Supporting Information

Metal-free and benign approach for the synthesis of dihydro-5'h-spiro[benzo[c]chromene-8,4'-oxazole]-5',6(7h)-dione scaffolds as masked amino acids

Behnaz Shafiee,† Joseph Duffield,‡ Rudy Timm,‡ Rohana Liyanage,‡ Jackson O. Lay Jr.,‡ Hadi Amiri Rudbari,† Ahmad R. Khosropour,*,†,‡ and M. Hassan Beyzavi*,‡

†Department of Chemistry, University of Isfahan, Isfahan, 81746-73441, Iran.
‡Department of Chemistry and Biochemistry, University of Arkansas, Fayetteville, Arkansas 72701, United States

Email: khosropour@chem.ui.ac.ir
Email: beyzavi@uark.edu

Supporting Information

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I. General Methods
Chemicals were purchased from Aldrich and Merck chemical companies. Reactions were monitored by thin layer chromatography (TLC) using 0.25 mm pre-coated silica gel HF254 plates. Azlactones were prepared using literature procedures.1 NMR spectra were recorded on Brüker Avance 400 MHz Fourier-transform spectrometers.1H, 13C and 19F NMR spectra were referenced to residual solvent. Coupling constants are reported in hertz. FT-IR spectra were recorded on a Nicolet-Impact 400D instrument in the range of 400–4000 cm⁻¹ High resolution mass spectrometry (HRMS) data were obtained on a Bruker Apex II-FTMS using electrospray ionization (ESI) in positive or negative mode, depending on the analyte. Melting points were determined using Stuart Scientific SMP2 apparatus and are uncorrected. Silica gel (230-400 mesh) was used for column chromatography. Few compounds contain grease peak, which could not be eliminated completely. The yields for those compounds are reduced accordingly.

The X-ray data of 3c was collected at room temperature with a Bruker APEX II CCD area detector diffractometer using Mo Kα radiation (λ = 0.71073 Å). Data collections, cell refinements, data reductions and absorption corrections were performed using multiscan methods with Bruker software.2 The structure was solved by direct methods using SIR2004.3 The non-hydrogen atoms were refined anisotropically by the full matrix least squares method on F² using SHELXL.4 All hydrogen atoms were added at ideal positions and constrained to ride on their parent atoms. Crystallographic data are listed in Table S3.

For TLC-MALDI-MS imaging, TLC was run using n-hexanes:ethyl acetate (1:0.7) with TLC Silica Gel 60 T254, Merck, Darmstadt, Germany. TLC plate developed as described above was used for thin layer chromatography matrix assisted laser desorption ionization mass spectrometry (TLC-MALDI-MS) imaging analysis. Conventional air brush device was used for homogeneously coating the entire TLC plate with a 2,5-Dihydroxybenzoic acid (DHB) matrix aerosol (10 mL of 300 mg/mL DHB in in 90% Methanol). High purity nitrogen served as the nebulizing and drying gas. After complete drying, the plate was attached to a Bruker Daltonics MTP TLC adapter. MALDI-MS imaging and scanning of lanes on the TLC plate was performed using Bruker MALDI fleximaging 4.1software on Ultraflex II MALDI-TOF/TOF mass spectrometer equipped with a smartbeam™ solid state laser (Bruker Daltonik, Bremen, Germany) operated in positive ion reflectron mode. Matrix suppression was set to m/z <500. A pixel raster width of 600 μm spots
was defined with fleximaging 4.1 software on the entire TLC lane. For each pixel 200 laser shots were accumulated. The data were processed using Bruker Flex Imaging 4.1, and FlexAnalysis 3.4.

LC-ESI-MS: Liquid chromatography electrospray ionization mass spectrometry analysis of all samples were conducted using a Hewlet Packard 1100 series HPLC with a Bruker ESQUIRE 2000 (Billerica, MA) quadrupole ion trap mass spectrometer (Bruker, Daltonics Corp., Germany). For HPLC analysis, Discovery Bio Wide Pore reverse phase C8 columns (4.6 x 150 mm; 5 µm) was used. A solvent gradient, 25% acetonitrile in water to 100% acetonitrile in 25 min with a flow rate of 1 mL/min, was used in successfully separating all the products and intermediates in each sample. Samples were automatically injected using an autosampler with an injection volume of 2 µL. MS analysis was conducted in positive ion mode with a capillary voltage at 4 kV. A nebulizing gas (N2) pressure of 32 psi and a drying gas flow of 12 L/min were used. Bruker DataAnalysis 4.0 software program was used to analyze LC-ESI-MS data.
II. Experimental Procedure and Characterization Data

1. General procedure for synthesis of azlactone (d1·1i)1

The azlactone d1·1i was prepared according to the literatures. In a 25 ml round bottom flask, a mixture 4-methoxybenzaldehyde-α-d (1 mmol, 0.137 g), hippuric acid (1.1 mmol, 0.197 g) and calcium acetate (0.05 g) were prepared. The freshly distilled Ac2O (2 mmol, 0.204 g) was added to the mixture and heated at 80°C for 4 h. The reaction progress was monitored by TLC (petroleum ether/ethyl acetate: 7/1). After the reaction was completed, the reaction mixture was cooled to room temperature. Cold ethanol (15 mL) was added and the mixture was stirred for 10 min. The resulting mixture was filtered and washed with an aqueous solution (20 %) of NaHCO3 (15 mL). The crude product we purified by recrystallization from EtOH.

Characterization Data

(Z)-4-(4-methoxybenzylidene-d1)-2-phenyloxazol-5(4H)-one (d1·1i):

mp 156-157 °C (lit.1, 155-157 °C); IR (KBr): Vmax = 3054, 2936, 1177, 1644, 1253, 1152, 824, 692 cm⁻¹; ¹H NMR (400 MHz, CDCl3): δ = 8.09-8.16 (m, 4H), 7.53 (t, J = 7.4 Hz, 1H), 7.46 (m, 2H), 6.94 (d, J = 9.0 Hz, 2H), 3.83 (s, 3H).
2. General method for preparation of (3)

A mixture of azlactone 1 (1.0 mmol), 4-hydroxycoumarine 2 (0.5 mmol), and diisopropylethylamine (1.0 mmol) in propylene carbonate (1 mL) was stirred at 80 °C for 8 h. After completion of the reaction as monitored by TLC (eluent: n-hexane/ethyl acetate, 1:1). The resulting mixture was cooled to room temperature. The reaction was treated with water (10 mL) and the product was filtered off and the PC was recovered by evaporating the water. The recovered PC was subjected to the next cycle without further purification. The crude product was recrystallized from hot ethanol to obtain 3 as white solids.

Characterization data of products

(±) N-(5′,6-dioxo-2′,7,9-triphenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3a):

white solid; yield 52% (160 mg); d. r. = 96:4; mp 288-289 °C; IR (KBr): ν_{max} = 3414, 3032, 2924, 2854, 1813, 1728, 1654, 1602, 1313, 1451 cm^{-1}; ^1H NMR (400 MHz, DMSO- d_6): δ = 9.06 (br s, 1H), 8.04 (br s, 1H), 7.70 (t, J = 7.7 Hz, 1H), 7.56-7.64 (m, 6H), 7.42-7.53 (m, 6H), 7.34-7.40 (m, 3H), 7.15-7.27 (m, 6H), 6.91 (d, J = 6.5 Hz, 1H), 6.69 (br s, 1H), 4.87 (d, J = 1.4 Hz, 1H), 4.27 (br
s, 1H); $^{13}$C NMR (100 MHz, DMSO- $d_6$): $\delta$ = 176.5, 165.9, 165.8, 159.3, 158.3, 151.9, 150.5, 136.6, 150.0, 133.5, 133.5, 133.1, 131.5, 130.8, 129.0, 128.4, 1287.1, 127.9, 127.4, 127.1, 126.8, 125.4, 125.0, 124.4, 124.1, 122.8, 117.8, 116.8, 76.5, 52.5, 49.9, 46.8; HRMS (ESI, [M + H]$^+$): m/z calcd for C$_{40}$H$_{27}$F$_2$N$_2$O$_5$, 653.1888, found 653.1895.

($\pm$)N-(7,9-bis(4-fluorophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3b):

![Chemical Structure Image]

white solid; yield 85% (277 mg); d. r. = 97:3; mp 301-302 °C; IR (KBr): $\nu_{\text{max}}$ = 3358, 3068, 2927, 2857, 1813, 1722, 1653, 1604, 1315, 1450 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO- $d_6$): $\delta$ = 9.00 (br s, 1H), 7.92 (br s, 1H), 7.57-7.63 (m, 2H), 7.53-7.55 (m, 4H), 7.41-7.50 (m, 4H), 7.32-7.39 (m, 6H), 6.99-7.07 (m, 3H), 6.90-6.95 (m, 2H), 6.55 (br s, 1H), 4.83 (d, $J = 1.7$ Hz, 1H), 4.22 (br s, 1H); $^{13}$C NMR (100 MHz, DMSO- $d_6$): $\delta$ = 176.4, 166.0, 165.9, 162.6, 162.4, 160.2, 160.0, 159.5, 158.2, 152.0, 150.5, 133.4, 133.4, 132.8, 131.6, 131.1, 129.1, 128.4, 127.5, 127.2, 126.8, 125.0, 124.4, 123.9, 122.5, 117.7, 116.8, 115.3, 115.1, 114.9, 114.4, 114.2, 76.5, 51.5, 49.0, 46.8; $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ = -113.47 (tt, $J = 8.7$, 5.5 Hz), -114.06 (m); HRMS (ESI, [M + H]$^+$): m/z calcd for C$_{46}$H$_{27}$F$_2$N$_2$O$_5$, 653.1888, found 653.1895.

($\pm$)N-(7,9-bis(4-chlorophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3c):

![Chemical Structure Image]
White solid; yield 90% (308 mg); d. r. = 98:2; mp 310-311 °C; IR (KBr): \( \nu_{\text{max}} = 3363, 3062, 2924, 2854, 1807, 1707, 1661, 1604, 1314, 1451 \text{ cm}^{-1} \); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.95 \) (dd, \( J = 8.2, J = 1.1 \text{ Hz}, 1H \)), 7.56 (t, \( J = 7.8 \text{ Hz}, 1H \)), 7.40-7.46 (m, 4H), 7.22-7.32 (m, 9H), 7.06-7.10 (m, 5H), 6.68-6.74 (m, 3H), 6.55 (br s, 1H), 4.25 (d, \( J = 1.6 \text{ Hz}, 1H \)), 3.98 (d, \( J = 10.8 \text{ Hz}, 1H \)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 176.3, 166.7, 160.8, 160.0, 152.3, 152.2, 134.9, 134.1, 133.5, 133.3, 133.0, 132.7, 131.8, 131.7, 128.9, 128.7, 128.5, 128.0, 127.6, 127.0, 126.7, 126.3, 125.4, 124.4, 122.4, 118.1, 117.0, 76.4, 53.2, 49.7, 47.5; HRMS (ESI, [M + H]\(^+\)): m/z calcd for C\(_{40}\)H\(_{27}\)Cl\(_2\)N\(_2\)O\(_5\), 685.1297, 687.1268, found 685.1309, 687.1287.

\(^{(\pm)}\)N-(7,9-bis(4-bromophenyl)-5′,6-dioxo-2′-phenyl-6,7,9,10-tetrahydro-5′H-spiro[benzo[c]chromene-8,4′-oxazole]-10-yl)benzamide (3d):

White solid; yield 89% (344 mg); d. r. = 97:3; mp 315-316 °C; IR (KBr): \( \nu_{\text{max}} = 3365, 3061, 2922, 2852, 1806, 1710, 1663, 1603, 1314, 1451 \text{ cm}^{-1} \); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.94 \) (d, \( J = 7.6 \text{ Hz}, 1H \)), 7.53 (t, \( J = 7.5 \text{ Hz}, 1H \)), 7.44-7.46 (m, 2H), 7.38 (t, \( J = 8.5 \text{ Hz}, 2H \)), 7.24-7.33 (m, 8H), 6.96-7.14 (m, 6H), 6.68-6.89 (m, 4H), 4.34 (s, 1H), 3.93 (d, \( J = 10.8 \text{ Hz}, 1H \)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 176.2, 166.8, 160.9, 159.8, 152.2, 152.0, 135.4, 133.3, 133.2, 133.1, 132.2, 131.8, 131.6, 128.7, 128.6, 128.5, 127.7, 127.4, 126.7, 126.2, 125.3, 124.4, 122.5, 122.4, 121.8, 118.0, 117.0, 113.7, 76.3, 53.4, 49.8, 47.4; HRMS (ESI, [M + H]\(^+\)): m/z calcd for C\(_{40}\)H\(_{27}\)Br\(_2\)N\(_2\)O\(_5\), 773.0287, 775.0266, 777.0246, found 773.0295, 775.0278, 777.0280.
(±)N-(7,9-bis(3-bromophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3e):

![Chemical Structure of 3e](image)

white solid; yield 86% (332 mg); d. r. = 96:4; mp 288-289 °C; IR (KBr): $v_{\text{max}} = 3372, 3062, 2938, 2850, 1810, 1725, 1658, 1602, 1541 \text{ cm}^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.04$ (d, $J = 7.8$ Hz, 1H), 7.49-7.64 (m, 6H), 7.37-7.44 (m, 8H), 7.02-7.26 (m, 6H), 6.94 (d, $J = 9.6$ Hz, 1H), 7.87 (br s, 1H), 6.79 (t, $J = 10.2$ Hz, 1H), 4.52 (s, 1H), 3.99 (d, $J = 10.4$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.9, 159.7, 152.3, 152.0, 136.4, 133.5, 133.0, 131.8, 131.7, 131.5, 130.9, 130.1, 128.7, 128.5, 127.7, 126.7, 126.2, 125.3, 124.5, 122.1, 117.9, 117.0, 76.3, 53.6, 50.1, 47.6; HRMS (ESI, [M + H]$^+$): m/z calcd for C$_{40}$H$_{27}$Br$_2$N$_2$O$_5$, 773.0287, 775.0266, 777.0246, found 773.0296, 775.0285, 777.0274.

(±)N-(7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3f):

![Chemical Structure of 3f](image)

white solid; yield 81% (286 mg); d. r. = 98:2; mp 305-306 °C; IR (KBr): $v_{\text{max}} = 3396, 3076, 2919, 2854, 1789, 1725, 1658, 1608, 1314, 1450 \text{ cm}^{-1}$; $^1$H NMR (400 MHz, DMSO- $d_6$): $\delta = 9.16$ (br s, 1H), 8.11 (d, $J = 6.8$ Hz, 2H), 8.05 (d, $J = 8.1$ Hz, 1H), 7.97 (d, $J = 7.6$ Hz, 1H), 7.90 (br s, 1H), 7.61-7.66 (m, 4H), 7.44-7.56 (m, 7H), 7.34-7.41 (m, 5H), 7.23 (d, $J = 7.9$ Hz, 1H), 6.58 (br s, 1H), 5.11 (s, 1H), 4.53 (br s, 1H); $^{13}$C NMR (100 MHz, DMSO- $d_6$): $\delta = 175.9, 166.1, 166.0, 160.2, 158.4, 152.1, 150.7, 147.1, 146.7, 144.3, 142.6, 133.7, 133.2, 133.1, 132.2, 131.9, 131.8, 129.2,
128.6, 128.5, 127.3, 126.8, 124.9, 124.6, 123.6, 123.4, 122.4, 121.7, 117.5, 116.9, 75.9, 51.7, 49.4, 47.0; HRMS (ESI, [M + H]+): m/z calcd for C_{40}H_{27}N_{4}O_{9}, 707.1778, found 707.1785.

(±)N-(7,9-bis(3-nitrophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3g):

white solid; yield 73% (706 mg); d. r. = 96:4; mp 312-313 °C; IR (KBr): ν_{max} = 3350, 3083, 2884, 1815, 1700, 1653, 1605, 1312, 1451 cm\(^{-1}\); \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): δ = 8.21 (br s, 1H), 7.82-7.94 (m, 4H), 7.60-7.70 (m, 2H), 7.31-7.43 (m, 7H), 7.22-7.30 (m, 7H), 7.05-7.09 (m, 2H), 6.82 (t, J = 9.8 Hz, 1H), 4.52, 4.62 (s, 1H, that split into two separate signals due to magnetically nonequivalent environments), 4.18 (d, J = 10.6 Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): δ = 175.7, 166.7, 161.4, 160.0, 152.5, 152.3, 147.5, 138.1, 136.1, 133.6, 132.9, 132.5, 132.0, 131.6, 129.8, 128.9, 128.5, 127.6, 126.6, 126.2, 125.8, 125.5, 123.6, 122.9, 121.3, 117.6, 117.1, 76.0, 53.5, 50.1, 47.3; HRMS (ESI, [M + H]+): m/z calcd for C_{40}H_{27}N_{4}O_{9}, 707.1778, found 707.1788.

(±)N-(7,9-bis(4-cyanophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3h):

white solid; yield 82% (273 mg); d. r. = 97:3; mp 325-326 °C; IR (KBr): ν_{max} = 3362, 3065, 2928, 2854, 2230, 1811, 1709, 1657, 1605, 1314, 1451 cm\(^{-1}\); \(^{1}\)H NMR (400 MHz, DMSO- \(d_6\)): δ = 9.10 (br s, 1H), 7.88 (br s, 1H), 7.73 (d, J = 7.4 Hz, 2H), 7.65-7.68 (m, 1H), 7.57-7.63 (m, 3H), 7.50-
7.53 (m, 8H), 7.41-7.47 (m, 3H), 7.35-7.39 (m, 3H), 7.11 (d, \( J = 7.8 \) Hz, 1H), 6.53 (br s, 1H), 5.00 (d, \( J = 1.5 \) Hz, 1H), 4.42 (br s, 1H); \(^{13}\)C NMR (100 MHz, DMSO- \( d_6 \)): \( \delta = 176.0, 166.0, 165.9, 159.9, 158.3, 152.0, 150.7, 142.2, 140.6, 133.7, 133.1, 132.4, 132.2, 131.9, 131.8, 131.3, 129.2, 128.5, 127.8, 126.8, 124.9, 124.5, 123.4, 121.7, 118.4, 118.2, 117.5, 116.9, 110.8, 110.3, 75.9, 52.0, 49.6, 46.7; HRMS (ESI, [M + H]): m/z calcd for C\(_{42}\)H\(_{33}\)N\(_2\)O\(_5\), 667.1981, found 667.1992.

(\( \pm \))N-(7,9-bis(4-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3i):

white solid; yield 81% (272 mg); d. r. = 96:4; mp 293-294 °C; IR (KBr): \( \nu_{\max } = 3367, 3071, 2923, 2854, 1814, 1715, 1656, 1605, 1313, 1451 \) cm\(^{-1}\); \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 8.07 \) (d, \( J = 8.1 \) Hz, 1H), 7.55-7.61 (m, 3H), 7.42-7.48 (m, 2H), 7.31-7.37 (m, 8H), 7.17 (t, \( J = 7.7 \) Hz, 2H), 7.08 (d, \( J = 9.8 \) Hz, 1H), 6.70-6.83 (m, 6H), 6.45 (br s, 1H) 4.47 (s, 1H), 3.99 (d, \( J = 10.8 \) Hz, 1H), 3.66 (s, 3H), 3.65 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 176.7, 166.9, 160.4, 159.8, 159.1, 158.7, 152.3, 151.3, 133.8, 132.5, 131.7, 131.4, 131.3, 128.5, 128.3, 127.7, 126.8, 126.2, 126.2, 125.1, 125.0, 123.4, 118.3, 116.9, 113.6, 113.5, 77.1, 55.0, 55.0, 53.2, 49.6, 47.8; HRMS (ESI, [M + H]): m/z calcd for C\(_{42}\)H\(_{33}\)N\(_2\)O\(_7\), 677.2288, found 677.2300.

(\( \pm \))N-(7,9-bis(3-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3j):

(±)N-(7,9-bis(4-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3i):

(±)N-(7,9-bis(3-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3j):

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white solid; yield 84% (284 mg); d. r. = 96:4; mp 275-276 °C; IR (KBr): \( \nu_{\text{max}} = 3358, 3061, 2930, 2882, 1809, 1722, 1659, 1598, 1316, 1450 \text{ cm}^{-1} \); \(^1\)H NMR (400 MHz, CDCl\(_3\), 25 °C): \( \delta = 8.10 \) (dd, \( J = 8.2, 1.2 \text{ Hz}, 1H \)), 7.56-7.62 (m, 3H), 7.44-7.47 (m, 2H), 7.31-7.37 (m, 6H), 7.01-7.23 (m, 7H), 6.85 (t, \( J = 9.6 \text{ Hz}, 1H \)), 6.65 (d, \( J = 7.5 \text{ Hz}, 2H \)), 6.36-6.51 (m, 2H), 4.43, 4.50 (s, 1H, that split into two separate signals due to magnetically nonequivalent environments), 4.10 (s, 1H), 3.72 (s, 3H), 3.21, 3.66 (s, 3H, that split into two separate signals due to magnetically nonequivalent environments); \(^1\)H NMR (400 MHz, CDCl\(_3\), 50 °C): \( \delta = 8.21 \) (dd, \( J = 8.1, J = 1.2 \text{ Hz}, 1H \)), 7.65-7.68 (m, 3H), 7.51-7.54 (m, 2H), 7.38-7.46 (m, 6H), 7.28-7.30 (m, 1H), 7.24 (t, \( J = 7.8 \text{ Hz}, 2H \)), 7.12-7.18 (m, 4H), 6.94 (t, \( J = 10.3 \text{ Hz}, 1H \)), 6.74 (d, \( J = 9.1 \text{ Hz}, 2H \)), 6.61 (d, \( J = 7.7 \text{ Hz}, 1H \)), 6.54 (s, 1H), 4.60 (s, 1H, the coalescence of the two separate signals to a single average signal), 4.20 (d, \( J = 10.8 \text{ Hz}, 1H \)), 3.81 (s, 3H), 3.43 (br s, 3H, the coalescence of the two separate signals to a single average signal); \(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 176.6, 166.9, 160.6, 160.0, 159.5, 159.12, 158.6, 152.2, 151.9, 137.9, 135.8, 133.8, 132.6, 131.4, 129.5, 129.2, 128.5, 128.4, 127.6, 126.7, 126.3, 125.1, 123.3, 123.0, 118.3, 118.1, 117.0, 114.8, 114.4, 112.8, 111.7, 76.6, 53.7, 55.2, 55.1 and 54.6 (singlet that split into two separate signals due to magnetically nonequivalent environments), 50.7 and 50.5 (singlet that split into two separate signals due to magnetically nonequivalent environments), 47.7; HRMS (ESI, [M + H]+): m/z calcd for C\(_{42}\)H\(_{33}\)N\(_2\)O\(_7\), 677.2288, found 677.2290.

\( \pm \)N-(5',6-dioxo-2'-phenyl-7,9-dip-tolyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3k):

white solid; yield 70% (225 mg); d. r. = 96:4; mp 315-316 °C; IR (KBr): \( \nu_{\text{max}} = 3372, 3056, 2921, 2860, 1814, 1710, 1656, 1605, 1314, 1448 \text{ cm}^{-1} \); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 8.05 \) (dd, \( J = 8.1, 1.1 \text{ Hz}, 1H \)), 7.53-7.58 (m, 3H), 7.48 (t, \( J = 7.5 \text{ Hz}, 1H \)), 7.36-7.40 (m, 5H), 7.31-7.35 (m, 4H), 7.22 (t, \( J = 7.7 \text{ Hz}, 2H \)), 6.77-7.00 (m, 7H), 6.62 (d, \( J = 9.4 \text{ Hz}, 1H \)), 4.66 (s, 1H), 3.95 (d, \( J = 10.6 \text{ Hz}, 1H \)), 2.19 (s, 3H), 2.16 (s, 3H); \(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 176.6, 167.0, 160.5, 159.6, 152.3, 150.9, 137.7, 137.0, 134.0, 133.3, 132.4, 131.4, 131.2, 131.2, 129.1, 128.4, 128.4, 127.7, 126.7, 126.0, 125.2, 124.8, 123.7, 118.2, 116.9, 76.9, 53.8, 50.0, 48.0, 21.1, 21.1; HRMS (ESI, [M + H]+): m/z calcd for C\(_{42}\)H\(_{33}\)N\(_2\)O\(_7\), 645.2389, found 645.2403.
(±)N-(7,9-bis(4-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3l):

white solid; yield 62% (195 mg); d. r. = 97:3; mp 270-271 °C; IR (KBr): νmax = 3337, 3070, 2951, 1806, 1721, 1643, 1604, 1315, 1450 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ = 8.97 (br s, 1H), 7.96 (br s, 1H), 7.67 (d, J = 7.4 Hz, 2H), 7.58-7.64 (m, 4H), 7.46-7.49 (m, 4H), 7.34-7.41 (m, 3H), 7.29-7.30 (m, 2H), 7.02 (d, J = 3.0 Hz, 1H), 6.81-6.85 (m, 2H), 6.75 (d, J = 2.7 Hz, 1H), 6.48 (br s, 1H), 5.03 (s, 1H), 4.44 (br s, 1H); ¹³C NMR (100 MHz, DMSO-d₆): δ = 176.2, 166.1, 166.0, 160.7, 157.9, 151.9, 149.7, 138.6, 137.1, 133.4, 131.8, 129.2, 128.4, 127.5, 126.9, 126.5, 126.2, 126.0, 125.9, 125.3, 125.1, 124.5, 124.1, 122.5, 117.6, 116.8, 76.8, 48.1, 47.0, 44.7; HRMS (ESI, [M + H]⁺): m/z calcd for C₃₆H₂₅N₂O₅S₂, 629.1205, found 629.1221.

(±)N-(7,9-bis(4-chlorophenyl)-5',6-dioxo-2'-p-tolyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)-4-methylbenzamide (3m):

white solid; yield 74% (263 mg); d. r. = 96:4; mp 311-312 °C; IR (KBr): νmax = 3410, 3032, 2919, 2849, 1820, 1721, 1648, 1607, 1313, 1460 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ = 7.90 (br s, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.43-7.49 (m, 5H), 7.22-7.35 (m, 10H), 7.16-7.18 (m, 3H), 6.86 (d, J = 7.7 Hz, 1H), 6.51 (br s, 1H), 4.79 (s, 1H), 4.22 (br s, 1H), 2.70 (br s, 1H), 2.26 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆): δ = 176.4, 165.8, 165.7, 159.6, 158.3, 151.9, 150.7, 144.0, 141.7, 135.7, 134.1, 132.5, 132.4, 132.0, 131.6, 130.4, 129.7, 128.9, 128.4, 128.1, 127.4, 127.2, 126.9, 125.0, 124.4, 122.3, 121.0, 117.6, 116.8, 76.2, 51.7, 49.2, 46.8, 21.1, 20.8; HRMS (ESI, [M + H]⁺): m/z calcd for C₄₂H₃₁Cl₂N₂O₅, 713.1610, 715.1581, found 713.1626, 715.1598.
(±)N-(7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-p-tolyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)-4-methylbenzamide (3n):

white solid; yield 64% (235 mg); d. r. = 96:4; mp 311-312 °C; IR (KBr): \( \nu_{\text{max}} = 3421, 3074, 2925, 2860, 1808, 1725, 1654, 1607, 1313, 1453 \text{ cm}^{-1} \); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \( \delta = 9.09 \) (br s, 1H), 8.16 (d, \( J = 7.8 \) Hz, 2H), 8.11 (d, \( J = 8.7 \) Hz, 1H), 8.03 (d, \( J = 8.3 \) Hz, 1H), 7.95 (br s, 1H), 7.64-7.72 (m, 4H), 7.56 (d, \( J = 7.8 \) Hz, 1H), 7.45-7.51 (m, 4H), 7.42 (t, \( J = 7.6 \) Hz, 1H), 7.21-7.27 (m, 5H), 6.61 (br s, 1H), 5.12 (d, \( J = 1.7 \) Hz, 1H), 4.55 (br s, 1H), 2.34 (s, 3H), 2.32 (s, 3H); \(^13\)C NMR (100 MHz, DMSO-\(d_6\)): \( \delta = 177.0, 165.8, 160.1, 158.4, 152.0, 150.9, 147.1, 146.7, 144.4, 144.2, 142.8, 141.8, 132.2, 131.9, 130.3, 129.7, 128.9, 127.3, 126.9, 125.0, 124.5, 123.6, 123.2, 122.4, 121.7, 120.6, 117.5, 116.9, 75.8, 51.8, 49.5, 47.0, 21.1, 20.8; HRMS (ESI, [M + H]+): m/z calcd for C\(_{42}\)H\(_{31}\)N\(_4\)O\(_9\), 735.2091, found 735.2095.

(±)N-(7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-p-tolyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)-4-methylbenzamide (3o):

white solid; yield 69% (243 mg); d. r. = 96:4; mp 309-310 °C; IR (KBr): \( \nu_{\text{max}} = 3372, 3071, 2921, 2835, 1808, 1713, 1657, 1608, 1304, 1451 \text{ cm}^{-1} \); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \( \delta = 8.87 \) (br s, 1H), 8.01 (br s, 1H), 7.66 (t, \( J = 7.2 \) Hz, 1H), 7.50-7.54 (m, 5H), 7.40 (t, \( J = 7.6 \) Hz, 1H), 7.23-7.30 (m, 7H), 6.80 (m, 4H), 6.68 (d, \( J = 7.7 \) Hz, 1H), 6.60 (br s, 1H), 4.73 (d, \( J = 2.0 \) Hz, 1H), 4.13 (br s, 1H), 3.68 (s, 3H), 3.62 (s, 3H), 2.37 (s, 3H), 2.34 (s, 3H); \(^13\)C NMR (100 MHz, DMSO-\(d_6\)):
δ = 176.7, 167.0, 165.8, 159.2, 158.3, 158.2, 158.2, 151.9, 150.4, 143.5, 141.6, 131.9, 131.7, 131.6, 131.4, 130.8, 129.6, 128.8, 128.7, 127.2, 126.9, 126.4, 125.1, 124.3, 123.1, 121.5, 117.9, 116.7, 113.2, 76.7, 51.7, 49.0, 46.8, 54.8, 54.7, 21.1, 20.8; HRMS (ESI, [M + H]+): m/z calcd for C₄₄H₃₇N₂O₇, 705.2601, found 705.2612.

(±)N-(2-chloro-7,9-bis(4-chlorophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3p):

white solid; yield 51% (183 mg); d. r. = 97:3; mp 308-309 ℃; IR (KBr): ν max = 3407, 3072, 2922, 2857, 1811, 1725, 1651, 1605, 1305, 1450 cm⁻¹; ¹H NMR (400 MHz, DMSO- d₆): δ = 9.06 (br s, 1H), 7.95 (br s, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.55-7.56 (m, 6H), 7.38-7.48 (m, 5H), 7.24-7.31 (m, 6H), 7.16 (d, J = 6.8 Hz, 1H), 6.93 (d, J = 8.4 Hz, 1H), 4.85 (s, 1H), 4.26 (br s, 1H); ¹³C NMR (100 MHz, DMSO- d₆): δ = 176.2, 167.0, 166.3, 159.7, 157.8, 150.6, 149.6, 135.4, 133.8, 133.5, 133.3, 132.5, 132.1, 131.8, 131.7, 131.6, 131.3, 129.2, 128.5, 128.3, 127.7, 127.4, 127.3, 126.7, 124.5, 123.7, 118.8, 76.2, 51.5, 49.0, 46.6; HRMS (ESI, [M + H]+): m/z calcd for C₄₀H₂₆Cl₂N₂O₅, 719.0907, 721.0878, found 719.0905, 721.0895.

(±)N-(2-chloro-7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3q):

white solid; yield 50% (185 mg); d. r. = 97:3; mp 308-309 ℃; IR (KBr): ν max = 3370, 3075, 2925, 2856, 1809, 1725, 1655, 1602, 1314, 1451 cm⁻¹; ¹H NMR (400 MHz, DMSO- d₆): δ = 9.17 (br s, 1H), 8.12 (d, J = 7.6 Hz, 2H), 8.05 (d, J = 8.4 Hz, 1H), 7.97 (d, J = 7.8 Hz, 1H), 7.70 (dd, J = 8.8,
2.1 Hz, 1H), 7.56-7.63 (m, 5H), 7.46-7.54 (m, 6H), 7.37-7.42 (m, 4H), 7.28 (dd, J = 8.2 Hz, 1H),
6.51 (br s, 1H), 5.13 (dd, J = 1.2 Hz, 1H), 4.55 (br s, 1H); $^{13}$C NMR (100 MHz, DMSO- $d_6$): δ =
175.8, 160.2, 157.9, 150.7, 149.7, 149.5, 147.1, 146.7, 144.0, 142.4, 136.8, 133.7, 133.1, 132.2,
131.9, 131.5, 129.2, 128.6, 128.6, 127.4, 126.7, 123.5, 123.3, 122.4, 118.9, 118.7, 75.8, 51.9, 49.3,
46.6; HRMS (ESI, [M + H]$^+$): m/z calcd for C$_{40}$H$_{26}$ClN$_4$O$_9$, 741.1388, 743.1359, found 741.1399,
743.1368.

(±)N-(7,9-bis(4-chlorophenyl)-3-hydroxy-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-
spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3r):

white solid; yield 65% (228 mg); d. r. = 97:3; mp 314-315 °C; IR (KBr): $\nu_{\text{max}}$ = 3358, 3067,
2925, 2854, 1809, 1707, 1654, 1577, 1319, 1446 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO- $d_6$): δ = 9.01 (br s,
1H), 7.69 (br s, 1H), 7.53-7.60 (m, 5H), 7.36-7.49 (m, 6H), 7.28 (m, 6H), 7.14 (d, J = 7.1 Hz, 1H),
6.86 (d, J = 7.6 Hz, 1H), 6.72-6.75 (m, 2H), 6.41 (br s, 1H), 4.73 (s, 1H), 4.21 (br s, 1H); $^{13}$C NMR
(100 MHz, DMSO- $d_6$): δ = 176.3, 165.9, 161.6, 159.5, 158.8, 154.0, 151.1, 136.1, 134.2, 133.5,
133.4, 132.5, 132.3, 131.8, 131.6, 129.2, 128.4, 128.1, 127.4, 127.2, 126.8, 126.2, 123.8, 117.5,
113.3, 109.4, 102.3, 76.3, 51.7, 49.0, 47.0; HRMS (ESI, [M + H]$^+$): m/z calcd for C$_{40}$H$_{27}$Cl$_2$N$_2$O$_6$,
701.1246, 703.1217, found 701.1262, 703.1244.

(±)N-(3-hydroxy-7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-
spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3s):
white solid; yield 62% (224 mg); d. r. = 96:4; mp 312-313 °C; IR (KBr): ν_{max} = 3388, 3073, 2918, 2854, 1792, 1727, 1656, 1609, 1314, 1450 cm^{-1}; \textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}_6): δ = 9.26 (br s, 1H), 8.22-8.24 (m, 3H), 8.08 (d, J = 6.3 Hz, 1H), 7.85 (m, 2H), 7.71-7.73 (m, 3H), 7.58-7.66 (m, 6H), 7.50-7.54 (m, 4H), 7.33 (d, J = 7.3 Hz, 1H), 6.91-6.95 (m, 2H), 6.60 (br s, 1H), 5.15 (s, 1H), 4.62 (br s, 1H); \textsuperscript{13}C NMR (100 MHz, DMSO-\textit{d}_6): δ = 175.9, 166.0, 165.9, 160.9, 160.0, 158.8, 154.0, 151.2, 147.1, 146.6, 144.7, 142.8, 133.6, 133.3, 133.2, 132.1, 131.7, 129.2, 128.4, 127.3, 127.2, 126.8, 126.3, 123.6, 123.4, 122.4, 117.4, 113.2, 109.7, 102.4, 75.7, 51.9, 49.4, 46.9; HRMS (ESI, [M + H]^+): m/z calcd for C_{40}H_{27}N_{10}O_{10}, 723.1727, found 723.1738.

(±)-N-(7,9-bis(4-chlorophenyl)-3-methoxy-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3t):

white solid; yield 64% (228 mg); d. r. = 98:2; mp 317-318 °C; IR (KBr): ν_{max} = 3369, 3073, 2938, 2843, 1806, 1709, 1655, 1604, 1449 cm^{-1}; \textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}_6): δ = 9.18 (br s, 1H), 8.11-8.17 (m, 3H), 8.02 (d, J = 7.8 Hz, 1H), 7.86 (br s, 1H), 7.64-7.66 (m, 3H), 7.55-7.61 (m, 5H), 7.51 (d, J = 7.3 Hz, 1H), 7.40-7.47 (m, 4H), 7.25 (d, J = 8.2 Hz, 1H), 7.15 (d, J = 2.3 Hz, 1H), 7.04 (dd, J = 9.0, 2.7 Hz, 1H), 6.56 (br s, 1H), 5.10 (s, 1H), 4.57 (br s, 1H), 3.90 (s, 3H); \textsuperscript{13}C NMR (100 MHz, DMSO-\textit{d}_6): δ = 175.9, 166.0, 165.9, 162.1, 160.0, 158.7, 154.0, 151.0, 147.1, 146.7, 144.6, 142.7, 133.6, 133.2, 133.1, 132.2, 131.8, 129.2, 128.5, 127.3, 127.2, 126.8, 126.1, 123.6, 123.4, 123.3, 122.4, 118.3, 112.5, 110.8, 101.0, 75.86, 56.0, 51.8, 49.4, 47.0; HRMS (ESI, [M + H]^+): m/z calcd for C_{41}H_{29}Cl_{2}N_{2}O_{6}, 715.1403, 717.1373, found 715.1412, 717.1385.

(±)-N-(7,9-bis(4-chlorophenyl)-3-methoxy-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3u):

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white solid; yield 62% (228 mg); d. r. = 96:4; mp 310-311 °C; IR (KBr): ν_{max} = 3398, 3076, 2927, 2843, 1811, 1724, 1657, 1616, 1305, 1450 cm\(^{-1}\); \(^1\)H NMR (400 MHz, DMSO- \(d_6\)): δ = 9.01 (br s, 1H), 7.80 (br s, 1H), 7.53-7.60 (m, 5H), 7.41-7.49 (m, 3H), 7.37 (t, \(J = 7.5\) Hz, 2H), 7.25-7.29 (m, 6H), 7.15 (d, \(J = 7.6\) Hz, 1H), 7.07 (d, \(J = 2.4\) Hz, 1H), 6.96 (dd, \(J = 9.0, 2.5\) Hz, 1H), 6.86 (d, \(J = 7.8\) Hz, 1H), 6.46 (br s, 1H), 4.77 (d, \(J = 1.3\) Hz, 1H), 4.23 (br s, 1H), 3.84 (s, 3H); \(^13\)C NMR (100 MHz, DMSO- \(d_6\)): δ = 176.3, 165.9, 165.9, 161.9, 159.6, 158.6, 153.8, 150.8, 135.9, 134.1, 133.4, 133.3, 132.5, 132.4, 131.9, 131.7, 129.2, 128.4, 128.2, 127.4, 127.2, 126.8, 126.1, 123.8, 118.9, 112.4, 110.95, 101.0, 76.3, 55.9, 51.7, 49.0, 46.8; HRMS (ESI, [M + H]^+) : m/z calcd for C\(_{41}\)H\(_{29}\)N\(_4\)O\(_{10}\), 737.1884, found 737.1903.

\((\pm)\)N-(7,9-bis(4-chlorophenyl)-3-methyl-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3v):

white solid; yield 71% (248 mg); d. r. = 98:2; mp 301-302 °C; IR (KBr): ν_{max} = 3352, 3065, 2923, 2857, 1809, 1707, 1656, 1614, 1312, 1451 cm\(^{-1}\); \(^1\)H NMR (400 MHz, DMSO- \(d_6\)): δ = 9.00 (br s, 1H), 7.75 (br s, 1H), 7.53-7.60 (m, 5H), 7.40-7.49 (m, 5H), 7.35-7.38 (m, 2H), 7.24-7.34 (m, 6H), 7.15 (d, \(J = 7.6\) Hz, 1H), 6.84 (d, \(J = 8.0\) Hz, 1H), 6.49 (br s, 1H), 4.81 (d, \(J = 1.3\) Hz, 1H), 4.24 (br s, 1H), 2.29 (s, 3H); \(^13\)C NMR (100 MHz, DMSO- \(d_6\)): δ = 176.3, 166.1, 166.0, 159.6, 158.4, 150.6, 150.0, 135.7, 134.1, 133.6, 133.5, 133.4, 132.5, 132.5, 132.3, 132.0, 131.6, 129.2, 128.5, 128.2, 127.4, 127.3, 126.7, 125.0, 123.8, 122.2, 117.3, 116.4, 76.3, 51.6, 49.1, 46.7, 20.5; HRMS (ESI, [M + H]^+) : m/z calcd for C\(_{41}\)H\(_{29}\)Cl\(_2\)N\(_2\)O\(_5\), 699.1454, 701.1424, found 699.1459, 701.1439.
(±)N-(3-methyl-7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3w):

white solid; yield 73% (263 mg); d. r. = 97:3; mp 300-301 °C; IR (KBr): \( \nu_{\text{max}} = 3395, 3068, 2925, 2860, 1811, 1716, 1657, 1604, 1306, 1451 \text{ cm}^{-1}; \)

\(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \( \delta = 9.16 \) (br s, 1H), 8.11 (d, \( J = 7.8 \text{ Hz}, 2\)H), 8.06 (d, \( J = 8.1 \text{ Hz}, 1\)H), 7.97 (d, \( J = 7.6 \text{ Hz}, 1\)H), 7.75 (br s, 1H), 7.58-7.63 (m, 3H), 7.49-7.56 (m, 5H), 7.46 (d, \( J = 7.5 \text{ Hz}, 2\)H), 7.36-7.43 (m, 5H), 7.18 (d, \( J = 8.1 \text{ Hz}, 1\)H), 6.52 (br s, 1H), 5.08 (s, 1H), 4.56 (br s, 1H), 2.29 (s, 3H);

\(^{13}\)C NMR (100 MHz, DMSO-\(d_6\)): \( \delta = 175.9, 166.2, 166.1, 160.1, 158.5, 150.7, 150.1, 147.1, 146.7, 144.4, 142.7, 133.7, 133.4, 132.6, 132.2, 131.7, 129.2, 128.5, 127.3, 127.2, 126.7, 125.0, 123.6, 123.4, 123.3, 122.4, 121.6, 117.1, 116.5, 75.9, 51.5, 49.4, 47.1, 20.5; HRMS (ESI, [M + H]\(^+\)): m/z calcd for C\(_{41}\)H\(_{29}\)N\(_4\)O\(_9\), 721.1935, found 721.1950.

3. General procedure for the synthesis of d\(^2\)-3i

The mixture of azlactone d\(^1\)-1i (1.0 mmol, 0.279 gr), 4-hydroxycoumarins 2 (0.5 mmol, 0.81 gr), diisopropylethylamine (1.0 mmol, 0.129 gr) in propylene carbonate (1 mL) was stirred at 80 °C for about 8 h. After completion of the reaction as monitored by TLC (eluent: n-hexane/ethyl acetate, 1:1), the mixture was cooled to room temperature. The reaction was treated with water.
(10 mL) and the product was filtered off and the PC was recovered by evaporating the water. The recovered PC was subjected to the next cycle without further purification. The crude product was recrystallized from hot ethanol to obtain d²-3j as white solids.

**Characterization Data**

(±)N-(7,9-bis(4-methoxyphenyl)-5′,6-dioxo-2′-phenyl-6,7,9,10-tetrahydro-5′H-spiro[benzo[c]chromene-8,4′-oxazole]-10-yl-7,9-d₂)benzamide (d²-3i):

white solid; yield 81% (275 mg); d. r. = 98:2; mp 295-296 °C; IR (KBr): νmax = 3403, 3041, 2852, 1818, 1716, 1650, 1607, 1312, 1452 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 8.07 (dd, J = 8.2, J = 1.2 Hz, 1H), 7.55-7.62 (m, 3H), 7.44-7.50 (m, 2H), 7.31-7.38 (m, 8H), 7.12-7.18 (m, 3H), 6.44-6.79 (m, 7H), 3.65 (s, 3H), 3.64 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 176.8, 166.8, 160.4, 159.9, 159.1, 158.6, 152.3, 151.6, 133.8, 132.5, 131.7, 131.3, 128.5, 128.3, 127.7, 126.8, 126.2, 126.2, 125.1, 125.0, 123.3, 118.3, 116.9, 113.6, 113.5, 55.0, 55.0, 52.7, 49.1, 47.8; HRMS (ESI, [M + H⁺]): m/z calcd for C₄₂H₃₁D₂N₂O₇, 679.2413, found 679.2425.
4. **Cross reaction procedure:**

The mixture of azlactone **d1-1i** (0.5 mmol, 0.140 gr), azlactone **1c** (0.5 mmol, 0.142 gr), 4-hydroxycoumarine **2** (0.5 mmol, 0.81 gr), DIPEA (1.0 mmol, 0.129 gr) in propylene carbonate (1 mL) was stirred at 80 °C for about 8 h until complete consumption of starting materials as monitored by TLC (eluent: *n*-hexane/ethyl acetate, 1:1). After completion of the reaction, the mixture was cooled to room temperature. Water (20 mL) was added and the organic layer was extracted with CHCl₃ (2 × 20 mL). The combined organic layer were dried over MgSO₄, filtered and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography with hexane/AcOEt (3/2).
Characterization Data

(±)N-(7-(4-chlorophenyl)-9-(4-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl-9-d1)benzamide (d1-3x):

white solid; yield 38% with respect to 2 (259 mg); d. r. = 97:3; mp 298-299 °C; IR (KBr): νmax = 3358, 3061, 2955, 2840, 1806, 1712, 1655, 1605, 1313, 1451 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 7.99 (d, J = 7.7 Hz, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.44-7.46 (m, 2H), 7.37-7.40 (m, 2H), 7.23-7.30 (m, 8H), 7.05-7.13 (m, 4H), 6.61-6.75 (m, 6H), 4.31 (d, J = 1.5 Hz, 1H), 3.56 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 176.5, 166.8, 160.5, 159.9, 159.2, 152.3, 152.2, 135.2, 133.6, 133.3, 132.8, 131.6, 131.5, 128.6, 128.4, 127.9, 127.6, 127.0, 126.7, 126.3, 125.8, 125.2, 124.7, 122.6, 118.2, 117.0, 113.7, 55.0, 52.6, 49.6, 47.7; HRMS (ESI, [M + H]⁺): m/z calcd for C₄₁H₂₉DClN₂O₆, 682.1855, 684.1826, found 682.1863, 684.1832.

III. The screening reaction with different hydroxypyranones and arylidene azlactones

The screening reaction with different hydroxypyranones, such as cyclohexan-1.3-dione (Table S1) and dimedone (Table S2) instead of 4-hydroxycoumarin were performed and the results are illustrated as the following.

As shown in Tables S1 and S2 with changing the azlactone, with cyclohexan-1.3-dione (Table S1) and dimedone (Table S2) as 4-hydroxy-5,6-dihydro-2H-pyran-2-one derivatives. These results are consistent with our previous report.⁵
Table S1. Reaction of arylidene azlactones and cyclohexan-1.3-dione under the reaction condition.

![Reaction diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>68</td>
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<tr>
<td>2</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>4-CH&lt;sub&gt;3&lt;/sub&gt;O</td>
<td>73</td>
</tr>
<tr>
<td>3</td>
<td>4-Cl</td>
<td>4-CH&lt;sub&gt;3&lt;/sub&gt;O</td>
<td>62</td>
</tr>
<tr>
<td>4</td>
<td>4-CH&lt;sub&gt;3&lt;/sub&gt;O</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>79</td>
</tr>
</tbody>
</table>

Table S2. Reaction of arylidene azlactones and dimedone under the reaction condition.

![Reaction diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
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<td>4-CH&lt;sub&gt;3&lt;/sub&gt;O</td>
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<tr>
<td>3</td>
<td>4-Cl</td>
<td>4-CH&lt;sub&gt;3&lt;/sub&gt;O</td>
<td>61</td>
</tr>
<tr>
<td>4</td>
<td>4-CH&lt;sub&gt;3&lt;/sub&gt;O</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>69</td>
</tr>
</tbody>
</table>
IV. Green chemistry metric analysis for 3c:

**Experimental procedure:** A mixture of azlactone 1 (1.0 mmol), 4-hydroxycoumarine 2 (0.5 mmol), and diisopropylethylamine (1.0 mmol) in propylene carbonate (1 mL) was stirred at 80 °C for 8 h. After completion of the reaction as monitored by TLC (eluent: n-hexane/ethyl acetate, 1:1) The resulting mixture was cooled to room temperature. The reaction was treated with water (5 mL) and the product was filtered off and the PC was recovered by evaporating the water. The recovered PC was subjected to the next cycle without further purification. The crude product was recrystallized from hot ethanol to obtain 3 as white solids.

Materials used for metrics calculations (atom efficiency): azlactone 1c (0.283 g, 1 mmol), 4-hydroxycoumarine 2a (0.081 g, 0.5 mmol), diisopropylethylamine (0.129 g, 1.0 mmol), propylene carbonate (1.0 mL, 1.25 g, the solvent is recovered ), and compound 3c (0.309 g, 90% yield).

\[
AE = \frac{\text{Molecular weight of product}}{\text{Total molecular weight of reactants}} \times 100
\]

\[
AE = \frac{685.6}{283.7+283.7+162.1} \times 100 = 93.98\%
\]
V. X-Ray crystal structure and crystal data of 3c (CCDC: 1838514)

Figure S1. X-Ray crystal structure of 3c
### Table S3. Crystal Data and Structure Refinement for 3c

<table>
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<th>Crystal Data</th>
<th>Compound 3c</th>
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<td>shelx</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C_{40}H_{26}Cl_{2}N_{2}O_{5}</td>
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<tr>
<td>Formula weight</td>
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<tr>
<td>Temperature</td>
<td>296(2) k</td>
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<tr>
<td>Wavelength</td>
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<tr>
<td>Crystal system, space group</td>
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<tr>
<td>Unit cell dimensions</td>
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</tr>
<tr>
<td>a = 9.9687(8) Å</td>
<td>alpha = 92.312(2)°</td>
</tr>
<tr>
<td>b = 14.9432(11) Å</td>
<td>beta = 97.145(2)°</td>
</tr>
<tr>
<td>c = 24.3238(17) Å</td>
<td>gamma = 107.847(2)°</td>
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<tr>
<td>Z, Calculated density</td>
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<tr>
<td>Absorption coefficient</td>
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<tr>
<td>F(000)</td>
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</tr>
<tr>
<td>Theta range for data collection</td>
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</tr>
<tr>
<td>Limiting indices</td>
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</tr>
<tr>
<td>Reflections collected / unique</td>
<td>92109/11859[R(int) = 0.1630]</td>
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<tr>
<td>Completeness to theta = 24.999°</td>
<td>98.8%</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
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<tr>
<td>Data / restraints / parameters</td>
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<tr>
<td>Goodness-of-fit on F²</td>
<td>0.999</td>
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<tr>
<td>Final R indices [I&gt;2sigma(I)]</td>
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<td>R indices (all data)</td>
<td>R₁ = 0.1961, wR₂ = 0.2183</td>
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<tr>
<td>Largest diff. peak and hole</td>
<td>0.456 and -0.383 e.Å⁻³</td>
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</table>
VI. References


VII. $^1$H and $^{13}$C NMR Spectra
(±) N-(5′,6-dioxo-2′,7,9-triphenyl-6,7,9,10-tetrahydro-5′H-spiro[benzo[c]chromene-8,4′-oxazole]-10-yl)benzamide (3a):
$^{13}\text{C} \text{NMR (400 MHz, DMSO-}$d_6$)$

$(\pm) \text{N-($5',6$-dioxo-$2',7,9$-triphenyl-$6,7,9,10$-tetrahydro-$5$H-spiro[benzo[c]chromene-$8,4'$-oxazole]-$10$-yl)benzamide (3a):}$

S29
$^1$H NMR (400 MHz, DMSO-$d_6$)

$\text{(+)}N$-(7,9-bis(4-fluorophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3b)
$^{13}$C NMR (400 MHz, DMSO-$d_6$)

(±)-N-(7,9-bis(4-fluorophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3b):
^{19}F NMR (376 MHz, CDCl₃)

(+)-N-(7,9-bis(4-fluorophenyl)-5',6-dioxa-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3b):
\textit{\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3})}

(±)-\textit{N}-(7,9-bis(4-chlorophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3c):
$^{13}$C NMR (400 MHz, CDC$_3$)

(±)N-(7,9-bis(4-chlorophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3c)
(±)-N-(7,9-bis(4-bromophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3d)
$^1$H NMR (400 MHz, CDCl$_3$)

(±)N-(7,9-bis(4-bromophenyl)-5',6'-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3d):
\( ^1\text{H NMR (400 MHz, CDC\textsubscript{3})} \)

\( \text{(+)}\text{N-[(7,9-bis(3-bromophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl]benzamide (3e):} \)
$^{13}$C NMR (400 MHz, CDC$_3$)

(±)N-(7,9-bis(3-bromophenyl)-5′,6-dioxo-2′-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4′-oxazole]-10-yl)benzamide (3e)
$^1$H NMR (400 MHz, DMSO-$d_6$)

(+)-N-(7,9-bis(4-nitrophenyl)-5,6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3f)
\(^{13}\)C NMR (400 MHz, DMSO-\(d_6\))

\((\pm)\)N-(7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3f)
$^1$H NMR (400 MHz, CDCl$_3$)

(+)-N-(7,9-bis(3-nitrophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3g)
$^{13}$C NMR (400 MHz, CDCl$_3$)

(±)N-(7,9-bis(3-nitrophenyl)-5′,6-dioxo-2′-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4′-oxazole]-10-yl)benzamide (3g)
$^1$H NMR (400 MHz, DMSO- $d_6$)

$(\pm)$N-(7',9'-bis(4-cyanophenyl)-5',6'-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3h)
(±)-N-(7,9-bis(4-cyanophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3h)
$^{1}H$ NMR (400 MHz, CDC$_3$)

(±)-N-(7,9-bis(4-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3i)
($\pm$)N-(7,9-bis(4-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3i)
$^1$H NMR (400 MHz, CDCl$_3$)

(±)N-(7,9-bis(4-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl-7,9-d2)benzamide (d2-3i)
$^{13}$C NMR (400 MHz, CDCl$_3$)

($\pm$)N-(7,9-bis(4-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl-7,9-d2)benzamide (d2-3i)
\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, 25 °C)

\[ \text{\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, 25 °C)} \]

\[(\pm)\text{-}(7,9\text{-bis(3-methoxyphenyl)}\text{)}-5',6\text{-dioxo-2'-phenyl}-6,7,9,10\text{-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3j)} \]
$^{1}$H NMR (400 MHz, CDCl$_3$, 50 °C)

(±)N-(7,9-bis(3-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3j)
$^{13}$C NMR (100 MHz, CDCl$_3$, 25 °C)

(±)-N-(7,9-bis(3-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3j)
\(^1\text{H NMR (400 MHz, CDCl}_3\)\)

(±)N-(5',6'-dioxo-2'-phenyl-7,9-dip-tolyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3k)
$^{13}\text{C NMR (400 MHz, CDCl}_3$)

(±)N-(5',6-dioxo-2'-phenyl-7,9-dip-toly1-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3k)
$^{1}$H NMR (400 MHz, DMSO- $d_6$)

(±)-N-(7,9-bis(4-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (31)
$^{13}$C NMR (400 MHz, DMSO-$d_6$)

(±)N-(7,9-bis(4-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (31)
\( ^1 \text{H NMR (400 MHz, DMSO-} \, d_6) \)

\[ (+)N-(7,9-bis(4-chlorophenyl)-5',6-dioxo-2'-p-tolyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)-4-methylbenzamide (3m) \]
\textbf{$^{13}$C NMR (400 MHz, DMSO-$d_6$)}

\(\text{(±)N-[(7,9-bis(4-chlorophenyl)]-5',6-dioxo-2'-p-tolyl-6,7,9,10-tetrahydro-\textit{5}'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl]-4-methylbenzamide (3m)}\)
$^1$H NMR (400 MHz, DMSO- $d_6$)

(±)-N-(7,9-bis(4-nitrophenyl)-5,6-dioxo-2'-p-tolyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)-4-methylbenzamide (3n)
$^{13}$C NMR (400 MHz, DMSO-$d_6$)

$\text{(\pm)N-}(7,9\text{-bis}(4\text{-nitrophenyl})-5',6\text{-dioxo-}2\text{-p-tolyl}-6,7,9,10\text{-tetrahydro}-5\text{H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl})\text{-4-methylbenzamide (3n)}$
$^1$H NMR (400 MHz, DMSO-$d_6$)

(±)-N-(7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-tolyl-6,7,9,10-tetrahydro-5'H-spiro[indeno[1,2-b]chromene-8,4'-oxazole]-10-yl)-4-methylbenzamide (3o)
$^{13}$C NMR (400 MHz, DMSO-$d_6$)

(±)-N-(7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-p-tolyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)-4-methylbenzamide (3o)
$^1$H NMR (400 MHz, DMSO-$d_6$)

(±)N-(2-chloro-7,9-bis(4-chlorophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3p)
$^{13}$C NMR (400 MHz, DMSO-d$_6$)
$^1$H NMR (400 MHz, DMSO-$d_6$)

(±)N-(-2-chloro-7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazol]-10-yl)benzamide (3q)
$^{13}$C NMR (400 MHz, DMSO-$d_6$)

(±)N-[(2-chloro-7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazol]-10-yl)benzamide (3q)
$^1$H NMR (400 MHz, DMSO- $d_6$)

(±)N-(7,9-bis(4-chlorophenyl)-3-hydroxy-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3r)
$^1$H NMR (400 MHz, DMSO, D2O)
H-D exchange NMR

$^1$H-NMR-DMSO, D$_2$O

$^1$H-NMR-DMSO

amide N-H proton
\(^{13}\text{C} \text{NMR (400 MHz, DMSO-}d_6\text{)}\)

(\pm)N-(7,9-bia(4-chlorophenyl)-3-hydroxy-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3r)
(±)-N-(3-hydroxy-7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3s)
\( ^{13} \text{C NMR (400 MHz, DMSO-} d_6) \)

(\( \pm \))N-(3-hydroxy-7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3s)
$^1$H NMR (400 MHz, DMSO-$d_6$)

(±)-N-(7,9-bis(4-chlorophenyl)-3-methoxy-5'-6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3t)
\(^{13}\)C NMR (400 MHz, DMSO-\(d_6\))

(±)N-(7,9-bis(4-chlorophenyl)-3-methoxy-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3t)
$^1$H NMR (400 MHz, DMSO-$d_6$)

(+)-N-(7,9-bis(4-chlorophenyl)-3-methoxy-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3u)
$^{13}$C NMR (400 MHz, DMSO-$d_6$)

($\pm$)N-[(7,9-bis(4-chlorophenyl)-3-methoxy-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3u)
$^{1}$H NMR (400 MHz, DMSO- $d_6$)

$\text{(+)N-}(7,9$-bis(4-chlorophenyl)$)-3$-methyl-$5',6$-dioxo-$2$'-phenyl-$6,7,9,10$-tetrahydro-$5$H-spiro[benzo[c]chromene-$8,4'$-oxazole]-10-yl)benzamide (3v)
$^{13}$C NMR (400 MHz, DMSO-$d_6$)

$^{13}$C NMR spectrum of $\pm$N-(7,9-bis(4-chlorophenyl)-3-methyl-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3v)
$^1$H NMR (400 MHz, DMSO- $d_6$)

(±)N-(3-methyl-7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3w)
$^{13}$C NMR (400 MHz, DMSO-$d_6$)

(+)-N-(3-methyl-7,9-bis(4-nitrophenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl)benzamide (3w)
$^1$H NMR (400 MHz, CDCl$_3$)

(±)-N-(7-(4-chlorophenyl)-9-(4-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-yl-9-d1)benzamide (d$^1$-3x)
$^{13}$C NMR (400 MHz, CDCl$_3$)

(±)-$N$-(7-(4-chlorophenyl)-9-(4-methoxyphenyl)-5',6-dioxo-2'-phenyl-6,7,9,10-tetrahydro-5'H-spiro[benzo[c]chromene-8,4'-oxazole]-10-y1-9-d1)benzamide (d$^1$-3x)
Screening of the reaction path using LC-MS after 30 min from the beginning of the reaction at 80 °C.
The LC-MS spectrum of each individual observed peak. (Peaks 1–7)

Peak 1
MH$^+$ 88.2 130.1 162.9 130.1 281.2 402.4 430.3 517.3 592.2 859.3
+MS, 3.1-3.2min #(120-125)

Peak 2
MH$^+$ 130.1 281.2 402.4 430.3
+MS, 10.5-10.7min #(418-426)

Exact Mass: 430.11
Peak 3
MH+ 105.0
268.1
592.3
+MS, 13.0-13.1min #(525-529), Background Subtracted

Peak 4
MH+ 593.5
697.5
+MS, 13.5-13.9min #(547-566), Background Subtracted

S84
Peak 5
MH+ 130.0 308.3 531.5 654.5 697.5 +MS, 14.2-14.4min #578-589

Peak 6
MH+ 653.6 +MS, 14.0-14.2min #571-579

Exact Mass: 697.18
Exact Mass: 653.19

S85
Peak 7

+MS, 15.2-15.3 min #618-626

Intens. x10

0 2 4 6

100 200 300 400 500 600 700 800 900 m/z

Exact Mass: 653.19

S86
TLC-MALDI-MS imaging of the spots taken during the course of the reaction showing the formation of the diastereomers of the main product.