,6-triphenyl-3-azaspiro-[bicyclo[3.1.0]hexane-2,3′-indolin]-2′-one (**7bcb**).* Prepared according to general procedure **B** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin **2c** (95 mg, 0.4 mmol), and sarcosine (**3b**) (45 mg, 0.5 mmol). Purification of the crude by PTLC (hexane−EtOAc, 5:1) furnished **6bcb** and **7bcb** as separated diastereomers. Data for major diastereomer **6bcb**: colorless solid; yield: 113 mg (53%); mp 218−220 °C (MeOH); R_f 0.64 (SiO_2, hexane−EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (dd, J = 7.6, 2.9 Hz, 1H), 7.60 (d, J = 6.9 Hz, 2H), 7.29−7.23 (m, 4H), 7.15−7.07 (m, 7H), 7.02−6.98 (m, 1H), 6.95−6.89 (m, 4H), 6.50 (d, J = 7.2 Hz, 2H), 6.45 (d, J = 7.4 Hz, 2H), 6.33 (dd, J = 7.7, 2.9 Hz, 1H), 5.00 (d, J = 16.1 Hz, 1H), 4.39 (d, J = 16.1 Hz, 1H), 4.04 (d, J = 9.0 Hz, 1H), 3.91 (s, 1H), 3.53 (d, J = 9.0 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.6, 143.7, 137.3, 135.2, 135.0, 132.8 (4C), 132.1, 130.9 (2C), 129.2, 128.6 (4C), 127.7 (2C), 127.5, 127.0, 126.9, 126.7, 126.5, 126.5, 126.3 (2C), 125.1, 124.5, 122.8, 109.0, 78.3, 66.3, 52.1, 43.0, 42.6, 34.5, 32.5. IR (KBr): 3025, 2928, 2861, 1710, 1602, 1496, 1465, 1352, 1173, 1098, 1000, 926, 750, 700 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{38}H_{33}N_2O$: 533.2587; found: 533.2586. Data for minor diastereomer **7bcb**: colorless solid; yield: 32 mg (15%); mp 224−226 °C (MeOH); R_f 0.42 (SiO_2, hexane−EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, J = 6.6 Hz, 1H), 7.41 (d, J = 6.9 Hz, 2H), 7.31−7.24 (m, 2H), 7.22−7.18 (m, 3H), 7.15−7.08 (m, 3H), 7.01−6.99 (m, 2H), 6.95−6.84 (m, 6H), 6.82−6.78 (m, 2H), 6.46−6.42 (m, 3H), 4.78−4.76 (m, 2H), 4.36 (s, 1H), 3.73 (d, J = 9.5 Hz, 1H), 3.65 (d, J = 9.5 Hz, 1H), 2.20 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.4, 142.5, 137.4, 135.6, 135.0, 133.0, 132.2 (2C), 132.0, 131.2 (2C), 128.6, 128.5 (2C), 128.0 (2C), 127.8, 127.3, 127.1 (2C), 127.0 (2C), 126.5, 126.3 (4C), 125.1, 124.9, 121.8, 109.5, 77.5, 67.3, 52.9, 43.8, 43.6, 35.1, 32.5. IR (KBr): 3039, 2943, 2793, 1717, 1603, 1497, 1350, 1175, 756, 701 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{38}H_{33}N_2O$: 533.2587; found: 533.2584.

*Methyl (±)-(3′R,5aR,6R,6aS,6bS)-1′-Benzyl-2′-oxo-5a,6a-diphenyl-1,3,5a,6,6a,6b-hexahydrospiro[cyclopropa[3,4]pyrrolo[1,2-c]-thiazole-5,3′-indoline]-6-carboxylate (**6acc**) and Methyl (±)-(3′R,5aS,6S,6aR,6bR)-1′-Benzyl-2′-oxo-5a,6a-diphenyl-1,3,5a,6,6a,6b-hexahydrospiro[cyclopropa[3,4]pyrrolo[1,2-c]-thiazole-5,3′-indoline]-6-carboxylate (**7acc**).* Prepared according to general procedure **B** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin **2c** (95 mg, 0.4 mmol), and *L*-4-thiazolidinecarboxylic acid (**3c**) (67 mg, 0.5 mmol). Purification of the crude by PTLC (hexane−EtOAc, 4:1) furnished **6acc** and **7acc** as an inseparable mixture in ratio 10:1, respectively. Data for mixture of diastereomers **6acc** and **7acc**: colorless amorphous powder; yield: 112 mg (50%). IR (KBr): 3071, 3052, 2964, 2824, 1737, 1706, 1613, 1489, 1467, 1355, 1288, 1172, 1008, 751, 698 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{35}H_{31}N_2O_3S$: 559.2050; found: 559.2049. NMR data for major diastereomer **6acc**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75−7.71 (m, 1H), 7.65 (d, J = 7.5 Hz, 2H), 7.38 (t, J = 7.5 Hz, 2H), 7.30−7.27 (m, 1H), 7.20−7.09 (m, 6H), 7.05−6.97 (m, 4H), 6.48 (d, J = 7.2 Hz, 2H), 6.40 (dd, J = 6.4, 2.2 Hz, 1H), 5.01 (d, J = 16.1 Hz, 1H), 4.78 (dd, J = 8.9, 5.4 Hz, 1H), 4.35 (d, J = 16.1 Hz, 1H), 3.66 (s, 1H), 3.66−3.62 (m, 2H), 3.41 (s, 3H), 2.84 (t, J = 9.0 Hz, 1H), 2.68 (dd, J = 9.1, 5.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.6, 169.7, 143.5, 134.8, 133.8, 132.1, 130.9 (2C), 130.8 (2C), 130.0, 128.7 (2C), 128.1 (2C), 127.6 (2C), 127.5, 127.4, 127.2, 126.3 (2C), 125.0, 124.8, 123.1, 109.6, 75.3, 72.5, 56.2, 51.4, 45.4, 44.9, 43.3, 29.8, 27.2.

*(±)-(3′R,5aR,6R,6aS,6bS)-1′-Methyl-5a,6,6a-triphenyl-1,3,5a,6,6a,6b-hexahydrospiro[cyclopropa[3,4]pyrrolo[1,2-c]-thiazole-5,3′-indolin]-2′-one (**6bbc**) and (±)-(3′R,5aS,6S,6aR,6bR)-1′-Methyl-5a,6,6a-triphenyl-1,3,5a,6,6a,6b-hexahydrospiro[cyclopropa[3,4]pyrrolo[1,2-c]thiazole-5,3′-indolin]-2′-one (**7bbc**).* Prepared according to general procedure **B** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin **2b** (65 mg, 0.4 mmol), and *L*-4-thiazolidinecarboxylic acid (**3c**) (67 mg, 0.5 mmol). Purification of the crude by PTLC (hexane−EtOAc, 4:1) furnished **6bbc** and **7bbc** as an inseparable mixture in ratio 5:1, respectively. Data for mixture of diastereomers **6bbc** and **7bbc**: colorless amorphous powder; yield: 94 mg (47%). IR (KBr): 3057, 3041, 2980, 2891, 1704, 1613, 1495, 1472, 1348, 1209, 1118, 1092, 1022, 905, 754, 730, 700 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{33}H_{29}N_2OS$: 501.1995; found: 501.2004. NMR data for major diastereomer **6bbc**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, J = 6.7 Hz, 1H), 7.49 (dd, J = 8.0, 1.4 Hz, 2H), 7.31−7.23 (m, 2H), 7.13 (t, J = 7.5 Hz, 2H), 7.03−6.77 (m, 9H), 6.54 (d, J = 7.7 Hz, 1H), 6.43 (d, J = 7.8 Hz, 2H), 4.83 (dd, J = 8.9, 5.3 Hz, 1H), 3.90 (s, 1H), 3.76 (d, J = 5.2 Hz, 1H), 3.72 (d, J = 5.2 Hz, 1H), 2.91 (t, J = 8.9 Hz, 1H), 2.80 (s, 3H), 2.67 (dd, J = 9.0, 5.3 Hz, 1H).

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^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.5, 144.2, 136.6, 134.1, 132.4 (4C), 132.3, 131.2, 131.0 (2C), 129.6, 128.0 (4C), 127.1, 127.0, 126.6 (2C), 125.4, 124.4, 122.7, 108.0, 76.4, 73.5, 56.6, 45.3, 44.0, 30.0, 29.6, 25.4.

General Procedure C for Three-Component Reaction of Cyclopropenes, Isatin, and Primary α-Amino Acids. A mixture of the corresponding cyclopropene **1** (0.4 mmol), isatin (**2a**) (0.4 mmol), and α-amino acid **3e**−**o** (0.8 mmol) in a 3:1 mixture of MeOH−H_2O (10 mL) was refluxed for 4−12 h; the reaction progress was monitored by TLC and by the change in the reaction mixture color from red to yellow. The solvent was evaporated under reduced pressure. The crude mixture was subjected by silica gel chromatography to obtain the pure products **8**. The compound **8bak** can also be purified by recrystallization from methanol (a gram-scale reaction).

*Methyl (±)-(1R,2R,4R,5S,6R)-4-Ethyl-2′-oxo-1,5-diphenyl-3-azaspiro[bicyclo[3.1.0]hexane-2,3′-indoline]-6-carboxylate (**8aae**).* Prepared according to general procedure **B** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-aminobutyric acid (**3e**) (82 mg, 0.8 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished **8aae** as a single diastereomer. Beige amorphous powder; yield: 72 mg (41%); R_f 0.28 (SiO_2, hexane−EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 7.2 Hz, 1H), 7.61−7.57 (m, 3H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.27−7.20 (m, 2H), 7.15 (td, *J* = 7.6, 0.9 Hz, 1H), 7.02−6.88 (m, 5H), 6.56 (d, *J* = 7.6 Hz, 1H), 4.35 (dd, *J* = 9.4, 3.4 Hz, 1H), 3.39 (s, 3H), 3.18 (s, 1H), 2.12 (br s, 1H), 1.60−1.50 (m, 1H), 1.49−1.37 (m, 1H), 0.87 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.6, 170.3, 141.2, 134.3, 132.0, 131.5 (2C), 130.7 (2C), 129.5, 128.5, 127.8 (2C), 127.2 (2C), 127.0 (2C), 124.1, 122.8, 109.8, 73.6, 68.6, 52.4, 51.3, 49.7, 26.2, 23.9, 11.3. IR (KBr): 3349, 3181, 3139, 3054, 2941, 2891, 1736, 1710, 1623, 1472, 1341, 1198, 747, 708 cm^{-1}. HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{27}N_2O_3$: 439.2016; found: 439.2017.

*(±)-(1R,2R,4R,5S,6R)-4-Isopropyl-1,5,6-triphenyl-3-azaspiro-[bicyclo[3.1.0]hexane-2,3′-indolin]-2′-one (**8baf**).* Prepared according to general procedure **C** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-valine (**3f**) (94 mg, 0.8 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished **8baf** as a single diastereomer. Colorless amorphous powder; yield: 83 mg (44%); R_f 0.46 (SiO_2, hexane−EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 7.3 Hz, 1H), 7.51−7.43 (m, 2H), 7.30−6.76 (m, 14H), 6.59 (d, *J* = 7.6 Hz, 1H), 6.46 (d, *J* = 7.4 Hz, 2H), 4.59 (d, *J* = 4.5 Hz, 1H), 3.70 (s, 1H), 2.08 (br s, 1H), 1.84−1.76 (m, 1H), 1.12 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.8, 141.0, 136.9, 135.1, 133.0 (4C), 131.5, 131.1 (2C), 129.6, 129.1, 127.5 (2C), 127.2, 126.8, 126.6 (4C), 125.2, 124.1, 122.6, 109.5, 73.3, 71.7, 50.4, 46.1, 29.8, 29.3, 21.1, 17.7. IR (KBr): 3249, 3030, 3005, 2958, 2863, 1712, 1621, 1496, 1470, 1189, 744, 702 cm^{-1}. HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{33}H_{31}N_2O$: 471.2431; found: 471.2428.

*(±)-(1R,2R,4R,5S,6R)-4-Isobutyl-1,5,6-triphenyl-3-azaspiro-[bicyclo[3.1.0]hexane-2,3′-indolin]-2′-one (**8bag**).* Prepared according to general procedure **C** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-leucine (**3g**) (105 mg, 0.8 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished an inseparable mixture of two diastereomers in ratio 6:1. Data for mixture of diastereomers: colorless amorphous powder; yield: 130 mg (67%). IR (KBr): 3253, 3045, 2954, 2896, 1714, 1621, 1497, 1471, 1193, 747, 701 cm^{-1}. HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{34}H_{33}N_2O$: 485.2587; found: 485.2597. NMR data for major diastereomer **8bag**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 7.3 Hz, 1H), 7.47 (d, *J* = 6.9 Hz, 2H), 7.34−7.14 (m, 6H), 7.08 (t, *J* = 7.4 Hz, 1H), 7.03−6.76 (m, 7H), 6.59 (d, *J* = 7.6 Hz, 1H), 6.45 (d, *J* = 7.5 Hz, 2H), 4.57 (dd, *J* = 9.7, 3.0 Hz, 1H), 3.39 (s, 1H), 2.25 (br s, 1H), 1.82−1.66 (m, 1H), 1.50 (ddd, *J* = 14.2, 9.8, 4.7 Hz, 1H), 1.27 (ddd, *J* = 13.4, 9.9, 3.2 Hz, 1H), 0.87 (d, *J* = 6.5 Hz, 3H, CH_3), 0.79 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.4, 141.1, 137.0, 134.5, 133.0 (4C), 131.6, 130.9 (3C), 129.2 (2C), 127.6 (2C), 127.2, 126.8, 126.6, 126.5 (2C), 125.2, 123.9, 122.6, 109.6, 74.4, 65.9, 51.6, 48.0, 40.0, 28.9, 25.6, 23.9, 21.6.

*(±)-(1R,2R,4R,5S,6R)-4-Benzyl-1,5,6-triphenyl-3-azaspiro[bicyclo-[3.1.0]hexane-2,3′-indolin]-2′-one (**8bah**).* Prepared according to general procedure **C** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-phenylalanine (**3h**) (132 mg, 0.8 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished **8bah** as a single diastereomer. Colorless amorphous powder; yield: 114 mg (55%); R_f 0.49 (SiO_2, hexane−EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 7.2 Hz, 1H), 7.54 (d, *J* = 7.0 Hz, 2H), 7.37−6.72 (m, 19H), 6.53 (d, *J* = 7.6 Hz, 1H), 6.41 (d, *J* = 7.5 Hz, 2H), 4.82 (dd, *J* = 9.1, 3.1 Hz, 1H), 3.54 (s, 1H), 2.83 (dd, *J* = 13.4, 3.0 Hz, 1H), 2.75 (dd, *J* = 13.4, 9.3 Hz, 1H), 2.20 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.6, 140.9, 139.2, 136.9, 134.3, 133.1 (2C), 132.5, 131.5, 131.0 (2C), 129.4 (5C), 129.2, 128.4 (2C), 127.8 (2C), 127.2, 126.8 (2C), 126.5 (2C), 126.1, 125.2, 124.3, 122.6, 109.4, 73.6, 68.1, 51.5, 47.0, 37.0, 29.1. IR (KBr): 3288, 3098, 3030, 1712, 1621, 1497, 1471, 1189, 751, 701 cm^{-1}. HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{37}H_{31}N_2O$: 519.2431; found: 519.2415.

*Methyl (±)-(1R,2R,4R,5S,6R)-4-(4-Hydroxybenzyl)-2′-oxo-1,5-diphenyl-3-azaspiro[bicyclo[3.1.0]hexane-2,3′-indoline]-6-carboxylate (**8aai**).* Prepared according to general procedure **C** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-tyrosine (**3i**) (145 mg, 0.8 mmol). Purification of the crude by PTLC (hexane−EtOAc, 1:1) furnished **8aai** as a single diastereomer. Colorless amorphous powder; yield: 122 mg (59%); R_f 0.49 (SiO_2, EtOAc−hexane, 3:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66−7.54 (m, 4H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.27 (t, *J* = 7.4 Hz, 1H), 7.13 (t, *J* = 7.3 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 7.00−6.84 (m, 7H), 6.59 (d, *J* = 8.4 Hz, 2H), 6.57 (br s, 1H), 6.45 (d, *J* = 7.6 Hz, 1H), 4.66 (dd, *J* = 10.2, 2.3 Hz, 1H), 3.40 (s, 3H), 3.34 (s, 1H), 2.74−2.68 (m, 1H), 2.56−2.48 (m, 1H), 1.83 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.4, 170.5, 154.5, 140.9, 133.9, 131.7, 131.5 (2C), 130.6 (2C), 130.3, 130.0 (2C), 129.5, 128.3, 128.0 (2C), 127.2 (3C), 127.1, 124.4, 122.9, 115.3 (2C), 109.9, 73.0, 67.8, 52.2, 51.4, 49.1, 36.0, 26.3. IR (KBr): 3349, 2985, 2855, 1713, 1621, 1515, 1472, 1446, 1196, 751, 699 cm^{-1}. HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{33}H_{29}N_2O_4$: 517.2122; found: 517.2100.

*(±)-(1R,2R,4R,5S,6R)-4-(4-Hydroxy-3,5-diiodobenzyl)-1,5,6-triphenyl-3-azaspiro[bicyclo[3.1.0]hexane-2,3′-indolin]-2′-one (**8baj**).* Prepared according to general procedure **C** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and 3,5-diiodo-*L*-tyrosine (**3j**) (346 mg, 0.8 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished **8baj** as a single diastereomer. Light gray amorphous powder; yield: 132 mg (42%); R_f 0.66 (SiO_2, hexane−EtOAc, 3:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 7.3 Hz, 1H), 7.51−7.47 (m, 4H), 7.36−6.75 (m, 14H), 6.55 (d, *J* = 7.5 Hz, 1H), 6.39 (d, *J* = 7.3 Hz, 2H), 5.59 (br s, 1H, OH), 4.74 (dd, *J* = 8.9, 3.7 Hz, 1H), 3.53 (s, 1H), 2.69 (dd, *J* = 13.7, 3.6 Hz, 1H), 2.61 (dd, *J* = 13.7, 8.9 Hz, 1H), 1.97 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.7, 152.0, 139.7 (2C), 139.5, 136.5, 133.0 (2C), 131.1, 130.9 (4C), 129.4, 128.6, 127.7 (2C), 127.3 (2C), 127.1, 127.0 (2C), 126.6 (4C), 125.4, 122.8, 109.6, 82.2 (2C), 73.5, 68.0, 51.3, 46.7, 35.4, 29.2. IR (KBr): 3394, 3217, 3086, 2999, 2941, 2870, 1716, 1621, 1470, 1320, 1188, 749, 704 cm^{-1}. HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{37}H_{29}I_2N_2O_2$: 787.0313; found: 787.0301.

*(±)-(1R,2R,4R,5S,6R)-1,4,5,6-Tetraphenyl-3-azaspiro[bicyclo-[3.1.0]hexane-2,3′-indolin]-2′-one (**8bak**).* Prepared according to general procedure **C** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *DL*-phenylglycine (**3k**) (121 mg, 0.8 mmol). Purification of the crude by PTLC (hexane−EtOAc, 3:1) furnished **8bak** as a single diastereomer. Colorless solid; yield: 139 mg (69%); mp > 260 °C (MeOH); R_f 0.44 (SiO_2, hexane−EtOAc, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 7.2 Hz, 1H), 7.33−7.11 (m, 13H), 7.07 (s, 1H), 7.02−6.84 (m, 7H), 6.61 (d, *J* = 7.6 Hz, 1H), 6.38 (d, *J* = 7.6 Hz, 2H), 5.76 (s, 1H), 3.85 (s, 1H), 2.50 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.1, 140.9, 139.2, 136.7, 133.9, 133.5 (2C), 132.5 (2C), 131.4, 130.9 (2C), 129.5, 129.3, 127.8 (2C), 127.4 (3C), 127.2 (4C), 126.9, 126.8, 126.4 (2C), 125.1, 124.5, 122.8, 109.6, 73.6, 69.8, 51.3, 48.4, 29.1. IR (KBr): 3321, 3184, 3058, 3042, 2875, 1694, 1619, 1495, 1468, 1328, 1303, 1201, 1034, 758, 702 cm^{-1}.

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HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{36}H_{29}N_2O$: 505.2274; found: 505.2293.

*(±)-Methyl (1R,2R,4R,5S,6R)-4-((1H-Indol-3-yl)methyl)-2′-oxo-1,5-diphenyl-3-azaspiro[bicyclo[3.1.0]hexane-2,3′-indoline]-6-carboxylate (**8aal**).* Prepared according to general procedure **C** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-tryptophan (**3l**) (163 mg, 0.8 mmol). Purification of the crude by PTLC (hexane−EtOAc, 1:1) furnished **8aal** as a single diastereomer. Colorless solid; yield: 104 mg (48%); mp > 260 °C (MeOH−H_2O); R_f 0.57 (SiO_2, EtOAc−hexane, 3:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (s, 1H), 7.71−7.64 (m, 3H), 7.48−7.36 (m, 3H), 7.35−7.29 (m, 2H), 7.22−6.90(m, 10H), 6.82 (s, 1H), 6.51 (d, J = 7.4 Hz, 1H), 4.81 (dd, J = 10.0, 2.3 Hz, 1H), 3.44 (s, 1H), 3.42 (s, 3H), 2.94 (dd, J = 14.2, 2.3 Hz, 1H), 2.88−2.79 (m, 1H), 2.13 (br s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 179.1, 170.0, 143.0, 136.4, 135.4, 133.0, 131.9 (2C), 131.0 (2C), 129.7, 128.4, 128.2 (2C), 127.6, 127.3 (2C), 127.2, 127.0, 124.8, 123.5, 121.8, 121.2, 118.5, 118.2, 112.2, 111.7, 109.6, 74.6, 69.2, 52.9, 51.7, 50.3, 25.7, 25.2. IR (KBr): 3390, 3241, 3054, 2987, 2891, 1746, 1711, 1620, 1472, 1174, 749 cm^{-1}. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{35}H_{29}N_3NaO_3$: 562.2101; found: 562.2117.

*(±)-(1R,2R,4R,5S,6R)-4-(2-(Methylthio)ethyl)-1,5,6-triphenyl-3-azaspiro[bicyclo[3.1.0]hexane-2,3′-indolin]-2′-one (**8bam**).* Prepared according to general procedure **C** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-methionine (**3m**) (119 mg, 0.8 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished **8bam** as a single diastereomer. Colorless amorphous powder; yield: 117 mg (58%); R_f 0.30 (SiO_2, hexane−EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, J = 7.3 Hz, 1H), 7.47 (d, J = 6.9 Hz, 2H), 7.32−7.22 (m, 5H), 7.19 (td, J = 7.7, 1.2 Hz, 1H), 7.09 (td, J = 7.6, 0.6 Hz, 1H), 7.04−6.78 (m, 7H), 6.59 (d, J = 7.6 Hz, 1H), 6.43 (d, J = 7.3 Hz, 2H), 4.60 (dd, J = 8.3, 4.0 Hz, 1H), 3.49 (s, 1H), 2.54 (ddd, J = 12.7, 9.2 Hz, 6.2 Hz, 1H), 2.45 (ddd, J = 12.7, 9.1, 6.7 Hz, 1H), 2.20 (br s, 1H), 2.02 (s, 3H), 1.90−1.76 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.5, 141.0, 136.7, 134.2, 133.0 (2C), 131.3, 130.9 (3C), 129.3, 129.1, 127.8 (2C), 127.2, 126.9 (2C), 126.6 (4C), 125.3, 124.1, 122.7, 109.6, 74.2, 67.2, 51.5, 47.4, 31.7, 30.6, 29.1, 15.5. IR (KBr): 3250, 3033, 3010, 2914, 1711, 1620, 1496, 1471, 1322, 1195, 745, 699 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{33}H_{31}N_2OS$: 503.2152; found: 503.2170.

*(±)-2-((1R,2R,4R,5S,6R)-2′-Oxo-1,5,6-triphenyl-3-azaspiro-[bicyclo[3.1.0]hexane-2,3′-indolin]-4-yl)acetamide (**8ban**).* Prepared according to general procedure **C** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-asparagine (**3n**) (106 mg, 0.8 mmol). Purification of the crude by PTLC (EtOAc) furnished **8ban** as a single diastereomer. Colorless amorphous powder; yield: 87 mg (45%); R_f 0.44 (SiO_2, EtOAc). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.94 (s, 1H), 7.72 (d, J = 7.2 Hz, 1H), 7.36−7.21 (m, 6H), 7.15 (t, J = 7.5 Hz, 1H), 7.03 (t, J = 7.4 Hz, 1H), 6.96−6.63 (m, 9H), 6.55 (d, J = 7.6 Hz, 1H), 6.38 (d, J = 7.4 Hz, 2H), 4.52 (m, 1H), 3.53 (s, 1H), 3.53−3.49 (m, 1H), 2.39 (dd, J = 14.1, 10.6 Hz, 1H), 2.03 (d, J = 13.2 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 179.7, 173.2, 143.0, 137.5, 134.9, 132.9 (2C), 132.4, 130.9 (2C), 129.6, 129.2, 128.2 (4C), 127.4 (2C), 127.2, 127.1, 126.9 (2C), 125.5, 124.6, 121.8, 109.6, 74.7, 65.7, 57.5, 47.7, 36.6, 28.1. IR (KBr): 3500 (br), 1732, 1670, 1621, 1474, 1446, 753, 705 cm^{-1}. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{32}H_{27}N_3NaO_2$: 508.1995; found: 508.2002.

*Methyl 4-((S)-sec-Butyl)-2′-oxo-1,5-diphenyl-3-azaspiro[bicyclo-[3.1.0]hexane-2,3′-indoline]-6-carboxylate (**8aao**).* Prepared according to general procedure **C** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-isoleucine (**3o**) (105 mg, 0.8 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished an inseparable mixture of two diastereomers **8aao** in ratio 1.9:1. Data for mixture of diastereomers **8aao**: colorless amorphous powder; yield: 106 mg (57%). IR (KBr): 3326, 3037, 2962, 2802, 1713, 1621, 1471, 1446, 1288, 1194, 750, 698 cm^{-1}. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{30}H_{30}N_2NaO_3$: 489.2149; found 489.2163. NMR data for major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, J = 7.2 Hz, 1H), 7.62−7.57 (m, 2H), 7.38−6.85 (m, 11H), 6.58 (d, J = 7.6 Hz, 1H), 4.62 (d, J = 3.9 Hz, 1H), 3.43 (s, 3H), 3.42 (s, 1H), 2.05 (br s, 1H), 1.71−1.11 (m, 3H), 1.09 (t, J = 6.8 Hz, 3H), 0.78 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.0, 170.3, 141.1−109.6 (18C), 72.7, 69.0, 51.3, 50.6, 47.9, 35.3, 27.8, 27.1, 13.8, 11.7. NMR data for minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, J = 7.2 Hz, 1H), 7.62−7.57 (m, 2H), 7.38−6.85 (m, 11H), 6.58 (d, J = 7.6 Hz, 1H), 4.55 (d, J = 5.2 Hz, 1H), 3.44 (s, 3H), 3.38 (s, 1H), 2.05 (br s, 1H), 1.71−1.11 (m, 3H), 0.87 (t, J = 7.3 Hz, 3H), 0.79−0.75 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.1, 170.4, 141.3−109.4 (18C), 73.3, 70.9, 51.1, 50.6, 47.8, 36.5, 27.1, 24.7, 16.6, 11.5.

*4-((S)-sec-Butyl)-1,5,6-triphenyl-3-azaspiro[bicyclo[3.1.0]hexane-2,3′-indolin]-2′-one (**8bao**).* Prepared according to general procedure **C** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and *L*-isoleucine (**3o**) (105 mg, 0.8 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished an inseparable mixture of two diastereomers **8bao** (116 mg, 60%) in ratio 2.3:1. Data for mixture of diastereomers **8bao**: colorless amorphous powder; yield: 116 mg (60%). IR (KBr), cm^{-1}: 3394, 3252, 3031, 2961, 1711, 1621, 1497, 1470, 1322, 1192, 744, 702 cm^{-1}. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{34}H_{32}N_2NaO$: 507.2407; found 507.2412. NMR data for major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71−6.41 (m, 20H), 4.72 (d, J = 3.7 Hz, 1H), 3.71 (s, 1H), 2.20 (br s, 1H), 1.72−1.18 (m, 3H), 1.15 (d, J = 6.7 Hz, 3H), 0.80 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.7, 141.3−109.4 (24C), 73.3, 69.7, 50.0, 46.1, 35.3, 30.0, 27.9, 13.9, 11.8; NMR data for minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71−6.41 (m, 20H), 4.66 (d, J = 4.8 Hz, 1H), 3.69 (s, 1H), 2.20 (br s, 1H), 1.72−1.18 (m, 3H), 0.88 (d, J = 7.4 Hz, 3H), 0.87 (t, J = 5.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.8, 141.3−109.4 (24C), 73.3, 71.6, 50.5, 45.7, 36.5, 30.1, 24.6, 16.7, 11.8.

General Procedure D for Three-Component Reaction of Cyclopropenes, Isatin, and Dipeptide Gly-Gly. A mixture of the corresponding cyclopropene **1** (0.4 mmol), isatin (**2a**) (0.4 mmol), and glycylglycine (**9**) (0.8 mmol) in a 3:1 mixture of EtOH−H_2O (10 mL) was refluxed for 6−8 h; the reaction progress was monitored by TLC and by the change in the reaction mixture color from red to yellow. The solvent was evaporated under reduced pressure. The crude mixture was purified by recrystallization or silica gel chromatography to give the pure products **10**.

*(±)-2-((1R,2R,4S,5S,6R)-6-(Methoxycarbonyl)-2′-oxo-1,5-diphenyl-3-azaspiro[bicyclo[3.1.0]hexane-2,3′-indolin]-4-ylcarboxamido)-acetic Acid (**10a**).* Prepared according to general procedure **D** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and glycyglycine (**9**) (106 mg, 0.8 mmol). Purification of the crude by PTLC (CH_2Cl_2−MeOH, 10:1) furnished **10a** as a single diastereomer. Colorless solid; yield: 117 mg (57%); mp 239−240 °C ($CHCl_3$); R_f 0.42 (CH_2Cl_2−MeOH, 10:1). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.47 (br s, 1H), 10.04 (s, 1H), 8.02 (t, J = 5.8 Hz, 1H), 7.70 (d, J = 7.3 Hz, 1H), 7.48 (d, J = 7.4 Hz, 2H), 7.30 (t, J = 7.5 Hz, 2H), 7.24−7.17 (m, 2H), 7.10 (t, J = 7.5 Hz, 1H), 7.03−6.83 (m, 5H), 6.57 (d, J = 7.6 Hz, 1H), 4.66 (d, J = 6.2 Hz, 1H), 3.92 (d, J = 6.5 Hz, 1H), 3.77 (dd, J = 17.3, 6.1 Hz, 1H), 3.67 (dd, J = 17.3, 5.6 Hz, 1H), 3.48 (s, 1H), 3.40 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 179.4, 171.4, 169.9, 169.4, 142.9, 133.8, 132.3 (2C), 132.2, 131.1 (2C), 129.9, 128.4, 127.7 (2C), 127.4 (2C), 127.3, 127.1, 124.6, 122.1, 109.8, 73.9, 69.4, 51.9, 51.7, 48.1, 41.2, 26.0. IR (KBr): 3400 (br), 1718, 1620, 1538, 1471, 1346, 1196, 754, 700 cm^{-1}. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{29}H_{25}N_3NaO_6$: 534.1636; found: 534.1643.

*(±)-2-((1R,2R,4S,5S,6R)-2′-Oxo-1,5,6-triphenyl-3-azaspiro-[bicyclo[3.1.0]hexane-2,3′-indolin]-4-ylcarboxamido)acetic Acid (**10b**).* Prepared according to general procedure **D** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin (**2a**) (59 mg, 0.4 mmol), and glycylglycine (**9**) (106 mg, 0.8 mmol). Purification of the crude by recrystallization from chloroform furnished **10b** (148 mg, 70%) as a single diastereomer. Colorless solid; yield: 148 mg (70%); mp > 260 °C ($CHCl_3$); R_f 0.42 (CH_2Cl_2−MeOH, 10:1). ^{1}H NMR (400 MHz, DMSO-d_6), zwitterionic form: δ = 10.29 (s, 1H), 8.32−8.26 (m, 1H), 7.89 (d, J = 7.3 Hz, 1H), 7.40−6.63 (m, 17H), 6.58 (d, J = 7.6 Hz, 1H), 6.33 (d, J = 7.3 Hz, 2H), 4.97 (s, 1H, CH), 3.91 (s, 1H), 3.80 (dd, J = 17.3, 6.0 Hz, 1H), 3.67 (dd, J = 17.3, 5.2 Hz, 1H). ^{13}C NMR

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(100 MHz, DMSO-d_6): δ = 176.8, 171.0, 168.0, 143.2, 136.1, 133.3 (2C), 132.7, 132.4, 131.2 (2C), 130.7, 130.3, 128.0 (2C), 127.7 (6C), 126.9 (2C), 126.2, 126.0, 122.1, 110.2, 74.1, 68.4, 49.5, 45.5, 41.3, 28.9. IR (KBr): 3400 (br), 1712, 1690, 1619, 1544, 1472, 1395, 1200, 756, 701 cm^{-1}. HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{33}H_{28}N_3O_4$: 530.2074; found: 530.2086.

General Procedure E for Three-Component Reaction of Cyclopropenes, *N*-Methylisatin, and Benzylamine. A mixture of the corresponding cyclopropene **1** (0.4 mmol), isatin **2b** (0.4 mmol), and benzylamine **11A** or **11B** (0.8 mmol) in a 3:1 mixture of MeOH−benzene (10 mL) was refluxed for 3 h. After completion of the reaction monitored by TLC, the solvent was evaporated under reduced pressure. The residue recrystallized from methyl alcohol to produce the pure products **8**.

*Methyl (±)-(1R,2R,4R,5S,6R)-1′-Methyl-2′-oxo-1,4,5-triphenyl-3-azaspiro[bicyclo[3.1.0]hexane-2,3′-indoline]-6-carboxylate (**8abA**).* Prepared according to general procedure **E** using cyclopropene **1a** (100 mg, 0.4 mmol), isatin **2b** (65 mg, 0.4 mmol), and benzylamine (**11A**) (86 mg, 0.8 mmol). Purification of the crude by recrystallization from methanol furnished **8abA** as an inseparable mixture of two diastereomers in ratio 13:1. Data for the mixture of diastereomers: colorless solid; yield: 158 mg (79%). IR (KBr): 3350, 3077, 3041, 2988, 1744, 1708, 1615, 1494, 1471, 1347, 1165, 956, 746, 699 cm^{-1}. HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{33}H_{28}N_2NaO_3$: 523.1992, found: 523.1987. NMR data for major diastereomer **8abA**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, J = 6.6 Hz, 1H), 7.43−7.41 (m, 2H), 7.36−7.22 (m, 8H), 7.15−7.13 (m, 2H), 7.03−6.91 (m, 5H), 6.59 (d, J = 7.6 Hz, 1H), 5.74 (s, 1H), 3.51 (s, 1H), 3.29 (s, 3H), 2.83 (s, 3H), 2.33 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.9, 170.0, 143.9, 138.5, 133.7, 132.0 (2C), 131.8, 130.5 (2C), 129.6, 128.2, 127.9 (2C), 127.6 (4C), 127.2 (2C), 127.1, 127.0 (2C), 124.1, 123.0, 108.0, 73.0, 69.2, 52.4, 51.1, 50.4, 26.3, 25.5.

*(±)-(1R,2R,4R,5S,6R)-1′-Methyl-1,4,5,6-tetraphenyl-3-azaspiro-[bicyclo[3.1.0]hexane-2,3′-indolin]-2′-one (**8bbA**).* Prepared according to general procedure **E** using cyclopropene **1b** (107 mg, 0.4 mmol), isatin **2b** (65 mg, 0.4 mmol), and benzylamine (**11A**) (86 mg, 0.8 mmol). Purification of the crude by recrystallization from methanol furnished **8bbA** as a single diastereomer. Colorless solid; yield: 180 mg (87%); mp 204−205 °C (MeOH); R_f 0.49 (SiO_2, hexane−EtOAc, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, J = 7.0 Hz, 1H), 7.32−7.15 (m, 14H), 6.99−6.84 (m, 6H), 6.55 (d, J = 7.8 Hz, 1H), 6.40 (d, J = 7.5 Hz, 2H), 5.81 (s, 1H), 3.84 (s, 1H), 2.84 (s, 3H), 2.44 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.6, 143.9, 139.4, 136.8, 133.9, 133.5 (2C), 132.3, 131.3, 131.0 (2C), 129.3, 128.9, 127.8 (2C), 127.4 (4C), 127.3 (3C), 127.0, 126.9, 126.8, 126.4 (2C), 125.1, 123.9, 122.7, 107.9, 73.8, 70.0, 51.7, 48.5, 29.1, 25.5. IR (KBr): 3342, 3103, 3067, 3008, 2988, 2891, 1701, 1616, 1501, 1451, 1370, 1298, 1195, 1025, 751, 696 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{37}H_{31}N_2O$: 519.2431, found: 519.2427.

*(±)-(1R,2R,4R,5S,6R)-1′-Methyl-2′-oxo-1,4,5-triphenyl-3-azaspiro-[bicyclo[3.1.0]hexane-2,3′-indoline]-6-carbonitrile (**8dbA**).* Prepared according to general procedure **E** using cyclopropene **1d** (87 mg, 0.4 mmol), isatin **2b** (65 mg, 0.4 mmol), and benzylamine (**11A**) (86 mg, 0.8 mmol). Purification of the crude by recrystallization from methanol furnished **8dbA** as a single diastereomer. Colorless solid; yield: 170 mg (91%); mp 252−253 °C (MeOH); R_f 0.27 (SiO_2, hexane−EtOAc, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, J = 7.3 Hz, 2H), 7.72 (d, J = 7.2 Hz, 1H), 7.40−7.23 (m, 8H), 7.14−7.08 (m, 5H), 7.05−7.01 (m, 2H), 6.62 (d, J = 7.8 Hz, 1H), 5.87 (d, J = 3.7 Hz, 1H), 3.34 (s, 1H), 2.87 (s, 3H), 2.38 (d, J = 4.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.2, 143.7, 137.8, 132.6, 131.2 (4C), 130.1, 129.5, 128.5 (2C), 128.3, 128.2 (2C), 128.1, 128.0, 127.7 (2C), 127.1, 126.7 (2C), 123.8, 123.2, 118.5, 108.3, 71.9, 67.0, 50.9, 48.4, 25.7, 11.7. IR (KBr): 3362, 3081, 3024, 2230, 1699, 1618, 1496, 1469, 1374, 1124, 1094, 1028, 754, 704 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{32}H_{26}N_3O$: 468.2070, found: 468.2060.

*(±)-(1R,2R,4R,5S)-1′-Methyl-1,4,5-triphenyl-3-azaspiro[bicyclo-[3.1.0]hexane-2,3′-indolin]-2′-one (**8ebA**).* Prepared according to general procedure **E** using cyclopropene **1e** (77 mg, 0.4 mmol), isatin **2b** (65 mg, 0.4 mmol), and benzylamine (**11A**) (86 mg, 0.8 mmol). Purification of the crude by recrystallization from methanol furnished **8ebA** as a single diastereomer. Colorless solid; yield: 166 mg (94%); mp 167−168 °C (MeOH); R_f 0.52 (SiO_2, hexane−EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, J = 7.2 Hz, 1H), 7.55 (d, J = 7.3 Hz, 2H), 7.39−7.34 (m, 2H), 7.31−7.22 (m, 6H), 7.20−7.13 (m, 2H), 7.00−6.88 (m, 5H), 6.59 (d, J = 7.7 Hz, 1H), 6.05 (s, 1H), 2.91 (s, 3H), 2.36 (d, J = 4.9 Hz, 1H), 2.30 (br s, 1H), 1.45 (d, J = 4.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.5, 143.7, 140.3, 137.6, 135.3, 131.3 (2C), 130.1 (2C), 129.2, 129.1, 128.1 (2C), 128.0 (2C), 127.2 (5C), 126.8, 126.6, 123.6, 122.6, 107.9, 72.6, 65.7, 47.0, 42.3, 25.6, 14.4. IR (KBr): 3312, 3071, 2952, 2875, 1699, 1611, 1601, 1493, 1470, 1447, 1371, 1348, 1300, 1092, 1024, 755, 698 cm^{-1}. HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{31}H_{26}N_2NaO$: 465.1937, found: 465.1940.

*(±)-(1R,2R,4R,5S,6R)-4-(4-Fluorophenyl)-1′-methyl-2′-oxo-1,5-diphenyl-3-azaspiro[bicyclo[3.1.0]hexane-2,3′-indoline]-6-carbonitrile (**8dbB**).* Prepared according to general procedure **E** using cyclopropene **1d** (87 mg, 0.4 mmol), isatin **2b** (65 mg, 0.4 mmol), and benzylamine **11B** (100 mg, 0.8 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished **8dbB** as a single diastereomer. Colorless solid; yield: 163 mg (84%); mp 249−251 °C (MeOH); R_f 0.37 (SiO_2, hexane−EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76−7.68 (m, 3H), 7.42−7.22 (m, 5H), 7.12−6.92 (m, 9H), 6.62 (d, J = 7.7 Hz, 1H), 5.84 (d, J = 4.2 Hz, 1H), 3.28 (s, 1H), 2.87 (s, 3H), 2.38 (d, J = 4.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.1, 162.2 (d, J = 246.5 Hz), 143.7, 133.4 (d, J = 2.9 Hz), 132.4, 131.2 (4C), 130.1, 129.4, 128.5 (2C), 128.3 (d, J = 11.7 Hz, 2C), 128.1 (2C), 127.7 (2C), 126.9, 123.8, 123.2, 118.4, 115.1 (d, J = 21.3 Hz, 2C), 108.4, 71.8, 66.3, 50.9, 48.4, 25.7, 11.6. ^{19}F NMR (376 MHz, $CDCl_3$): δ = −114.4. IR (KBr): 3364, 3083, 3049, 2991, 2864, 2232, 1701, 1612, 1510, 1495, 1468, 1445, 1371, 1352, 1304, 1217, 1161, 1119, 1094, 1078, 841, 756, 704 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{32}H_{25}FN_3O$: 486.1976, found: 486.1973.

General Procedure F for Oxidation of Spiroazabicyclo-[3.1.0]hexanes to Spiroazabicyclo[3.1.0]hex-3-nes. A stirred solution of the cycloadduct **8bak** or **8bbA** (0.25 mmol) and DDQ (0.75 mmol) in dry-xylene (10 mL) was heated at 110 °C under an argon atmosphere for 3 h. The reaction mixture was cooled and diluted with dichloromethane, and washed with aqueous K_2CO_3 (10%) and water. The washed organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude mixture was purified by silica gel chromatography to obtain spiroazabicyclo[3.1.0]-hex-3-enes **12**.

*(±)-(1R,2R,5S,6S)-1,4,5,6-Tetraphenyl-3-azaspiro[bicyclo[3.1.0]-hex[3]ene-2,3′-indolin]-2′-one (**12a**).* Prepared according to general procedure **F** using cycloadduct **8bak** (126 mg, 0.25 mmol) and DDQ (170 mg, 0.75 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished **12a**. Colorless solid; yield: 60 mg (48%); mp 201−202 °C (MeOH−H_2O); R_f 0.25 (SiO_2, hexane−EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73−7.71 (m, 2H), 7.65−7.56 (m, 3H), 7.39−7.19 (m, 8H), 7.14−6.99 (m, 9H), 6.73 (d, J = 7.7 Hz, 1H), 6.58 (d, J = 7.4 Hz, 2H), 3.27 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.0, 174.7, 141.6, 134.9, 133.1 (2C), 131.5, 131.1, 130.9 (4C), 130.6, 129.6, 129.3 (4C), 128.9, 128.0 (4C), 127.9, 127.5, 127.3, 127.0 (2C), 126.3, 124.6, 123.0, 110.0, 86.7, 53.2, 49.9, 39.8. IR (KBr): 3348, 3028, 3010, 2970, 1728, 1710, 1611, 1494, 1469, 1327, 1255, 1178, 1039, 769, 705 cm^{-1}. HRMS (ESI): m/z [M + H]$^+$calcd for $C_{36}H_{27}N_2O$: 503.2118, found: 503.2135.

*(±)-(1R,2R,5S,6S)-1′-Methyl-1,4,5,6-tetraphenyl-3-azaspiro-[bicyclo[3.1.0]hex[3]ene-2,3′-indolin]-2′-one (**12b**).* Prepared according to general procedure **F** using cycloadduct **8bbA** (130 mg, 0.25 mmol) and DDQ (170 mg, 0.75 mmol). Purification of the crude by PTLC (hexane−EtOAc, 2:1) furnished **12b**. Colorless solid; yield: 79 mg (61%); mp 134−136 °C (MeOH−H_2O); R_f 0.38 (SiO_2, hexane−EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74−7.72 (m, 2H), 7.66−7.55 (m, 3H), 7.36−7.28 (m, 3H), 7.25−7.09 (m, 9H), 7.03−6.99 (m, 4H), 6.70 (d, J = 7.6 Hz, 1H), 6.59 (d, J = 7.8 Hz, 2H), 3.25 (s, 1H), 2.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.9, 173.5, 144.6, 135.1, 133.3, 133.1, 131.6, 131.1, 130.9 (4C), 130.5, 129.6, 129.2 (4C), 128.7, 128.0 (4C), 127.9, 127.4, 127.1, 127.0 (2C), 126.2,

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124.1, 123.0, 108.2, 86.8, 53.2, 50.1, 39.8, 25.9. IR (KBr): 3056, 3041, 2998, 1731, 1716, 1620, 1497, 1471, 1195, 753, 700 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{37}H_{29}N_2O$: 517.2274, found: 517.2270.

Chlorination of Cycloadduct 8bak with *N*-Chlorosuccinimide (NCS). To a suspension of *N*-chlorosuccinimide (80 mg, 0.6 mmol) in anhydrous diethyl ether (10 mL) was added the compound **8bak** (252 mg, 0.5 mmol) under an argon atmosphere. The reaction mixture was stirred for 72 h at ambient temperature. Upon completion, monitored by TLC, the mixture was diluted with water (20 mL). The organic layer was separated, and aqueous phase was extracted with ether (2 × 10 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by PTLC (hexane−EtOAc, 2:1) to obtain the title compound **13**.

*(±)-(1R,2R,4R,5S,6R)-3-Chloro-1,4,5,6-tetraphenyl-3-azaspiro-[bicyclo[3.1.0]hexane-2,3′-indolin]-2′-one (**13**).* Colorless solid; yield: 168 mg (52%); mp 149−151 °C (MeOH); R_f 0.42 (SiO_2, hexane−EtOAc, 3:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, J = 7.2 Hz, 1H), 7.45 (s, 1H), 7.35−7.06 (m, 14H), 7.03−6.80 (m, 6H), 6.67 (d, J = 7.6 Hz, 1H), 6.34 (d, J = 7.5 Hz, 2H), 5.79 (s, 1H), 4.01 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.1, 141.5, 135.8, 135.5, 133.5 (2C), 132.7, 130.9 (4C), 130.1, 128.9, 128.0 (4C), 127.6 (4C), 127.5, 127.3 (2C), 126.5 (2C), 126.3, 125.5, 124.8, 123.1, 109.8, 80.1, 78.5, 49.5, 48.1, 30.1. IR (KBr): 3057, 3029, 1723, 1613, 1495, 1470, 1370, 1351, 1090, 1024, 758, 698 cm^{-1}. HRMS (ESI): m/z $[M - Cl]$ calcd for $C_{36}H_{27}N_2O$: 503.2123, found: 503.2124.

Reduction of Cycloadduct 4bba with Lithium Aluminum Hydride (LAH). To a solution of $LiAlH_4$ (152 mg, 4.0 mmol) in anhydrous diethyl ether (15 mL) under an argon atmosphere was added cycloadduct **4bba** (241 mg, 0.5 mmol), and the reaction mixture was stirred at room temperature for 4 h. After that, the mixture was cooled to 0 °C and 2 mL of H_2O was added to this mixture. Then, 2 mL of a 10% NaOH solution and 2 mL of another portion of H_2O were added to it. The reaction mixture was stirred for 5 min at ambient temperature. The organic layer was separated, and the aqueous phase was extracted with ether (3 × 10 mL). The total organic mixture was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was recrystallized from MeOH to afford the 2-hydroxyindoline **14** as a single diastereomer. The compound **15** was synthesized similarly by refluxing the reaction mixture containing cycloadduct **4bba** (241 mg, 0.5 mmol) and $LiAlH_4$ (152 mg, 4.0 mmol) in anhydrous ether (15 mL) for 24 h.

*(±)-(1R,1aR,2R,2′R,6aR,6bS)-1′-Methyl-1,1a,6b-triphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indolin]-2′-ol (**14**).* Colorless solid; yield: 172 mg (71%); mp 194−196 °C (MeOH); R_f 0.56 (SiO_2, hexane−EtOAc, 3:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.82−7.73 (m, 2H), 7.34−7.13 (m, 7H), 7.08−6.93 (m, 4H), 6.78−6.69 (m, 2H), 6.46 (t, J = 7.5 Hz, 2H), 6.35 (d, J = 7.8 Hz, 1H), 6.23 (d, J = 7.1 Hz, 1H), 5.20 (br s, 1H), 4.71 (s, 1H), 4.34 (t, J = 7.0 Hz, 1H), 3.35−3.25 (m, 1H), 3.02 (s, 1H), 2.67−2.61 (m, 1H), 2.59 (s, 3H), 2.16−2.06 (m, 1H), 2.02−1.88 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.7, 136.9, 134.8, 133.7, 133.6, 132.4 (2C), 131.8, 130.6 (2C), 130.0, 127.8 (2C), 127.6, 127.4, 126.7 (4C), 125.8 (2C), 125.2, 117.3, 107.5, 92.5, 79.0, 78.1, 55.9, 51.3, 49.0, 34.0, 32.2, 28.2, 27.4. IR (KBr): 3302, 3037, 2962, 2847, 1603, 1486, 1445, 1299, 1134, 1095, 1075, 966, 748, 702 cm^{-1}. HRMS (ESI): m/z $[M - OH]^+$calcd for $C_{34}H_{31}N_2$: 467.2482, found: 467.2496.

*(±)-(1R,1aR,2R,6aR,6bS)-1′-Methyl-1,1a,6b-triphenyl-1a,4,5,6,6a,6b-hexahydro-1H-spiro[cyclopropa[a]pyrrolizine-2,3′-indoline] (**15**).* Colorless solid; yield: 202 mg (86%); mp 160−161 °C (MeOH); R_f 0.46 (SiO_2, hexane−EtOAc, 3:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, J = 7.3 Hz, 2H), 7.27−7.17 (m, 7H), 7.06−6.94 (m, 4H), 6.79 (t, J = 7.5 Hz, 2H), 6.50−6.45 (m, 4H), 4.27 (t, J = 7.0 Hz, 1H), 3.50 (d, J = 8.4 Hz, 1H), 3.31−3.25 (m, 1H), 3.17 (d, J = 8.5 Hz, 1H), 3.12 (s, 1H), 2.63 (s, 3H), 2.57−2.53 (m, 1H), 2.05−1.91 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.7, 137.5, 135.3, 134.9, 132.3 (2C), 130.7 (2C), 129.2, 129.0, 127.8 (2C), 127.4, 126.6 (2C), 126.5, 126.3, 125.4, 125.1, 117.1, 108.4, 76.8, 75.2, 66.9, 55.1, 51.0, 49.6, 36.4, 33.2, 27.5, 26.6. IR (KBr): 3027, 2927, 2855, 1603, 1488, 1444, 1299, 1272, 1190, 1158, 1113, 1028, 765, 739, 702 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{34}H_{33}N_2$: 469.2638, found: 469.2638.

Bioassay Details. *Tumor Cell Line.* The erythroleukemia cells K562 cell line was obtained from the Bank of cell cultures of the Institute of Cytology of the Russian Academy of Sciences. K562 cells were cultured in the RPMI-1640 medium (Biolot, Russia) with addition of 10% fetal calf serum (FCS) (Biolot, Russia) and 40 μg/mL gentamicin (Sigma, USA).

Treatment of K562 Cells. Cells were ceded at 24 well plates and treated with each compound at 25 μM concentration. Imatinib mesylate was used as a positive control at 10 μM concentration.[29] The cells were analyzed after treatment for 24, 48, and 72 h.

Evaluation of Proliferative Activity and Viability of K562 Cells by Flow Cytometry. For analysis of the cell viability and the cell number, propidium iodide (Invitrogen, USA) at a concentration of 0.05 mg/mL was added. After incubation for 5 min at room temperature, the samples were analyzed on a flow cytometer (Coulter Epics XL, Beckman Coulter, USA). The data were processed with ModFit LT software (Verity Software House, Topsham).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02505.

Crystallographic data for **4aaa** (CCDC 1497000) (CIF)
Crystallographic data for **4bca** (CCDC 1497001) (CIF)
Crystallographic data for **6bcb** (CCDC 1497002) (CIF)
Crystallographic data for **14** (CCDC 1520839) (CIF)
Copies of ^1H, ^{13}C NMR, ^{19}F NMR, and H−H NOESY NMR spectra for all new compounds, bioassay details, and X-ray data (PDF)

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Notes

The authors declare no competing financial interest.

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