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Synthesis of spirocyclic Δ^4 -isoxazolines via [3 + 2] cycloaddition of indanone-derived ketonitrones with alkynes†

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A [3 + 2] cycloaddition of indanone-derived nitrones and alkynes under mild conditions is developed, allowing facile synthesis of spirocyclic indenyl isoxazolines with structural diversity. The sequential protocol of generated *in situ* ketonitron from unsaturated ketones and *N*-alkylhydroxylamines is also achieved successfully, affording the desired products in considerable yield with moderate to good diastereoselectivity. Moreover, the spirocyclic product can be conveniently transformed into indenyl-based allylic alcohol and enamide.

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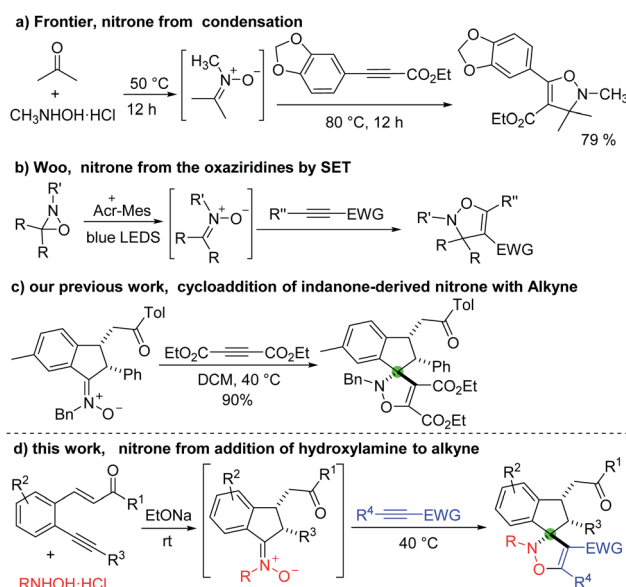
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Introduction

Isloxazolines are part of an important class of N,O-containing heterocycles, since they are well known for biological properties¹ and could be used as versatile intermediates for the synthesis of many complex compounds.² Among the many methods, the cycloaddition of nitrones has been widely used in the synthesis of this skeleton.³ Recently, one-pot cycloaddition reactions of nitrones generated *in situ* have attracted much attention due to their high efficiency and avoidance of complicated operation and the separation of unstable nitrones. Despite great progress being made in the cycloaddition of aldonitrones with cyclopropanes,⁴ olefins,⁵ and alkynes,⁶ however, the cycloaddition of ketonitrones generated *in situ* for preparation of 4-isoxazoline remains scarce. In 2009, Frontier and coworkers reported that the [3 + 2] dipolar cycloaddition of an electron-deficient alkyne and a ketonitron generated *in situ* from condensation of acetone and *N*-methylhydroxylamine gives an isolable isoxazoline in 79% yield (Scheme 1a).⁷ Recently, Woo developed an efficient visible-light photoredox-catalyzed [3 + 2] cycloaddition of oxaziridines with alkynes to give 4-isoxazoline in high yield, this novel strategy involves *in situ* generation of ketonitrones from oxaziridines through a SET way (Scheme 1b).⁸ However, most of these powerful approaches suffer from the use of transition metal catalysts and unstable

and expensive reagents,^{4,5,6c} or multistep manipulations as well as uneconomical atomic transformations.^{5f,6a} Consequently, the development of an environmentally friendly and atom-economical cycloaddition of novel nitron generated *in situ* for the synthesis of highly functionalized isoxazoline is still of great interest.

Spiroisoxazolines have been received intensive attention because the incorporation of a rigid spiro-ring can reduce the conformational entropy penalty upon binding with a protein target in modern drug discovery.⁹ However, the application of cycloaddition reaction of nitron to construct spiroisoxazolines



Scheme 1 Cycloadditions of ketonitron generated *in situ* with alkynes.

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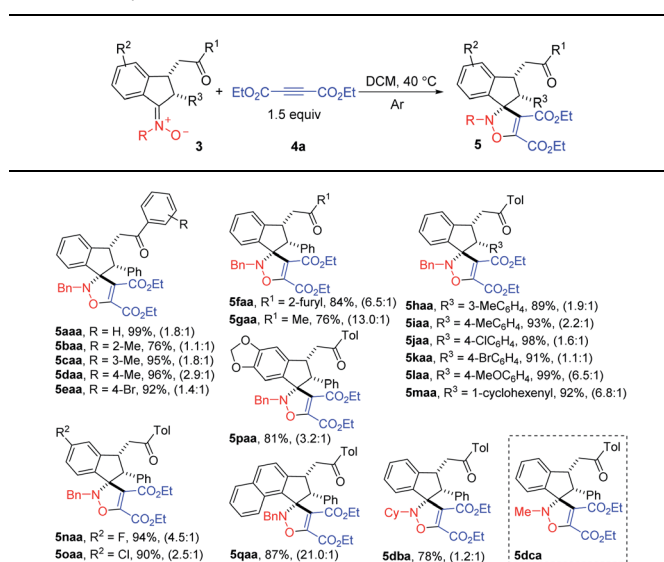
is largely undeveloped, because methods for the synthesis of cyclic ketonitrone are still not rich and mostly limited to specific substrates scope such as cyclic ketone derived nitrones,¹⁰ isatin ketonitrones,¹¹ sugar ketonitrones,¹² fluorenone nitrones.¹³ Therefore, only a few examples using these compounds as substrates to synthesize spirocyclic compounds have been reported. Oxyallyl cations,¹⁴ cyclopropanes,^{15f} aza-oxyallyl cations,¹⁵ olefins^{11a,b,d,12,16} gave the expected cycloadducts in high yields, while reactions with acetylenes seldom gave the corresponding spiroisoxazolines. Instead, non spiro products arising from transformations of the initially formed spiroisoxazoline are produced in these cases.^{13c,17} For example, in 2012, Anderson and co-workers reported that the reaction of alkynes with *N*-vinyl fluorenone nitrones provides the fluorene-tethered isoxazoles at high temperature *via* a cyclization and elimination process.^{13c} In contrast, Prathapan and co-workers discovered that the cycloadduct resulting from the reaction of *N*-phenyl fluorenone nitrones and electron deficient acetylenes was formed predominantly initially and then could undergo rearrangement easily to give 3(2*H*)-furanone at room temperature.^{17b} Therefore, the continuous development of novel cyclic ketonitrones for the discovery of spirocyclic drug candidates is highly desirable.

Recently, we developed a carbonyl-directed addition of *N*-alkylhydroxylamines to unactivated alkynes with high stereoselectivity. This strategy enables the facile synthesis of indanone-derived nitrones, which was subjected successfully to [3 + 2] cycloadditions with diethyl acetylenedicarboxylate (DEAD) in dichloromethane (DCM) to give spiro-isoxazoline in 90% yield (Scheme 1c).²⁰ This privilege skeleton prompted us to further expand the substrate scope. Herein, we wish to report our efforts on the [3 + 2] cycloaddition of indanone ketonitrones with alkynes under mild conditions (Scheme 1d).

Results and discussion

It was found that the amount of DEAD **4a** in cycloadditions could be decreased to 1.5 equivalent, and the same reactivity was observed. The relative configuration of product spiroindanyl isoxazoline **5** was assigned by its analogue X-ray diffraction analysis reported by us.²⁰ As shown in Table 1, a variety of *N*-benzyl indanone-derived nitrones underwent cycloadditions with DEAD **4a** in DCM at 40 °C smoothly, affording the corresponding spiroindanyl isoxazolines in good to excellent yields, albeit with low dr values (**5aaa–qaa**). It was interesting to find that when the R¹ group was methyl substituent, the nitrone **3ga** produced the desired products in higher dr value, compared to nitrones with aryl group at position R¹ (**5aaa–faa** vs. **5gaa**). Spiroindanyl isoxazolines could be obtained in excellent yields when indanone-derived nitrones **3ha–ma** were used as substrates. The reaction tolerated different groups at position R² in nitrones **3**, affording the desired products in good to excellent yields (**5naa–qaa**). It is worth noting that naphthalenyl isoxazoline **5qaa** was furnished in 87% yield with a high 21 : 1 dr, which may attribute to the steric hindrance effect. To our pleasure, *N*-cyclohexenyl indanone-derived nitrone **3db** was also an effective substrate for this reaction to

Table 1 Scope of indanone-derived nitrone^a

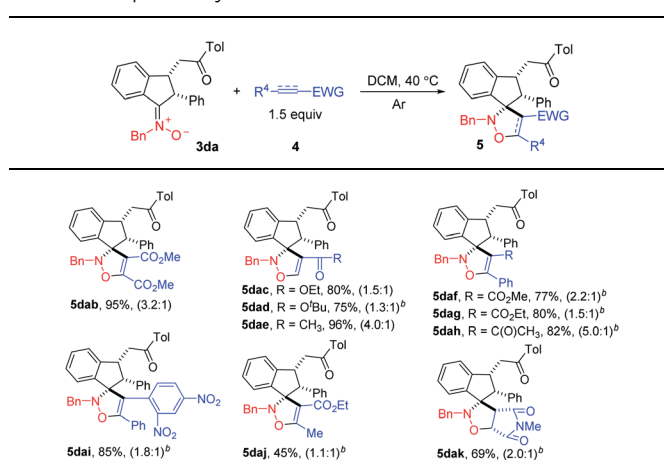


^a All reactions were carried out with **3** (0.20 mmol), **4a** (1.5 equiv.), and DCM (3.0 mL), 17–21 h unless otherwise stated; isolated yield based on **3**; the dr ratio is given in brackets and determined by ¹H NMR analysis (see ESI for details).

furnish the desired product **5dba** in good yield. However, *N*-methyl isoxazoline **5dca** failed to be furnished, because nitrone **3dc** is too unstable to be separated.

Next, to further probe the generality of this cycloaddition reaction, a variety of alkynes **4b–j** were treated with indanone-derived nitrone **3da**. The results are shown in Table 2 (**5dab–daj**). Although dimethyl acetylenedicarboxylate, ethyl propionate, and 3-butyn-2-one gave the corresponding spiroindanyl isoxazoline in high yields in dichloromethane, the reaction of

Table 2 Scope of alkynes^a



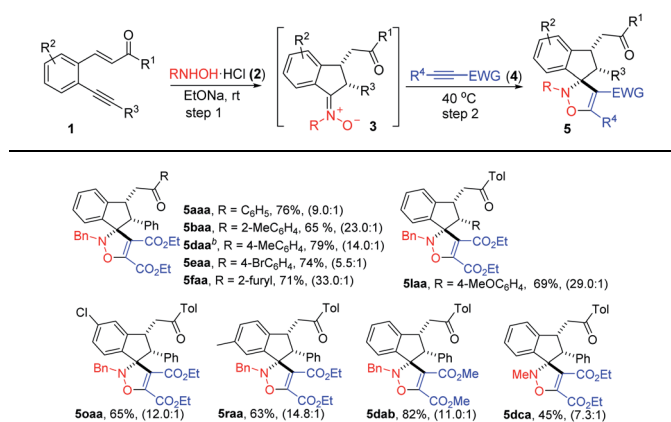
^a All reactions were carried out with **3da** (0.20 mmol), **4** (1.5 equiv.), and DCM (3.0 mL), 17–21 h unless otherwise stated; isolated yield based on **3da**; the dr ratio is given in brackets and determined by ¹H NMR analysis (see ESI for details). ^b The reaction was carried out in CHCl₃ (3.0 mL) at 80 °C.



tert-butyl propionate, methyl phenylpropiolate, ethyl phenylpropiolate, 4-phenyl-3-buten-2-one, and ethyl 2-butynoate needed to be carried out in chloroform at higher temperature to obtain satisfactory yields (**5dab**, **5dac**, **5dae** vs. **5dad**, **5daf**–**5dah**, **5daj**). To our delight, cycloaddition reaction of nitron **3da** with diphenylethyne also went smoothly to give diphenyl-4-isoxazoline (**5dai**), which may be a potential inhibitor of cyclooxygenase-2 with analgesic and antiinflammatory activity according to the study reported by Knaus.^{1a} It was found that electron deficient olefin was also a good partner in cycloaddition reaction with indanone-derived nitron, as *N*-methylmaleimide could afford the spiroindenyl isoxazolidine in moderate yield (**5dak**).

DCM was used as the solvent in both the preparation of indanone-derived nitron and the cycloaddition reaction of nitron with electron deficient alkyne, therefore, we envisioned that cycloaddition of nitrones generated *in situ* from unsaturated ketone **1**, and *N*-alkylhydroxylamine **2**, with alkyne **4** for synthesis of spiroindenyl isoxazoline was possible. Indeed, the cycloaddition of nitrones generated *in situ* went smoothly to afford the spiroindenyl isoxazoline in good yield, and the results are summarized in Table 3. Of note is that **5dca** can be afforded successfully in a yield of 45%. Surprisingly, this cycloaddition gave higher dr value than cycloaddition of pre-prepared nitron in Table 1. The mechanism is still not clear currently, according to the previous literature^{17–19} and experimental results, the reaction process may be determined by the attack of nucleophilic oxygen anion in nitron moiety on the carbon–carbon triple bond in alkynes,¹⁹ and the reason is probably that this cycloaddition, at least in part, follows a two-step mechanism, while cycloaddition of pre-prepared nitron in Table 1 proceeds in a concerted manner.

Table 3 [3 + 2] cycloaddition reaction of generated *in situ* ketonitron^a



Scheme 2 Transformations of spiroisoxazolines.

With the novel spiroisoxazolines in hand, subsequently, transformations of isoxazoline were investigated (Scheme 2). 4-Isloxazoline **5daa** underwent reductive cleavage of the N–O bond successfully in the presence of zinc powder and NH₄Cl at 75 °C, affording allylic alcohol **6** in a yield of 75%.^{8,21} Besides, it was found that Co₂(CO)₈ catalyzed rearrangement of 4-isloxazoline **5raa** could occur in MeCN, giving enamide **7** in 52% yield, instead of ring contraction product acylaziridines.²² While the mechanism for Co₂(CO)₈ catalyzed rearrangement is not clear at present, further examination of the rearrangement reaction conditions and mechanism will be carried out in due course.

Conclusions

In summary, we have reported a novel [3 + 2] cycloaddition between indanone-derived nitrones and electron deficient alkynes to give a series of spiroindenyl isoxazolines under mild conditions in moderate to good yields. To the best of our knowledge, this is the first example of [3 + 2] cycloaddition of indanone-derived nitrones generated *in situ*, giving the corresponding spiroindenyl isoxazolines in high diastereoselectivity. Application of these spiroindenyl isoxazolines and expansion of the scope of dipolarophiles for synthesis of other novel spiroindenyl compounds are currently under investigation in our laboratory.

Experimental

General information

All ¹H, ¹³C, and ¹⁹F NMR spectra were recorded at ambient temperatures on a Bruker 400 MHz or 500 MHz advance spectrometer with tetramethylsilane as internal standard. High-resolution mass spectra (HRMS) were recorded on an Agilent 1290 or GCT Premier Mass Spectrometer using ESI-TOF or EI (electrospray ionization time of flight). All reactions were monitored by thin-layer chromatography. Column chromatography (petroleum ether/ethyl acetate) was performed on silica gel (200–300 mesh). 2,4-Dinitro-1-(phenylethynyl)benzene **4i**²³ was prepared according to literature procedure, and other reagents were purchased from commercial suppliers and used without further purification.

Representative procedure for the synthesis of spiroindenyl isoxazoline 5 (Table 1, 5aaa). To a dried Schlenk flask was charged with **3aa** (0.0863 g, 0.20 mmol), diethyl acetylenedicarboxylate (0.0511 g, 0.30 mmol), and DCM (3.0 mL) under argon. The reaction mixture was stirred at 40 °C for 20 h, and then was concentrated. The crude residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate =

^a All reactions were carried out with **1** (0.50 mmol), **2** (0.50 mmol), EtONa (1.3 equiv.), and DCM (5.0 mL), 12–24 h for step one, then **4** (1.5 equiv.) was added, 17–21 h for step two unless otherwise stated; isolated yield based on **1**; the dr ratio is given in brackets and determined by ¹H NMR analysis (see ESI for details). ^b The reactions were carried out with 4 mmol scale of **1d**.



10 : 1, v/v) to afford the desired product **5aaa** as a light yellow solid (0.1191 g, 99% yield, 1.8 : 1 dr).

Diethyl 2'-benzyl-3-(2-oxo-2-phenylethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5aaa**), 1.8 : 1 dr. Purified by silica gel column chromatography (10 : 1 petroleum ether/ethyl acetate): 119.1 mg, 99% yield; light yellow solid, mp 120–122 °C, IR (film) 1739, 1709, 1474, 1303, 1231, 1188 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.93 (d, *J* = 10.0 Hz, 0.7H), 7.79 (d, *J* = 10.0 Hz, 1.3H), 7.67 (t, *J* = 5.0 Hz, 1.3H), 7.57–7.33 (m, 5.7H), 7.32–7.11 (m, 10H), 4.50 (t, *J* = 10.0 Hz, 0.3H), 4.25–4.07 (m, 5.3H), 4.02 (d, *J* = 15.0 Hz, 0.7H), 3.87 (dd, *J* = 15.0, 5.0 Hz, 0.7H), 3.57–3.43 (m, 2.3H), 3.36 (dd, *J* = 20.0, 10.0 Hz, 0.4H), 3.22 (dd, *J* = 15.0, 5.0 Hz, 0.3H), 1.29–1.20 (m, 4.1H), 1.13 (d, *J* = 10.0 Hz, 1.9H); ¹³C NMR (125 MHz, CDCl₃) δ 199.5, 199.1, 162.7, 162.4, 159.2, 155.4, 154.8, 148.0, 147.0, 139.8, 137.8, 137.5, 137.4, 137.4, 137.2, 137.0, 135.5, 133.6, 133.4, 133.1, 131.6, 130.5, 130.0, 129.7, 129.1, 129.0, 128.8, 128.7, 128.6, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.6, 127.6, 127.4, 127.2, 127.2, 127.1, 126.6, 126.3, 126.0, 124.7, 113.1, 108.7, 100.2, 85.3, 84.0, 62.6, 62.6, 61.4, 60.9, 60.8, 60.6, 60.2, 58.4, 43.9, 42.6, 42.3, 40.4, 14.2, 14.1, 14.0, 14.0; HRMS(ESI) calcd for C₃₈H₃₆NO₆ [M + H]⁺ 602.2537, found 602.2543.

Diethyl 2'-benzyl-3-(2-oxo-2-(*o*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5baa**), 1.1 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 93.6 mg, 76% yield; light yellow solid, mp 87–89 °C, IR (film) 1747, 1712, 1456, 1371, 1299, 1187 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.64–7.62 (m, 1H), 7.58 (d, *J* = 8.0 Hz, 0.5H), 7.45–7.43 (m, 2H), 7.39–7.36 (m, 1.5H), 7.34–7.26 (m, 4H), 7.25–7.10 (m, 9H), 4.49–4.43 (m, 0.6H), 4.21–4.12 (m, 4.8H), 4.00 (d, *J* = 12.0 Hz, 0.5H), 3.86 (d, *J* = 16.0 Hz, 0.5H), 3.82 (d, *J* = 12.0 Hz, 0.5H), 3.52 (d, *J* = 12.0 Hz, 0.5H), 3.50–3.42 (m, 1.3H), 3.32–3.25 (m, 0.6H), 3.16 (dd, *J* = 16.0, 4.0 Hz, 0.5H), 2.48 (s, 1.6H), 2.36 (s, 1.4H), 1.29–1.18 (m, 4.6H), 1.13 (d, *J* = 8.0 Hz, 1.4H); ¹³C NMR (100 MHz, CDCl₃) δ 203.3, 202.8, 162.7, 162.4, 159.3, 159.2, 155.5, 154.8, 148.2, 147.0, 138.7, 138.4, 138.3, 137.8, 137.6, 137.5, 137.3, 137.2, 137.0, 135.5, 132.3, 132.1, 131.7, 131.7, 131.4, 130.5, 130.0, 129.7, 129.1, 129.0, 128.7, 128.6, 128.5, 128.3, 128.2, 128.0, 127.6, 127.4, 127.2, 127.2, 127.1, 126.5, 126.4, 126.1, 125.9, 125.7, 124.5, 108.7, 127.2, 85.3, 84.1, 62.6, 61.5, 60.9, 60.8, 60.6, 60.2, 58.4, 45.6, 45.0, 43.9, 40.7, 29.9, 21.7, 21.4, 14.2, 14.1, 14.0, 14.0; HRMS(ESI) calcd for C₃₉H₃₈NO₆ [M + H]⁺ 616.2694, found 616.2690.

Diethyl 2'-benzyl-3-(2-oxo-2-(*m*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5caa**), 1.8 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 117.0 mg, 95% yield; light yellow oil, IR (film) 1745, 1701, 1496, 1370, 1181, 1108 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.69 (d, *J* = 10.0 Hz, 2H), 7.59 (s, 0.7H), 7.46–7.40 (m, 2H), 7.36–7.26 (m, 7H), 7.24–7.12 (m, 5H), 6.69 (t, *J* = 10.0 Hz, 0.5H), 6.79 (d, *J* = 5.0 Hz, 1H), 4.48 (t, *J* = 10.0 Hz, 0.6H), 4.26–4.10 (m, 4.5H), 4.02 (d, *J* = 15.0 Hz, 0.4H), 3.88–3.85 (m, 1.3H), 3.53–3.43 (m, 1.7H), 3.34 (dd, *J* = 20.0, 10.0 Hz, 0.7H), 3.20 (d, *J* = 15.0 Hz, 0.6H), 2.38 (s, 1.9H), 2.31 (s, 1.1H), 1.28–1.20 (m, 5H), 1.12 (t, *J* = 10.0 Hz, 1.3H); ¹³C NMR (125 MHz, CDCl₃) δ 200.0, 199.6, 162.9, 162.4, 159.3, 156.1, 155.6, 154.9,

148.0, 147.0, 138.6, 138.5, 137.5, 137.4, 137.2, 137.1, 137.0, 135.6, 134.2, 133.9, 131.6, 130.5, 130.0, 129.8, 129.7, 128.9, 128.7, 128.6, 128.6, 128.2, 128.2, 128.0, 127.6, 127.5, 127.3, 127.2, 127.2, 127.1, 126.6, 126.3, 126.0, 125.6, 125.4, 124.7, 120.6, 115.5, 107.3, 85.3, 84.0, 62.6, 61.4, 60.9, 60.7, 60.2, 58.4, 44.0, 42.6, 42.3, 40.5, 29.9, 21.5, 14.2, 14.1, 14.0, 14.0; HRMS(ESI) calcd for C₃₉H₃₈NO₆ [M + H]⁺ 616.2694, found 616.2696.

Diethyl 2'-benzyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5daa**), 2.9 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 118.2 mg, 96% yield; light yellow solid, mp 127–129 °C, IR (film) 1743, 1709, 1474, 1303, 1231, 1181 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.83 (d, *J* = 10.0 Hz, 1.5H), 7.70–7.66 (m, 1H), 7.47–7.12 (m, 15.5H), 4.50 (t, *J* = 10.0 Hz, 0.7H), 4.26–4.10 (m, 4.5H), 4.02 (d, *J* = 15.0 Hz, 0.3H), 3.87 (t, *J* = 10.0 Hz, 1.5H), 3.57–3.40 (m, 1.4H), 3.33 (dd, *J* = 20.0, 10.0 Hz, 0.8H), 3.18 (d, *J* = 20.0 Hz, 0.7H), 2.38 (s, 2.2H), 2.36 (s, 0.8H), 1.28–1.20 (m, 5.2H), 1.12 (t, *J* = 10.0 Hz, 0.8H); ¹³C NMR (125 MHz, CDCl₃) δ 199.1, 198.8, 162.8, 162.5, 159.2, 155.4, 154.8, 148.0, 147.0, 144.2, 143.8, 137.4, 137.0, 135.6, 135.0, 134.6, 131.6, 130.5, 130.0, 129.6, 129.4, 129.3, 129.0, 128.6, 128.6, 128.5, 128.3, 128.2, 128.2, 128.0, 127.6, 127.5, 127.3, 127.2, 127.1, 127.0, 126.6, 126.3, 125.9, 124.7, 108.8, 107.3, 85.3, 84.0, 62.5, 61.4, 60.8, 60.6, 60.2, 58.4, 43.9, 42.4, 42.1, 40.5, 29.9, 21.8, 14.2, 14.1, 14.0, 14.0; HRMS(ESI) calcd for C₃₉H₃₈NO₆ [M + H]⁺ 616.2694, found 616.2697.

Diethyl 2'-benzyl-3-(2-(4-bromophenyl)-2-oxoethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5eaa**), 1.4 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 125.2 mg, 92% yield; white solid, mp 96–98 °C, IR (film) 1735, 1701, 1499, 1373, 1223, 1167 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.77 (d, *J* = 5.0 Hz, 1H), 7.65–7.60 (m, 2H), 7.56 (d, *J* = 10.0 Hz, 1H), 7.49–7.38 (m, 4H), 7.33–7.09 (m, 10H), 4.44 (t, *J* = 10.0 Hz, 0.4H), 4.24–4.10 (m, 5.3H), 4.03 (d, *J* = 15.0 Hz, 0.6H), 3.86 (q, *J* = 10.0 Hz, 0.8H), 3.53–3.45 (m, 1.6H), 3.37–3.28 (m, 1H), 3.17 (d, *J* = 15.0 Hz, 0.4H), 1.28–1.20 (m, 4.3H), 1.13 (t, *J* = 10.0 Hz, 1.7H); ¹³C NMR (125 MHz, CDCl₃) δ 198.6, 198.1, 162.7, 162.4, 159.2, 159.2, 155.6, 154.8, 147.8, 146.7, 137.9, 137.5, 137.4, 137.1, 136.9, 136.2, 135.7, 135.4, 132.1, 132.0, 131.5, 130.5, 130.0, 129.9, 129.7, 129.7, 128.9, 128.6, 128.6, 128.3, 128.2, 128.0, 127.7, 127.6, 127.4, 127.3, 127.2, 127.2, 126.4, 126.4, 126.1, 124.5, 108.7, 107.2, 85.3, 84.0, 62.6, 62.6, 61.4, 60.9, 60.8, 60.6, 60.2, 58.3, 43.9, 42.4, 42.2, 40.6, 14.2, 14.1, 14.0, 14.0; HRMS(ESI) calcd for C₃₈H₃₅BrNO₆ [M + H]⁺ 680.1642, found 680.1648.

Diethyl 2'-benzyl-3-(2-(furan-2-yl)-2-oxoethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5faa**), 6.5 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 99.4 mg, 84% yield; light yellow solid, mp 65–67 °C, IR (film) 1740, 1710, 1467, 1300, 1253, 1189 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.53 (s, 1H), 7.43 (d, *J* = 10.0 Hz, 2H), 7.38–7.07 (m, 14H), 6.48 (t, *J* = 5.0 Hz, 1H), 6.42 (s, 0.1H), 4.41 (d, *J* = 5.0 Hz, 1H), 4.24–4.17 (m, 4H), 3.88–3.82 (m, 2H), 3.46 (d, *J* = 15.0 Hz, 1H), 3.20 (dd, *J* = 20.0, 10.0 Hz, 1H), 3.09 (dd, *J* = 15.0, 5.0 Hz, 1H), 1.28–1.19 (m, 5.7H), 1.12 (t, *J* = 5.0 Hz, 0.4H); ¹³C NMR (125 MHz, CDCl₃) δ 188.5, 162.7,



159.2, 155.5, 152.8, 146.7, 146.6, 137.4, 136.9, 135.4, 130.4, 130.0, 129.0, 128.6, 128.2, 127.9, 127.5, 127.2, 127.1, 126.0, 124.6, 117.4, 112.4, 107.2, 84.0, 62.6, 61.5, 60.8, 60.2, 41.9, 40.4, 29.9, 14.2, 14.0; HRMS(ESI) calcd for $C_{36}H_{34}NO_7$ $[M + H]^+$ 592.2330, found 592.2333.

Diethyl 2'-benzyl-3-(2-oxopropyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-is-oxazole]-4',5'-dicarboxylate (**5gaa**), 13.0 : 1 dr. Purified by silica gel column chromatography (30 : 1 petroleum ether/ethyl acetate): 82.0 mg, 76% yield; Light yellow oil, IR (film) 1712, 1685, 1448, 1370, 1223, 1108 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, $J = 4.0$ Hz, 2H), 7.45–7.21 (m, 12H), 4.20–4.05 (m, 5H), 4.01–3.84 (m, 2H), 3.52–3.42 (m, 1H), 3.03–2.98 (m, 1H), 2.88–2.81 (m, 1H), 2.75 (d, $J = 4.0$ Hz, 0.1H), 2.15 (s, 0.2H), 2.02 (s, 2.8H), 1.29–1.19 (m, 3.2H), 1.12 (d, $J = 8.0$ Hz, 2.8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.7, 162.4, 159.2, 154.7, 147.9, 137.6, 137.2, 137.1, 131.7, 129.7, 129.0, 128.6, 128.1, 127.6, 127.4, 127.2, 126.4, 126.2, 108.7, 85.2, 62.6, 60.9, 60.5, 58.0, 47.4, 43.4, 31.0, 14.1, 13.9. HRMS (ESI) calcd for $C_{33}H_{33}NO_6Na$ $[M + Na]^+$ 562.2200, found 562.2199.

Diethyl 2'-benzyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-(*m*-tolyl)-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5haa**), 1.9 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 112.1 mg, 89% yield; white yellow solid, mp 50–52 °C, IR (film) 1741, 1712, 1496, 1370, 1300, 1241, 1140 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, $J = 8.0$ Hz, 0.7H), 7.67 (d, $J = 8.0$ Hz, 1.3H), 7.55 (d, $J = 8.0$ Hz, 0.7H), 7.45–7.27 (m, 7.6H), 7.24–7.11 (m, 5.9H), 7.06 (d, $J = 8.0$ Hz, 0.4H), 7.01 (d, $J = 8.0$ Hz, 0.7H), 4.48 (t, $J = 8.0$ Hz, 0.3H), 4.26–4.07 (m, 5.1H), 4.02 (d, $J = 16.0$ Hz, 0.8H), 3.85 (dd, $J = 16.0, 8.0$ Hz, 0.7H), 3.55–3.45 (m, 1.6H), 3.34 (dd, $J = 20.0, 8.0$ Hz, 1H), 3.20 (dd, $J = 20.0, 4.0$ Hz, 0.4H), 2.39 (s, 0.9H), 2.36 (s, 1.9H), 2.32 (s, 1.1H), 2.21 (s, 2H), 1.30–1.19 (m, 4.1H), 1.12 (t, $J = 8.0$ Hz, 1.9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 198.8, 162.8, 162.4, 159.4, 159.3, 155.6, 154.8, 148.0, 147.0, 144.2, 143.8, 138.0, 137.6, 137.5, 137.4, 137.2, 137.1, 135.5, 135.0, 134.6, 132.6, 131.3, 129.9, 129.6, 129.4, 129.3, 128.8, 128.5, 128.5, 128.3, 128.2, 128.1, 127.9, 127.9, 127.5, 127.2, 127.1, 127.0, 126.4, 126.2, 125.9, 124.8, 108.8, 107.2, 85.2, 83.9, 62.6, 61.1, 60.8, 60.7, 60.6, 60.2, 58.2, 44.0, 42.4, 42.3, 40.4, 29.9, 21.8, 21.8, 21.7, 21.6, 14.2, 14.1, 14.1, 14.0; HRMS (ESI) calcd for $C_{40}H_{39}NO_6Na$ $[M + Na]^+$ 652.2670, found 652.2669.

Diethyl 2'-benzyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-(*p*-tolyl)-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5iaa**), 2.2 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 117.1 mg, 93% yield; light yellow solid, mp 55–57 °C, IR (film) 1739, 1709, 1497, 1371, 1302, 1241, 1140 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, $J = 8.0$ Hz, 1.5H), 7.69 (d, $J = 8.0$ Hz, 0.5H), 7.55 (d, $J = 8.0$ Hz, 0.6H), 7.44–7.39 (m, 0.7H), 7.37–7.32 (m, 3.3H), 7.29–7.09 (m, 10H), 7.05 (d, $J = 8.0$ Hz, 0.6H), 4.47 (t, $J = 8.0$ Hz, 0.8H), 4.25–4.07 (m, 4.5H), 4.01 (d, $J = 12.0$ Hz, 0.3H), 3.84 (dd, $J = 20.0, 12.0$ Hz, 1.5H), 3.53–3.38 (m, 1.5H), 3.31 (dd, $J = 16.0, 8.0$ Hz, 0.8H), 3.20 (dd, $J = 16.0, 4.0$ Hz, 0.8H), 2.39 (s, 2.1H), 2.36 (s, 0.9H), 2.30 (s, 2.1H), 2.27 (s, 0.9H), 1.29–1.19 (m, 5.1H), 1.12 (t, $J = 8.0$ Hz, 0.9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 198.9, 162.8, 162.4, 159.3, 155.3, 154.7, 148.1, 147.2, 144.2, 143.8, 137.8, 137.5, 137.1, 137.0, 136.7, 135.1, 134.6, 134.1, 132.5, 131.5, 130.4, 129.9, 129.6,

129.4, 129.3, 129.0, 128.9, 128.8, 128.6, 128.6, 128.5, 128.3, 128.3, 127.6, 127.2, 127.1, 127.0, 126.6, 126.3, 126.0, 124.7, 108.9, 107.5, 85.3, 84.0, 62.5, 61.1, 60.8, 60.6, 60.3, 58.1, 44.0, 42.5, 42.1, 40.5, 29.9, 21.8, 21.4, 21.3, 21.2, 14.2, 14.1, 14.0, 14.0; HRMS(ESI) calcd for $C_{40}H_{40}NO_6$ $[M + H]^+$ 630.2850, found 630.2852.

Diethyl 2'-benzyl-2-(4-chlorophenyl)-3-(2-oxo-2-(*p*-tolyl)ethyl)-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5jaa**), 1.6 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 127.4 mg, 98% yield; light yellow solid, mp 95–97 °C, IR (film) 1741, 1701, 1476, 1353, 1226, 1156 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, $J = 8.0$ Hz, 0.7H), 7.70 (d, $J = 8.0$ Hz, 1.2H), 7.60 (d, $J = 8.0$ Hz, 1.3H), 7.44–7.37 (m, 2.6H), 7.34–7.28 (m, 5H), 7.25–7.11 (m, 6.4H), 4.44 (t, $J = 8.0$ Hz, 0.4H), 4.25–4.08 (m, 5.2H), 4.01 (d, $J = 12.0$ Hz, 0.7H), 3.88 (d, $J = 16.0$ Hz, 0.4H), 3.79 (d, $J = 12.0$ Hz, 0.4H), 3.52–3.45 (m, 1.5H), 3.42–3.31 (m, 1.2H), 3.13 (dd, $J = 16.0, 4.0$ Hz, 0.4H), 2.40 (s, 1.2H), 2.38 (s, 1.8H), 1.30–1.20 (m, 4.2H), 1.13 (t, $J = 8.0$ Hz, 1.8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0, 198.5, 162.7, 162.3, 159.1, 155.4, 154.8, 147.9, 146.8, 144.3, 144.0, 137.3, 137.2, 137.1, 136.8, 135.7, 134.9, 134.4, 134.1, 133.3, 133.3, 132.9, 131.8, 130.1, 129.8, 129.5, 129.4, 129.0, 128.6, 128.4, 128.3, 128.3, 128.2, 128.1, 127.7, 127.4, 127.3, 127.2, 126.6, 126.3, 126.0, 124.7, 108.5, 107.2, 100.1, 85.2, 84.0, 62.8, 61.0, 60.6, 60.2, 57.6, 43.8, 42.4, 41.9, 40.7, 21.8, 14.2, 14.1, 14.0, 14.0; HRMS (ESI) calcd for $C_{39}H_{36}NO_6ClNa$ $[M + Na]^+$ 672.2123, found 672.2128.

Diethyl 2'-benzyl-2-(4-bromophenyl)-3-(2-oxo-2-(*p*-tolyl)ethyl)-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5kaa**), 1.1 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 126.4 mg, 91% yield; white solid, mp 82–84 °C, IR (film) 1749, 1712, 1488, 1371, 1299, 1180 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, $J = 8.0$ Hz, 1H), 7.69 (d, $J = 8.0$ Hz, 1H), 7.54 (d, $J = 8.0$ Hz, 1H), 7.44–7.27 (m, 8H), 7.25–7.10 (m, 6H), 4.43 (t, $J = 8.0$ Hz, 0.5H), 4.25–4.15 (m, 3H), 4.13–4.07 (m, 1.8H), 4.00 (d, $J = 16.0$ Hz, 0.5H), 3.88 (d, $J = 12.0$ Hz, 0.6H), 3.78 (d, $J = 12.0$ Hz, 0.6H), 3.52–3.30 (m, 2.5H), 3.12 (dd, $J = 16.0, 4.0$ Hz, 0.6H), 2.40 (s, 1.5H), 2.38 (s, 1.5H), 1.30–1.19 (m, 4.4H), 1.13 (t, $J = 8.0$ Hz, 1.6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0, 198.5, 162.7, 162.3, 159.1, 155.4, 154.8, 147.9, 146.8, 144.3, 144.0, 137.2, 137.1, 136.8, 136.2, 135.0, 134.7, 134.5, 133.3, 132.2, 131.3, 131.1, 130.1, 129.8, 129.5, 129.4, 129.0, 128.7, 128.6, 128.5, 128.3, 128.3, 127.7, 127.4, 127.3, 127.2, 126.6, 126.3, 126.0, 124.7, 121.6, 121.6, 108.5, 107.2, 85.3, 84.0, 62.8, 62.7, 61.1, 61.0, 60.6, 60.3, 57.7, 43.8, 42.4, 41.9, 40.7, 29.9, 21.9, 21.8, 14.2, 14.1, 14.0, 14.0; HRMS(ESI) calcd for $C_{39}H_{37}O_6BrNa$ $[M + H]^+$ 694.1799; found: 694.1799.

Diethyl 2'-benzyl-2-(4-methoxyphenyl)-3-(2-oxo-2-(*p*-tolyl)ethyl)-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5laa**), 6.5 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 127.9 mg, 99% yield; light yellow solid, mp 78–80 °C, IR (film) 1739, 1711, 1491, 1370, 1300, 1107 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, $J = 8.0$ Hz, 0.2H), 7.71 (d, $J = 8.0$ Hz, 1.8H), 7.59 (d, $J = 8.0$ Hz, 2H), 7.44–7.37 (m, 2H), 7.34–7.21 (m, 7H), 7.17 (t, $J = 8.0$ Hz, 2H), 6.83 (d, $J = 8.0$ Hz, 0.2H), 6.78 (d, $J = 8.0$ Hz, 1.8H),



4.22–4.05 (m, 5.9H), 4.01 (d, $J = 12.0$ Hz, 0.9H), 3.77 (s, 0.4H), 3.75 (s, 2.6H), 3.52–3.38 (m, 2.8H), 2.40 (s, 0.4H), 2.37 (s, 2.6H), 1.30–1.19 (m, 3.4H), 1.13 (t, $J = 8.0$ Hz, 2.6H); ^{13}C NMR (100 MHz, CDCl_3) δ 198.9, 162.4, 159.2, 158.8, 154.6, 148.1, 143.9, 137.7, 137.4, 135.0, 132.7, 131.5, 129.6, 129.3, 129.2, 129.0, 128.6, 128.6, 128.5, 128.3, 127.6, 127.1, 126.6, 126.3, 113.5, 108.9, 85.3, 62.6, 60.9, 60.6, 57.7, 55.3, 44.0, 42.5, 40.8, 21.8, 14.1, 14.0; HRMS (ESI) calcd for $\text{C}_{40}\text{H}_{39}\text{NO}_7\text{Na}$ [$\text{M} + \text{Na}$] $^+$ 668.2619, found 668.2615.

Diethyl 2'-benzyl-2-(cyclohex-1-en-1-yl)-3-(2-oxo-2-(*p*-tolyl)ethyl)-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5maa**), 6.8 : 1 dr. Purified by silica gel column chromatography (40 : 1 petroleum ether/ethyl acetate): 114.0 mg, 92% yield; light yellow solid, mp 85–87 °C, IR (film) 1733, 1710, 1372, 1298, 1200, 1175 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.95 (d, $J = 10.0$ Hz, 0.2H), 7.81 (d, $J = 10.0$ Hz, 1.7H), 7.39 (d, $J = 5.0$ Hz, 1H), 7.34–7.23 (m, 8.2H), 7.18 (d, $J = 10.0$ Hz, 1.8H), 6.22 (s, 0.8H), 4.34–4.28 (m, 2H), 4.16–4.06 (m, 2.8H), 3.99 (d, $J = 15.0$ Hz, 0.8H), 3.81–3.76 (m, 0.9H), 3.41 (dd, $J = 15.0, 10.0$ Hz, 0.9H), 3.32–3.20 (m, 1.1H), 3.01 (dd, $J = 15.0, 5.0$ Hz, 0.8H), 2.43 (s, 0.4H), 2.39 (s, 2.6H), 2.26–2.13 (m, 0.9H), 2.04–1.99 (m, 0.3H), 1.90–1.82 (m, 1.6H), 1.62–1.56 (m, 2.8H), 1.49–1.40 (m, 2.7H), 1.36–1.33 (m, 3H), 1.17 (d, $J = 10.0$ Hz, 0.4H), 1.13 (d, $J = 10.0$ Hz, 2.6H); ^{13}C NMR (100 MHz, CDCl_3) δ 199.4, 198.6, 162.7, 162.5, 160.0, 159.8, 155.3, 148.1, 147.1, 144.2, 143.7, 137.7, 137.6, 137.4, 135.1, 134.8, 133.2, 132.6, 129.8, 129.5, 129.3, 128.8, 128.6, 128.6, 128.5, 128.4, 128.3, 127.5, 127.3, 126.9, 126.8, 126.1, 126.0, 125.8, 124.6, 108.1, 85.0, 84.4, 62.7, 60.8, 60.6, 59.9, 58.2, 42.6, 42.3, 42.0, 38.4, 31.5, 29.9, 28.5, 27.8, 27.1, 25.9, 25.8, 23.5, 23.4, 22.6, 22.2, 21.9, 21.8, 14.2, 14.1; HRMS (ESI) calcd for $\text{C}_{39}\text{H}_{41}\text{NO}_6\text{Na}$ [$\text{M} + \text{Na}$] $^+$ 642.2826, found 642.2823.

Diethyl 2'-benzyl-5-fluoro-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5naa**), 4.5 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 119.1 mg, 94% yield; yellowish white solid, mp 116–118 °C, IR (film) 1743, 1709, 1474, 1303, 1231, 1181 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.83 (d, $J = 8.0$ Hz, 0.4H), 7.71 (d, $J = 8.0$ Hz, 1.6H), 7.65 (d, $J = 8.0$ Hz, 1.6H), 7.42–7.36 (m, 1.4H), 7.35–7.14 (m, 11H), 7.02–6.97 (m, 1H), 6.82 (d, $J = 8.0$ Hz, 0.2H), 4.45 (t, $J = 8.0$ Hz, 0.2H), 4.30–4.07 (m, 5.6H), 3.99 (d, $J = 12.0$ Hz, 0.8H), 3.87 (d, $J = 12.0$ Hz, 0.4H), 3.53–3.40 (m, 2.6H), 3.33–3.14 (m, 0.4H), 2.40 (s, 0.5H), 2.38 (s, 2.5H), 1.29–1.22 (m, 3.5H), 1.15 (t, $J = 8.0$ Hz, 2.5H); ^{13}C NMR (100 MHz, CDCl_3) δ 198.8, 198.4, 168.4, 163.7 (d, $J = 246.8$ Hz), 162.7, 162.3, 159.2, 159.1, 155.7, 155.0, 150.6, 150.5, 149.4, 144.4, 144.1, 141.1, 137.2, 136.8, 136.7, 135.2, 134.8, 134.3, 133.5 (d, $J = 2.6$ Hz), 131.6, 130.4, 130.2, 129.5, 129.4, 129.0, 128.6, 128.6, 128.5, 128.3, 128.3, 128.1, 127.7, 127.6, 127.5, 127.5, 127.3, 120.5, 114.6 (d, $J = 22.9$ Hz), 114.0 (d, $J = 22.4$ Hz), 112.4, 112.2, 108.2, 106.8, 92.9, 84.6, 84.0, 83.3, 62.7, 61.6, 61.0, 60.5, 60.1, 58.8, 43.7, 42.1, 41.9, 40.4, 29.9, 21.8, 14.2, 14.1, 14.0, 14.0; ^{19}F NMR (282 MHz, CDCl_3): δ –111.5 (s, 1F); HRMS (ESI) calcd for $\text{C}_{39}\text{H}_{37}\text{FNO}_6$ [$\text{M} + \text{H}$] $^+$ 634.2599, found 634.2603.

Diethyl 2'-benzyl-5-chloro-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5oaa**), 2.5 : 1 dr. Purified by silica gel column chromatography

(20 : 1 petroleum ether/ethyl acetate): 117.0 mg, 90% yield; light yellow solid, mp 112–114 °C, IR (film) 1740, 1709, 1466, 1304, 1261, 1180 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.83 (d, $J = 8.0$ Hz, 1.4H), 7.71 (d, $J = 12.0$ Hz, 0.5H), 7.64 (d, $J = 4.0$ Hz, 0.5H), 7.47 (d, $J = 1.6$ Hz, 0.3H), 7.42 (d, $J = 8.0$ Hz, 1.5H), 7.39–7.10 (m, 13H), 4.45 (t, $J = 8.0$ Hz, 0.7H), 4.26–4.09 (m, 4.4H), 3.99 (d, $J = 12.0$ Hz, 0.3H), 3.89–3.84 (m, 1.5H), 3.52–3.42 (m, 1.5H), 3.33–3.18 (m, 1.6H), 2.40 (s, 2H), 2.38 (s, 1H), 1.29–1.21 (m, 5.1H), 1.16 (t, $J = 8.0$ Hz, 0.9H); ^{13}C NMR (100 MHz, CDCl_3) δ 198.7, 198.3, 162.6, 162.3, 159.1, 155.8, 149.9, 149.0, 144.4, 144.1, 137.1, 136.7, 136.6, 136.5, 136.1, 135.9, 135.7, 135.1, 134.8, 134.3, 131.5, 130.4, 129.5, 129.4, 129.0, 128.6, 128.6, 128.5, 128.3, 128.3, 128.3, 128.1, 127.7, 127.6, 127.5, 127.4, 127.3, 127.0, 125.3, 108.1, 106.6, 84.7, 83.4, 62.7, 61.3, 60.9, 60.6, 60.2, 58.5, 43.6, 42.0, 41.9, 40.3, 29.9, 21.8, 14.2, 14.1, 14.0, 14.0; HRMS (ESI) calcd for $\text{C}_{39}\text{H}_{37}\text{ClNO}_6$ [$\text{M} + \text{H}$] $^+$ 650.2304, found 650.2308.

Diethyl 2'-benzyl-7-(2-oxo-2-(*p*-tolyl)ethyl)-6-phenyl-6,7-dihydro-2'*H*-spiro[indeno-[5,6-d][1,3]dioxole-5,3'-isoxazole]-4',5'-dicarboxylate (**5paa**), 3.2 : 1 dr. Purified by silica gel column chromatography (10 : 1 petroleum ether/ethyl acetate): 106.9 mg, 81% yield; yellowish white solid, mp 149–151 °C, IR (film) 1734, 1705, 1497, 1370, 1258, 1143 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.82 (d, $J = 12.0$ Hz, 1.6H), 7.71–7.65 (m, 1H), 7.42 (d, $J = 8.0$ Hz, 1.6H), 7.35 (t, $J = 4.0$ Hz, 1.3H), 7.31–7.15 (m, 9H), 6.86 (d, $J = 8.0$ Hz, 0.5H), 6.80 (s, 0.7H), 6.60 (s, 0.7H), 5.97–5.93 (m, 1.9H), 4.40–4.35 (m, 0.9H), 4.27–4.12 (m, 4.2H), 4.03–3.95 (m, 0.5H), 3.91–3.83 (m, 1.4H), 3.57 (dd, $J = 20.0, 12.0$ Hz, 1H), 3.41 (d, $J = 8.0$ Hz, 0.4H), 3.27 (dd, $J = 16.0, 8.0$ Hz, 0.8H), 3.16 (dd, $J = 16.0, 4.0$ Hz, 0.7H), 2.39 (s, 2.3H), 2.37 (s, 0.7H), 1.29–1.21 (m, 5.3H), 1.18 (t, $J = 8.0$ Hz, 0.7H); ^{13}C NMR (100 MHz, CDCl_3) δ 199.2, 198.9, 162.8, 162.4, 159.3, 155.5, 154.8, 149.4, 149.1, 147.3, 147.2, 144.3, 143.9, 142.0, 140.9, 137.5, 137.2, 137.0, 136.1, 135.7, 135.0, 134.5, 131.6, 130.5, 130.3, 129.5, 129.4, 129.0, 128.9, 128.6, 128.5, 128.5, 128.3, 128.3, 128.2, 128.0, 127.6, 127.5, 127.3, 127.2, 107.0, 106.9, 106.0, 105.9, 105.5, 101.6, 85.2, 83.9, 62.6, 61.5, 60.9, 60.9, 60.6, 60.0, 58.9, 43.7, 42.6, 42.4, 40.2, 21.8, 14.3, 14.2, 14.0, 14.0; HRMS (ESI) calcd for $\text{C}_{40}\text{H}_{37}\text{NO}_8\text{Na}$ [$\text{M} + \text{Na}$] $^+$ 682.2411, found 682.2406.

Diethyl 2'-benzyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[cyclopenta[*a*]naphthalene-1,3'-isoxazole]-4',5'-dicarboxylate (**5qaa**), 21.0 : 1 dr. Purified by silica gel column chromatography (40 : 1 petroleum ether/ethyl acetate): 115.8 mg, 87% yield; yellowish white solid, mp 158–160 °C, IR (film) 1747, 1711, 1370, 1300, 1181, 1094 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.34 (d, $J = 8.0$ Hz, 1H), 7.86 (d, $J = 8.0$ Hz, 1H), 7.79 (d, $J = 8.0$ Hz, 1H), 7.70 (t, $J = 8.0$ Hz, 4H), 7.55 (t, $J = 8.0$ Hz, 2H), 7.45 (t, $J = 8.0$ Hz, 1H), 7.32–7.20 (m, 8H), 7.15 (d, $J = 8.0$ Hz, 2H), 4.30–4.24 (m, 3H), 4.20 (d, $J = 8.0$ Hz, 2H), 4.05–3.90 (m, 2H), 3.75–3.55 (m, 3H), 2.37 (s, 3H), 1.23 (t, $J = 8.0$ Hz, 3H), 0.98 (d, $J = 8.0$ Hz, 0.1H), 0.85 (d, $J = 8.0$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 198.9, 162.4, 159.4, 154.9, 148.1, 143.9, 137.7, 137.2, 135.0, 133.6, 132.0, 132.0, 130.8, 129.4, 129.3, 128.8, 128.6, 128.3, 128.1, 127.5, 127.4, 127.1, 125.4, 124.4, 124.1, 108.7, 85.8, 62.7, 60.6, 60.6, 59.1, 44.0, 43.1, 21.8, 14.0, 13.9;



HRMS(ESI) calcd for $C_{43}H_{40}NO_6$ $[M + H]^+$ 666.2850, found 666.2855.

Diethyl 2'-cyclohexyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5dba**), 1.2 : 1 dr. Purified by silica gel column chromatography (10 : 1 petroleum ether/ethyl acetate): 94.8 mg, 78% yield; light yellow solid, mp 142–144 °C, IR (film) 1746, 1703, 1455, 1353, 1278, 1171 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, $J = 8.0$ Hz, 1H), 7.72 (d, $J = 8.0$ Hz, 1H), 7.68–7.65 (m, 1H), 7.42–7.11 (m, 10H), 4.47 (d, $J = 8.0$ Hz, 0.4H), 4.26–3.99 (m, 4H), 3.94 (d, $J = 8.0$ Hz, 0.5H), 3.57 (d, $J = 12.0$ Hz, 0.4H), 3.52–3.39 (m, 0.9H), 3.29 (dd, $J = 16.0, 8.0$ Hz, 0.4H), 3.12 (dd, $J = 16.0, 4.0$ Hz, 0.4H), 2.40 (s, 1.6H), 2.38 (s, 1.4H), 2.30–2.25 (m, 0.5H), 2.13 (d, $J = 12.0$ Hz, 0.5H), 1.97 (d, $J = 12.0$ Hz, 0.5H), 1.82–1.69 (m, 1.7H), 1.65–1.51 (m, 3H), 1.31–1.18 (m, 6H), 1.11 (t, $J = 8.0$ Hz, 2H), 1.02–0.86 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4, 199.4, 162.7, 162.4, 159.3, 159.2, 156.3, 155.7, 148.5, 147.9, 144.2, 143.8, 137.6, 137.5, 137.4, 135.7, 135.3, 134.6, 132.0, 130.7, 129.6, 129.4, 129.4, 129.4, 128.5, 128.2, 127.9, 127.6, 127.4, 127.3, 126.9, 126.7, 126.5, 125.7, 125.7, 124.5, 110.3, 108.8, 85.0, 83.7, 63.8, 63.7, 63.2, 62.4, 62.4, 60.7, 59.3, 44.0, 42.1, 41.8, 40.0, 33.8, 32.7, 29.9, 27.7, 27.6, 26.2, 25.9, 25.7, 25.2, 25.1, 21.8, 21.8, 14.2, 14.2, 14.1, 14.1, 14.0; HRMS (ESI) calcd for $C_{38}H_{42}NO_6$ $[M + H]^+$ 608.3007, found 608.3012.

Dimethyl 2'-benzyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5dab**), 3.2 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 111.7 mg, 95% yield; light yellow solid, mp 123–125 °C, IR (film) 1763, 1754, 1443, 1352, 1296, 1142 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, $J = 8.0$ Hz, 0.5H), 7.70–7.67 (m, 3H), 7.47–7.40 (m, 2.5H), 7.36–7.15 (m, 10H), 7.13 (d, $J = 4.0$ Hz, 2H), 4.50 (t, $J = 8.0$ Hz, 0.2H), 4.19–4.10 (m, 1.8H), 4.00 (d, $J = 16.0$ Hz, 0.9H), 3.91–3.81 (m, 0.7H), 3.75 (d, $J = 4.0$ Hz, 1.2H), 3.73 (s, 2.2H), 3.66 (s, 2.2H), 3.54–3.32 (m, 2.7H), 3.18 (dd, $J = 4.0, 16.0$ Hz, 0.2H), 2.39 (s, 0.7H), 2.36 (s, 2.2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.1, 198.8, 163.3, 162.9, 159.5, 154.9, 154.4, 148.0, 147.0, 144.2, 143.9, 137.6, 137.3, 137.1, 136.9, 135.5, 135.4, 135.0, 134.6, 131.6, 130.5, 130.1, 129.7, 129.4, 129.3, 128.9, 128.6, 128.5, 128.3, 128.2, 128.0, 127.6, 127.4, 127.3, 127.2, 126.7, 126.1, 125.8, 124.8, 109.2, 107.9, 100.2, 85.4, 84.1, 61.3, 60.7, 60.2, 58.4, 53.2, 52.1, 44.0, 42.4, 42.1, 40.5, 29.9, 21.8; HRMS (ESI) calcd for $C_{37}H_{34}NO_6$ $[M + H]^+$ 588.2381, found 588.2379.

Ethyl 2'-benzyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4'-carboxylate (**5dac**), 1.5 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 87.0 mg, 80% yield; light yellow oil, IR (film) 1704, 1682, 1454, 1372, 1278, 1106 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, $J = 8.0$ Hz, 1H), 7.73–7.71 (m, 1H), 7.67 (d, $J = 8.0$ Hz, 1H), 7.46–7.39 (m, 2H), 7.37 (d, $J = 4.0$ Hz, 2H), 7.34–7.27 (m, 4H), 7.26–7.21 (m, 4H), 7.19–7.12 (m, 3H), 4.45 (t, $J = 8.0$ Hz, 0.6H), 4.23–4.16 (m, 1.5H), 4.14–4.07 (m, 1.3H), 3.95–3.88 (m, 1H), 3.73 (d, $J = 16.0$ Hz, 0.6H), 3.50–3.33 (m, 2.4H), 3.17 (dd, $J = 16.0, 4.0$ Hz, 0.6H), 2.39 (s, 1.8H), 2.35 (s, 1.2H), 1.26–1.23 (m, 1.8H), 1.15 (d, $J = 8.0$ Hz, 1.2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 198.8, 163.8, 163.3, 156.4, 156.2, 147.8, 146.6, 144.2, 143.8, 138.3, 138.3, 138.0, 137.9, 137.5,

136.3, 135.1, 134.6, 131.6, 130.7, 129.7, 129.4, 129.4, 129.3, 128.7, 128.5, 128.4, 128.3, 128.3, 128.2, 127.9, 127.6, 127.4, 127.3, 127.0, 126.6, 126.0, 125.7, 124.7, 108.3, 127.7, 83.3, 82.1, 61.1, 60.6, 60.6, 60.1, 57.9, 43.9, 42.4, 42.3, 40.8, 29.9, 21.8, 21.8, 14.5, 14.4; HRMS (ESI) calcd for $C_{36}H_{34}NO_4$ $[M + H]^+$ 544.2482, found 544.2479.

tert-Butyl 2'-benzyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4'-carboxylate (**5dad**), 1.3 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 85.8 mg, 75% yield; reddish brown solid, mp 85–87 °C, IR (film) 1699, 1624, 1455, 1364, 1228, 1134 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, $J = 5.0$ Hz, 1H), 7.12 (d, $J = 5.0$ Hz, 1H), 7.68 (d, $J = 10.0$ Hz, 1H), 7.47–7.36 (m, 4H), 7.34–7.21 (m, 8H), 7.18–7.11 (m, 3H), 4.43 (t, $J = 10.0$ Hz, 0.5H), 4.13 (d, $J = 5.0$ Hz, 0.4H), 4.10–4.05 (m, 0.5H), 3.93–3.85 (m, 0.9H), 3.75 (d, $J = 20.0$ Hz, 0.5H), 3.51–3.37 (m, 1.8H), 3.31 (dd, $J = 20.0, 10.0$ Hz, 0.6H), 3.17 (dd, $J = 15.0, 5.0$ Hz, 0.5H), 2.40 (s, 1.7H), 2.36 (s, 1.3H), 1.40 (s, 5H), 1.30 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.3, 198.9, 163.3, 162.8, 156.0, 155.9, 147.9, 146.6, 144.2, 143.8, 138.6, 138.6, 138.1, 138.0, 137.7, 136.4, 135.1, 134.6, 131.7, 130.7, 129.6, 129.4, 129.4, 129.3, 129.2, 128.6, 128.5, 128.4, 128.3, 128.2, 128.2, 127.9, 127.5, 127.4, 127.2, 127.2, 126.9, 126.9, 126.5, 126.2, 125.8, 124.6, 109.9, 109.1, 83.3, 82.1, 80.6, 80.5, 61.1, 60.9, 60.7, 58.0, 43.9, 42.5, 42.4, 40.7, 28.4, 28.2, 21.8, 21.8; HRMS (ESI) calcd for $C_{38}H_{37}NO_6Na$ $[M + Na]^+$ 594.2615, found 594.2615.

2-(4'-Acetyl-2'-benzyl-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazol]-3-yl)-1-(*p*-tolyl)ethan-1-one (**5dae**), 4.0 : 1 dr. Purified by silica gel column chromatography (30 : 1 petroleum ether/ethyl acetate): 98.6 mg, 96% yield; white solid, mp 71–73 °C, IR (film) 1679, 1653, 1457, 1374, 1228, 1140 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, $J = 8.0$ Hz, 1.5H), 7.70–7.65 (m, 0.6H), 7.45–7.34 (m, 3H), 7.31–7.17 (m, 12H), 7.13 (d, $J = 4.0$ Hz, 1H), 4.44 (d, $J = 8.0$ Hz, 0.8H), 4.20 (d, $J = 8.0$ Hz, 0.2H), 4.13–4.07 (m, 0.2H), 4.03 (d, $J = 12.0$ Hz, 0.8H), 3.86 (d, $J = 16.0$ Hz, 0.2H), 3.70 (d, $J = 16.0$ Hz, 0.8H), 3.48–3.36 (m, 2H), 3.13 (dd, $J = 16.0, 4.0$ Hz, 0.8H), 2.38 (s, 2.4H), 2.35 (s, 0.6H), 2.32 (s, 2.3H), 2.22 (s, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4, 198.8, 191.7, 191.3, 157.7, 157.6, 147.6, 146.5, 144.1, 143.8, 138.2, 137.9, 137.9, 137.8, 137.4, 136.5, 135.0, 134.6, 131.6, 130.7, 129.6, 129.4, 129.3, 128.7, 128.5, 128.3, 128.2, 128.2, 127.9, 127.6, 127.3, 127.3, 127.2, 127.0, 126.7, 125.9, 125.4, 124.8, 118.1, 117.9, 83.6, 82.3, 61.2, 60.7, 59.8, 57.2, 43.9, 42.4, 42.2, 40.8, 29.9, 28.1, 28.0, 21.8, 21.8; HRMS (ESI) calcd for $C_{35}H_{32}NO_3$ $[M + H]^+$ 514.2377, found 514.2380.

Methyl 2'-benzyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2,5'-diphenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4'-carboxylate (**5daf**), 2.2 : 1 dr. Purified by silica gel column chromatography (10 : 1 petroleum ether/ethyl acetate): 93.2 mg, 77% yield; yellow white solid, mp 73–75 °C, IR (film) 1738, 1697, 1495, 1350, 1241, 1092 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, $J = 8.0$ Hz, 1.5H), 7.74 (t, $J = 8.0$ Hz, 1H), 7.53 (d, $J = 4.0$ Hz, 1.5H), 7.43–7.13 (m, 19H), 4.59 (t, $J = 8.0$ Hz, 0.7H), 4.25 (d, $J = 8.0$ Hz, 0.3H), 4.17–4.12 (m, 0.3H), 4.05 (d, $J = 16.0$ Hz, 0.3H), 3.93–3.85 (m, 1.3H), 3.59 (s, 2.7H), 3.55–3.45 (m, 1.5H), 3.41–3.34 (m, 0.8H), 3.22–3.17 (m, 0.8H), 2.39 (s, 2.1H), 2.37 (s, 0.9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4, 199.2, 166.7, 164.9, 148.1, 147.1,



144.1, 143.8, 138.6, 138.1, 138.0, 137.8, 136.4, 134.7, 131.9, 130.6, 130.5, 129.6, 129.4, 129.4, 129.3, 129.2, 128.6, 128.6, 128.5, 128.4, 128.3, 128.3, 128.2, 128.0, 127.9, 127.9, 127.8, 127.4, 127.3, 127.0, 127.0, 126.8, 126.7, 126.2, 125.8, 124.7, 101.7, 86.1, 84.8, 62.2, 60.5, 60.2, 58.8, 51.2, 3.9, 42.9, 42.2, 40.5, 29.9, 21.8, 21.8; HRMS (ESI) calcd for $C_{41}H_{36}NO_4$ $[M + H]^+$ 606.2639, found 606.2646.

Ethyl 2'-benzyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2,5'-diphenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4'-carboxylate (**5dag**), 1.5 : 1 dr. Purified by silica gel column chromatography (10 : 1 petroleum ether/ethyl acetate): 99.2 mg, 80% yield; yellow white solid, mp 81–83 °C, IR (film) 1695, 1646, 1454, 1372, 1336, 1091 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, $J = 8.0$ Hz, 1.3H), 7.74 (t, $J = 8.0$ Hz, 1.4H), 7.53 (d, $J = 8.0$ Hz, 1.4H), 7.44–7.13 (m, 19H), 4.58 (t, $J = 8.0$ Hz, 0.6H), 4.26 (d, $J = 8.0$ Hz, 0.4H), 4.17–3.96 (m, 2.3H), 3.94–3.86 (m, 1.5H), 3.66–3.59 (m, 1.1H), 3.53 (d, $J = 12.0$ Hz, 0.7H), 3.35 (dd, $J = 20.0, 8.0$ Hz, 0.7H), 3.20 (dd, $J = 16.0, 4.0$ Hz, 0.6H), 2.40 (s, 1.8H), 2.37 (s, 1.2H), 0.99 (d, $J = 8.0$ Hz, 1.8H), 0.90 (d, $J = 8.0$ Hz, 1.2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4, 199.2, 166.5, 166.4, 166.0, 148.2, 147.1, 144.1, 143.8, 141.3, 138.9, 138.8, 138.2, 138.0, 137.9, 136.5, 135.2, 134.7, 131.9, 130.6, 130.6, 129.5, 129.4, 129.4, 129.3, 129.2, 128.6, 128.6, 128.5, 128.4, 128.3, 128.3, 128.2, 128.0, 127.9, 127.8, 127.8, 127.4, 127.2, 127.0, 126.9, 126.8, 126.6, 126.3, 125.9, 124.6, 102.7, 102.0, 86.0, 84.8, 62.2, 60.5, 60.2, 60.0, 59.9, 58.8, 43.9, 42.9, 42.2, 40.6, 32.1, 29.9, 21.8, 21.8, 14.0, 13.9; HRMS (ESI) calcd for $C_{42}H_{37}NO_4Na$ $[M + Na]^+$ 642.2615, found 642.2610.

2-(4'-Acetyl-2'-benzyl-2,5'-diphenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazol]-3-yl)-1-(*p*-tolyl)ethan-1-one (**5dah**), 5.0 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 96.7 mg, 82% yield; light yellow solid, mp 70–72 °C, IR (film) 1736, 1680, 1454, 1371, 1241, 1118 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, $J = 8.0$ Hz, 1.5H), 7.75–7.72 (m, 0.6H), 7.53 (d, $J = 8.0$ Hz, 1.5H), 7.42–7.13 (m, 19H), 6.97 (d, $J = 8.0$ Hz, 0.6H), 4.59 (t, $J = 8.0$ Hz, 0.8H), 4.32–4.26 (m, 0.2H), 4.17–4.09 (m, 0.2H), 4.05 (d, $J = 12.0$ Hz, 0.1H), 3.95–3.88 (m, 1.7H), 3.64 (t, $J = 8.0$ Hz, 0.5H), 3.52–3.39 (m, 1.8H), 3.16 (dd, $J = 16.0, 4.0$ Hz, 1H), 2.39 (s, 2.4H), 2.37 (s, 0.6H), 1.97 (s, 2.5H), 1.83 (s, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 199.2, 194.0, 167.9, 148.2, 147.1, 144.1, 143.7, 138.3, 138.1, 137.8, 136.6, 135.3, 134.7, 132.0, 131.0, 130.9, 130.7, 129.5, 129.4, 129.4, 129.3, 129.2, 128.9, 128.8, 128.7, 128.6, 128.5, 128.3, 128.0, 127.8, 127.5, 127.3, 127.1, 126.9, 126.8, 126.2, 125.7, 124.8, 113.4, 85.5, 61.7, 60.3, 58.5, 43.8, 43.0, 42.1, 40.7, 30.2, 30.0, 29.9, 21.8; HRMS (ESI) calcd for $C_{41}H_{36}NO_3$ $[M + H]^+$ 590.2690, found 590.2692.

2-(2'-Benzyl-4'-(2,4-dinitrophenyl)-2,5'-diphenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazol]-3-yl)-1-(*p*-tolyl)ethan-1-one (**5dai**), 1.8 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 121.3 mg, 85% yield; brownish red solid, mp 135–137 °C, IR (film) 1721, 1680, 1536, 1453, 1345, 1180 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 8.31 (d, $J = 8.0$ Hz, 1H), 7.87 (d, $J = 8.0$ Hz, 2H), 7.53–7.14 (m, 20H), 6.97 (d, $J = 8.0$ Hz, 2H), 4.70 (s, 0.7H), 4.25–4.03 (m, 1.6H), 3.90 (d, $J = 8.0$ Hz, 1H), 3.63 (d, $J = 12.0$ Hz, 1H), 3.41 (d, $J = 4.0$ Hz, 1.7H), 2.42 (s, 1.9H), 2.37 (s, 1.1H), 3.71 (d, $J = 16.0$ Hz,

0.6H), 3.49–3.28 (m, 2.4H), 3.17 (dd, $J = 16.0, 4.0$ Hz, 0.5H), 2.39 (s, 1.6H), 2.35 (s, 1.4H), 2.06 (s, 1.5H), 2.00 (s, 1.4H), 1.14 (t, $J = 8.0$ Hz, 1.6H), 1.05 (d, $J = 8.0$ Hz, 1.4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.7, 150.5, 145.5, 144.4, 144.0, 138.1, 137.8, 135.7, 135.6, 135.4, 134.7, 131.1, 131.0, 130.1, 129.5, 129.3, 129.0, 128.8, 128.7, 128.6, 128.5, 128.4, 128.1, 128.0, 127.8, 127.6, 127.4, 127.2, 126.8, 126.6, 124.6, 121.0, 117.9, 88.8, 86.9, 59.6, 41.3, 34.6, 29.8, 21.9; HRMS (ESI) calcd for $C_{45}H_{35}N_3O_6Na$ $[M + Na]^+$ 736.2418, found 736.2425.

Ethyl 2'-benzyl-5'-methyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4'-carboxylate (**5daj**), 1.1 : 1 dr. Purified by silica gel column chromatography (20 : 1 petroleum ether/ethyl acetate): 50.2 mg, 45% yield; brown solid, mp 39–41 °C, IR (film) 1734, 1696, 1473, 1374, 1258, 1107 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, $J = 8.0$ Hz, 1H), 7.69 (t, $J = 8.0$ Hz, 2H), 7.41–7.33 (m, 4H), 7.31–7.09 (m, 11H), 4.48 (t, $J = 8.0$ Hz, 0.5H), 4.23–3.98 (m, 3H), 3.87–3.78 (m, 1H), 3.71 (d, $J = 16.0$ Hz, 0.6H), 3.49–3.28 (m, 2.4H), 3.17 (dd, $J = 16.0, 4.0$ Hz, 0.5H), 2.39 (s, 1.6H), 2.35 (s, 1.4H), 2.06 (s, 1.5H), 2.00 (s, 1.4H), 1.14 (t, $J = 8.0$ Hz, 1.6H), 1.05 (d, $J = 8.0$ Hz, 1.4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4, 199.1, 168.5, 168.3, 164.9, 164.6, 147.7, 146.7, 144.1, 143.7, 139.4, 139.1, 138.3, 137.9, 136.6, 135.1, 134.7, 131.6, 130.5, 129.4, 129.3, 129.3, 129.0, 128.6, 128.5, 128.5, 128.3, 128.2, 128.1, 127.7, 127.4, 127.3, 127.0, 126.7, 126.7, 126.4, 126.2, 125.9, 124.5, 102.1, 101.6, 84.7, 83.5, 61.4, 60.8, 60.3, 59.7, 59.6, 58.1, 43.9, 42.6, 42.3, 40.3, 29.9, 21.8, 21.8, 14.4, 14.3, 13.2, 13.1; HRMS (ESI) calcd for $C_{37}H_{35}NO_4Na$ $[M + Na]^+$ 580.2458, found 580.2460.

2'-Benzyl-5'-methyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3,3a',6a'-tetrahydro-2'*H*,4'*H*-spiro[indene-1,3'-pyrrolo[3,4-d]isoxazole]-4',6'(5'*H*)-dione (**5dak**), 2.0 : 1 dr. Purified by silica gel column chromatography (10 : 1 petroleum ether/ethyl acetate): 76.8 mg, 69% yield; yellowish white solid, mp 110–112 °C, IR (film) 1709, 1677, 1453, 1377, 1281, 1181 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, $J = 8.0$ Hz, 0.7H), 7.54 (d, $J = 8.0$ Hz, 1.2H), 7.41–7.17 (m, 15H), 7.10 (d, $J = 4.0$ Hz, 0.8H), 7.00 (d, $J = 8.0$ Hz, 0.5H), 4.94 (d, $J = 8.0$ Hz, 0.6H), 4.66 (d, $J = 8.0$ Hz, 0.3H), 4.56–4.51 (m, 0.1H), 4.37–4.29 (m, 0.5H), 4.11–3.95 (m, 2.1H), 3.90–3.78 (m, 1H), 3.73–3.67 (m, 0.4H), 3.51–3.44 (m, 0.4H), 3.36–3.29 (m, 1.2H), 3.21–3.15 (m, 1.3H), 3.00 (s, 1H), 2.50 (s, 2H), 2.39 (s, 1H), 2.38 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.8, 175.2, 173.9, 172.7, 146.5, 145.0, 144.3, 141.3, 137.4, 137.2, 136.8, 134.9, 134.7, 134.4, 134.4, 132.1, 130.7, 129.8, 129.6, 129.5, 128.8, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.7, 127.6, 127.2, 127.1, 125.3, 124.9, 124.7, 124.7, 79.8, 78.8, 75.4, 60.3, 58.7, 58.1, 56.8, 56.4, 56.0, 46.5, 43.4, 43.0, 42.6, 29.9, 24.9, 24.4, 21.8. HRMS (ESI) calcd for $C_{36}H_{32}N_2O_4Na$ $[M + Na]^+$ 579.2254, found 579.2259.

Representative procedure for the cycloaddition reaction of generated *in situ* ketonitrone (Table 3, 5aaa). A 10 mL round-bottom flask was charged with **1a** (0.1542 g, 0.50 mmol), **2a** (0.0798 g, 0.50 mmol), EtONa (0.0443 g, 0.65 mmol), and DCM (5.0 mL) under air atmosphere. The reaction mixture was stirred at room temperature for 12 h, then filtered through a short pad of silica gel, and diethyl acetylenedicarboxylate (0.1277 g, 0.75 mmol) was added. The reaction was allowed to stir under argon at 40 °C for 23 h, and then was concentrated. The crude residue



was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate from 50 : 1 to 10 : 1) to afford the desired product **5aaa** as a light yellow solid (0.2286 g, 76% yield, 9 : 1 dr).

Diethyl 2'-benzyl-3-(2-oxo-2-phenylethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5aaa**), 9 : 1 dr. Purified by silica gel column chromatography (petroleum ether/ethyl acetate from 50 : 1 to 10 : 1): 228.6 mg, 76% yield; light yellow solid, mp 127–129 °C, IR (film) 1740, 1706, 1454, 1393, 1239, 1106 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.52–7.42 (m, 3H), 7.39–7.20 (m, 12H), 4.21–4.08 (m, 6H), 4.02 (d, *J* = 16.0 Hz, 1H), 3.56–3.42 (m, 3H), 1.31–1.19 (m, 3.3H), 1.13 (t, *J* = 8.0 Hz, 2.7H); ¹³C NMR (100 MHz, CDCl₃) δ 199.2, 162.4, 159.2, 154.8, 148.0, 137.8, 137.5, 137.4, 137.2, 133.1, 131.6, 129.7, 129.0, 128.7, 128.6, 128.2, 128.1, 127.6, 127.3, 127.2, 126.6, 126.3, 108.7, 85.3, 62.6, 60.9, 60.6, 58.4, 43.9, 42.6, 14.1, 14.0.

Diethyl 2'-benzyl-3-(2-oxo-2-(*o*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5baa**), 23.0 : 1 dr. Purified by silica gel column chromatography (petroleum ether/ethyl acetate from 50 : 1 to 10 : 1): 200.1 mg, 65% yield; light yellow solid, mp 96–97 °C, IR (film) 1743, 1719, 1495, 1393, 1300, 1176 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.64–7.62 (m, 2H), 7.46–7.43 (m, 2H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.34–7.31 (m, 3H), 7.29–7.18 (m, 9H), 7.16–7.12 (m, 1H), 4.19–4.08 (m, 6H), 3.99 (d, *J* = 12.0 Hz, 1H), 3.52 (d, *J* = 12.0 Hz, 1H), 3.48–3.41 (m, 2H), 2.49 (s, 0.1H), 2.36 (s, 3H), 1.22 (t, *J* = 8.0 Hz, 3H), 1.13 (t, *J* = 8.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 202.8, 162.4, 159.2, 154.8, 148.2, 138.4, 138.3, 137.8, 137.3, 137.2, 132.1, 131.7, 131.4, 129.7, 129.0, 128.7, 128.5, 128.2, 127.6, 127.4, 127.2, 126.4, 126.3, 125.7, 108.7, 85.3, 62.6, 60.9, 60.6, 58.4, 45.6, 43.9, 21.4, 14.1, 14.0.

Diethyl 2'-benzyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5daa**), 14.0 : 1 dr. Purified by silica gel column chromatography (petroleum ether/ethyl acetate from 50 : 1 to 10 : 1): 243.2 mg, 79% yield; 112.1 mg, 89% yield; light yellow solid, mp 140–142 °C, IR (film) 1740, 1713, 1474, 1370, 1241, 1140 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.68 (d, *J* = 8.0 Hz, 4H), 7.43–7.39 (m, 2H), 7.32–7.15 (m, 12H), 4.21–4.10 (m, 6H), 4.02 (d, *J* = 12.0 Hz, 1H), 3.54–3.39 (m, 3H), 2.40 (s, 0.2H), 2.37 (s, 2.8H), 1.23 (t, *J* = 8.0 Hz, 3.2H), 1.13 (t, *J* = 8.0 Hz, 2.8H); ¹³C NMR (100 MHz, CDCl₃) δ 198.8, 162.4, 159.2, 154.8, 148.1, 143.9, 137.8, 137.5, 137.2, 135.1, 131.6, 129.7, 129.4, 129.0, 128.6, 128.3, 128.2, 127.6, 127.3, 127.1, 126.6, 126.3, 108.8, 85.3, 62.6, 60.9, 60.6, 58.4, 44.0, 42.5, 21.8, 14.1, 14.0.

Diethyl 2'-benzyl-3-(2-(4-bromophenyl)-2-oxoethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5eaa**), 5.5 : 1 dr. Purified by silica gel column chromatography (petroleum ether/ethyl acetate from 50 : 1 to 10 : 1): 251.8 mg, 74% yield; light yellow solid, mp 115–117 °C, IR (film) 1735, 1707, 1499, 1370, 1242, 1169 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, *J* = 8.0 Hz, 0.4H), 7.66–7.56 (m, 3.5H), 7.50–7.37 (m, 4H), 7.35–7.14 (m, 10H), 4.22–4.08 (m, 5.2H), 4.03 (d, *J* = 12.0 Hz, 0.9H), 3.89–3.76 (m, 0.4H), 3.54–3.48 (m, 1.8H), 3.38–3.28 (m, 1H), 3.20–3.14 (m, 0.2H), 1.29–1.20 (m, 3.6H), 1.13 (t, *J* = 8.0 Hz, 2.5H); ¹³C NMR (100 MHz, CDCl₃) δ 198.1, 162.4,

159.2, 154.8, 147.7, 137.8, 137.4, 137.1, 136.1, 132.1, 131.9, 131.5, 130.5, 129.9, 129.7, 129.7, 128.9, 128.6, 128.6, 128.3, 128.2, 128.0, 127.7, 127.4, 127.3, 126.4, 126.4, 108.6, 85.3, 62.7, 60.9, 60.6, 58.3, 43.9, 42.4, 14.1, 14.0.

Diethyl 2'-benzyl-3-(2-(furan-2-yl)-2-oxoethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5faa**), 33.0 : 1 dr. Purified by silica gel column chromatography (petroleum ether/ethyl acetate from 50 : 1 to 10 : 1): 210.1 mg, 71% yield; light yellow solid, mp 141–143 °C, IR (film) 1739, 1710, 1465, 1371, 1189, 1140 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.68 (d, *J* = 10.0 Hz, 2H), 7.45–7.42 (m, 2H), 7.40 (d, *J* = 5.0 Hz, 2H), 7.36–7.33 (m, 3H), 7.30–7.20 (m, 6H), 7.00 (d, *J* = 5.0 Hz, 1H), 6.50–6.49 (m, 0.03H), 6.44–6.43 (m, 1H), 4.20–4.15 (m, 3H), 4.14–4.06 (m, 3H), 4.01 (d, *J* = 15.0 Hz, 1H), 3.54 (d, *J* = 15.0 Hz, 1H), 3.47 (dd, *J* = 20.0, 10.0 Hz, 1H), 3.21 (dd, *J* = 20.0, 5.0 Hz, 1H), 1.23 (t, *J* = 10.0 Hz, 3H), 1.12 (t, *J* = 10.0 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 188.7, 162.4, 159.2, 154.9, 153.3, 147.5, 146.2, 137.8, 137.5, 137.0, 131.6, 129.6, 129.1, 128.6, 128.1, 127.6, 127.4, 127.2, 126.4, 126.3, 116.8, 112.5, 108.5, 85.2, 62.7, 60.9, 60.7, 58.3, 44.0, 42.3, 14.1, 14.0.

Diethyl 2'-benzyl-2-(4-methoxyphenyl)-3-(2-oxo-2-(*p*-tolyl)ethyl)-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5laa**), 29.0 : 1 dr. Purified by silica gel column chromatography (petroleum ether/ethyl acetate from 50 : 1 to 10 : 1): 222.8 mg, 69% yield; light yellow solid, mp 85–86 °C, IR (film) 1738, 1712, 1496, 1393, 1305, 1140 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.71 (d, *J* = 5.0 Hz, 2H), 7.59 (d, *J* = 10.0 Hz, 2H), 7.44–7.39 (m, 2H), 7.36–7.32 (m, 4H), 7.30–7.27 (m, 3H), 7.17 (d, *J* = 10.0 Hz, 2H), 6.78 (d, *J* = 10.0 Hz, 2H), 4.21–4.16 (m, 2H), 4.15–4.05 (m, 4H), 4.01 (d, *J* = 15.0 Hz, 1H), 3.75 (s, 3H), 3.52–3.48 (m, 2H), 3.44–3.38 (m, 1H), 2.37 (s, 2.9H), 1.25 (t, *J* = 10.0 Hz, 3.1H), 1.13 (t, *J* = 10.0 Hz, 2.9H); ¹³C NMR (125 MHz, CDCl₃) δ 198.9, 162.5, 159.2, 158.9, 154.6, 148.1, 143.9, 137.7, 137.5, 135.1, 132.7, 129.6, 129.3, 129.2, 129.0, 128.6, 128.3, 127.6, 127.1, 126.6, 126.3, 113.6, 108.9, 85.3, 62.6, 60.9, 60.6, 57.7, 55.3, 44.1, 42.5, 21.8, 14.1, 14.0.

Diethyl 2'-benzyl-5-chloro-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5oaa**), 12.0 : 1 dr. Purified by silica gel column chromatography (petroleum ether/ethyl acetate from 50 : 1 to 10 : 1): 211.3 mg, 65% yield; light yellow solid, mp 118–120 °C, IR (film) 1740, 1710, 1454, 1394, 1304, 1143 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.83 (d, *J* = 8.0 Hz, 0.2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.65–7.62 (m, 2H), 7.48 (d, *J* = 4.0 Hz, 1H), 7.38–7.16 (m, 12H), 4.21–4.09 (m, 6H), 3.99 (d, *J* = 12.0 Hz, 1H), 3.52–3.38 (m, 3H), 2.40 (s, 0.2H), 2.38 (s, 2.7H), 1.23 (t, *J* = 8.0 Hz, 3H), 1.16 (t, *J* = 8.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 198.3, 162.3, 159.1, 155.1, 149.9, 144.1, 137.1, 136.7, 136.5, 135.6, 134.8, 131.5, 129.4, 129.0, 128.6, 128.3, 128.2, 127.7, 127.6, 127.5, 127.3, 127.1, 108.1, 84.7, 62.7, 61.0, 60.6, 58.5, 43.6, 42.0, 21.8, 14.1, 14.0.

Diethyl 2'-benzyl-6-methyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydrospiro[indene-1,3'-isoxazolidine]-4',5'-dicarboxylate (**5raa**), 14.8 : 1 dr. Purified by silica gel column chromatography (petroleum ether/ethyl acetate from 50 : 1 to 10 : 1): 198.4 mg, 63% yield; yellowish white solid, mp 145–147 °C, IR (film) 1749, 1712, 1453, 1305, 1200, 1178 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.70–7.65 (m, 4H), 7.34 (t, *J* = 4.0 Hz, 4H), 7.30–7.20 (m, 6H),



7.16 (d, $J = 8.0$ Hz, 2H), 7.19 (d, $J = 8.0$ Hz, 1H), 4.21–4.05 (m, 6H), 4.00 (d, $J = 16.0$ Hz, 1H), 3.53 (d, $J = 12.0$ Hz, 1H), 3.49–3.37 (m, 2H), 2.37 (s, 3H), 2.36 (s, 3H), 1.25 (t, $J = 8.0$ Hz, 3.2H), 1.13 (t, $J = 8.0$ Hz, 2.8H); ^{13}C NMR (100 MHz, CDCl_3) δ 199.0, 162.5, 159.2, 154.5, 145.0, 143.8, 137.8, 137.5, 137.3, 136.8, 135.1, 131.6, 130.6, 129.3, 129.1, 128.6, 128.3, 128.2, 127.6, 127.3, 126.6, 126.2, 123.0, 109.0, 100.1, 93.3, 85.3, 62.6, 60.8, 60.6, 58.6, 43.7, 42.6, 21.8, 21.6, 14.1, 14.0.

Dimethyl 2'-benzyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydro-2'*H*-spiro[indene-1,3'-isoxazole]-4',5'-dicarboxylate (**5dab**), 11.0 : 1 dr. Purified by silica gel column chromatography (petroleum ether/ethyl acetate from 50 : 1 to 10 : 1): 241.0 mg, 82% yield; light yellow solid, mp 132–134 °C, IR (film) 1765, 1750, 1448, 1352, 1307, 1140 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.68 (t, $J = 8.0$ Hz, 4H), 7.47–7.41 (m, 2H), 7.36–7.20 (m, 10H), 7.16 (d, $J = 8.0$ Hz, 2H), 4.19–4.10 (m, 2H), 4.00 (d, $J = 16.0$ Hz, 1H), 3.73 (s, 3H), 3.66 (s, 3H), 3.52–3.39 (m, 3H), 2.39 (s, 0.3H), 2.37 (s, 2.7H); ^{13}C NMR (100 MHz, CDCl_3) δ 198.8, 162.9, 159.5, 154.4, 148.0, 143.9, 137.6, 137.3, 137.1, 135.0, 131.6, 129.7, 129.3, 128.9, 128.6, 128.3, 128.2, 127.6, 127.4, 127.3, 126.7, 126.1, 109.2, 85.3, 60.7, 58.4, 53.3, 52.1, 44.0, 42.4, 21.8.

Diethyl 2'-methyl-3-(2-oxo-2-(*p*-tolyl)ethyl)-2-phenyl-2,3-dihydro-spiro[indene-1,3'-isoxazolidine]-4',5'-dicarboxylate (**5dca**), 7.3 : 1 dr. Purified by silica gel column chromatography (petroleum ether/ethyl acetate from 50 : 1 to 10 : 1): 121.4 mg, 45% yield; brown solid, mp 74–76 °C, IR (film) 1737, 1702, 1460, 1370, 1291, 1186 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.84 (d, $J = 10.0$ Hz, 0.3H), 7.72 (d, $J = 10.0$ Hz, 1.7H), 7.68 (d, $J = 5.0$ Hz, 1.7H), 7.44 (d, $J = 5.0$ Hz, 0.3H), 7.37 (d, $J = 10.0$ Hz, 1H), 7.32 (t, $J = 5.0$ Hz, 1H), 7.29–7.19 (m, 7H), 7.14 (d, $J = 10.0$ Hz, 0.2H), 4.26–4.14 (m, 2.3H), 4.13–4.04 (m, 3.5H), 3.43 (dd, $J = 15.0$, 5.0 Hz, 0.9H), 3.32 (dd, $J = 15.0$, 10.0 Hz, 1H), 2.62 (s, 2.6H), 2.45 (s, 0.4H), 2.40 (s, 0.4H), 2.38 (s, 2.6H), 1.31–1.19 (m, 3.4H), 1.11 (t, $J = 10.0$ Hz, 2.6H); ^{13}C NMR (125 MHz, CDCl_3) δ 199.0, 162.6, 159.1, 153.8, 148.0, 143.8, 137.3, 137.2, 135.1, 131.8, 130.4, 129.9, 129.5, 129.4, 129.4, 128.5, 128.3, 128.0, 127.9, 127.4, 126.9, 126.5, 126.5, 108.9, 85.6, 62.6, 60.9, 58.1, 43.9, 43.7, 42.5, 21.8, 14.1, 14.0. HRMS (ESI) calcd for $\text{C}_{33}\text{H}_{34}\text{NO}_6$ [$\text{M} + \text{H}$] $^+$ 540.2381, found 540.2386.

Procedure for the synthesis of allylic alcohol 6 from spiroindanyl isoxazoline 5daa (Scheme 2). To a dried Schlenk flask was charged with **5daa** (0.1847 g, 0.30 mmol), zinc dust (0.1962 g, 3.00 mmol), NH_4Cl (0.3210 g, 6.00 mmol), and MeOH (3.0 mL) under air atmosphere. The reaction mixture was stirred at 75 °C for 5 h, then filtered through a short pad of silica gel and washed with ethyl acetate. After removal of solvent, the crude residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5 : 1, v/v) to afford the product **6** as a white solid (0.1153 g, 75% yield), mp. 50–52 °C, IR (film) 3486, 1730, 1680, 1606, 1453, 1366, 1224, 1079 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.02 (d, $J = 10.0$ Hz, 0.1H), 7.88–7.82 (m, 0.3H), 7.75 (d, $J = 10.0$ Hz, 0.1H), 7.67 (d, $J = 5.0$ Hz, 0.7H), 7.57–7.51 (m, 1.9H), 7.42 (d, $J = 10.0$ Hz, 0.2H), 7.40–7.35 (m, 1H), 7.32–7.22 (m, 2.6H), 7.19 (d, $J = 5.0$ Hz, 0.3H), 7.17–7.13 (m, 2H), 7.04–6.96 (m, 2.8H), 6.85 (d, $J = 5.0$ Hz, 0.2H), 6.74 (t, $J = 10.0$ Hz, 1.7H), 5.79 (d, $J = 10.0$ Hz, 0.2H), 5.47 (d, $J = 10.0$ Hz, 0.2H), 5.05–5.02 (m, 0.8H), 4.87 (d, $J = 10.0$ Hz, 0.8H), 3.40 (t, $J =$

10.0 Hz, 0.9H), 4.31–4.24 (m, 2.1H), 4.10–3.90 (m, 0.5H), 3.89–3.75 (m, 1.8H), 3.43 (d, $J = 5.0$ Hz, 0.8H), 3.19–3.01 (m, 1H), 2.84–2.74 (m, 0.9H), 2.41 (s, 0.2H), 2.37 (s, 0.5H), 2.36 (s, 2.2H), 1.30–1.21 (m, 3.5H), 1.11 (t, $J = 5.0$ Hz, 0.5H), 0.82 (t, $J = 10.0$ Hz, 2.1H); ^{13}C NMR (125 MHz, CDCl_3) δ 198.9, 173.4, 173.3, 167.5, 156.5, 152.7, 150.0, 143.8, 140.6, 140.3, 139.2, 134.7, 131.0, 130.5, 129.5, 129.3, 129.2, 128.9, 128.5, 128.5, 128.2, 128.1, 128.0, 127.5, 127.0, 127.0, 126.9, 126.7, 126.4, 125.7, 124.9, 124.6, 124.0, 70.3, 68.6, 62.3, 62.0, 61.2, 60.9, 55.4, 54.8, 43.4, 43.1, 39.7, 39.0, 21.8, 14.3, 14.2, 14.0, 13.8; HRMS (ESI) calcd for $\text{C}_{32}\text{H}_{33}\text{O}_6$ [$\text{M} + \text{H}$] $^+$ 513.2272, found 513.2277.

Procedure for the $\text{Co}_2(\text{CO})_8$ catalyzed rearrangement of spiroindanyl isoxazoline 5raa (Scheme 2). To a dried Schlenk flask was charged with **5raa** (0.1260 g, 0.20 mmol), $\text{Co}_2(\text{CO})_8$ (0.0342 g, 0.10 mmol), and MeCN (4.0 mL) under argon. The reaction mixture was stirred at 100 °C for 12 h, then filtered through a short pad of silica gel and washed with ethyl acetate. After removal of solvent, the crude residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5 : 1, v/v) to afford the product **7** as a light yellow solid (0.0655 g, 52% yield), mp 45–47 °C, IR (film) 1733, 1710, 1679, 1494, 1284, 1215, 1093 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.89 (d, $J = 8.0$ Hz, 0.3H), 7.77 (d, $J = 8.0$ Hz, 1.7H), 7.39–7.33 (m, 2H), 7.29 (d, $J = 8.0$ Hz, 2H), 7.15–7.09 (m, 4H), 7.07–6.98 (m, 3H), 5.48 (d, $J = 16.0$ Hz, 0.8H), 5.20 (d, $J = 16.0$ Hz, 0.2H), 4.69 (d, $J = 16.0$ Hz, 0.2H), 4.19 (d, $J = 16.0$ Hz, 0.9H), 4.08–4.02 (m, 1.3H), 3.98–3.92 (m, 1.7H), 3.83–3.73 (m, 2.9H), 3.62–3.56 (m, 0.2H), 3.32–3.26 (m, 0.9H), 3.15–3.03 (m, 0.3H), 2.89 (dd, $J = 16.0$, 4.0 Hz, 0.9H), 2.44 (s, 2.5H), 2.38 (s, 0.5H), 2.36 (s, 2.5H), 2.08 (s, 0.5H), 1.07 (d, $J = 8.0$ Hz, 0.6H), 1.03–0.97 (m, 5.4H); ^{13}C NMR (100 MHz, CDCl_3) δ 197.9, 165.8, 162.0, 161.7, 144.3, 141.5, 141.4, 137.3, 136.8, 135.7, 134.8, 131.9, 131.8, 130.9, 130.6, 129.5, 129.4, 129.3, 129.2, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 127.8, 127.7, 127.3, 127.0, 62.3, 61.7, 61.4, 51.4, 46.0, 45.9, 45.4, 44.9, 44.0, 40.2, 21.9, 21.6, 13.8, 13.7; HRMS (ESI) calcd for $\text{C}_{40}\text{H}_{40}\text{NO}_6$ [$\text{M} + \text{H}$] $^+$ 630.2850, found 630.2857.

Conflicts of interest

There are no conflicts to declare.

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