Electronic supplementary information

Catalytic [4+1]-annulation of thioamides with carbenoid precursors

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General information

All chemicals were obtained from commercial sources and were used without further purification. Dry solvents were obtained according to the literature protocols and stored over molecular sieves. Analytical thin-layer chromatography was performed on aluminum foil plates coated with 0.2 mm silica gel. Column chromatography was performed using 60–120 mesh silica gel. Melting points were determined on a melting point apparatus Stuart SMP10 and are uncorrected. Enantioselectivity was determined on an Azura P6.1L Knauer HPLC using a Chiralpak AD column (250 × 4.6 mm, 5 μm) (Daicel, Japan). The elution rate for the Chiralpak AD column was 1 mL min–1. Detection was carried out on a wavelength of 220 (230) nm (Diode Array Detector). Optical rotation was measured using a PerkinElmer polarimeter 343 plus. IR spectra were recorded on a Bruker Alpha FT-IR spectrometer equipped with a ZnSe ATR accessory. All NMR spectra were recorded at 400 MHz, 600 MHz (1H NMR) and 100 MHz, 150 MHz (13C NMR) in CDCl3, DMSO-d6, CD3CN-d3. The chemical shifts are given in parts per million (ppm) relative to the resonance of the solvents [1H: δ (CHCl3) = 7.26, 13C: δ (CDCl3) = 77.16 ppm; 1H: δ (DMSO-d6) = 2.50, 13C: δ (DMSO-d6) = 39.52 ppm; 1H: δ (CD3CN-d3) = 1.94, 13C: δ (CD3CN-d3) = 1.32, 118.26 ppm]. Multiplicities were given as: s (singlet), d (doublet), t (triplet), q (quartet), dd (double of doublet), and m (multiplet). Coupling constants are reported as J value in Hertz (Hz). The minor isomer (Z/E-isomerism) signal is highlighted with an asterisk (*). High-resolution mass spectra (HRMS) were recorded using an ultra-high-resolution quadrupole time-of-flight mass spectrometer with an electrospray ionization probe installed coupled with an Agilent 1260 HPLC system. The XRD analysis was carried out using equipment of the Center for Joint Use “Spectroscopy and Analysis of Organic Compounds” at the Postovsky Institute of Organic Synthesis of the Russian Academy of Sciences (Ural Branch). The experiments were accomplished on the automated X-ray diffractometer «Xcalibur 3» with CCD detector on standard procedure (MoKα-irradiation, graphite monochromator, ω-scans with 1o step at T= 295(2) K). Empirical absorption correction was applied. The solution and refinement of the structures were accomplished with using Olex program package.\textsuperscript{1} The structures were solved by method of the intrinsic phases in ShelXT program and refined by ShelXL by full-matrix least-squared method for non-hydrogen atoms.\textsuperscript{2} The H-atoms at were placed in the calculated positions and were refined in isotropic approximation. The XRD data were deposited in the Cambridge Structural Database with numbers CCDC 2288489–2288498. This data can be requested free of charge via www.ccdc.cam.ac.uk.
Preparation of starting reagents

3-Morpholino-3-thioxopropanenitrile (S1a), 3-(piperidin-1-yl)-3-thioxopropanenitrile (S1b), 3-(pyrrolidin-1-yl)-3-thioxopropanenitrile (S1c), 3-(azepan-1-yl)-3-thioxopropanenitrile (S1d), 2-cyano-\(N-(p\)-tolyl)ethanethioamide (S1e), 4-morpholino-4-thioxobutan-2-one (S1f), methyl 3-morpholino-3-thioxopropanoate (S1g), 3-\((4\)-chlorophenyl\)amino)-2-(pyrrolidine-1-carbonyl)acrylonitrile (1t), 2-morpholino-N-\(N\)-phenyl-2-thioxoacetohydrazonoyl cyanide (1u), 3-(dimethylamino)-2-(pyrrolidine-1-carbonyl)acrylonitrile (1v), 1-sulfonyl-1,2,3-triazoles 2a-c, 2d, 2e-f, diazo compounds 2h-o, 2q, 2r, 2t, 2v, 4,7-dibromoisobenzofuran-1,3-dione (S3) were synthesized according to literature procedures. 3-Morpholino-3-thioxopropanethioamide (1e), 4-cyclopropyl-1-tosyl-1\(H\)-1,2,3-triazole (2g), \(N-(4\)-chlorophenyl\)-\(N\)-tosylformimidamide (3ta) were synthesized according to modified literature procedures. 3-Diazo-7-methylindolin-2-one (2p) was purchased from commercial source and characterized. Copper, ruthenium, silver, palladium catalysts, Rh\(_2\)(OAc)\(_4\), Rh\(_2\)(Oct)\(_4\), Rh\(_2\)(esp)\(_2\), Rh\(_2\)(S-PTAD)\(_4\), Rh\(_2\)(S-DOSP)\(_4\) were purchased from commercial sources. Rh\(_2\)(Piv)\(_4\) was synthesized according to literature procedure. Other chiral rhodium catalysts, Rh\(_2\)(S-PTTL)\(_4\), Rh\(_2\)(S-PTV)\(_4\), Rh\(_2\)(S-NTTL)\(_4\) were synthesized according to literature protocols. Heteroaromatic thioamides T1-2, T3 were synthesized according to literature procedures.
Starting compounds were used in the research

**Thioamides**

1a 1b 1c 1d 1g

1h 1i 1j 1k 1l

1n 1o 1p 1q 1r 1s

1t 1u 1v

**Amide**

Am1

**1-Sulfonyl-1,2,3-triazoles**

2a 2b 2c

2d 2e 2f 2g

**Diazocompounds**

2h

2i 2j 2k 2l

2m 2n 2o

2p 2q 2r

2s 2t 2u 2v

**Figure S1.** Starting compounds were used in the research
Chiral rhodium(II) catalysts were used in the research

**Figure S2.** Chiral catalysts were used in the research
Synthesis of thioamides 1a-p

General procedure for the synthesis of thioamides 1a-d

A mixture of 3-morpholino-3-thioxopropanenitrile (S1a) (1.0 equiv), appropriate aldehyde S2a-d (1.3–1.4 equiv) and DBU (0.1 equiv) in ethanol (2–5 mL) was stirred for 10–18 h at room temperature. The formed precipitate was filtered off and washed with cold ethanol and diethyl ether for 1a-b or with cold ethanol with subsequent centrifugation with hexane for 1d. The product 1c after filtration was washed with ethanol and diethyl ether, the precipitate was dissolved in boiling methanol and filtered off. The mother liquor was evaporated under reduced pressure.

2-(Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a)

Compound 1a was obtained according to the general procedure from 3-morpholino-3-thioxopropanenitrile (S1a) (1000 mg, 1.0 equiv, 5.87 mmol), benzaldehyde S2a (872 mg, 8.22 mmol, 1.4 equiv), DBU (89 mg, 0.1 equiv, 0.59 mmol), and ethanol (5 mL), reaction time is 15 h. Product 1a was isolated as a yellow powder (1255 mg, 83%), mp 118–120 °C. 1H NMR (400 MHz, DMSO-d6): δ 7.89 – 7.87 (m, 2H), 7.55 – 7.52 (m, 4H), 4.23 (br. s, 2H), 3.96 (br. s, 2H), 3.78 (br. s, 2H), 3.70 (br. s, 2H). 13C{1H} NMR (150 MHz, DMSO-d6): δ 189.2, 144.7, 132.3, 131.6, 129.3, 129.1, 116.2, 110.8, 65.9, 65.5, 52.7, 49.6. HRMS (ESI) m/z: [M + Na]+ calcd. for C14H14N2OSNa+ 281.0719; found 281.0719.

(Z/E)-2-(Morpholine-4-carbonothioyl)-3-(p-tolyl)acrylonitrile (1b)
Compound 1b was obtained according to the general procedure from 3-morpholino-3-thioxopropanenitrile (S1a) (600 mg, 1.0 equiv, 3.52 mmol), 4-methylbenzaldehyde (S2b) (593 mg, 4.93 mmol, 1.4 equiv), DBU (54 mg, 0.1 equiv, 0.35 mmol), and ethanol (5 mL), reaction time is 18 h. Product 1b was isolated as a bright-yellow powder (815 mg, 85%), mp 160–162 °C. 1H NMR (400 MHz, DMSO-d6): δ 7.42 (s, 1H), 7.39 (d, J = 4.2 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 4.28 – 4.16 (m, 2H), 3.80 – 3.72 (m, 2H), 3.68 – 3.62 (m, 1H), 3.52 – 3.47 (m, 2H), 3.08 – 3.02 (m, 1H), 2.34 (s, 3H). 13C{1H} NMR (100 MHz, DMSO-d6): δ 189.6*, 187.5, 144.9, 142.0*, 141.4, 140.9, 129.7, 129.7, 129.5*, 129.4*, 117.4, 116.3*, 110.5, 109.7*, 65.8*, 65.5*, 65.2, 64.9, 52.7*, 51.4, 49.6*, 48.3, 21.1*, 21.1. HRMS (ESI) m/z: [M + Na]+ calcd. for C15H16N2OSNa+ 295.0876; found 295.0876.

(Z/E)-3-(4-Chlorophenyl)-2-(morpholine-4-carbonothioyl)acrylonitrile (1c)

![Image](image)

Compound 1c was obtained according to the general procedure from 3-morpholino-3-thioxopropanenitrile (S1a) (1000 mg, 1.0 equiv, 5.87 mmol), 4-chlorobenzaldehyde (S2c) (1073 mg, 7.64 mmol, 1.3 equiv), DBU (89 mg, 0.1 equiv, 0.59 mmol), and ethanol (5 mL), reaction time is 14 h. Product 1c was isolated as a yellow powder (1390 mg, 81%), mp 194–196 °C. 1H NMR (400 MHz, DMSO-d6): δ 7.58 – 7.50 (m, 4H), 7.45 (s, 1H), 4.26 – 4.16 (m, 2H), 3.81 – 3.65 (m, 3H), 3.54 – 3.49 (m, 2H), 3.08 – 3.04 (m, 1H). 13C{1H} NMR (100 MHz, DMSO-d6): δ 188.9*, 186.8, 143.2, 139.6, 136.1*, 135.7, 131.3, 131.3, 131.2*, 131.0*, 129.3, 129.2*, 117.0, 115.9*, 112.0, 111.3*, 65.3, 64.9, 51.5, 48.3. HRMS (ESI) m/z: [M + Na]+ calcd. for C14H13ClN2OSNa+ 315.0329; found 315.0327.

(Z/E)-2-(Morpholine-4-carbonothioyl)-5-phenylpenta-2,4-dienonitrile (1d)

![Image](image)

Compound 1d was obtained according to the general procedure from 3-morpholino-3-thioxopropanenitrile (S1a) (200 mg, 1.0 equiv, 1.17 mmol), 3-phenylacrylaldehyde (S2d) (217 mg, 1.64 mmol, 1.4 equiv), DBU (18 mg, 0.1 equiv, 0.12 mmol), and ethanol (2 mL), reaction time is 10 h. Product 1d was isolated as a yellow powder (220 mg, 66%), mp 139–141 °C. 1H
NMR (400 MHz, DMSO-\textit{d}_6): \(\delta\) 7.65 (d, \(J = 7.6\) Hz, 2H), 7.47 – 7.34 (m, 5H), 7.15 – 7.09 (m, 1H), 4.32* and 4.20 (both br. s, 2H), 3.91 and 3.81* (both br. s, 2H), 3.73 and 3.64 – 3.61* (br. s and m, 4H). \(^{13}\text{C}\{1\text{H}\}\text{ NMR (100 MHz, DMSO-\textit{d}_6):} \delta \) 188.9, 186.5*, 146.3, 144.9, 143.7*, 142.1*, 135.1, 135.0*, 130.2, 130.1*, 129.1, 129.0*, 128.0*, 127.9, 123.2, 121.9*, 117.4*, 115.26, 111.9, 110.8*, 66.0, 65.8*, 65.7*, 65.6, 52.8*, 52.0, 49.7*, 48.6. HRMS (ESI) m/z: [M + H]\(^+\) calcd. for C\(_{16}\)H\(_{17}\)N\(_2\)O\(_2\)S 285.1056; found 285.1056.

\textbf{3-Morpholino-3-thioxopropanethioamide (1e)}

\[
\text{H}_2\text{N} \quad \text{S} \quad \text{S} \quad \text{N} \quad \text{O} \quad \text{S} \quad \text{N} \quad \text{O}
\]

Sodium (40 mg, 0.1 equiv, 1.76 mmol) was dissolved in dry ethanol (35 mL), and the solution was cooled to 0 °C. Then the solution was saturated with hydrogen sulfide obtained from sodium sulfide nonahydrate (50 g) and phosphoric acid (15 mL). The hydrogen sulfide-saturated solution was transferred to an autoclave containing 3-morpholino-3-thioxopropanenitrile (\(\text{S1a}\)) (3000 mg, 1.0 equiv, 17.62 mmol) and stirred at 70 °C for 5 h. The formed suspension was cooled to room temperature and kept in the fridge for 1 h. Filtration of the precipitate and washing with ethanol afforded \(1e\) in 83% (3000 mg) yield as a colorless powder, mp 167–170 °C (lit.\(^{20}\) 143–150 °C). \(^1\text{H}\) NMR (400 MHz, DMSO-\textit{d}_6): \(\delta\) 9.59 (s, 1H, NH), 9.18 (s, 1H, NH), 4.20 – 4.17 (m, 4H), 3.84 (br. s, 2H), 3.72 – 3.66 (m, 4H). \(^{13}\text{C}\{1\text{H}\}\text{ NMR (100 MHz, DMSO-\textit{d}_6):} \delta \) 200.0, 194.3, 65.9, 65.5, 56.7, 51.2, 49.7.

\textbf{\((Z/E)-2-(Morpholine-4-carbonothioyl)-3-phenylprop-2-enethioamide (1f)\)}

\[
\text{H}_2\text{N} \quad \text{Ph} \quad \text{S} \quad \text{S} \quad \text{N} \quad \text{O} \quad \text{S} \quad \text{N} \quad \text{O}
\]

3-Morpholino-3-thioxopropanethioamide (\(1e\)) (680 mg, 1.0 equiv, 3.33 mmol), benzaldehyde (\(\text{S2a}\)) (494 mg, 1.4 equiv, 4.66 mmol) and DIPEA (43 mg, 0.1 equiv, 0.33 mmol) were dissolved in \(n\)-butanol (4 mL), and the solution was stirred at 100 °C for 13.5 h. The solvent was evaporated, and the residue was purified by column chromatography on SiO\(_2\) (PE/EtOAc, gradient 50:0 to 25:25) afforded \(1f\) (33%, 321 mg) as pale-yellow powder, mp 118–120 °C. \(^1\text{H}\) NMR (400 MHz, DMSO-\textit{d}_6): \(\delta\) 9.79 (s, 1H, NH), 9.18 (s, 1H, NH), 7.54 (d, \(J = 7.2\) Hz, 2H), 7.43 – 7.35 (m, 3H), 6.86 (s, 1H), 4.24 – 4.14 (m, 2H), 3.73 – 3.61 (m, 2H), 3.58 – 3.51 (m, 2H), 3.31 – 3.27 (m, 1H), 2.87 – 2.82 (m, 1H). \(^{13}\text{C}\{1\text{H}\}\text{ NMR (100 MHz, DMSO-\textit{d}_6):} \delta \) 197.0, 196.9*, 193.6, 139.1, 139.1*,
133.9, 129.4, 129.2, 128.8*, 128.7, 125.4, 65.0, 64.8, 51.5, 47.6. HRMS (ESI) m/z: [M - H]− calcd. for C_{14}H_{15}N_{2}OS_{2}− 291.0631; found 291.0628.

1-Morpholino-3-phenyl-2-(4-phenylthiazol-2-yl)prop-2-ene-1-thione (1g)

A mixture of 2-(morpholine-4-carbonothioyl)-3-phenylprop-2-enethioamide (1f) (100 mg, 1.0 equiv, 0.34 mmol) and freshly prepared 2-bromo-1-phenylethan-1-one (102 mg, 1.5 equiv, 0.51 mmol) in dry ethanol (2 mL) was stirred at room temperature for 3 h. The solvent was evaporated, and the residue was purified by column chromatography on SiO_{2} (PE/EtOAc, gradient 50:0 to 40:10). The obtained precipitate was centrifugated with diethyl ether to afford 1g (71 mg, 53%) as a pale-yellow powder, mp 167–168 °C. \(^{1}\)H NMR (400 MHz, CDCl_{3}-d): \(\delta\) 7.94 (d, \(J\) = 7.6 Hz, 2H), 7.64 (d, \(J\) = 7.3 Hz, 2H), 7.48 – 7.31 (m, 8H), 4.59 – 4.54 (m, 1H), 4.35 – 4.29 (m, 1H), 3.89 – 3.74 (m, 3H), 3.63 – 3.50 (m, 2H), 3.23 – 3.19 (m, 1H). \(^{13}\)C\{^{1}\}H NMR (100 MHz, CDCl_{3}-d): \(\delta\) 195.4, 165.6, 156.2, 134.4, 134.4, 134.0, 129.7, 129.2, 129.0, 128.9, 128.5, 126.9, 126.6, 113.9, 66.3, 66.1, 51.6, 48.3. HRMS (ESI) m/z: [M + H]⁺ calcd. for C_{22}H_{21}N_{2}OS_{2}⁺ 393.1090; found 393.1095.
General procedure for the synthesis of thioamides 1h-s

A mixture of 2-cyanothioacetamide S1a-c (1.0 equiv), appropriate ketone S3a-g (2.5–4.0 equiv) and DBU (0.1–1 equiv) in dry 1,4-dioxane (for 1k) or in neat (for 1h,i,j,l-s) was stirred for 14–48 h at 70–85 °C in an oven-dried 10 mL standard microwave vial. The vial was cooled to room temperature, then SiO₂ was added, and the solvent was evaporated under reduced pressure. The purification of the crude product by column chromatography on SiO₂ afforded the desired products 1h-s.
3-Methyl-2-(morpholine-4-carbonothioyl)but-2-enenitrile (1h)

Compound 1h was obtained according to the general procedure from 3-morpholino-3-thioxopropanenitrile (S1a) (500 mg, 1.0 equiv, 2.94 mmol), acetone S3a (2 mL), DBU (45 mg, 0.1 equiv, 0.29 mmol), 80 °C, reaction time is 14 h. The purification of the crude product by column chromatography (PE/EtOAc, gradient 40:10 to 20:30) afforded 1h as a pale-yellow oil (94%, 580 mg). 

$^1$H NMR (400 MHz, CDCl$_3$-$d$): $\delta$ 4.42 – 4.40 (m, 1H), 4.16 – 4.13 (m, 1H), 3.81 – 3.70 (m, 6H), 2.14 (s, 3H), 1.89 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$-$d$): $\delta$ 189.8, 154.7, 115.3, 111.7, 66.5, 66.2, 51.8, 48.8, 23.9, 21.4. HRMS (ESI) m/z: [M + Na$^+$] calcd. for C$_{10}$H$_{14}$N$_2$OSNa$^+$ 233.0719; found 233.0716.

2-Cyclopentylidene-3-morpholino-3-thioxopropanenitrile (1i)

Compound 1i was obtained according to the general procedure from 3-morpholino-3-thioxopropanenitrile (S1a) (400 mg, 1.0 equiv, 2.35 mmol), cyclopentanone (S3b) (791 mg, 4.0 equiv, 9.40 mmol), DBU (36 mg, 0.1 equiv, 0.24 mmol), 70 °C, reaction time is 24 h. The purification of the crude product by column chromatography (PE/EtOAc, gradient 50:0 to 30:20) afforded 1i as a pale-yellow oil (84%, 465 mg) that crystallizes into powder when stored at room temperature, mp 109–112 °C. $^1$H NMR (400 MHz, CDCl$_3$-$d$): $\delta$ 4.26 (br. s, 2H), 3.82 – 3.74 (m, 6H), 2.69 (t, $J = 6.0$ Hz, 2H), 2.46 (br. s, 2H), 1.81 – 1.89 (m, 4H). $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$-$d$): $\delta$ 190.1, 169.2, 115.4, 107.5, 66.7, 66.4, 51.9, 49.0, 34.9, 33.1, 26.4, 25.8. HRMS (ESI) m/z: [M + H$^+$] calcd. for C$_{12}$H$_{17}$N$_2$OS$^+$ 237.1056; found 237.1059.

2-Cyclohexylidene-3-morpholino-3-thioxopropanenitrile (1j)
Compound **1j** was obtained according to the general procedure from 3-morpholino-3-thioxopropanenitrile (**S1a**) (1000 mg, 1.0 equiv, 5.87 mmol), cyclohexanone (**S3c**) (1730 mg, 3.0 equiv, 17.62 mmol), DBU (89 mg, 0.1 equiv, 0.59 mmol), 80 °C, reaction time is 16 h. The purification of the crude product by column chromatography (PE/EtOAc, gradient 50:0 to 25:25) afforded **1j** as a pale-yellow oil (85%, 1250 mg) that crystallizes into powder when stored at room temperature, mp 91–93 °C. $^1$H NMR (400 MHz, CDCl$_3$-d): $\delta$ 4.42 – 4.37 (m, 1H), 4.21 – 4.15 (m, 1H), 3.86 – 3.68 (m, 6H), 2.59 – 2.46 (m, 2H), 2.39 – 2.33 (m, 1H), 2.20 – 2.13 (m, 1H), 1.78 – 1.52 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$-d): $\delta$ 189.8, 161.4, 115.1, 108.3, 66.5, 66.3, 51.8, 48.9, 34.2, 31.7, 27.7, 27.1, 25.5. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{13}$H$_{19}$N$_2$O$_2$S$^+$ 251.1212; found 251.1214.

**3-Morpholino-2-(tetrahydro-4H-pyran-4-ylidene)-3-thioxopropanenitrile (1k)**

![Chemical structure](image)

Compound **1k** was obtained according to the general procedure from 3-morpholino-3-thioxopropanenitrile (**S1a**) (300 mg, 1.0 equiv, 1.76 mmol), tetrahydro-4H-pyran-4-one (**S3d**) (529 mg, 3.0 equiv, 5.29 mmol), DBU (27 mg, 0.1 equiv, 0.18 mmol), 1,4-dioxane (1 mL), 80 °C, reaction time is 24 h. The purification of the crude product by column chromatography (PE/EtOAc, gradient 50:0 to 25:25) afforded **1k** as a colorless powder (81%, 360 mg), mp 191–193 °C. $^1$H NMR (400 MHz, CDCl$_3$-d): $\delta$ 4.45 – 4.41 (m, 1H), 4.17 – 4.12 (m, 1H), 3.87 – 3.72 (m, 10H), 2.73 – 2.57 (m, 3H), 2.34 – 2.29 (m, 1H). $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$-d): $\delta$ 188.6, 156.0, 114.6, 110.0, 68.1, 67.5, 66.5, 66.4, 52.0, 49.0, 34.5, 32.4. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{12}$H$_{17}$N$_2$O$_2$S$^+$ 253.1005; found 253.1005.

**2-Cycloheptylidene-3-morpholino-3-thioxopropanenitrile (1l)**

![Chemical structure](image)

Compound **1l** was obtained according to the general procedure from 3-morpholino-3-thioxopropanenitrile (**S1a**) (300 mg, 1.0 equiv, 1.76 mmol), cycloheptanone (**S3e**) (593 mg, 3.0 equiv, 17.62 mmol), DBU (27 mg, 0.1 equiv, 0.18 mmol), 80 °C, reaction time is 23 h. The
purification of the crude product by column chromatography (PE/EtOAc, gradient 50:0 to 35:15) afforded 1l as a yellow oil (70%, 326 mg) that crystallizes into powder when stored at room temperature, mp 99–100 °C. 1H NMR (400 MHz, CDCl₃-d): δ 4.48 – 4.42 (m, 1H), 4.17 – 4.11 (m, 1H), 3.86 – 3.76 (m, 4H), 3.73 – 3.65 (m, 2H), 2.74 – 2.56 (m, 3H), 2.31 – 2.25 (m, 1H), 1.78 – 1.71 (m, 3H), 1.59 (br. s, 4H), 1.50 – 1.44 (m, 1H). 13C{1H} NMR (100 MHz, CDCl₃-d): δ 190.3, 164.0, 115.3, 110.9, 66.6, 66.4, 51.8, 48.8, 35.4, 33.1, 29.8, 29.0, 27.2, 25.9. HRMS (ESI) m/z: [M + H]+ calcd. for C₁₄H₂₁N₂OS+ 265.1369; found 265.1374.

2-Cyclohexylidene-3-(piperidin-1-yl)-3-thioxopropanenitrile (1m)

Compound 1m was obtained according to the general procedure from 3-(piperidin-1-yl)-3-thioxopropanenitrile (S₁b) (350 mg, 1.0 equiv, 2.08 mmol), cyclohexanone (S₃c) (612 mg, 3.0 equiv, 6.24 mmol), DBU (32 mg, 0.1 equiv, 0.21 mmol), 80 °C, reaction time is 14 h. The purification of the crude product by column chromatography (PE/EtOAc, gradient 100:0 to 85:15) afforded 1m as a pale-yellow powder (94%, 484 mg), mp 116–117 °C. 1H NMR (400 MHz, CDCl₃-d): δ 4.32 – 4.29 (m, 1H), 4.14 – 4.10 (m, 1H), 3.79 – 3.75 (m, 1H), 3.67 – 3.62 (m, 1H), 2.52 (br. s, 2H), 2.37 – 2.31 (m, 1H), 2.20 – 2.14 (m, 1H), 1.73 (br. s, 8H), 1.65 – 1.48 (m, 4H). 13C{1H} NMR (100 MHz, CDCl₃-d): δ 188.5, 160.0, 115.3, 108.9, 52.7, 50.0, 34.1, 31.7, 27.7, 27.1, 26.8, 25.6, 25.3, 24.0. HRMS (ESI) m/z: [M + H]+ calcd. for C₁₄H₂₁N₂S+ 249.1420; found 249.1422.

2-Cyclohexylidene-3-(pyrrolidin-1-yl)-3-thioxopropanenitrile (1n)

Compound 1n was obtained according to the general procedure from 3-(pyrrolidin-1-yl)-3-thioxopropanenitrile (S₁c) (400 mg, 1.0 equiv, 2.59 mmol), cyclohexanone (S₃c) (764 mg, 3.0 equiv, 7.78 mmol), DBU (39 mg, 0.1 equiv, 0.26 mmol), 80 °C, reaction time is 21 h. The purification of the crude product by column chromatography (PE/EtOAc, gradient 100:0 to 80:20) afforded 1n as a colorless powder (86%, 526 mg), mp 84–86 °C. 1H NMR (400 MHz, CDCl₃-d):
$\delta$ 3.82 – 3.52 (m, 4H), 2.52 (br. s, 2H), 2.31 (br. s, 2H), 2.06 (br. s, 2H), 1.73 – 1.61 (m, 6H).

$^{13}$C\{1H\} NMR (100 MHz, CDCl$_3$-d): $\delta$ 186.7, 161.4, 115.1, 110.0, 53.0, 52.3, 34.2, 31.7, 27.8, 27.2, 26.3, 25.6, 24.5. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{13}$H$_{19}$N$_2$S$^+$ 235.1263; found 235.1265.

2-Cyclooctylidene-3-morpholino-3-thioxopropanenitrile (1o)

![Image](https://via.placeholder.com/150)

Compound 1o was obtained according to the general procedure from 3-morpholino-3-thioxopropanenitrile (S1a) (360 mg, 1.0 equiv, 2.11 mmol), cyclooctanone (S3f) (801 mg, 3.0 equiv, 6.34 mmol), DBU (32 mg, 0.1 equiv, 0.21 mmol), 80 °C, reaction time is 48 h. The purification of the crude product by column chromatography (PE/EtOAc, gradient 100:0 to 70:30) afforded 1o as a pale-yellow oil (68%, 401 mg) that crystallizes into powder when stored at room temperature, mp 117–119 °C. $^1$H NMR (400 MHz, CDCl$_3$-d): $\delta$ 4.45 – 4.40 (m, 1H), 4.20 – 4.14 (m, 1H), 3.84 – 3.75 (m, 4H), 3.72 – 3.63 (m, 2H), 2.69 – 2.63 (m, 1H), 2.50 – 2.42 (m, 2H), 2.25 – 2.19 (m, 1H), 1.93 – 1.84 (m, 2H), 1.80 – 1.76 (m, 2H), 1.66 – 1.60 (m, 1H), 1.56 – 1.43 (m, 5H). $^{13}$C\{1H\} NMR (100 MHz, CDCl$_3$-d): $\delta$ 190.4, 165.6, 115.4, 109.8, 66.6, 66.4, 51.7, 48.7, 33.2, 33.0, 29.2, 28.0, 25.6, 25.1, 23.1. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{15}$H$_{23}$N$_2$OS$^+$ 279.1525; found 279.1528.

2-Cycloheptylidene-3-(piperidin-1-yl)-3-thioxopropanenitrile (1p)

![Image](https://via.placeholder.com/150)

Compound 1p was obtained according to the general procedure from 3-(piperidin-1-yl)-3-thioxopropanenitrile (S1b) (300 mg, 1.0 equiv, 1.78 mmol), cycloheptanone (S3e) (600 mg, 3.0 equiv, 5.35 mmol), DBU (27 mg, 0.1 equiv, 0.18 mmol), 80 °C, reaction time is 40 h. The purification of the crude product by column chromatography (PE/EtOAc, gradient 100:0 to 70:30) afforded 1p as a pale-yellow oil (91%, 468 mg) that crystallizes into powder when stored at room temperature, mp 87–88 °C. $^1$H NMR (400 MHz, CDCl$_3$-d): $\delta$ 4.42 – 4.36 (m, 1H), 4.05 – 3.99 (m, 1H), 3.82 – 3.76 (m, 1H), 3.63 – 3.57 (m, 1H), 2.70 – 2.53 (m, 3H), 2.31 – 2.24 (m, 1H), 1.78 –
1.54 (m, 13H), 1.48 – 1.42 (m, 1H). $^{13}$C{1H} NMR (100 MHz, CDCl$_3$-d): $\delta$ 188.9, 162.5, 115.4, 111.5, 52.6, 49.9, 35.2, 32.9, 29.8, 29.0, 27.1, 26.8, 25.9, 25.3, 24.0. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{15}$H$_{23}$N$_2$S$^+$ 263.1576; found 263.1576.

2-Cyclooctylidene-3-(pyrrolidin-1-yl)-3-thioxopropanenitrile (1q)

![Structure of 2-Cyclooctylidene-3-(pyrrolidin-1-yl)-3-thioxopropanenitrile (1q)]

Compound 1q was obtained according to the general procedure from 3-(pyrrolidin-1-yl)-3-thioxopropanenitrile (S1c) (500 mg, 1.0 equiv, 3.24 mmol), cyclooctanone (S3f) (1023 mg, 2.5 equiv, 8.10 mmol), DBU (493 mg, 1 equiv, 3.24 mmol), 85 °C, reaction time is 24 h. The purification of the crude product by column chromatography (PE/EtOAc, gradient 50:0 to 42:8) afforded 1q as a pale-yellow oil (65%, 558 mg) that crystallizes into powder when stored at room temperature, mp 81–83 °C. $^1$H NMR (400 MHz, CDCl$_3$-d): $\delta$ 3.86 – 3.83 (m, 2H), 3.62 (br s, 2H), 2.58 (br s, 2H), 2.40 (br s, 2H), 2.09 – 2.06 (m, 4H), 1.92 – 1.86 (m, 2H), 1.80 – 1.76 (m, 2H), 1.50 (br s, 6H). $^{13}$C{1H} NMR (100 MHz, CDCl$_3$-d): $\delta$ 187.2, 165.6, 115.3, 111.5, 52.8, 52.0, 33.2, 32.8, 28.9, 27.9, 26.3, 25.7, 25.2, 24.4, 23.3. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{15}$H$_{23}$N$_2$S$^+$ 263.1576; found 263.1575.

2-Cyclooctylidene-3-(piperidin-1-yl)-3-thioxopropanenitrile (1r)

![Structure of 2-Cyclooctylidene-3-(piperidin-1-yl)-3-thioxopropanenitrile (1r)]

Compound 1r was obtained according to the general procedure from 3-(piperidin-1-yl)-3-thioxopropanenitrile (S1b) (500 mg, 1.0 equiv, 2.97 mmol), cyclooctanone (S3f) (1125 mg, 3.0 equiv, 8.91 mmol), DBU (821 mg, 1 equiv, 2.97 mmol), 85 °C, reaction time is 24 h. The purification of the crude product by column chromatography (PE/EtOAc, gradient 100:0 to 82:18) afforded 1r as a pale-yellow oil (70%, 573 mg) that crystallizes into powder when stored at room temperature, mp 114–116 °C. $^1$H NMR (400 MHz, CDCl$_3$-d): $\delta$ 4.40 – 4.35 (m, 1H), 4.09 – 4.03 (m, 1H), 3.79 – 3.74 (m, 1H), 3.63 – 3.57 (m, 1H), 2.67 – 2.61 (m, 1H), 2.50 – 2.41 (m, 1H), 2.26 – 2.19 (m, 1H), 1.95 – 1.82 (m, 2H), 1.81 – 1.68 (m, 7H), 1.66 – 1.58 (m, 2H), 1.56 – 1.38 (m, 5H). $^{13}$C{1H} NMR (100 MHz, CDCl$_3$-d): $\delta$ 189.1, 164.0, 115.6, 110.5, 52.6, 49.9, 33.1, 32.9,
29.1, 28.0, 26.8, 25.6, 25.3, 25.1, 24.1, 23.1. HRMS (ESI) m/z: [M + H]^+ calcd. for C_{16}H_{25}N_{2}S^+ 277.1733; found 277.1733.

3-(Azepan-1-yl)-2-cyclooctylidene-3-thioxopropanenitrile (1s)

Compound 1s was obtained according to the general procedure from 3-(azepan-1-yl)-3-thioxopropanenitrile (S1d) (500 mg, 1.0 equiv, 2.74 mmol), cyclooctanone (S3f) (1038 mg, 3.0 equiv, 8.23 mmol), DBU (417 mg, 1 equiv, 2.74 mmol), 85 °C, reaction time is 40 h. The purification of the crude product by column chromatography (PE/EtOAc, gradient 50:0 to 42:8) afforded 1s as a pale-yellow oil (42%, 338 mg) that crystallizes into powder when stored at room temperature, mp 106–108 °C. ^1H NMR (400 MHz, CDCl_3-d): δ 4.24 – 4.18 (m, 1H), 3.97 – 3.90 (m, 1H), 3.86 – 3.80 (m, 1H), 3.65 – 3.58 (m, 1H), 2.68 – 2.62 (m, 1H), 2.52 – 2.40 (m, 2H), 2.20 – 2.13 (m, 1H), 2.05 – 1.95 (m, 1H), 1.93 – 1.81 (m, 4H), 1.79 – 1.73 (m, 3H), 1.67 – 1.58 (m, 4H), 1.57 – 1.37 (m, 6H). ^13C{1H} NMR (100 MHz, CDCl_3-d): δ 190.3, 163.8, 115.7, 110.9, 53.8, 52.8, 33.0, 32.9, 29.4, 28.7, 28.1, 27.8, 26.1, 25.5, 25.4, 25.1, 22.8. HRMS (ESI) m/z: [M + H]^+ calcd. for C_{17}H_{27}N_{2}S^+ 291.1889; found 291.1887.

(Z/E)-3-((4-Chlorophenyl)amino)-2-(pyrrolidine-1-carbonothioyl)acrylonitrile (1t)

To a solution of 3-(dimethylamino)-2-(pyrrolidine-1-carbonothioyl)acrylonitrile (S1d) (261 mg, 1.0 equiv, 1.25 mmol), 4-chloroaniline (175 mg, 1.1 equiv, 1.375 mmol) in EtOH (5 mL) concentrated HCl (127 mg, 1.0 equiv, 1.25 mmol) was added and the mixture was stirred for 3 h at 60 °C. The suspension was cooled down to room temperature, filtered and washed with EtOH afforded 1p as a yellow powder (65%, 238 mg), mp 159–161 °C. ^1H NMR (400 MHz, DMSO-d_6): δ 10.52* and 10.46 (both d, J = 13.4* and 12.1 Hz, 1H), 8.52 and 7.95* (both d, J = 11.1 and 13.3* Hz, 1H), 7.42 – 7.34 (m, 4H), 3.81 – 3.72 (m, 4H), 1.96 (br. s, 4H). ^13C{1H} NMR (100 MHz,
DMSO-$d_6$): $\delta$ 186.9, 183.8*, 152.2, 144.3*, 139.2, 138.6*, 129.4, 129.3*, 128.0, 127.4*, 119.2*, 119.1, 118.3*, 116.2, 86.9, 85.6*, 55.1, 53.4*, 53.3, 52.7*, 26.6, 26.0*, 24.0, 23.8°. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{14}$H$_{15}$ClN$_3$S$^+$ 292.0670; found 292.0672.

3-(Morpholine-4-carbonothioyl)-4-phenylbut-3-en-2-one (1w)

A mixture of 4-morpholino-4-thioxobutan-2-one (S1f) (374 mg, 1.0 equiv, 2.0 mmol), benzaldehyde S2a (261 mg, 1.25 equiv, 2.5 mmol), DBU (30 mg, 0.1 equiv, 0.20 mmol) and glacial acetic acid (12 mg, 0.1 equiv, 0.20 mmol) in toluene (3 mL) was stirred for 16 h at 80 °C. The solvent was evaporated under reduced pressure. Ethanol (3 mL) was added to a residue and the formed suspension was kept in the fridge for 1 h. The precipitate was filtered off and washed with cold ethanol afforded 1w as a yellow powder (57%, 315 mg), mp 131–133 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 7.65 – 7.63 (m, 2H), 7.48 – 7.40 (m, 3H), 7.36 (s, 1H), 4.35 – 4.30 (m, 1H), 4.27 – 4.21 (m, 1H), 3.77 – 3.65 (m, 2H), 3.62 – 3.54 (m, 1H), 3.50 – 3.44 (m, 2H), 3.13 – 3.07 (m, 1H), 2.43 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, DMSO-$d_6$): $\delta$ 195.5, 194.3, 139.6, 133.8, 133.2, 130.2, 128.8, 65.5, 65.2, 51.1, 47.7, 26.6. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{15}$H$_{18}$NO$_2$S$^+$ 276.1053; found 276.1053.

Methyl 2-(morpholine-4-carbonothioyl)-3-phenylacrylate (1x)

A mixture of methyl 3-morpholino-3-thioxopropanoate (S1g) (406 mg, 1.0 equiv, 2.0 mmol), benzaldehyde S2a (233 mg, 1.10 equiv, 2.2 mmol), DBU (30 mg, 0.1 equiv, 0.20 mmol) and glacial acetic acid (12 mg, 0.1 equiv, 0.20 mmol) in toluene (4 mL) was stirred for 16 h at 80 °C. The solvent was evaporated under reduced pressure. Ethanol (3 mL) was added to a residue and the formed suspension was kept in the fridge for 1 h. The precipitate was filtered off and washed with cold ethanol afforded 1x as a yellow powder (71%, 412 mg), mp 138–139 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 7.62 – 7.60 (m, 2H), 7.47 – 7.43 (m, 3H), 7.35 (s, 1H), 4.30 – 4.27 (m, 2H), 3.77 (s, 3H), 3.73 – 3.63 (m, 3H), 3.58 – 3.47 (m, 2H), 3.20 – 3.14 (m, 1H). $^{13}$C{$^1$H} NMR (100 MHz, DMSO-$d_6$): $\delta$ 192.4, 164.4, 134.3, 132.8, 131.0, 130.1, 128.8, 65.4, 65.1, 52.5, 51.3, 47.8. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{15}$H$_{18}$NO$_3$S$^+$ 292.1002; found 292.1001.
2-Cyano-3-phenyl-N-(p-tolyl)prop-2-enethioamide (1y)

![Structural formula]

A mixture of 2-cyano-N-(p-tolyl)ethanethioamide (S1e) (1000 mg, 1.0 equiv, 5.25 mmol), benzaldehyde S2a (781 mg, 1.4 equiv, 7.36 mmol) and DBU (80 mg, 0.1 equiv, 5.25 mmol) in ethanol (5 mL) was stirred for 15 h at room temperature. The formed suspension was kept in the fridge for 1 h. The precipitate was filtered off and washed with cold ethanol. The product was recrystallized from ethanol and filtered off. The mother liquor was evaporated under reduced pressure and the formed precipitate was filtered off and washed with cold ethanol afforded 1y as a bright-red powder (27%, 400 mg), mp 131–132 °C. 1H NMR (400 MHz, DMSO-d6): δ 12.02 (s, 1H), 8.02 (s, 1H), 8.00 – 7.97 (m, 2H), 7.68 (d, J = 8.1 Hz, 2H), 7.61 – 7.55 (m, 3H), 7.26 (d, J = 8.1 Hz, 2H), 2.33 (s, 3H). 13C{1H} NMR (100 MHz, DMSO-d6): δ 188.4, 145.5, 136.6, 136.1, 132.1, 132.0, 130.0, 129.2, 129.1, 123.8, 116.5, 114.2, 20.7. HRMS (ESI) m/z: [M + H]+ calcd. for C17H15N2S+ 279.0950; found 279.0950.
2-Cycloheptylidene-3-morpholino-3-oxopropanenitrile (Am-1)

A mixture of 3-morpholino-3-oxopropanenitrile (300 mg, 1.0 equiv, 1.94 mmol), cycloheptanone (S3e) (873 mg, 4.0 equiv, 7.78 mmol) and DBU (30 mg, 0.1 equiv, 0.19 mmol) was stirred for 24 h at 80 °C in an oven-dried 10 mL standard microwave vial. The vial was cooled to room temperature. The purification of the crude product by column chromatography on SiO2 afforded Am-1 as a white powder (75%, 364 mg), mp 60–62 °C. ¹H NMR (400 MHz, CDCl₃-d): δ 3.70 – 3.65 (m, 3H), 3.51 – 3.49 (m, 1H), 2.71 – 2.68 (m, 1H), 2.50 – 2.47 (m, 1H), 1.76 – 1.65 (m, 2H), 1.60 – 1.53 (m, 2H). ¹³C{¹H} NMR (100 MHz, CDCl₃-d): δ 171.1, 161.9, 115.2, 105.9, 66.8, 47.4, 42.5, 35.8, 33.7, 29.4, 29.1, 26.8, 26.5. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₁₄H₂₁N₂O₂⁺ 249.1597; found 249.1599.

Synthesis of 1-Sulfonyl-1,2,3-Triazole 2g and Diazo Compounds 2p,s-v

4-Cyclopropyl-1-tosyl-1H-1,2,3-triazole (2g)

To a solution of ethynylcyclopropane (500 mg, 1.0 equiv, 7.56 mmol) and CuTC (144 mg, 0.1 equiv, 0.76 mmol) in toluene (17 mL) tosyl azide (1490 mg, 1.0 equiv, 7.56 mmol) in toluene (10 mL) was added dropwise at room temperature and the solution was stirred for 2 h. The solvent was evaporated, and the formed precipitate was triturated with the mixture of PE/DCM (8:1). Purification of the crude product by flash chromatography (PE/EtOAc, gradient 50:0 to 40:10) afforded 2g (70%, 1390 mg) as a colorless powder, mp 105–106 °C (lit.¹⁶ 105–106 °C). ¹H NMR (400 MHz, DMSO-d₆): δ 7.96 (d, J = 8.3 Hz, 2H), 7.79 (s, 1H), 7.36 (d, J = 8.1 Hz, 2H), 2.43 (s, 3H), 1.96 – 1.89 (m, 1H), 0.99 – 0.94 (m, 2H), 0.88 – 0.84 (m, 2H).
3-Diazo-7-methylindolin-2-one (2p)

3-Diazo-7-methylindolin-2-one (2p) was purchased from a commercial source. Mp 178–176 °C (decomp.). \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta\) 10.68 (br. s, 1H), 7.23 (d, \(J = 4.4\) Hz, 1H), 6.92 (d, \(J = 4.4\) Hz, 2H), 2.23 (s, 3H). \(^1\)C\{\(^1\)H\} NMR (100 MHz, DMSO-\(d_6\)): \(\delta\) 168.2, 131.2, 126.4, 121.3, 119.4, 116.7, 116.5, 60.2, 16.3. HRMS (ESI) m/z: [M + H]\(^+\) calcd. for C\(_9\)H\(_8\)N\(_3\)O\(^+\) 174.0662; found 174.0661.

Dimethyl 2-diazomalonate (2s)

To a solution of dimethyl malonate (500 mg, 1.0 equiv, 3.78 mmol) and Et\(_3\)N (383 mg, 1.0 equiv, 3.78 mmol) in acetonitrile (10 mL) tosyl azide (830 mg, 1.1 equiv, 4.16 mmol) in acetonitrile (10 mL) was added dropwise at 0 °C and the solution was stirred for 16 h at room temperature. The solvent was evaporated, and the formed precipitate was triturated CCl\(_4\) and filtered off. The mother liquor was evaporated under reduced pressure. The residue was dissolved in DCM and purified by flash chromatography (DCM/EtOAc, gradient 25:0 to 24:1) afforded 2s (93%, 557 mg) as a pale-yellow liquid. \(^1\)H NMR (400 MHz, CDCl\(_3\)-\(d\)): \(\delta\) 3.83 (s, 6H).

Methyl 2-diazo-2-phenylacetate (2t)

Red oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)-\(d\)): \(\delta\) 7.48 (d, \(J = 8.3\) Hz, 2H), 7.39 (t, \(J = 7.9\) Hz, 2H), 7.19 (t, \(J = 7.4\) Hz, 1H), 3.87 (s, 3H).
**2-Diazo-1-phenylbutane-1,3-dione (2u)**

![Structure of 2-Diazo-1-phenylbutane-1,3-dione](image)

To a solution of 1-phenylbutane-1,3-dione (300 mg, 1.0 equiv, 1.85 mmol) and Et₃N (187 mg, 1.0 equiv, 1.85 mmol) in acetonitrile (4 mL) mesyl azide (246 mg, 1.1 equiv, 2.03 mmol) in acetonitrile (7 mL) was added dropwise at 0 °C and the solution was stirred for 16 h at room temperature. The solvent was evaporated, and the residue was dissolved in minimal volume of DCM and purified by flash chromatography (PE/EtOAc, gradient 9:1 to 4:1) afforded 2u (80%, 280 mg) as a pale-yellow solid, mp 62–63 °C (lit. 27 63.5–64.5 °C). ¹H NMR (400 MHz, CDCl₃-d₆): δ 7.64 (d, J = 7.3 Hz, 2H), 7.58 (t, J = 7.3 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 2.58 (s, 3H).

**3-Diazo-5-methylindolin-2-one (2v)**

![Structure of 3-Diazo-5-methylindolin-2-one](image)

Red powder, mp 178–180 °C (lit. 28 184–185 °C). ¹H NMR (400 MHz, DMSO-d₆): δ 10.53 (s, 1H), 7.21 (s, 1H), 6.90 (d, J = 7.9 Hz, 1H), 6.79 (d, J = 7.9 Hz, 1H), 2.27 (s, 3H).

**Synthesis of catalysts Rh₂(S-DBPTTL)₄ and Rh₂(S-PTTR)₄ (S)-2-(1,3-Dioxoisindolin-2-yl)-3-(1H-indol-3-yl)propanoic acid (L1)**

![Structure of L1](image)

A 50 mL round-bottom flask was charged with L-tryptophan (1000 mg, 4.9 mmol), phthalic anhydride (725 mg, 1.0 equiv, 4.9 mmol), triethylamine (50 mg, 0.1 equiv, 0.49 mmol), toluene (25 mL) and equipped with a Dean-Stark apparatus. The mixture was heated to reflux and stirred for 18 h. The solvent was evaporated and the crude product was purified by column chromatography on SiO₂ (PE/EtOAc, gradient 50:0 to 25:25) afforded after trituration in diethyl ether and n-hexane and filtration L₁ as a yellow powder (72%, 1182 mg), mp 172–174 °C (lit. 22 170 °C), [α]₀²⁰ = −184 (C = 0.49, EtOH) (lit. 29 [α]₀²⁰ = −212 (C = 1, EtOH)) ¹H NMR (400 MHz, DMSO-d₆): δ 10.53 (s, 1H), 7.21 (s, 1H), 6.90 (d, J = 7.9 Hz, 1H), 6.79 (d, J = 7.9 Hz, 1H), 2.27 (s, 3H).
MHz, DMSO-$d_6$): $\delta$ 13.30 (s, 1H), 10.73 (s, 1H), 7.81 (s, 3H), 7.48 (d, $J = 7.8$ Hz, 1H), 7.25 (d, $J = 8.0$ Hz, 1H), 7.03 – 6.98 (m, 2H), 6.89 (t, $J = 7.4$ Hz, 1H), 5.14 – 5.10 (m, 1H), 3.62 – 3.54 (m, 2H).

**(S)-2-(4,7-Dibromo-1,3-dioxoisindolin-2-yl)-3,3-dimethylbutanoic acid (L2)**

![Chemical structure of L2]

A 50 mL round-bottom flask was charged with $L$-tert-leucine (500 mg, 3.8 mmol), 4,7-dibromoisobenzofuran-1,3-dione (S3) (1170 mg, 1.0 equiv, 3.8 mmol), triethylamine (38 mg, 0.1 equiv, 0.38 mmol), dry toluene (15 mL) and equipped with a Dean-Stark apparatus. The mixture was heated to reflux and stirred for 15 h. The solvent was evaporated, and the crude product was purified by column chromatography on SiO$_2$ (PE/EtOAc, gradient 50:0 to 35:15) afforded after trituration in $n$-hexane and centrifugation L2 as a colorless powder (80%, 1284 mg), mp 195–197 °C, $[\alpha]_D^0 = +20.4$ (C = 1.8, CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$-$d_6$): $\delta$ 10.67 (br. s, 1H), 8.10 (s, 2H), 4.69 (s, 1H), 1.16 (s, 9H). $^{13}$C{1H} NMR (100 MHz, CDCl$_3$-$d_6$): $\delta$ 173.6, 166.1, 131.9, 131.4, 128.9, 60.4, 35.9, 28.1. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{14}$H$_{14}$Br$_2$NO$_4^+$ 417.9285; found 417.9283.

**Rh$_2$(S-PTTR)$_4$**

![Chemical structure of Rh$_2$(S-PTTR)$_4$]

To a mixture of Rh$_2$(OAc)$_4$ (100 mg, 1.0 equiv, 0.23 mmol) and (S)-PTTR (454 mg, 6.0 equiv, 1.36 mmol) was added dry chlorobenzene (25 mL). The flask was adapted with a Soxhlet extractor containing a cartridge filled with a mixture of Na$_2$CO$_3$ and sand (1:1). The solution was heated to 150 °C for 24 h. The reaction mixture was cooled down to room temperature and concentrated under reduced pressure. The residue was dissolved in acetonitrile, concentrated under reduced pressure, then dissolved in ethyl acetate, the obtained solution was heated to reflux and filtered
The mother liquor was cooled down and washed with saturated solution of Na2CO3 (3 times) and with water, dried over anhydrous Na2SO4, filtered, and concentrated in vacuo. The green residue was then dissolved in DCM and was purified by column chromatography on SiO2 (DCM/EtOAc, gradient 30:0 to 25:5) to provide the title product as a green solid (256 mg, 73%), \( \alpha = -5.1 \) (C = 0.7, MeCN). 1H NMR (400 MHz, DMSO-d6): \( \delta 10.74 \) (s, 4H, NH), 7.78 – 7.76 (m, 8H), 7.56 (d, \( J = 7.8 \) Hz, 4H), 7.27 (d, \( J = 8.0 \) Hz, 4H), 7.07 (s, 4H), 7.01 (t, \( J = 7.5 \) Hz, 4H), 6.90 (t, \( J = 7.4 \) Hz, 4H), 5.21 (t, \( J = 7.9 \) Hz, 4H), 3.56 (d, \( J = 7.6 \) Hz, 8H).

13C{1H} NMR (100 MHz, CDCl3-d): \( \delta 188.5, 166.8, 136.0, 134.6, 130.9, 127.1, 123.4, 123.1, 120.9, 118.3, 118.0, 111.4, 109.7, 53.8, 24.7. \) HRMS (ESI) m/z: [M + H]+ calcd. for C76H53N8O16Rh2 1539.1684; found 1539.1697.

**Rh2(S-DBPTTL)4**

To a mixture of Rh2(OAc)4 (70 mg, 1.0 equiv, 0.16 mmol) and (S)-DBPTTL (398 mg, 6.0 equiv, 0.95 mmol) was added dry chlorobenzene (15 mL). The flask was adapted with a Soxhlet extractor containing a cartridge filled with a mixture of Na2CO3 and sand (1:1). The solution was heated to 150 °C for 24 h. The reaction mixture was cooled down and concentrated under reduced pressure. The residue was dissolved in DCM and washed with saturated solution of Na2CO3 (3 times) and with water, dried over anhydrous Na2SO4 and concentrated in vacuo. The green residue was then dissolved in DCM and was purified by column chromatography on SiO2 (PE/EtOAc, gradient 50:0 to 36:14) to provide the title product as a light green solid (281 mg, 95%), \( \alpha = +55.3 \) (C = 0.07, CHCl3). 1H NMR (400 MHz, CDCl3-d): \( \delta 8.05 \) (br. s, 8H), 4.82 (s, 4H), 1.08 (s, 36H).

13C{1H} NMR (100 MHz, CDCl3-d): \( \delta 187.2, 166.1, 131.7, 131.5, 128.7, 62.0, 35.7, 28.0. \) HRMS (ESI) m/z: [M + H]+ calcd. for C56H48Br8N4O16Rh2Na+ 1892.4539; found 1892.4535.
Optimization study for the reaction of thioamide 1a with 1-sulfonyl-1,2,3-triazole 2a

Table S1. Optimization of the synthesis of dihydrothiophene 3aa

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent (T, °C)</th>
<th>Catalyst (mol %)</th>
<th>Time, h</th>
<th>Equiv of 2a</th>
<th>Yielda, %</th>
<th>drb</th>
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<td>Rh₂(Oct)₄ (2.0)</td>
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<td>52</td>
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<td>1.1</td>
<td>NR</td>
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</table>

Conditions: thioamide 1a (0.19 mmol), triazole 2a (0.21 mmol, 1.1 equiv), solvent (1 mL).

aIsolated yields. b(4RS,5SR:4RS,5RS). Determined by ¹H NMR analysis of the crude mixture.

Synthesis of dihydrothiophenes 3

General procedure for the synthesis of dihydrothiophenes 3

To an oven-dried 10 mL standard microwave vial, a mixture of rhodium (II) pivalate dimer (2.0 mol %), thioamide 1 (1.0 equiv), 1-sulfonyl-1,2,3-triazole 2 (1.1–1.5 equiv) and dry chloroform (1–1.5 mL) were added. The resulting solution was stirred for 9–17 h at 80 °C. Reaction solution was cooled down to room temperature and directly transferred on SiO₂ or neutral alumina (for 3da) and purified.
(4RS,5SR)-5-Formyl-2-morpholino-4,5-diphenyl-4,5-dihydrothiophene-3-carbonitrile (3aa)

![Chemical Structure](image)

Compound 3aa was obtained according to the general procedure from 2-(morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (50 mg, 1.0 equiv, 0.19 mmol), 1-sulfonyl-1,2,3-triazole 2a (64 mg, 1.1 equiv, 0.21 mmol), Rh2(Piv)4 (2.6 mg), chloroform (1 mL), 80 °C, reaction time is 13 h. The purification of the crude product by column chromatography on SiO2 (PE/EtOAc, gradient 50:0 to 35:15) afforded 3aa as a colorless powder (81%, 59 mg), mp 213–214 °C. 1H NMR (400 MHz, DMSO-d6): δ 9.43 (s, 1H), 7.21 – 7.18 (m, 3H), 7.13 – 7.02 (m, 7H), 4.88 (s, 1H), 3.73 – 3.68 (m, 4H), 3.65 – 3.61 (m, 4H). 13C{1H} NMR (100 MHz, DMSO-d6): δ 188.7, 159.2, 137.1, 130.1, 128.7, 128.6, 128.5, 128.1, 128.0, 127.3, 118.4, 75.2, 73.5, 65.5, 55.0, 50.5. HRMS (ESI) m/z: [M + H]+ calcd. for C22H21N2O2S+ 377.1318; found 377.1320.

(4RS,5SR)-5-Formyl-5-(4-methoxyphenyl)-2-morpholino-4-phenyl-4,5-dihydrothiophene-3-carbonitrile (3ac)

![Chemical Structure](image)

Compound 3ac was obtained according to the general procedure from 2-(morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (50 mg, 1.0 equiv, 0.19 mmol), 1-sulfonyl-1,2,3-triazole 2c (70 mg, 1.1 equiv, 0.21 mmol), Rh2(Piv)4 (2.6 mg), chloroform (1 mL), 80 °C, reaction time is 13 h. The purification of the crude product by column chromatography on SiO2 (DCM/EtOAc, gradient 25:0 to 24:1) afforded 3ac as a colorless gum. It was triturated with n-hexane and centrifugated afforded 3ac as a colorless powder (85%, 53 mg), mp 174–179 °C. 1H NMR (400 MHz, CDCl3-d): δ 9.35 (s, 1H), 7.10 – 7.06 (m, 3H), 7.01 – 6.99 (m, 2H), 6.86 (d, J = 8.8 Hz, 2H), 6.64 (d, J = 8.8 Hz, 2H), 4.84 (s, 1H), 3.82 – 3.77 (m, 4H), 3.73 – 3.62 (m, 7H). 13C{1H} NMR
(100 MHz, CDCl₃-d): δ 188.1, 159.8, 159.3, 136.8, 129.5, 128.9, 128.2, 127.6, 121.6, 118.3, 114.2, 77.4, 73.9, 66.4, 55.9, 55.3, 50.9. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₂₃H₂₃N₂O₃S⁺ 407.1424; found 407.1425.

(4RS,5SR)-5-Formyl-2-morpholino-5-phenyl-4-(p-tolyl)-4,5-dihydrothiophene-3-carbonitrile (3ba)

![Structure of 3ba](image)

Compound 3ba was obtained according to the general procedure from 2-(morpholine-4-carbonothioyl)-3-(p-tolyl)acrylonitrile (1b) (40 mg, 1.0 equiv, 0.15 mmol), 1-sulfonyl-1,2,3-triazole 2a (48 mg, 1.1 equiv, 0.16 mmol), Rh₂(Piv)₄ (2.0 mg), chloroform (1 mL), 70 °C, reaction time is 16 h. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 50:0 to 35:15) afforded 3ba as a colorless powder (70%, 57 mg), mp 228–229 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 9.41 (s, 1H), 7.23 – 7.17 (m, 3H), 7.05 – 7.02 (m, 4H), 6.90 (d, J = 7.6 Hz, 2H), 4.85 (s, 1H), 3.71 (br. s, 4H), 3.66 – 3.61 (m, 4H). ¹³C{¹H} NMR (100 MHz, DMSO-d₆): δ 188.9, 159.2, 136.3, 134.1, 130.2, 128.7, 128.4, 128.4, 128.3, 128.2, 128.2, 118.4, 75.6, 73.5, 65.5, 54.6, 50.5, 20.5. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₂₃H₂₃N₂O₂S⁺ 391.1475; found 391.1473.

(4RS,5SR)-4-(4-Chlorophenyl)-5-formyl-2-morpholino-5-phenyl-4,5-dihydrothiophene-3-carbonitrile (3ca)

![Structure of 3ca](image)

Compound 3ca was obtained according to the general procedure from 3-(4-chlorophenyl)-2-(morpholine-4-carbonothioyl)acrylonitrile (1c) (50 mg, 1.0 equiv, 0.17 mmol), 1-sulfonyl-1,2,3-triazole 2a (56 mg, 1.1 equiv, 0.19 mmol), Rh₂(Piv)₄ (2.3 mg), chloroform (1 mL), 80 °C, reaction time is 13 h. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc,
gradient 50:0 to 30:20) afforded 3ca as a colorless powder (64%, 45 mg), mp 235–236 °C. 1H NMR (400 MHz, DMSO-d6): δ 9.42 (s, 1H), 7.25 – 7.22 (m, 3H), 7.16 (br. s, 4H), 7.06 – 7.03 (m, 2H), 4.94 (s, 1H), 3.73 – 3.70 (m, 4H), 3.65 – 3.62 (m, 4H). 13C{1H} NMR (100 MHz, DMSO-d6): δ 188.5, 159.3, 136.3, 131.9, 130.6, 130.0, 128.8, 128.7, 128.1, 127.9, 118.2, 74.7, 73.3, 65.5, 54.2, 50.5. HRMS (ESI) m/z: [M + H]+ calcd. for C22H20ClN2O2S+ 411.0928; found 411.0929.

(E)-5-Formyl-2-morpholino-5-phenyl-4-styryl-4,5-dihydrothiophene-3-carbonitrile (3da)

Compound 3da was obtained according to the general procedure from 2-(morpholine-4-carbonothioyl)-5-phenylpenta-2,4-dienenitrile (1d) (70 mg, 1.0 equiv, 0.25 mmol), 1-sulfonyl-1,2,3-triazole 2a (81 mg, 1.1 equiv, 0.27 mmol), Rh2(Piv)4 (3.3 mg), chloroform (1.5 mL), 80 °C, reaction time is 13 h. The purification of the crude product by column chromatography on neutral Al2O3 (PE/EtOAc, gradient 50:0 to 35:15) with subsequent centrifugation with n-hexane afforded 3da as a colorless powder (68%, 48 mg), mp 121–123 °C. 1H NMR (400 MHz, DMSO-d6): δ 9.39 (s, 1H), 7.41 (t, J = 7.4 Hz, 2H), 7.33 (t, J = 7.3 Hz, 1H), 7.27 – 7.17 (m, 7H), 6.49 (d, J = 15.7 Hz, 1H), 5.86 (dd, J = 15.7, 9.1 Hz, 1H), 4.47 (d, J = 9.0 Hz, 1H), 3.70 – 3.68 (m, 4H), 3.60 – 3.59 (m, 4H). 13C{1H} NMR (100 MHz, DMSO-d6): δ 189.6, 158.7, 136.2, 131.9, 130.5, 129.1, 128.8, 128.5, 128.4, 127.6, 126.2, 124.9, 118.4, 73.1, 72.5, 65.4, 53.2, 50.4. HRMS (ESI) m/z: [M + H]+ calcd. for C24H23N2O2S+ 403.1475; found 403.1470.

4-Methyl-N-((5-morpholino-2,3-diphenyl-4-(4-phenylthiazol-2-yl)-2,3-dihydrothiophen-2-yl)methylene)benzenesulfonamide (3ga)

Compound 3ga was obtained according to the general procedure from 1-morpholino-3-phenyl-2-(4-phenylthiazol-2-yl)prop-2-ene-1-thione (1g) (44 mg, 1.0 equiv, 0.11 mmol), 1-sulfonyl-1,2,3-
triazole 2a (40 mg, 1.2 equiv, 0.13 mmol), Rh$_2$(Piv)$_4$ (1.6 mg), chloroform (1.0 mL), 80 °C, reaction time is 14 h. The purification of the crude product by column chromatography on SiO$_2$ (PE/EtOAc, gradient 50:0 to 40:10) with subsequent centrifugation with cold diethyl ether afforded 3ga as a colorless powder (53%, 30 mg), mp 216–218 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 8.41 (s, 1H), 7.99 (s, 1H), 7.88 (d, $J = 7.6$ Hz, 2H), 7.54 (d, $J = 7.9$ Hz, 2H), 7.41 (t, $J = 7.5$ Hz, 2H), 7.33 – 7.19 (m, 8H), 7.12 (d, $J = 6.7$ Hz, 2H), 7.04 – 6.94 (m, 3H), 5.45 (s, 1H), 2.74 – 2.70 (m, 2H), 2.35 (s, 3H), 2.24 – 2.20 (m, 2H). $^{13}$C{$^1$H} NMR (100 MHz, DMSO-$d_6$): δ 167.4, 158.5, 152.6, 149.0, 144.7, 136.4, 134.3, 134.1, 132.3, 129.9, 129.0, 128.7, 128.6, 128.4, 128.0, 127.9, 127.7, 127.3, 126.9, 126.8, 125.9, 114.2, 70.1, 65.7, 55.9, 51.4, 21.0. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{37}$H$_{34}$N$_3$O$_3$S$_3$+ 664.1757; found 664.1768.

4-Acetyl-5-morpholino-2,3-diphenyl-2,3-dihydrothiophene-2-carbaldehyde (3wa)

Compound 3wa was obtained according to the general procedure from 3-(morpholine-4-carbonothioyl)-4-phenylbut-3-en-2-one (1w) (50 mg, 1.0 equiv, 0.18 mmol), 1-sulfonyl-1,2,3-triazole 2a (65 mg, 1.2 equiv, 0.22 mmol), Rh$_2$(Piv)$_4$ (2.6 mg), chloroform (2.0 mL), 80 °C, reaction time is 14 h. The purification of the crude product by column chromatography on SiO$_2$ (PE/EtOAc, gradient 100:0 to 40:60) with subsequent flash chromatography on SiO$_2$ (DCM/EtOAc, gradient 50:0 to 25:25) afforded 3wa as a pale-yellow gum (52%, 37 mg). $^1$H NMR (400 MHz, CDCl$_3$-$d_6$): δ 9.42 (s, 1H), 7.14 – 7.10 (m, 3H), 7.06 - 6.97 (m, 7H), 5.10 (s, 1H), 3.96 – 3.90 (m, 2H), 3.85 – 3.79 (m, 2H), 3.70 – 3.65 (m, 2H), 3.45 – 3.40 (m, 2H), 2.06 (m, 3H). $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$-$d_6$): δ 189.1, 188.6, 162.4, 137.9, 130.4, 129.1, 128.7, 128.7, 128.3, 128.1, 127.2, 112.4, 73.9, 66.9, 57.0, 53.5, 30.4. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{23}$H$_{24}$NO$_3$S+ 394.1471; found 394.1475.

(4RS,5RS)-2-Morpholino-6-oxo-4-phenyl-1-thiaspiro[4.5]dec-2-ene-3-carbonitrile (3ad)
Compound 3ad was obtained according to the general procedure from 2-(morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (50 mg, 1.0 equiv, 0.19 mmol), 1-sulfonyl-1,2,3-triazole 2d (79 mg, 1.4 equiv, 0.27 mmol), Rh₂(Piv)₄ (3.3 mg), chloroform (1.5 mL), 80 °C, reaction time is 14 h. The purification of the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 25:0 to 22.5:2.5) with subsequent flash chromatography on neutral Al₂O₃ (PE/EtOAc, gradient 100:0 to 85:15) afforded 3ad as a colorless powder (69%, 48 mg), mp 164–166 °C. ¹H NMR (600 MHz, CD₃CN-d₃): δ 7.38 (t, J = 7.3 Hz, 2H), 7.34 – 7.31 (m, 3H), 4.70 (s, 1H), 3.69 (t, J = 4.9 Hz, 4H), 3.59 – 3.52 (m, 4H), 3.20 (td, J = 14.2, 6.3 Hz, 1H), 2.36 – 2.32 (m, 1H), 2.00 – 1.95 (m, 1H), 1.74 – 1.69 (m, 1H), 1.61 – 1.53 (m, 2H), 1.45 – 1.35 (m, 2H). ¹³C{¹H} NMR (150 MHz, CD₃CN-d₃): δ 205.5, 162.5, 138.6, 130.2, 129.5, 128.9, 119.8, 76.7, 67.8, 66.9, 56.8, 51.5, 37.7, 37.3, 27.2, 25.1. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₂₀H₂₃N₂O₂S⁺ 355.1475; found 355.1473.

(2RS,3SR)-(E)-N-(1-(2-Acetyl-4-cyano-5-morpholino-3-phenyl-2,3-dihydrothiophen-2-yl)ethylidene)-4-methylbenzenesulfonamide (3ae)

[Diagram]

Compound 3ae was obtained according to the general procedure from 2-(morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (40 mg, 1.0 equiv, 0.15 mmol), 1-sulfonyl-1,2,3-triazole 2e (65 mg, 1.5 equiv, 0.23 mmol), Rh₂(Piv)₄ (2.8 mg, 2 mol %), chloroform (1 mL), 80 °C, reaction time is 14 h. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 80:20 to 50:50) afforded 3ae as a pale-yellow gum. It was triturated with n-hexane until a powder was obtained and centrifugated with cold diethyl ether afforded 3ae as a colorless powder (78%, 62 mg), mp 184–185 °C. ¹H NMR (400 MHz, CDCl₃-d): δ 7.70 (d, J = 8.1 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.30 – 7.21 (m, 5H), 4.92 (s, 1H), 3.73 – 3.67 (m, 4H), 3.58 – 3.48 (m, 2H), 2.47 (s, 3H), 2.30 (s, 3H), 2.00 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃-d): δ 195.7, 180.4, 159.1, 144.6, 136.7, 136.7, 129.8, 129.1, 128.8, 128.5, 127.4, 118.0, 81.7, 66.2, 55.5, 50.6, 25.0, 21.9, 21.8. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₂₆H₂₈N₃O₄S₂⁺ 510.1516; found 510.1520.
\(N-((4\text{-Cyano-3,3-dimethyl-5-morpholino-2-phenyl-2,3-dihydrothiophen-2-yl})\text{methylene})-4\text{-methylbenzenesulfonamide (3ha)}\)

![Chemical Structure of 3ha](image)

Compound 3ha was obtained according to the general procedure from 3-methyl-2-(morpholine-4-carbonothioyl)but-2-enenitrile (1h) (40 mg, 1.0 equiv, 0.19 mmol), 1-sulfonyl-1,2,3-triazole 2a (56 mg, 1.1 equiv, 0.21 mmol), Rh2(Piv)4 (2.3 mg), chloroform (1 mL), 80 °C, reaction time is 13 h. The purification of the crude product by column chromatography on SiO2 (PE/EtOAc, gradient 50:0 to 30:20) afforded 3ha as a pale-yellow powder (68%, 63 mg), mp 173–175 °C. 1H NMR (400 MHz, CDCl3-\(d_2\)): \(\delta\) 8.65 (s, 1H), 7.81 (d, \(J = 8.1\) Hz, 2H), 7.39 – 7.34 (m, 7H), 3.71 – 3.62 (m, 4H), 3.53 – 3.48 (m, 2H), 3.45 – 3.49 (m, 2H), 2.44 (s, 3H), 1.38 (s, 3H), 0.88 (s, 3H). 13C{1H} NMR (100 MHz, CDCl3-\(d_2\)): \(\delta\) 169.9, 157.8, 145.0, 135.0, 131.4, 130.0, 129.2, 128.9, 128.6, 128.1, 118.4, 82.2, 72.2, 66.2, 52.2, 50.8, 25.7, 21.8, 21.4. HRMS (ESI) m/z: [M + H]\(^+\) calcd. for C25H28N3O3S2\(^+\) 482.1566; found 482.1569.

\(N-((4\text{-Cyano-3-morpholino-1-phenyl-2-thiaspiro[4.4]non-3-en-1-yl})\text{methylene})-4\text{-methylbenzenesulfonamide (3ia)}\)

![Chemical Structure of 3ia](image)

Compound 3ia was obtained according to the general procedure from 2-cyclopentylidene-3-morpholino-3-thioxopropanenitrile (1i) (40 mg, 1.0 equiv, 0.17 mmol), 1-sulfonyl-1,2,3-triazole 2a (56 mg, 1.1 equiv, 0.19 mmol), Rh2(Piv)4 (2.3 mg), chloroform (1 mL), 80 °C, reaction time is 10 h. The purification of the crude product by column chromatography on SiO2 (DCM/EtOAc, gradient 25:0 to 24.5:0.5) afforded 3ia as a pale-yellow powder (78%, 67 mg), mp 183–184 °C. 1H NMR (400 MHz, CDCl3-\(d_2\)): \(\delta\) 8.42 (s, 1H), 7.89 (d, \(J = 8.1\) Hz, 2H), 7.38 – 7.34 (m, 7H), 3.59 – 3.49 (m, 4H), 3.39 – 3.34 (m, 2H), 3.25 – 3.20 (m, 2H), 2.57 – 2.50 (m, 1H), 2.45 (s, 3H), 1.80

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S31
N-((4-Cyano-3-morpholino-1-phenyl-2-thiaspiro[4.5]dec-3-en-1-yl)methylene)-4-methylbenzenesulfonamide (3ja)

$\delta$ 167.2, 157.0, 145.0, 135.3, 131.5, 130.0, 129.6, 129.1, 129.0, 128.2, 118.6, 85.4, 73.2, 66.2, 62.4, 50.8, 38.6, 31.7, 25.5, 23.9, 21.8. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{27}$H$_{30}$N$_3$O$_3$S$_2$$^+$ 508.1723; found 508.1719.

Compound 3ja was obtained according to the general procedure from 2-cyclohexylidene-3-morpholino-3-thioxopropanenitrile (1j) (40 mg, 1.0 equiv, 0.16 mmol), 1-sulfonyl-1,2,3-triazole 2a (53 mg, 1.1 equiv, 0.17 mmol), Rh$_2$(Piv)$_4$ (2.2 mg), chloroform (1 mL), 80 °C, reaction time is 12 h. The purification of the crude product by column chromatography on SiO$_2$ (DCM/EtOAc, gradient 24.5:0.5 to 24:1) afforded 3ja as a yellow gum (81%, 67 mg), which solidified within 48 h when stored at room temperature, mp 187–189 °C. $^1$H NMR (400 MHz, CDCl$_3$-$d$): $\delta$ 8.57 (s, 1H), 7.90 (d, $J$ = 8.2 Hz, 2H), 7.42 – 7.35 (m, 7H), 3.68 – 3.63 (m, 2H), 3.61 – 3.56 (m, 2H), 3.54 – 3.48 (m, 2H), 3.33 – 3.28 (m, 2H), 2.53 – 2.45 (m, 4H), 2.24 – 2.12 (m, 1H), 2.01 (d, $J$ = 12.5 Hz, 1H), 1.65 – 1.50 (m, 4H), 1.41 (td, $J$ = 13.1, 4.7 Hz, 1H), 0.92 – 0.82 (m, 1H), 0.77 – 0.70 (m, 1H). $^{13}$C{1H} NMR (100 MHz, CDCl$_3$-$d$): $\delta$ 168.8, 161.1, 145.0, 135.0, 131.4, 130.0, 129.7, 129.4, 128.6, 128.2, 120.1, 80.9, 74.4, 66.4, 54.2, 51.1, 35.0, 28.8, 25.3, 22.2, 22.2, 21.8. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{28}$H$_{32}$N$_3$O$_3$S$_2$$^+$ 522.1879; found 522.1874.

N-((4-Cyano-3-morpholino-1-phenyl-8-oxa-2-thiaspiro[4.5]dec-3-en-1-yl)methylene)-4-methylbenzenesulfonamide (3ka)
Compound 3ka was obtained according to the general procedure from 3-morpholino-2-(tetrahydro-4H-pyran-4-ylidene)-3-thioxopropanenitrile (1k) (40 mg, 1.0 equiv, 0.16 mmol), 1-sulfonyl-1,2,3-triazole 2a (52 mg, 1.1 equiv, 0.17 mmol), Rh₂(Piv)₄ (2.1 mg), chloroform (1 mL), 80 °C, reaction time is 9 h. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 30:20 to 15:35) afforded 3ka as a pale-yellow powder (93%, 77 mg), mp 184–185 °C. ¹H NMR (400 MHz, CDCl₃-d): δ 8.43 (s, 1H), 7.94 (d, J = 8.1 Hz, 2H), 7.44 – 7.40 (m, 5H), 7.34 – 7.33 (m, 2H), 4.19 (t, J = 11.6, 1H), 3.80 (dd, J = 12.3, 5.6 Hz, 1H), 3.75 – 3.65 (m, 2H), 3.62 – 3.56 (m, 2H), 3.53 – 3.45 (m, 4H), 3.29 – 3.23 (m, 2H), 2.66 (d, J = 13.2, 1H), 2.48 (s, 3H), 1.86 – 1.73 (m, 2H), 1.36 – 1.29 (m, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃-d): δ 166.3, 160.6, 145.1, 135.0, 130.6, 130.0, 129.9, 129.6, 129.1, 128.3, 119.7, 79.9, 74.4, 66.3, 64.2, 64.1, 51.2, 35.2, 29.8, 28.7, 21.8. HRMS (ESI) m/z: [M + H]+ calcd. for C₂₇H₃₀N₃O₄S₂+ 524.1672; found 524.1669.

N-((4-Cyano-3-morpholino-1-phenyl-2-thiaspiro[4.6]undec-3-en-1-yl)methylene)-4-methylbenzenesulfonamide (3la)

Compound 3la was obtained according to the general procedure from 2-cycloheptylidene-3-morpholino-3-thioxopropanenitrile (1l) (40 mg, 1.0 equiv, 0.15 mmol), 1-sulfonyl-1,2,3-triazole 2a (50 mg, 1.1 equiv, 0.17 mmol), Rh₂(Piv)₄ (2.0 mg), chloroform (1 mL), 80 °C, reaction time is 12 h. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 50:0 to 30:20) afforded 3la as a pale-yellow powder (78%, 63 mg), mp 160–162 °C. ¹H NMR (400 MHz, CDCl₃-d): δ 8.62 (s, 1H), 7.83 (d, J = 8.1 Hz, 2H), 7.44 – 7.34 (m, 7H), 3.69 – 3.59 (m, 4H), 3.53 – 3.48 (m, 2H), 3.38 – 3.33 (m, 2H), 2.51 – 2.42 (m, 4H), 1.90 – 1.82 (m, 2H), 1.76 – 1.68 (m, 2H), 1.61 – 1.47 (m, 2H), 1.25 – 1.08 (m, 4H), 0.37 – 0.29 (m, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃-d): δ 170.1, 159.0, 144.9, 135.0, 131.5, 130.0, 129.5, 129.4, 128.6, 128.2, 119.3, 84.1, 74.0, 66.4, 58.4, 50.9, 35.6, 34.1, 31.1, 30.9, 24.9, 22.9, 21.8. HRMS (ESI) m/z: [M + H]+ calcd. for C₂₉H₃₆N₃O₄S₂⁺ 536.2036; found 536.2030.
**N-((4-Cyano-1-phenyl-3-(piperidin-1-yl)-2-thiaspiro[4.5]dec-3-en-1-yl)methylene)-4-methylbenzenesulfonamide (3ma)**

![Chemical Structure](image)

Compound **3ma** was obtained according to the general procedure from 2-cyclohexylidene-3-(piperidin-1-yl)-3-thioxopropanenitrile (**1m**) (40 mg, 1.0 equiv, 0.16 mmol), 1-sulfonyl-1,2,3-triazole **2a** (53 mg, 1.1 equiv, 0.18 mmol), Rh$_2$(Piv)$_4$ (2.2 mg), chloroform (1 mL), 80 °C, reaction time is 12 h. The purification of the crude product by column chromatography on SiO$_2$ (PE/EtOAc, gradient 50:0 to 35:15) with subsequent centrifugation with cold diethyl ether afforded **3ma** as a pale-yellow powder (65%, 55 mg), mp 174–176 °C. $^1$H NMR (400 MHz, CDCl$_3$-d): $\delta$ 8.58 (s, 1H), 7.86 (d, $J = 8.1$ Hz, 2H), 7.35 – 7.34 (m, 7H), 3.51 – 3.46 (m, 2H), 3.36 – 3.31 (m, 2H), 2.44 (s, 3H), 2.23 – 2.13 (m, 1H), 1.95 (d, $J = 13.2$, 1H), 1.61 – 1.37 (m, 12H), 0.87 – 0.81 (m, 1H), 0.72 – 0.65 (m, 1H). $^{13}$C{1H} NMR (100 MHz, CDCl$_3$-d): $\delta$ 169.9, 161.2, 144.7, 135.0, 131.7, 129.9, 129.8, 129.1, 128.5, 128.2, 120.8, 77.8, 73.8, 54.1, 52.7, 35.2, 29.1, 26.1, 25.5, 24.2, 22.2, 21.8. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{29}$H$_{34}$N$_3$O$_2$S$_2^+$ 520.2087; found 520.2085.

**N-((4-Cyano-1-phenyl-3-(pyrrolidin-1-yl)-2-thiaspiro[4.5]dec-3-en-1-yl)methylene)-4-methylbenzenesulfonamide (3na)**

![Chemical Structure](image)

Compound **3na** was obtained according to the general procedure from 2-cyclohexylidene-3-(pyrrolidin-1-yl)-3-thioxopropanenitrile (**1n**) (40 mg, 1.0 equiv, 0.17 mmol), 1-sulfonyl-1,2,3-triazole **2a** (56 mg, 1.1 equiv, 0.19 mmol), Rh$_2$(Piv)$_4$ (2.3 mg), chloroform (1 mL), 80 °C, reaction time is 12 h. The purification of the crude product by column chromatography on SiO$_2$ (PE/EtOAc, gradient 50:0 to 20:30) with subsequent centrifugation with cold diethyl ether afforded **3na** as a yellow powder (70%, 60 mg), mp 182–183 °C. $^1$H NMR (400 MHz, CDCl$_3$-d): $\delta$ 8.73 (s, 1H), 7.82 (d, $J = 7.9$ Hz, 2H), 7.37 – 7.32 (m, 7H), 3.54 – 3.47 (m, 4H), 2.43 (s, 3H), 2.27 – 2.15 (m, 2H),
1.93 – 1.90 (m, 4H), 1.66 – 1.53 (m, 4H), 1.45 – 1.40 (m, 2H), 0.87 – 0.78 (m, 1H), 0.67 – 0.60 (m, 1H). 13C{1H} NMR (100 MHz, CDCl3-d): δ 171.4, 157.7, 144.6, 135.2, 131.8, 129.9, 129.0, 128.3, 128.1, 121.9, 75.6, 74.4, 54.3, 51.9, 35.4, 29.8, 25.7, 25.5, 22.1, 22.0, 21.8. HRMS (ESI) m/z: [M + H]^+ calcd. for C28H32N3O2S2^+ 506.1930; found 506.1929.

**N-(15-Cyano-14-morpholino-13-thiadispiro[5.0.5.7.3.6]pentadeca-8,14-dien-8-yl)-4-methoxybenzenesulfonamide (3jd)**

Compound 3jd was obtained according to the general procedure from 2-cyclohexylidene-3-morpholino-3-thioxopropanenitrile (1j) (40 mg, 1.0 equiv, 0.16 mmol), 1-sulfonyl-1,2,3-triazole 2d (56 mg, 1.2 equiv, 0.19 mmol), Rh2(Piv)4 (2.3 mg), chloroform (1 mL), 80 °C, reaction time is 17 h. The purification of the crude product by column chromatography on SiO2 (DCM/EtOAc, gradient 24:1 to 23:2) with subsequent centrifugation with cold diethyl ether afforded 3jd as a colorless powder (63%, 44 mg), mp 154–155 °C. 1H NMR (400 MHz, CDCl3-d): δ 7.85 (d, J = 8.9 Hz, 2H), 6.98 (d, J = 8.9 Hz, 2H), 6.71 (s, 1H), 5.59 (dd, J = 5.8, 2.4 Hz, 1H), 3.89 (s, 3H), 3.81 – 3.71 (m, 5H), 3.63 – 3.58 (m, 2H), 2.30 – 2.19 (m, 1H), 2.15 – 2.07 (m, 2H), 2.03 – 1.45 (m, 11H), 1.36 – 1.26 (m, 2H), 1.18 – 1.06 (m, 1H). 13C{1H} NMR (100 MHz, CDCl3-d): δ 167.5, 163.1, 135.2, 132.5, 129.6, 120.9, 115.1, 114.1, 76.9, 66.6, 64.7, 55.8, 54.0, 51.4, 34.4, 32.0, 29.3, 25.7, 24.5, 22.1, 22.1, 21.2. HRMS (ESI) m/z: [M + H]^+ calcd. for C26H34N3O4S2^+ 516.1985; found 516.1994.
The reaction of 3-amino-2-cyanothioacrylamide 1t with 1-sulfonyl-1,2,3-triazole 2a afforded N-sulfonylamidine 3ta

\[
\begin{align*}
1t & \quad 2a \quad \text{Rh}_2(Piv)_4 \quad \text{2 mol % Rh}_2(Piv)_4 \\
& \quad \text{1 mL CHCl}_3 \quad 80 \, ^\circ\text{C}, 15 \, \text{h} \quad \text{Ts} \quad \text{N} = \text{C} = \text{N} \quad \text{Ar} \quad \text{Ar}' \\
\end{align*}
\]

**Compound 3ta was obtained according to the general procedure from 3-((4-chlorophenyl)amino)-2-(pyrrolidine-1-carbonothioyl)acrylonitrile (1t) (40 mg, 1.0 equiv, 0.14 mmol), 1-sulfonyl-1,2,3-triazole 2a (57 mg, 1.4 equiv, 0.19 mmol), Rh2(Piv)4 (2.3 mg), chloroform (1 mL), 80 °C, reaction time is 15 h. The purification of the crude product by column chromatography on SiO2 (PE/EtOAc, gradient 50:0 to 30:20) with subsequent centrifugation with cold diethyl ether and then with EtOAc afforded 3ta as a pale-red powder (50%, 21 mg).**

\[
\begin{align*}
\delta & \quad \text{11.29}^\circ \text{ and} \quad \text{10.87 (both d, } J^\circ = 12.3 \, \text{Hz, } J = 5.3 \, \text{Hz, 1H), 8.74}^\circ \text{ and} \quad \text{8.28 (both d, } J^\circ = 12.0 \, \text{Hz, } J = 5.0 \, \text{Hz, 1H), 7.76 – 7.66 (m, 3H), 7.46 – 7.42 (m, 2H), 7.38 – 7.32 (m, 3H), 2.36 (s, 3H).}
\end{align*}
\]
The failure of experiments for the synthesis of dihydrothiophenes

\[
\text{S1c} + \text{2a} \xrightarrow{[\text{Rh}]} \text{No reaction}
\]
\[
[\text{Rh}] = \text{Rh}_2(\text{Piv})_4, 2 \text{ mol }\%
\]
\[
\text{Conditions: 1,2-DCE (1 mL), 100 °C, 24 h}
\]

\[
\text{1r} + \text{2a} \xrightarrow{[\text{Rh}]} \text{Decomposition}
\]
\[
[\text{Rh}] = \text{Rh}_2(\text{Piv})_4, 2 \text{ mol }\%
\]
\[
\text{Conditions: 1,2-DCE (1 mL), 80 °C, 24 h}
\]

\[
\text{1s} + \text{2a} \xrightarrow{[\text{Rh}]} \text{No reaction}
\]
\[
[\text{Rh}] = \text{Rh}_2(\text{Piv})_4, 2 \text{ mol }\%
\]
\[
\text{Conditions: 1,2-DCE (1 mL), 100 °C, 24 h}
\]
Figure S3. The failure of experiments for the synthesis of dihydrothiophenes
Optimization study for the reaction of thioamide 1a with diazo compound 2h

Table S2. Optimization of the synthesis of dihydrothiophenes 4ah/4’ah

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent (T, °C)</th>
<th>Catalyst (mol %)</th>
<th>Time, h</th>
<th>Equiv of 2h</th>
<th>Yielda 4ah/4’ah, %</th>
<th>drb</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CHCl₃ (rt)</td>
<td>Rh₂(Piv)₄ (2.0)</td>
<td>24</td>
<td>1.1</td>
<td>51/34</td>
<td>56:44</td>
</tr>
<tr>
<td>2</td>
<td>CHCl₃ (rt)</td>
<td>Rh₂(esp)₂ (0.5)</td>
<td>24</td>
<td>1.1</td>
<td>46/28</td>
<td>56:44</td>
</tr>
<tr>
<td>3</td>
<td>CHCl₃ (rt)</td>
<td>Rh₂(OAc)₄ (0.5)</td>
<td>24</td>
<td>1.1</td>
<td>NR</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>CHCl₃ (75)</td>
<td>Rh₂(OAc)₄ (0.5)</td>
<td>3.5</td>
<td>1.1</td>
<td>52/34</td>
<td>51:49</td>
</tr>
<tr>
<td>5</td>
<td>CHCl₃ (75)</td>
<td>Rh₂(Oct)₄ (0.5)</td>
<td>3.5</td>
<td>1.1</td>
<td>57/28</td>
<td>54:46</td>
</tr>
<tr>
<td>6</td>
<td>CHCl₃ (rt)</td>
<td>Rh₂(Piv)₄ (0.5)</td>
<td>2</td>
<td>1.1</td>
<td>45/24</td>
<td>54:46</td>
</tr>
<tr>
<td>7</td>
<td>CHCl₃ (rt)</td>
<td>Rh₂(Piv)₄ (0.5)</td>
<td>24</td>
<td>1.1</td>
<td>49/33</td>
<td>56:44</td>
</tr>
<tr>
<td>8</td>
<td>CHCl₃ (rt)</td>
<td>Rh₂(Piv)₄ (0.5)</td>
<td>19</td>
<td>2.0</td>
<td>55/40</td>
<td>55:45</td>
</tr>
<tr>
<td>9</td>
<td>MeCN (rt)</td>
<td>Rh₂(Piv)₄ (0.5)</td>
<td>19</td>
<td>2.0</td>
<td>Trace</td>
<td>–</td>
</tr>
<tr>
<td>10</td>
<td>MeCN (75)</td>
<td>Rh₂(Piv)₄ (0.5)</td>
<td>3.5</td>
<td>2.0</td>
<td>48/22</td>
<td>53:47</td>
</tr>
<tr>
<td>11</td>
<td>C₆H₆ (rt)</td>
<td>Rh₂(Piv)₄ (0.5)</td>
<td>19</td>
<td>2.0</td>
<td>61/36</td>
<td>57:43</td>
</tr>
<tr>
<td>12</td>
<td>CCl₄ (rt)</td>
<td>Rh₂(Piv)₄ (0.5)</td>
<td>19</td>
<td>2.0</td>
<td>55/35</td>
<td>50:50</td>
</tr>
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<td>13</td>
<td>1,2-DCE (100)</td>
<td>[CuOTf]₂·C₆H₆ (10.0)</td>
<td>24</td>
<td>2.0</td>
<td>24/52</td>
<td>28:72</td>
</tr>
<tr>
<td>14</td>
<td>1,2-DCE (100)</td>
<td>[Cu(MeCN)₄]CF₃SO₃ (10.0)</td>
<td>24</td>
<td>2.0</td>
<td>32/65</td>
<td>33:67</td>
</tr>
<tr>
<td>15</td>
<td>1,2-DCE (90)</td>
<td>[Cu(MeCN)₄]CF₃SO₃ (10.0)</td>
<td>24</td>
<td>2.0</td>
<td>31/57</td>
<td>29:71</td>
</tr>
<tr>
<td>16</td>
<td>1,2-DCE (100)</td>
<td>[Cu(MeCN)₄]PF₆ (10.0)</td>
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<td>2.0</td>
<td>19/49</td>
<td>32:68</td>
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<tr>
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<td>1,2-DCE (100)</td>
<td>AgOTf (10.0)</td>
<td>24</td>
<td>2.0</td>
<td>20/34</td>
<td>33:67</td>
</tr>
<tr>
<td>18</td>
<td>1,2-DCE (100)</td>
<td>[Ru(ρ-cymene)Cl₂]₂ (5.0)</td>
<td>24</td>
<td>2.0</td>
<td>18/47</td>
<td>31:69</td>
</tr>
<tr>
<td>19</td>
<td>1,2-DCE (100)</td>
<td>RuCl(PPh₃)₃:Cp</td>
<td>24</td>
<td>2.0</td>
<td>24/56</td>
<td>27:73</td>
</tr>
<tr>
<td>20</td>
<td>n-Hexane (rt)</td>
<td>Rh₂(Piv)₄ (0.5)</td>
<td>24</td>
<td>2.0</td>
<td>NR</td>
<td>–</td>
</tr>
<tr>
<td>21</td>
<td>1,4-Dioxane (rt)</td>
<td>Rh₂(Piv)₄ (0.5)</td>
<td>24</td>
<td>2.0</td>
<td>NR</td>
<td>–</td>
</tr>
<tr>
<td>22</td>
<td>CHCl₃ (rt)</td>
<td>Pd₂(OAc)₄ (2.0)</td>
<td>24</td>
<td>1.1</td>
<td>NR</td>
<td>–</td>
</tr>
<tr>
<td>23</td>
<td>CHCl₃ (75)</td>
<td>Pd₂(OAc)₄ (2.0)</td>
<td>3.5</td>
<td>1.1</td>
<td>NR</td>
<td>–</td>
</tr>
</tbody>
</table>

Conditions: thioamide 1a (0.15 mmol), diazo compound 2h (0.17 mmol, 1.1 equiv or 0.31 mmol, 2.0 equiv), solvent (1.5 mL). aIsolated yields. b(2RS,3SR):2RS,3RS). Determined by ¹H NMR analysis of the crude mixture.
General procedure for the synthesis of dihydrothiophenes 4a,i-l and 4’a,i-l

**Method A.** A 10 mL standard microwave vial was charged with Rh$_2$(Piv)$_4$ (0.5–1.0 mol %), 2-(morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (1.0 equiv) and dry benzene (0.5 mL). A solution of diazo compounds 2h-o (1.1–2.0 equiv) in dry benzene (0.5–3 mL) was added slowly to the vial at room temperature. The reaction solution was stirred for 19–27 h at room temperature, and then the solution was concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel.

**Method B.** A 10 mL standard microwave vial was charged with [Cu(MeCN)$_4$]CF$_3$SO$_3$ (10 mol %), (morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (1.0 equiv), diazo compounds 2h-l (1.2–2.0 equiv) and dry 1,2-DCE (1.0–1.5 mL). The reaction solution was stirred for 24 h at 70–100 °C, and then the solution was concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel.

(2RS,3SR)-2-Acetyl-4-cyano-N-(cyclohexa-2,4-dien-1-yl)-5-morpholino-3-phenyl-2,3-dihydrothiophene-2-carboxamide (4ah)

![Structure of 4ah]

**Method A.** (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (40 mg, 1.0 equiv, 0.15 mmol), 2-diazo-3-oxo-N-phenylbutanamide (2h) (63 mg, 2.0 equiv, 0.31 mmol), Rh$_2$(Piv)$_4$ (0.9 mg, 0.5 mol %), benzene (1 mL), reaction time is 19 h. The purification of the crude product by column chromatography on SiO$_2$ (DCM/EtOAc, gradient 25:0 to 21:4) afforded 4ah as a colorless powder (61%, 41 mg), mp 105–106 °C. **Method B.** 1a (50 mg, 1.0 equiv, 0.19 mmol), 2h (78 mg, 2.0 equiv, 0.39 mmol), [Cu(MeCN)$_4$]CF$_3$SO$_3$ (14 mg), 1,2-DCE (1 mL), 100 °C, reaction time is 24 h. The product 4ah was isolated as a colorless powder (32%, 27 mg), mp 105–106 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.13 (s, 1H), 7.64 (d, $J = 7.8$ Hz, 2H), 7.41 – 7.44 (m, 7H), 7.13 (t, $J = 7.4$ Hz, 1H), 5.33 (s, 1H), 3.71 – 3.68 (m, 4H), 3.59 – 3.56 (m, 4H), 1.78 (s, 3H). $^{13}$C{1H} NMR (100 MHz, DMSO-$d_6$): $\delta$ 199.0, 166.1, 161.4, 138.5, 136.5, 129.0, 128.7, 128.7, 128.4, 124.3, 120.4, 118.5, 78.2, 72.7, 65.5, 56.4, 50.2, 27.7. HRMS (ESI) m/z: [M + Na]$^+$ calcd. for C$_{24}$H$_{25}$N$_3$O$_3$SNa$^+$ 456.1351; found 456.1352.
(2RS,3RS)-2-Acetyl-4-cyano-N-(cyclohexa-2,4-dien-1-yl)-5-morpholino-3-phenyl-2,3-dihydrothiophene-2-carboxamide (4′ah)

Method A. (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (40 mg, 1.0 equiv, 0.15 mmol), 2-diazo-3-oxo-N-phenylbutanamide (2h) (63 mg, 2.0 equiv, 0.31 mmol), Rh$_2$(Piv)$_4$ (0.9 mg, 0.5 mol %), benzene (1 mL), reaction time is 19 h. The purification of the crude product by column chromatography on SiO$_2$ (DCM/EtOAc, gradient 25:0 to 21:4) afforded 4′ah as an amorphous solid (36%, 25 mg).

Method B. 1a (50 mg, 1.0 equiv, 0.19 mmol), 2h (78 mg, 2.0 equiv, 0.39 mmol), [Cu(MeCN)$_4$]CF$_3$SO$_3$ (14 mg), 1,2-DCE (1 mL), 100 °C, reaction time is 24 h. The product 4′ah was isolated as an amorphous solid (65%, 55 mg). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 9.82 (s, 1H), 7.50 (d, $J$ = 7.3 Hz, 2H), 7.26 (t, $J$ = 7.4 Hz, 2H), 7.22 – 7.18 (m, 3H), 7.12 – 7.09 (m, 2H), 7.03 (t, $J$ = 7.3 Hz, 1H), 4.94 (s, 1H), 3.69 – 3.67 (m, 4H), 3.56 – 3.53 (m, 4H), 2.39 (s, 3H). $^{13}$C{1H} NMR (100 MHz, DMSO-$d_6$): $\delta$ 195.4, 162.3, 159.9, 137.5, 137.2, 128.5, 128.4, 128.2, 127.9, 124.7, 121.2, 118.5, 78.6, 74.8, 65.5, 53.4, 50.3, 24.3. HRMS (ESI) m/z: [M + Na]$^+$ calcd. for C$_{24}$H$_{23}$N$_3$O$_3$SNa$^+$ 456.1352; found 456.1356.

(2RS,3SR)-4-Cyano-5-morpholino-N,3-diphenyl-2-((E)-3-(p-tolyl)acryloyl)-2,3-dihydrothiophene-2-carboxamide (4ai)

Method A. (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (40 mg, 1.0 equiv, 0.15 mmol), 2-diazo-3-oxo-N-phenyl-5-(p-tolyl)pent-4-enamide (2i) (71 mg, 1.5 equiv, 0.23 mmol), Rh$_2$(Piv)$_4$ (1.4 mg, 1 mol %), benzene (3 mL), reaction time is 24 h. The purification of the crude product by column chromatography on SiO$_2$ (DCM/EtOAc, gradient 25:0 to 24.5:0.5) afforded 4ai as a pale-yellow powder (54%, 45 mg), mp 204–206 °C. Method B. 1a (50 mg, 1.0 equiv,
0.19 mmol), 2i (89 mg, 1.5 equiv, 0.29 mmol), [Cu(MeCN)₄]CF₃SO₃ (14.5 mg), 1,2-DCE (1.5 mL), 90 °C, reaction time is 24 h. The product 4(ai) was isolated as a pale-yellow powder (27%, 28 mg), mp 204–206 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 10.13 (s, 1H), 7.63 (d, J = 7.8 Hz, 2H), 7.45 (br. s, 4H), 7.32 (t, J = 7.3 Hz, 2H), 7.24 – 7.07 (m, 7H), 6.84 (d, J = 15.8 Hz, 1H), 5.45 (s, 1H), 3.71 (br. s, 4H), 3.61 (br. s, 4H), 2.31 (s, 3H). ¹³C{¹H} NMR (100 MHz, DMSO-d₆): δ 188.9, 166.3, 161.5, 143.1, 141.3, 138.6, 136.8, 131.0, 129.6, 129.0, 128.8, 128.7, 128.2 (2C), 124.2, 120.3, 120.1, 118.6, 78.2, 73.4, 65.5, 56.2, 50.3, 21.1. HRMS (ESI) m/z: [M + H]^+ calcd. for C₃₂H₃₀N₃O₃S⁺ 536.2002; found 536.2001.

(2RS,3RS)-4-Cyano-5-morpholino-N,3-diphenyl-2-((E)-3-(p-tolyl)acryloyl)-2,3-dihydrothiophene-2-carboxamide (4’ai)

**Method A.** (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (40 mg, 1.0 equiv, 0.15 mmol), 2-diazo-3-oxo-N-phenyl-5-(p-tolyl)pent-4-enamide (2i) (71 mg, 1.5 equiv, 0.23 mmol), Rh₂(Piv)₄ (1.4 mg, 1 mol %), benzene (3 mL), reaction time is 24 h. The purification of the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 25:0 to 24.5:0.5) afforded 4’ai as a bright-yellow powder (30%, 25 mg), mp 217–219 °C. **Method B.** 1a (50 mg, 1.0 equiv, 0.19 mmol), 2i (89 mg, 1.5 equiv, 0.29 mmol), [Cu(MeCN)₄]CF₃SO₃ (14.5 mg), 1,2-DCE (1.5 mL), 90 °C, reaction time is 24 h. The product 4’ai was isolated as a bright-yellow powder (49%, 51 mg), mp 217–219 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 9.90 (s, 1H), 7.86 (d, J = 15.6 Hz, 1H), 7.61 – 7.55 (m, 4H), 7.30 – 7.11 (m, 9H), 7.02 – 6.98 (m, 2H), 5.14 (s, 1H), 3.70 – 3.61 (m, 4H), 3.58 – 3.48 (m, 4H), 2.32 (s, 3H). ¹³C{¹H} NMR (100 MHz, DMSO-d₆): δ 185.9, 162.3, 159.8, 144.8, 141.4, 137.4, 137.3, 131.0, 129.7, 128.7, 128.4, 128.2, 127.9, 124.6, 121.1, 119.4, 118.6, 78.0, 75.2, 65.5, 53.3, 50.2, 21.1. HRMS (ESI) m/z: [M + H]^+ calcd. for C₃₂H₃₀N₃O₃S⁺ 536.2002; found 536.1997.
(2RS,3SR)-4-Cyano-2-((E)-3-(4-methoxyphenyl)acryloyl)-5-morpholino-N,3-diphenyl-2,3-dihydrothiophene-2-carboxamide (4aj)

**Method A.** (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (40 mg, 1.0 equiv, 0.15 mmol), 2-diazo-5-(4-methoxyphenyl)-3-oxo-\(-N\)-phenylpent-4-enamide (2j) (75 mg, 1.5 equiv, 0.23 mmol), Rh\(_2\)(Piv)\(_4\) (0.7 mg, 0.5 mol %), benzene (3 mL), reaction time is 24 h. The purification of the crude product by column chromatography on SiO\(_2\) (DCM/EtOAc, gradient 50:0 to 49:1) afforded 4aj as a yellow amorphous solid (59%, 50 mg) that crystallizes into powder when stored at 40 °C for 12 h, mp 214–216 °C. **Method B.** 1a (50 mg, 1.0 equiv, 0.19 mmol), 2j (93 mg, 1.5 equiv, 0.29 mmol), [Cu(MeCN)\(_4\)]CF\(_3\)SO\(_3\) (10.7 mg), 1,2-DCE (1.5 mL), 90 °C, reaction time is 24 h. The product 4aj was isolated as a yellow amorphous solid (36%, 39 mg) that crystallizes into powder when stored at 40 °C for 12 h, mp 214–216 °C. \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta\) 10.14 (s, 1H), 7.65 (d, \(J = 7.9\) Hz, 2H), 7.54 (d, \(J = 8.7\) Hz, 2H), 7.47 (d, \(J = 7.4\) Hz, 2H), 7.32 (t, \(J = 7.9\) Hz, 2H), 7.24 – 7.13 (m, 4H), 7.09 (t, \(J = 7.4\) Hz, 1H), 6.95 (d, \(J = 8.7\) Hz, 2H), 6.78 (d, \(J = 15.6\) Hz, 1H), 5.46 (s, 1H), 3.79 (s, 3H), 3.71 – 3.68 (m, 4H), 3.61 – 3.59 (m, 4H). \(^{13}\)C{\(^1\)H} NMR (100 MHz, DMSO-\(d_6\)): \(\delta\) 188.6, 166.4, 161.7, 161.5, 143.2, 138.6, 136.9, 130.7, 129.0, 128.6, 128.2, 128.1, 126.3, 124.2, 120.4, 118.6, 118.6, 114.5, 78.5, 73.6, 65.5, 56.2, 55.4, 50.3. HRMS (ESI) m/z: [M + Na]\(^+\) calcd. for C\(_{32}\)H\(_{29}\)N\(_3\)O\(_4\)SNa\(^+\) 574.1771; found 574.1771.

(2RS,3RS)-4-Cyano-2-((E)-3-(4-methoxyphenyl)acryloyl)-5-morpholino-N,3-diphenyl-2,3-dihydrothiophene-2-carboxamide (4aj)

**Method A.** (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (40 mg, 1.0 equiv, 0.15 mmol), 2-diazo-5-(4-methoxyphenyl)-3-oxo-\(-N\)-phenylpent-4-enamide (2j) (75 mg, 1.5 equiv, 0.23 mmol), Rh\(_2\)(Piv)\(_4\) (0.7 mg, 0.5 mol %), benzene (3 mL), reaction time is 24 h. The purification of
the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 50:0 to 46:4) afforded 4aj as a yellow powder (32%, 27 mg, mp 222–223 °C. Method B. 1a (50 mg, 1.0 equiv, 0.19 mmol), 2j (93 mg, 1.5 equiv, 0.29 mmol), [Cu(MeCN)₄]CF₃SO₃ (10.7 mg), 1,2-DCE (1.5 mL), 90 °C, reaction time is 24 h. The product 4aj was isolated as a yellow powder (56%, 60 mg, mp 222–223 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 9.90 (s, 1H), 7.85 (d, J = 15.5 Hz, 1H), 7.67 (d, J = 8.7 Hz, 2H), 7.57 (d, J = 7.3 Hz, 2H), 7.28 (t, J = 7.4 Hz, 2H), 7.23 – 7.12 (m, 5H), 7.02 – 6.97 (m, 3H), 6.91 (d, J = 15.5 Hz, 1H), 5.14 (s, 1H), 3.79 (s, 3H), 3.69 – 3.64 (m, 4H), 3.58 – 3.49 (m, 4H). ¹³C{¹H} NMR (100 MHz, DMSO-d₆): δ 185.8, 185.8, 162.4, 162.3, 161.7, 159.9, 144.6, 137.5, 137.3, 137.2, 130.7, 128.7, 128.4, 128.2, 127.9, 126.4, 124.6, 121.1, 121.0, 118.5, 117.8, 114.6, 78.0, 75.2, 65.5, 55.4, 53.3, 50.2. HRMS (ESI) m/z: [M + H]+ calcd. for C₃₂H₃₀N₃O₄S+ 552.1951; found 552.1949.

(2RS,3SR)-4-Cyano-2-((E)-3-(4-cyanophenyl)acryloyl)-5-morpholino-N,3-diphenyl-2,3-dihydrothiophene-2-carboxamide (4ak)

Method A. (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (40 mg, 1.0 equiv, 0.15 mmol), 5-(4-cyanophenyl)-2-diazo-3-oxo-N-phenylpent-4-enamide (2k) (73 mg, 1.5 equiv, 0.23 mmol), Rh₂(Piv)₄ (1.4 mg, 1.0 mol %), benzene (3 mL), reaction time is 24 h. The purification of the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 25:0 to 23.5:1.5) afforded 4ak as a yellow powder (59%, 50 mg, mp 166–168 °C. Method B. 1a (50 mg, 1.0 equiv, 0.19 mmol), 2k (92 mg, 1.5 equiv, 0.29 mmol), [Cu(MeCN)₄]CF₃SO₃ (10.9 mg), 1,2-DCE (1.5 mL), 90 °C, reaction time is 24 h. The product 4ak was isolated as a yellow powder (21%, 20 mg, mp 166–168 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 10.16 (s, 1H), 7.85 (d, J = 8.3 Hz, 2H), 7.77 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 7.9 Hz, 2H), 7.47 (d, J = 7.4 Hz, 2H), 7.32 (t, J = 7.9 Hz, 2H), 7.25 – 7.21 (m, 3H), 7.15 – 7.03 (m, 3H), 5.50 (s, 1H), 3.74 – 3.70 (m, 4H), 3.65 – 3.58 (m, 4H). ¹³C{¹H} NMR (150 MHz, DMSO-d₆): δ 189.4, 166.0, 161.5, 140.6, 138.6, 138.2, 136.6, 132.8, 129.3, 129.1, 128.7, 128.3 (2C), 124.2, 124.0, 120.3, 118.6, 118.5, 112.7, 77.6, 73.3, 65.5, 56.2, 50.3. HRMS (ESI) m/z: [M + H]+ calcd. for C₃₂H₂₇N₄O₃S⁺ 547.1798; found 547.1789.
**Method A.** (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (40 mg, 1.0 equiv, 0.15 mmol), 5-(4-cyanophenyl)-2-diazo-3-oxo-\(N\)-phenylpent-4-enamide (2k) (73 mg, 1.5 equiv, 0.23 mmol), \(\text{Rh}_2\text{(Piv)}_4\) (1.4 mg, 1.0 mol %), benzene (3 mL), reaction time is 24 h. The purification of the crude product by column chromatography on SiO\(_2\) (DCM/EtOAc, gradient 25:0 to 23.5:1.5) afforded \(4ak\) as a yellow powder (28%, 24 mg), mp 242–244 °C. **Method B.** 1a (50 mg, 1.0 equiv, 0.19 mmol), 2k (92 mg, 1.5 equiv, 0.29 mmol), \([\text{Cu(MeCN)}_4]\text{CF}_3\text{SO}_3\) (10.9 mg), 1,2-DCE (1.5 mL), 90 °C, reaction time is 24 h. The product \(4ak\) was isolated as a yellow powder (57%, 60 mg), mp 242–244 °C. \(^1\text{H NMR}\) (400 MHz, DMSO-\(d_6\)): \(\delta\) 9.91 (s, 1H), 7.96 – 7.92 (m, 3H), 7.87 (d, \(J = 8.3\) Hz, 2H), 7.54 (d, \(J = 7.3\) Hz, 2H), 7.29 (t, \(J = 7.4\) Hz, 2H), 7.24 – 7.10 (m, 6H), 7.01 (t, \(J = 7.2\) Hz, 1H), 5.14 (s, 1H), 3.69 – 3.65 (m, 4H), 3.59 – 3.49 (m, 4H). \(^{13}\text{C}\{^1\text{H}\}\) NMR (100 MHz, DMSO-\(d_6\)): \(\delta\) 185.5, 162.0, 159.7, 142.6, 138.2, 137.2, 137.1, 132.9, 129.3, 128.7, 128.4, 128.3, 128.0, 124.7, 123.9, 121.3, 118.5, 112.7, 77.7, 75.0, 65.5, 53.4, 50.3. HRMS (ESI) m/z: [M + H]\(^+\) calcd. for C\(_{32}\)H\(_{27}\)N\(_4\)O\(_3\)S\(^+\) 547.1798; found 547.1792.

**Method A.** (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (40 mg, 1.0 equiv, 0.15 mmol), 2-diazo-3-oxo-\(N\)-phenyl-5-(4-(trifluoromethyl)phenyl)pent-4-enamide (2l) (83 mg, 1.5 equiv, 0.23 mmol), \(\text{Rh}_2\text{(Piv)}_4\) (1.4 mg, 1.0 mol %), benzene (3 mL), reaction time is 24 h. The purification of the crude product by column chromatography on SiO\(_2\) (DCM) afforded \(4al\) as a yellow amorphous solid (59%, 54 mg), that crystallizes into powder when treated with cold diethyl...
ether, mp 209–210 °C. **Method B.** 1a (40 mg, 1.0 equiv, 0.15 mmol), 2l (83 mg, 1.5 equiv, 0.23 mmol), [Cu(MeCN)₄]CF₃SO₃ (8.7 mg), 1,2-DCE (1.5 mL), 90 °C, reaction time is 24 h. The product 4al was isolated as a yellow amorphous solid (30%, 26 mg), that crystallizes into powder when treated with cold diethyl ether, mp 209–210 °C. 

\[ ^1H \text{NMR (400 MHz, DMSO-}d_6\text{): } \delta \text{ } 10.17 \text{ (s, 1H), 7.80 (d, } J = 8.2 \text{ Hz, 2H), 7.74 (d, } J = 8.3 \text{ Hz, 2H), 7.64 (d, } J = 7.9 \text{ Hz, 2H), 7.48 (d, } J = 7.5 \text{ Hz, 2H), 7.34 – 7.22 \text{ (m, 5H), 7.16 – 7.02 (m, 3H), 5.50 (s, 1H), 3.73 – 3.71 (m, 4H), 3.66 – 3.62 (m, 4H).} \]

\[ ^19F\{^1H\} \text{NMR (376 MHz, DMSO-}d_6\text{): } \delta \text{ } -61.38. \]

\[ ^{13}C\{^1H\} \text{NMR (150 MHz, DMSO-}d_6\text{): } \delta \text{ } 189.3, 166.1, 161.5, 140.9, 138.6, 137.7, 136.7, 130.4 \text{ (q, } J = 31.9 \text{ Hz), 129.3, 129.1, 128.7, 128.4, 126.6, 125.8 \text{ (q, } J = 3.1 \text{ Hz), 123.6 \text{ (q, } J = 272 \text{ Hz), 121.2, 120.3, 118.6, 77.7, 73.3, 65.5, 56.3, 50.3.} \]

HRMS (ESI) m/z: [M + H]^+ calcd. for C₃₂H₂₇F₃N₃O₃S⁺ 590.1719; found 590.1709.

**(2RS,3RS)-4-Cyano-5-morpholino-N,3-diphenyl-2-((E)-3-(4-(trifluoromethyl)phenyl)acryloyl)-2,3-dihydrothiophene-2-carboxamide (4’al)**

**Method A.** (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (40 mg, 1.0 equiv, 0.15 mmol), 2-diazo-3-oxo-N-phenyl-5-(4-(trifluoromethyl)phenyl)pent-4-enamide (2l) (83 mg, 1.5 equiv, 0.23 mmol), Rh₂(Piv)₄ (1.4 mg, 1.0 mol %), benzene (3 mL), reaction time is 24 h. The purification of the crude product by column chromatography on SiO₂ (DCM) afforded 4’al as a yellow amorphous solid (25%, 23 mg), that crystallizes into powder when treated with cold diethyl ether, mp 218–220 °C. **Method B.** 1a (40 mg, 1.0 equiv, 0.15 mmol), 2l (83 mg, 1.5 equiv, 0.23 mmol), [Cu(MeCN)₄]CF₃SO₃ (8.7 mg), 1,2-DCE (1.5 mL), 90 °C, reaction time is 24 h. The product 4’al was isolated as a yellow amorphous solid (60%, 51 mg), that crystallizes into powder when treated with cold diethyl ether, mp 218–220 °C. 

\[ ^1H \text{NMR (400 MHz, DMSO-}d_6\text{): } \delta \text{ } 9.93 \text{ (s, 1H), 7.98 – 7.94 (m, 3H), 7.77 (d, } J = 8.3 \text{ Hz, 2H), 7.55 (d, } J = 7.3 \text{ Hz, 2H), 7.29 (t, } J = 7.4 \text{ Hz, 2H), 7.24 – 7.10 \text{ (m, 6H), 7.01 (t, } J = 7.2 \text{ Hz, 1H), 5.14 (s, 1H), 3.68 – 3.65 (m, 4H), 3.59 – 3.49 (m, 4H).} \]

\[ ^19F\{^1H\} \text{NMR (376 MHz, DMSO-}d_6\text{): } \delta \text{ -61.37.} \]

\[ ^{13}C\{^1H\} \text{NMR (150 MHz, DMSO-}d_6\text{): } \delta \text{ } 185.6, 162.0, 159.7, 142.8, 137.7, 137.2, 137.1, 130.43 \text{ (q, } J = 31.9 \text{ Hz), 129.4, 128.7, 128.4, 128.3, 128.0, 125.9 \text{ (q, } J = 4.0 \text{ Hz), 124.7, 123.9 \text{ (q, } J = 272.3 \text{ Hz), 123.2, 121.3, 118.5, 77.8, 75.1, 65.5, 53.4, 50.3.} \]

HRMS (ESI) m/z: [M + H]^+ calcd. for C₃₂H₂₇F₃N₃O₃S⁺ 590.1719; found 590.1713.

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General procedure for the synthesis of dihydrothiophenes 4a,m-o and 4’a,m-o

Method A. A 10 mL standard microwave vial was charge with Rh₂(Piv)₄ (0.5 mol %), (morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (1.0 equiv) and dry chloroform (0.5 mL). A solution of diazo compounds 2m,n (1.1 equiv) in dry chloroform (0.5 mL) was added slowly to the vial at 0 °C. The order of mixing the reagents for diazo compounds 2o (1.6 equiv) was reversed. The reaction solution was stirred for 1 h at room temperature, and then the solution was directly subjected to SiO₂.

Method B. A 10 mL standard microwave vial was charge with [Cu(MeCN)₄]CF₃SO₃ (10 mol %), (morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (1.0 equiv), 2-cyano-2-diazo-N-phenylacetamide (2m) (1.2 equiv) and dry chloroform (1 mL). The reaction solution was stirred for 24 h at 70 °C, and then the solution was directly subjected to SiO₂ afforded 4f.

(2RS,3RS)-2,4-Dicyano-5-morpholino-N,3-diphenyl-2,3-dihydrothiophene-2-carboxamide (4am)

Method A. (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (40 mg, 1.0 equiv, 0.15 mmol), 2-cyano-2-diazo-N-phenylacetamide (2m) (35 mg, 1.1 equiv, 0.18 mmol), Rh₂(Piv)₄ (0.5 mg, 0.5 mol %), chloroform (1 mL), reaction time is 1 h. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 0:50 to 30:20) afforded 4am as a yellow amorphous solid, that crystallizes into colorless powder when treated with cold diethyl ether (56%, 36 mg, dr 93:7), mp 181–183 °C. Method B. 1a (40 mg, 1.0 equiv, 0.15 mmol), 2m (35 mg, 1.2 equiv, 0.23 mmol), [Cu(MeCN)₄]CF₃SO₃ (7.1 mg). The product 4am was isolated as a yellow amorphous solid, that crystallizes into colorless powder when treated with cold diethyl ether (51%, 33 mg), mp 218–220 °C. Diastereomer 4’am was isolated in a trace amount. ¹H NMR (400 MHz, DMSO-d₆): δ 10.76 (NH, s, 1H), 10.70 (NH, s, 1H, minor isomer), 7.64 (d, J = 7.7 Hz, 2H), 7.45 – 7.37 (m, 7H), 7.30 – 7.24 (m, xH, minor isomer), 7.18 (t, J = 7.2 Hz, 1H), 5.35 (s, 1H), 5.06 (s, 1H, minor isomer), 3.73 – 3.70 (m, 4H), 3.64 – 3.61 (m, 4H). ¹³C {¹H} NMR (100 MHz, DMSO-d₆): δ 160.9, 160.8 (minor isomer), 160.5, 137.7, 137.6 (minor isomer), 135.2, 129.1, 128.9, 128.8 (minor isomer), 128.7, 128.4 (minor isomer), 125.1 (minor isomer), 125.0, 120.8, 120.6 (minor
(2RS,3RS)-2,4-Dicyano-5-morpholino-N-phenethyl-3-phenyl-2,3-dihydrothiophene-2-carboxamide (4an)

**Method A.** (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (50 mg, 1.0 equiv, 0.19 mmol), N-benzyl-2-cyano-2-diazoacetamide (2n) (43 mg, 1.1 equiv, 0.21 mmol), Rh₂(Piv)₄ (0.65 mg, 0.5 mol %), chloroform (1 mL), reaction time is 1 h. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 0:50 to 30:20) afforded 4an as a colorless solid (44%, 37 mg, dr 96:4), mp 216–217 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 9.42 (t, J = 5.3 Hz, 2H, minor isomer), 9.31 (t, J = 5.5 Hz, 2H), 7.44 – 7.40 (m, 2H), 7.38 – 7.30 (m, 3H), 7.28 – 7.23 (m, 3H), 6.94 – 6.92 (m, 2H), 5.16 (s, 1H, minor isomer), 4.86 (s, 1H), 4.10 (dd, J = 15.0, 5.9 Hz, 1H), 3.99 (dd, J = 15.1, 5.4 Hz, 1H), 3.73 – 3.71 (m, 4H), 3.67 – 3.64 (m, 4H). ¹³C{¹H} NMR (150 MHz, DMSO-d₆): δ 161.0, 159.6, 137.3, 134.6, 128.9, 128.6, 128.5, 128.3, 127.3, 127.1, 119.9, 118.2, 71.0, 65.5, 62.1, 57.8, 50.5, 43.5. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₂₄H₂₃N₄O₂S⁺ 431.1536; found 431.1537.

(2RS,3SR)-2,4-Dicyano-5-morpholino-N-phenethyl-3-phenyl-2,3-dihydrothiophene-2-carboxamide (4’an)

**Method A.** (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (50 mg, 1.0 equiv, 0.19 mmol), N-benzyl-2-cyano-2-diazoacetamide (2n) (43 mg, 1.1 equiv, 0.21 mmol), Rh₂(Piv)₄ (0.65 mg, 0.5 mol %), chloroform (1 mL), reaction time is 1 h. The purification of the crude product by
column chromatography on SiO₂ (PE/EtOAc, gradient 0:50 to 30:20) afforded 4’an that crystallizes into colorless powder when treated with cold diethyl ether (44%, 37 mg, dr 96:4), mp 138–140 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 9.43 (t, J = 5.8 Hz, 2H), 9.31 (t, J = 5.3 Hz, 2H, minor isomer), 7.44 – 7.40 (m, 3H), 7.37 – 7.34 (m, 4H), 7.30 – 7.26 (m, 3H), 5.17 (s, 1H), 4.86 (s, 1H, minor isomer), 4.39 (d, J = 5.8 Hz, 2H), 3.71 – 3.69 (m, 4H), 3.63 – 3.61 (m, 4H). ¹³C{¹H} NMR (100 MHz, DMSO-d₆): δ 162.4, 160.5, 138.2, 135.0, 129.0, 129.0, 128.6, 128.4, 127.2, 127.1, 118.0, 115.9, 70.1, 65.5, 56.8, 50.5, 43.7. HRMS (ESI) m/z: [M + H]+ calcd. for C₂₄H₂₃N₄O₂S+ 431.1536; found 431.1533.

(2RS,3RS)-2,4-Dicyano-5-morpholino-3-phenyl-2,3-dihydrothiophene-2-carboxamide (4ao)

Method A. (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (50 mg, 1.0 equiv, 0.19 mmol), 2-cyano-2-diazoacetamide (2o) (34 mg, 1.6 equiv, 0.31 mmol), Rh₂(Piv)₄ (0.94 mg, 0.5 mol %), chloroform (1 mL), reaction time is 1 h. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 20:30 to 10:40) afforded 4ao as a colorless solid (56%, 37 mg, single isomer), mp 208–209 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 8.25 (s, 1H, NH₂), 7.91 (s, 1H, NH₂), 7.48 – 7.46 (m, 2H), 7.38 – 7.34 (m, 3H), 4.81 (s, 1H), 3.73 – 3.71 (m, 4H), 3.66 – 3.65 (m, 4H). ¹³C{¹H} NMR (150 MHz, DMSO-d₆): δ 161.3, 161.0, 134.7, 128.9, 128.8, 128.4, 120.0, 118.2, 70.9, 65.5, 62.7, 57.7, 50.5. HRMS (ESI) m/z: [M + H]+ calcd. for C₁₇H₁₇N₄O₂S⁺ 341.1067; found 341.1064.

(2RS,3SR)-2,4-Dicyano-5-morpholino-3-phenyl-2,3-dihydrothiophene-2-carboxamide (4’ao)

Method A. (Morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (50 mg, 1.0 equiv, 0.19 mmol), 2-cyano-2-diazoacetamide (2o) (34 mg, 1.6 equiv, 0.31 mmol), Rh₂(Piv)₄ (0.94 mg, 0.5 mol %), chloroform (1 mL), reaction time is 1 h. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 20:30 to 10:40) afforded 4’ao as a yellow
amorphous solid (39%, 26 mg, single isomer). $^1$H NMR (600 MHz, DMSO-$d_6$): $\delta$ 8.32 (s, 1H, NH$_2$), 8.19 (s, 1H, NH$_2$), 7.45 – 7.39 (m, 5H), 5.14 (s, 1H), 3.71 – 3.70 (m, 4H), 3.62 – 3.61 (m, 4H). $^{13}$C{$^1$H} NMR (150 MHz, DMSO-$d_6$): $\delta$ 164.0, 160.6, 135.3, 129.0, 128.9, 128.6, 118.1, 116.0, 70.0, 65.5, 58.2, 50.5. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{17}$H$_{17}$N$_4$O$_2$S$^+$ 341.1067; found 341.1072.
General procedure for the synthesis of dihydrothiophenes 5

A 10 mL standard microwave vial was charge with Rh$_2$(Piv)$_4$ (0.5 mol %), thioamide 1 (1.0 equiv) and dry chloroform (0.5-1 mL). A solution of diazo compound 2n (1.5 equiv), 2h (1.5 equiv), 2p (1.5–2.0 equiv), 2q (1.5 equiv), 2s (1.5 equiv) or 2t (1.2 equiv) in dry chloroform (1-2 mL) was added slowly to the vial via syringe at room temperature. The reaction solution was stirred for 10 min–14 h at room temperature or at 40 °C (for 5kp), 60 °C (for 5jq) or 45 °C (for 5as,xs), and then the solution was directly subjected to SiO$_2$ or neutral alumina (for 5at).

$N$-Benzyl-2,4-dicyano-3,3-dimethyl-5-morpholino-2,3-dihydrothiophene-2-carboxamide (5hn)

Product 5hn was obtained according to the general procedure from 3-methyl-2-(morpholine-4-carbonothioyl)but-2-enenitrile (1h) (75 mg, 1.0 equiv, 0.36 mmol), $N$-benzyl-2-cyano-2-diazoacetamide (2n) (107 mg, 1.5 equiv, 0.53 mmol), Rh$_2$(Piv)$_4$ (1.6 mg), chloroform (3.0 mL), reaction time is 13 min. The purification of the crude product by column chromatography on SiO$_2$ (DCM/EtOAc, gradient 25:0 to 23.5:1.5) afforded 5hn as a yellow gum (98%, 134 mg). $^1$H NMR (400 MHz, CDCl$_3$-d): $\delta$ 7.38 – 7.32 (m, 3H), 7.28 – 7.26 (m, 2H), 6.61 (t, $J$ = 5.1 Hz, 1H), 4.55 – 4.42 (m, 2H), 3.74 – 3.72 (m, 4H), 3.58 – 3.56 (m, 4H), 1.63 (s, 3H), 1.25 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$-d): $\delta$ 160.7, 158.5, 136.5, 129.1, 128.4, 128.1, 117.6, 117.3, 79.2, 66.2, 63.4, 53.7, 50.9, 45.2, 25.0, 22.8. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{20}$H$_{23}$N$_4$O$_2$S$^+$ 383.1536; found 383.1539.

$N$-Benzyl-1,4-dicyano-3-morpholino-2-thiaspiro[4.4]non-3-ene-1-carboxamide (5in)
Product 5in was obtained according to the general procedure from 2-cyclopentylidene-3-morpholino-3-thioxopropanenitrile (1i) (69 mg, 1.0 equiv, 0.29 mmol), N-benzyl-2-cyano-2-diazoacetamide (2n) (88 mg, 1.5 equiv, 0.44 mmol), Rh$_2$(Piv)$_4$ (1.3 mg), chloroform (3.0 mL), reaction time is 15 min. The purification of the crude product by column chromatography on SiO$_2$ (DCM/EtOAc, gradient 25:0 to 23.5:1.5) afforded 5in as a pale-yellow gum (83%, 99 mg), that crystallizes into powder when stored at 50 °C for 8 h, mp 143–145 °C. $^1$H NMR (400 MHz, CDCl$_3$-d): $\delta$ 7.38 – 7.27 (m, 5H), 6.66 (t, $J$ = 5.8 Hz, 1H), 4.54 – 4.42 (m, 2H), 3.73 – 3.71 (m, 4H), 3.58 – 3.56 (m, 4H), 2.40 – 2.33 (m, 1H), 2.21 – 2.15 (m, 1H), 2.05 – 1.97 (m, 1H), 1.91 – 1.72 (m, 4H), 1.63 – 1.54 (m, 1H). $^{13}$C{1H} NMR (100 MHz, CDCl$_3$-d): $\delta$ 161.5, 159.3, 136.5, 129.1, 128.4, 128.1, 117.9, 117.3, 80.3, 66.3, 64.6, 62.1, 51.1, 45.1, 36.8, 35.7, 25.4, 24.9. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{22}$H$_{25}$N$_4$O$_2$S$^+$ 409.1693; found 409.1695.

**N-Benzyl-1,4-dicyano-3-morpholino-2-thiaspiro[4.5]dec-3-ene-1-carboxamide (5jn)**

Product 5jn was obtained according to the general procedure from 2-cyclohexylidene-3-morpholino-3-thioxopropanenitrile (1j) (68 mg, 1.0 equiv, 0.27 mmol), N-benzyl-2-cyano-2-diazoacetamide (2n) (81 mg, 1.5 equiv, 0.40 mmol), Rh$_2$(Piv)$_4$ (1.2 mg), chloroform (3.0 mL), reaction time is 10 min. The purification of the crude product by column chromatography on SiO$_2$ (DCM/EtOAc, gradient 25:0 to 24:1) afforded 5jn as a colorless powder (90%, 104 mg), mp 178–179 °C. $^1$H NMR (400 MHz, CDCl$_3$-d): $\delta$ 7.39 – 7.28 (m, 5H), 6.61 (t, $J$ = 4.5 Hz, 1H), 4.55 (dd, $J$ = 14.6, 5.8 Hz, 1H), 4.43 (dd, $J$ = 14.5, 5.3 Hz, 1H), 3.74 – 3.72 (m, 4H), 3.64 – 3.54 (m, 4H), 2.28 (d, $J$ = 11.1 Hz, 1H), 2.04 – 1.89 (m, 3H), 1.77 – 1.61 (m, 4H), 1.37 – 1.30 (m, 1H), 1.20 – 1.08 (m, 1H). $^{13}$C{1H} NMR (100 MHz, CDCl$_3$-d): $\delta$ 162.3, 161.0, 136.5, 129.1, 128.4, 128.1, 119.3, 117.1, 77.6, 66.4, 64.6, 56.0, 51.4, 45.2, 33.4, 32.7, 25.0, 22.3, 22.3. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{23}$H$_{27}$N$_4$O$_2$S$^+$ 423.1849; found 423.1851.
N-Benzyl-1,4-dicyano-3-morpholino-8-oxa-2-thiaspiro[4.5]dec-3-ene-1-carboxamide (5kn)

Product 5kn was obtained according to the general procedure from 3-morpholino-2-(tetrahydro-4H-pyran-4-ylidene)-3-thioxopropanenitrile (1k) (50 mg, 1.0 equiv, 0.20 mmol), N-benzyl-2-cyano-2-diazoacetamide (2n) (59 mg, 1.5 equiv, 0.30 mmol), Rh₂(Piv)₄ (0.9 mg), chloroform (3.0 mL), reaction time is 15 min. The purification of the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 24:1 to 22.5:2.5) afforded 5kn as a colorless solid (73%, 61 mg), mp 212–214 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 9.24 (t, J = 5.4 Hz, 1H), 7.35 – 7.24 (m, 5H), 4.35 (d, J = 5.6 Hz, 1H), 3.97 – 3.85 (m, 2H), 3.72 – 3.60 (m, 9H), 3.48 (t, J = 11.4 Hz, 1H), 2.31 – 2.23 (m, 1H), 1.93 (d, J = 13.7 Hz, 1H), 1.83 (d, J = 13.3 Hz, 1H), 1.51 – 1.44 (m, 1H). ¹³C{¹H} NMR (100 MHz, DMSO-d₆): δ 163.0, 160.1, 138.1, 128.3, 127.4, 127.1, 119.4, 117.2, 73.2, 65.6, 64.7, 63.2, 63.2, 52.0, 51.0, 43.9, 32.6, 32.1. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₂₂H₂₅N₄O₃S⁺ 425.1642; found 425.1640.

N-Benzyl-1,4-dicyano-3-morpholino-2-thiaspiro[4.6]undec-3-ene-1-carboxamide (5ln)

Product 5ln was obtained according to the general procedure from 2-cycloheptylidene-3-morpholino-3-thioxopropanenitrile (1l) (75 mg, 1.0 equiv, 0.28 mmol), N-benzyl-2-cyano-2-diazoacetamide (2n) (85 mg, 1.5 equiv, 0.42 mmol), Rh₂(Piv)₄ (1.3 mg), chloroform (3.0 mL), reaction time is 10 min. The purification of the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 25:0 to 24:1) afforded 5ln as a pale-yellow gum (71%, 88 mg), that crystallizes into powder when stored at 50 °C for 8 h, mp 176–177 °C. ¹H NMR (400 MHz, CDCl₃-d): δ 7.39 – 7.29 (m, 5H), 6.69 (t, J = 4.9 Hz, 1H), 4.55 (dd, J = 14.5, 5.8 Hz, 1H), 4.39 (dd, J = 14.5, 5.0 Hz, 1H), 3.73 – 3.71 (m, 4H), 3.62 – 3.52 (m, 4H), 2.44 – 2.38 (m, 1H), 2.24 – 2.16 (m, 2H), 1.81 – 1.72 (m, 4H), 1.56 – 1.49 (m, 2H), 1.41 – 1.25 (m, 2H), 1.21 – 1.13 (m, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃-d): δ 160.7, 160.1, 136.3, 129.1, 128.4, 128.3, 118.5, 117.8, 80.9, 66.3,
N-Benzyl-1,4-dicyano-3-morpholino-2-thiaspiro[4.7]dodec-3-ene-1-carboxamide (5on)

Product 5on was obtained according to the general procedure from 2-cyclooctylidene-3-morpholino-3-thioxopropanenitrile (1o) (50 mg, 1.0 equiv, 0.18 mmol), N-benzyl-2-cyano-2-diazoacetamide (2n) (54 mg, 1.5 equiv, 0.27 mmol), Rh₂(Piv)₄ (0.8 mg), chloroform (3.0 mL), reaction time is 60 min. The purification of the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 24:1 to 23:2) afforded 5on as a pale-yellow gum (79%, 64 mg). ¹H NMR (400 MHz, CDCl₃-d): δ 7.38 – 7.29 (m, 5H), 6.63 (br. s, 1H, NH), 4.54 (dd, J = 14.3, 5.7 Hz, 1H), 4.42 (dd, J = 14.4, 5.0 Hz, 1H), 3.72 (br. s, 4H), 3.63 – 3.55 (m, 4H), 2.43 – 2.36 (m, 1H), 2.30 – 2.25 (m, 1H), 2.17 – 2.13 (m, 1H), 1.80 – 1.57 (m, 9H), 1.47 – 1.39 (m, 2H). ¹³C{¹H} NMR (100 MHz, CDCl₃-d): 162.0, 160.7, 136.5, 129.1, 128.4, 128.2, 118.7, 117.1, 78.7, 66.3, 60.3, 51.3, 45.2, 32.3, 29.6, 28.7, 28.1, 25.3, 23.0, 22.9. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₂₅H₃₁N₄O₂S⁺ 451.2162; found 451.2165.

N-Benzyl-1,4-dicyano-3-(pyrrolidin-1-yl)-2-thiaspiro[4.7]dodec-3-ene-1-carboxamide (5qn)

Product 5qn was obtained according to the general procedure from 2-cyclooctylidene-3-(pyrrolidin-1-yl)-3-thioxopropanenitrile (1q) (40 mg, 1.0 equiv, 0.15 mmol), N-benzyl-2-cyano-2-diazoacetamide (2n) (46 mg, 1.5 equiv, 0.23 mmol), Rh₂(Piv)₄ (0.7 mg), chloroform (3.0 mL), reaction time is 10 min. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 25:0 to 37.5:12.5) afforded 5qn as a colorless solid (91%, 60 mg), mp 87–89 °C. ¹H NMR (400 MHz, CDCl₃-d): δ 7.38 – 7.29 (m, 5H), 6.71 (t, J = 5.1 Hz, 1H), 4.54 (dd, J = 14.6, 5.9 Hz, 1H), 4.43 (dd, J = 14.6, 5.4 Hz, 1H), 3.62 (br. s, 4H), 2.44 – 2.38 (m, 1H), 2.29 – 2.23 (m, 1H), 2.16 – 2.10 (m, 1H), 1.96 – 1.94 (m, 4H), 1.78 – 1.73 (m, 2H), 1.68 – 1.56 (m, 7H), 1.47 – 1.39 (m, 2H). HRMS (ESI) m/z: [M + H]⁺ calcd. for C₂₇H₃₅N₄O₂S⁺ 473.2380; found 473.2386.
1.47 – 1.36 (m, 2H). $^{13}$C{1H} NMR (100 MHz, CDCl$_3$-d): 162.4, 156.8, 136.7, 129.0, 128.2, 128.1, 120.2, 117.2, 73.6, 60.3, 52.0, 45.0, 32.7, 30.0, 28.7, 28.2, 25.7, 25.4, 23.1, 22.9. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{25}$H$_{31}$N$_4$OS$^+$ 435.2213; found 435.2216.

1-Acetyl-4-cyano-3-morpholino-N-phenyl-2-thiaspiro[4.4]non-3-ene-1-carboxamide (5ih)

Product 5ih was obtained according to the general procedure from 2-cyclopentylidene-3-morpholino-3-thioxopropanenitrile (1i) (155 mg, 1.0 equiv, 0.65 mmol), 2-diazo-3-oxo-N-phenylbutanamide (2h) (199 mg, 1.5 equiv, 0.98 mmol), Rh$_2$(Piv)$_4$ (3.0 mg), chloroform (3.5 mL), reaction time is 13 h. The purification of the crude product by column chromatography on SiO$_2$ (DCM/EtOAc, gradient 25:0 to 23.8:1.2) with subsequent centrifugation with $n$-hexane afforded 5ih as a colorless powder (74%, 199 mg), mp 154–155 °C. $^1$H NMR (400 MHz, CDCl$_3$-d): $\delta$ 8.27 (s, 1H, NH), 7.50 (d, $J = 8.1$ Hz, 2H), 7.37 (t, $J = 7.5$ Hz, 2H), 7.20 (t, $J = 6.9$ Hz, 1H), 3.74 (br. s, 4H), 3.64 – 3.52 (m, 4H), 2.46 – 2.41 (m, 1H), 2.36 (s, 3H), 2.15 – 2.07 (m, 2H), 1.98 – 1.71 (m, 4H), 1.62 – 1.56 (m, 1H). $^{13}$C{1H} NMR (100 MHz, CDCl$_3$-d): 197.1, 164.3, 158.5, 136.5, 129.4, 125.8, 120.6, 118.3, 84.0, 78.5, 66.39, 62.8, 51.0, 38.7, 34.1, 27.2, 25.3, 24.7. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{22}$H$_{25}$N$_3$O$_3$SNa$^+$ 434.1509; found 434.1511.

1-Acetyl-4-cyano-3-morpholino-N-phenyl-2-thiaspiro[4.5]dec-3-ene-1-carboxamide (5jh)

Product 5jh was obtained according to the general procedure from 2-cyclohexylidene-3-morpholino-3-thioxopropanenitrile (1j) (128 mg, 1.0 equiv, 0.50 mmol), 2-diazo-3-oxo-N-phenylbutanamide (2h) (156 mg, 1.5 equiv, 0.77 mmol), Rh$_2$(Piv)$_4$ (2.3 mg), chloroform (3.5 mL), reaction time is 14 h. The purification of the crude product by column chromatography on SiO$_2$ (PE/EtOAc, gradient 25:0 to 25:25) afforded 5jh as a colorless powder (82%, 178 mg), mp 198–
200 °C. $^1$H NMR (400 MHz, CDCl$_3$-$d$): $\delta$ 8.60 (s, 1H), 7.50 (d, $J$ = 7.9 Hz, 2H), 7.36 (t, $J$ = 7.7 Hz, 2H), 7.18 (t, $J$ = 7.4 Hz, 1H), 3.79 – 3.72 (m, 4H), 3.70 – 3.56 (m, 4H), 2.45 (s, 3H), 2.36 – 2.29 (m, 1H), 2.23 – 2.16 (m, 1H), 2.03 – 1.96 (m, 1H), 1.77 – 1.67 (m, 5H), 1.62 – 1.55 (m, 1H), 1.18 – 1.07 (m, 1H). $^{13}$C{1H} NMR (100 MHz, CDCl$_3$-$d$): $\delta$ 200.5, 163.6, 163.4, 136.8, 129.3, 125.5, 120.6, 119.9, 81.5, 79.3, 66.5, 55.4, 51.3, 34.4, 31.0, 29.6, 25.2, 22.6. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{23}$H$_{28}$N$_3$O$_3$S$^+$ 426.1846; found 426.1840.

1-Acetyl-4-cyano-3-morpholino-$N$-phenyl-2-thiaspiro[4.6]undec-3-ene-1-carboxamide (5lh)

Product 5lh was obtained according to the general procedure from 2-cycloheptylidene-3-morpholino-3-thioxopropanenitrile (1l) (80 mg, 1.0 equiv, 0.30 mmol), 2-diazo-3-oxo-$N$-phenylbutanamide (2h) (92 mg, 1.5 equiv, 0.45 mmol), Rh$_2$(Piv)$_4$ (1.4 mg), chloroform (2.0 mL), reaction time is 14 h. The purification of the crude product by column chromatography on SiO$_2$ (DCM/EtOAc, gradient 25:0 to 23.5:1.5) afforded 5lh as a colorless powder (92%, 123 mg), mp 174–175 °C. $^1$H NMR (400 MHz, CDCl$_3$-$d$): $\delta$ 8.51 (s, 1H, NH), 7.50 (d, $J$ = 7.8 Hz, 2H), 7.37 (t, $J$ = 7.8 Hz, 2H), 7.19 (t, $J$ = 7.4 Hz, 1H), 3.78 – 3.70 (m, 4H), 3.66 – 3.54 (m, 4H), 2.57 – 2.46 (m, 1H), 2.41 (s, 3H), 2.38 – 2.32 (m, 1H), 2.05 – 1.99 (m, 2H), 1.80 – 1.73 (m, 3H), 1.68 – 1.55 (m, 2H), 1.48 – 1.31 (m, 3H). $^{13}$C{1H} NMR (100 MHz, CDCl$_3$-$d$): 198.8, 164.2, 160.4, 136.8, 129.4, 125.6, 120.6, 119.1, 83.5, 80.9, 66.5, 58.9, 51.2, 35.8, 34.1, 30.8, 30.6, 28.5, 24.7, 24.1. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{24}$H$_{28}$N$_3$O$_3$SNa$^+$ 462.1822; found 462.1823.

1-Acetyl-4-cyano-3-morpholino-$N$-phenyl-2-thiaspiro[4.7]dodec-3-ene-1-carboxamide (5oh)

Product 5oh was obtained according to the general procedure from 2-cyclooctylidene-3-morpholino-3-thioxopropanenitrile (1o) (80 mg, 1.0 equiv, 0.29 mmol), 2-diazo-3-oxo-$N$-
phenylbutanamide (2h) (87 mg, 1.5 equiv, 0.43 mmol), Rh₂(Piv)₄ (1.3 mg), chloroform (2.0 mL), reaction time is 14 h. The purification of the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 25:0 to 23.5:1.5) afforded 5oh as a colorless powder (75%, 98 mg), mp 241–243 °C. ¹H NMR (400 MHz, CDCl₃-d): δ 8.88 (s, 1H, NH), 7.51 (d, J = 7.8 Hz, 2H), 7.36 (t, J = 7.8 Hz, 2H), 7.17 (t, J = 7.4 Hz, 1H), 3.79 – 3.58 (m, 8H), 2.51 (s, 3H), 2.31 – 2.10 (m, 3H), 1.99 – 1.92 (m, 1H), 1.73 – 1.40 (m, 10H). ¹³C{¹H} NMR (100 MHz, CDCl₃-d): 203.2, 163.4, 161.9, 136.9, 129.3, 125.4, 120.4, 119.4, 82.2, 81.0, 66.5, 59.9, 51.2, 31.6, 30.6, 30.2, 28.7, 28.2, 25.9, 23.2, 23.2. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₂₅H₃₂N₃O₃S + 454.2159; found 454.2155.

1-Acetyl-4-cyano-N-phenyl-3-(piperidin-1-yl)-2-thiaspiro[4.6]undec-3-ene-1-carboxamide (5ph)

Product 5ph was obtained according to the general procedure from 2-cycloheptylidene-3-(piperidin-1-yl)-3-thioxopropanenitrile (1p) (60 mg, 1.0 equiv, 0.23 mmol), 2-diazo-3-oxo-N-phenylbutanamide (2h) (70 mg, 1.5 equiv, 0.34 mmol), Rh₂(Piv)₄ (1.0 mg), chloroform (2.0 mL), reaction time is 14 h. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 25:0 to 37.5:12.5) afforded 5ph as a colorless powder (79%, 79 mg), mp 79–81 °C. ¹H NMR (400 MHz, CDCl₃-d): δ 8.59 (s, 1H, NH), 7.52 (d, J = 7.6 Hz, 2H), 7.38 (t, J = 7.9 Hz, 2H), 7.19 (t, J = 7.4 Hz, 1H), 3.65 – 3.60 (m, 4H), 2.50 – 2.32 (m, 5H), 2.12 – 1.96 (m, 2H), 1.82 – 1.59 (m, 1H), 1.53 – 1.45 (m, 2H), 1.39 – 1.32 (m, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃-d): 199.4, 164.8, 160.6, 136.8, 129.2, 125.3, 120.4, 119.8, 81.1, 80.4, 58.3, 52.6, 35.9, 34.1, 30.6, 30.2, 28.7, 26.1, 24.5, 24.3, 24.0. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₂₅H₃₂N₃O₂S⁺ 438.2201; found 438.2212.

1-Acetyl-4-cyano-N-phenyl-3-(piperidin-1-yl)-2-thiaspiro[4.7]dodec-3-ene-1-carboxamide (5rh)

SS7
Product 5rh was obtained according to the general procedure from 2-cyclooctylidene-3-(piperidin-1-yl)-3-thioxopropanenitrile (1r) (90 mg, 1.0 equiv, 0.32 mmol), 2-diazo-3-oxo-N-phenylbutanamide (2h) (99 mg, 1.5 equiv, 0.49 mmol), Rh2(Piv)4 (1.5 mg), chloroform (2.0 mL), reaction time is 14 h. The purification of the crude product by column chromatography on SiO2 (PE/EtOAc, gradient 25:0 to 37.5:12.5) afforded 5rh as a colorless powder (76%, 112 mg), mp 155–157 °C. 1H NMR (400 MHz, CDCl3-d): δ 8.90 (s, 1H, NH), 7.51 (d, J = 7.7 Hz, 2H), 7.36 (t, J = 7.9 Hz, 2H), 7.16 (t, J = 7.4 Hz, 1H), 3.66 – 3.58 (m, 4H), 2.51 (s, 3H), 2.35 – 2.08 (m, 3H), 1.99 – 1.93 (m, 1H), 1.77 – 1.68 (m, 10H), 1.60 – 1.39 (m, 6H). 13C{1H} NMR (100 MHz, CDCl3-d): *the product decomposes while recording a carbon spectrum.* HRMS (ESI) m/z: [M + H]+ calcd. for C26H34N3O2S+ 452.2366; found 452.2369.

1-Acetyl-3-(azepan-1-yl)-4-cyano-N-phenyl-2-thiaspiro[4.7]dodec-3-ene-1-carboxamide (5sh)

Product 5sh was obtained according to the general procedure from 2-cyclooctylidene-3-(piperidin-1-yl)-3-thioxopropanenitrile (1s) (90 mg, 1.0 equiv, 0.31 mmol), 2-diazo-3-oxo-N-phenylbutanamide (2h) (94 mg, 1.5 equiv, 0.46 mmol), Rh2(Piv)4 (1.4 mg), chloroform (2.0 mL), reaction time is 14 h. The purification of the crude product by column chromatography on SiO2 (PE/EtOAc, gradient 25:0 to 37.5:12.5) afforded 5sh as a colorless powder (83%, 119 mg), mp 160–162 °C. 1H NMR (400 MHz, CDCl3-d): δ 8.93 (s, 1H, NH), 7.51 (d, J = 7.7 Hz, 2H), 7.35 (t, J = 7.9 Hz, 2H), 7.16 (t, J = 7.4 Hz, 1H), 3.74 – 3.64 (m, 4H), 2.53 (s, 3H), 2.35 – 2.29 (m, 1H), 2.24 – 2.18 (m, 2H), 2.11 – 2.05 (m, 1H), 2.00 – 1.93 (m, 1H), 1.87 – 1.81 (m, 4H), 1.78 – 1.41 (m, 14H). 13C{1H} NMR (100 MHz, CDCl3-d): 203.8, 164.1, 161.0, 137.1, 129.3, 125.2, 120.7, 120.4, 83.0, 75.6, 59.6, 54.3, 31.8, 30.8, 30.7, 29.1, 28.9, 28.3, 26.9, 26.0, 23.4, 23.3. HRMS (ESI) m/z: [M + H]+ calcd. for C27H36N3O2S+ 466.2522; found 466.2524.
7''-Methyl-5''-morpholino-2''-oxodispiro[cyclohexane-1,3'-thiophene-2',3''-indoline]-4''-carbonitrile (5jp)

Product 5jp was obtained according to the general procedure from 2-cyclohexylidene-3-morpholino-3-thioxopropanenitrile (1j) (40 mg, 1.0 equiv, 0.16 mmol), 3-diazo-7-methylindolin-2-one (2p) (41 mg, 1.5 equiv, 0.24 mmol), Rh₂(Piv)₄ (0.70 mg), chloroform (2.0 mL), reaction time is 1 h. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 30:20 to 20:30) afforded 5jp as a colorless powder (75%, 47 mg), mp 222–223 °C. ¹H NMR (400 MHz, CDCl₃-d): δ 9.62 (s, 1H), 7.26 (d, J = 7.3 Hz, 1H), 7.11 (d, J = 7.6 Hz, 1H), 6.96 (t, J = 7.5 Hz, 1H), 3.78 – 3.58 (m, 7H), 2.32 (s, 3H), 2.25 (d, J = 9.9 Hz, 1H), 2.14 – 2.00 (m, 2H), 1.70 – 1.61 (m, 4H), 1.51 (d, J = 14.1 Hz, 1H), 1.31 – 1.23 (m, 1H), 1.07 – 0.97 (m, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃-d): δ 178.0, 165.6, 140.2, 131.4, 124.7, 124.3, 122.4, 121.0, 120.1, 78.1, 66.7, 66.5, 55.2, 51.4, 34.0, 30.5, 25.3, 22.3, 22.3, 16.5. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₂₂H₂₆N₃O₂S⁺ 396.1740; found 396.1740.

7-Methyl-5'-morpholino-2-oxo-2'',3'',5'',6''-tetrahydrodispiro[indoline-3,2'-thiophene-3',4''-pyran]-4'-carbonitrile (5kp)

Product 5kp was obtained according to the general procedure from 3-morpholino-2-(tetrahydro-4H-pyran-4-ylidene)-3-thioxopropanenitrile (1k) (41 mg, 1.0 equiv, 0.15 mmol), 3-diazo-7-methylindolin-2-one (2p) (39 mg, 1.5 equiv, 0.24 mmol), Rh₂(Piv)₄ (0.70 mg), chloroform (2.0 mL), 40 °C, reaction time is 30 min. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 30:20 to 40:10) afforded 5kp as a colorless powder (89%, 56 mg), mp 288–290 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 10.82 (s, 1H), 7.25 (d, J = 7.5 Hz, 1H), 7.13 (d, J = 7.6 Hz, 1H), 6.95 (t, J = 7.6 Hz, 1H), 3.87 (t, J = 11.1 Hz, 1H), 3.71 – 3.63
(m, 6H), 3.60 – 3.54 (m, 4H), 2.20 (s, 3H), 1.98 – 1.92 (m, 1H), 1.85 – 1.78 (m, 2H), 1.51 – 1.44 (m, 1H). 13C{1H} NMR (100 MHz, DMSO-d6): δ 174.7, 165.3, 140.6, 131.2, 123.7, 123.7, 121.5, 120.2, 119.7, 74.7, 65.6, 63.1, 51.3, 50.8, 33.7, 30.6, 16.1. HRMS (ESI) m/z: [M + H]⁺ calcd. for C21H24N3O3S⁺ 398.1533; found 398.1530.

7''-Methyl-5'-morpholino-2''-oxodispiro[cycloheptane-1,3'-thiophene-2',3''-indoline]-4'-carbonitrile (5lp)

Product 5lp was obtained according to the general procedure from 2-cycloheptylidene-3-morpholino-3-thioxopropanenitrile (II) (39 mg, 1.0 equiv, 0.15 mmol), 3-diazo-7-methylindolin-2-one (2p) (39 mg, 1.5 equiv, 0.23 mmol), Rh₂(Piv)₄ (0.68 mg), chloroform (2.0 mL), reaction time is 20 min. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 30:20 to 25:25) afforded 5lp as a colorless powder (79%, 49 mg), mp 209–211 °C. ¹H NMR (400 MHz, CDCl₃-d): δ 9.34 (s, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.10 (d, J = 7.6 Hz, 1H), 6.94 (t, J = 7.6 Hz, 1H), 3.78 – 3.76 (m, 4H), 3.69 – 3.57 (m, 4H), 2.31 (s, 3H), 2.27 – 2.18 (m, 2H), 2.00 – 1.94 (m, 1H), 1.86 – 1.73 (m, 2H), 1.66 – 1.53 (m, 2H), 1.46 – 1.41 (m, 3H), 1.25 – 1.14 (m, 2H). ¹³C{1H} NMR (100 MHz, CDCl₃-d): δ 178.0, 163.1, 139.9, 131.4, 125.1, 124.2, 122.6, 120.0, 81.4, 66.6, 66.0, 59.6, 51.2, 35.0, 34.6, 31.0, 30.8, 24.4, 24.2, 16.6. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₂₃H₂₈N₃O₂S⁺ 410.1897; found 410.1897.

7''-Methyl-5'-morpholino-2''-oxodispiro[cyclooctane-1,3'-thiophene-2',3''-indoline]-4'-carbonitrile (5op)

A 10 mL standard microwave vial was charge with Rh₂(Piv)₄ (0.60 mg, 1.0 mol %), 2-cyclooctylidene-3-morpholino-3-thioxopropanenitrile (1o) (40 mg, 1.0 equiv, 0.14 mmol) and dry
chloroform (1 mL). A solution of diazocompound 2p (37 mg, 1.5 equiv, 0.21 mmol) in dry chloroform (1 mL) was added slowly to the vial at room temperature. The reaction solution was stirred for 20 min at room temperature, and then a portion of 2p (25 mg, 1.0 equiv, 0.14 mmol) in 0.5 mL dry chloroform was added. The reaction solution was stirred for 40 min at room temperature, and then the solution was directly subjected to SiO2. The purification of the crude product by column chromatography on SiO2 (PE/EtOAc, gradient 30:20 to 40:10) with subsequent centrifugation with cold diethyl ether afforded 5op as a colorless powder (57%, 35 mg), mp 228–230 °C. 1H NMR (400 MHz, CDCl3-d): δ 9.49 (s, 1H), 7.32 (d, J = 7.5 Hz, 1H), 7.09 (d, J = 7.6 Hz, 1H), 6.96 (t, J = 7.6 Hz, 1H), 3.77 – 3.75 (m, 4H), 3.70 – 3.58 (m, 4H), 2.45 – 2.37 (m, 1H), 2.29 (s, 3H), 2.24 – 2.21 (m, 2H), 2.06 – 2.00 (m, 1H), 1.66 (br. s, 1H), 1.55 (br. s, 4H), 1.47 – 1.42 (m, 1H), 1.32 (br. s, 3H), 0.91 (br. s, 1H). 13C{1H} NMR (100 MHz, CDCl3-d): δ 178.3, 163.4, 139.6, 131.3, 124.0, 122.5, 120.1, 120.0, 79.7, 66.6, 66.2, 58.8, 51.3, 30.1, 29.7, 29.3, 28.0, 25.4, 22.9, 22.1, 16.5. HRMS (ESI) m/z: [M + H]+ calcd. for C24H30N3O2S+ 424.2053; found 424.2055.

1-Methyl-13-morpholino-4-oxo-3-phenyl-14-thia-2,3-diazadispiro[4.0.56.35]tetradeca-1,12-diene-12-carbonitrile (5jq)

Product 5jq was obtained according to the general procedure from 2-cyclohexylidene-3-morpholino-3-thioxopropanenitrile (1j) (40 mg, 1.0 equiv, 0.16 mmol), 4-diazo-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (2q) (48 mg, 1.5 equiv, 0.23 mmol), Rh2(Piv)4 (0.70 mg), chloroform (2.0 mL), 60 °C, reaction time is 1 h. The purification of the crude product by column chromatography on SiO2 (DCM/EtOAc, gradient 25:0 to 20:5) afforded 5jq as a pale-yellow oil (79%, 53 mg). 1H NMR (400 MHz, CDCl3-d): δ 7.88 (d, J = 7.8 Hz, 2H), 7.40 (t, J = 8.0 Hz, 2H), 7.20 (t, J = 7.4 Hz, 1H), 3.82 – 3.67 (m, 6H), 3.62 – 3.57 (m, 2H), 2.30 (s, 3H), 2.19 – 2.15 (m, 1H), 2.10 – 2.02 (m, 2H), 1.95 – 1.91 (m, 1H), 1.73 – 1.68 (m, 1H), 1.65 – 1.59 (m, 2H), 1.51 – 1.47 (m, 1H), 1.39 – 1.32 (m, 1H), 1.21 – 1.15 (m, 1H). 13C{1H} NMR (100 MHz, CDCl3-d): δ 167.6, 163.9, 159.6, 137.6, 129.0, 125.7, 119.8, 119.0, 78.2, 68.5, 66.6, 55.6, 51.5, 32.6, 31.1, 25.1, 22.4, 22.4, 16.3. HRMS (ESI) m/z: [M + H]+ calcd. for C23H27N4O2S+ 423.1849; found 423.1853.
Dimethyl 4-cyano-5-morpholino-3-phenylthiophene-2,2,3(3H)-dicarboxylate (5as)

Product 5as was obtained according to the general procedure from 2-(morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (50 mg, 1.0 equiv, 0.19 mmol), dimethyl 2-diazomalonate (2s) (46 mg, 1.5 equiv, 0.29 mmol), Rh2(Piv)4 (0.90 mg), chloroform (2.0 mL), 45 °C, reaction time is 1 h. The purification of the crude product by column chromatography on SiO2 (PE/EtOAc, gradient 25:0 to 20:30) afforded 5as as a colorless powder (95%, 71 mg), mp 153–154 °C. 1H NMR (400 MHz, DMSO-d6): δ 7.35 (br. s, 5H), 4.89 (s, 1H), 3.81 (s, 6H), 3.69 (br. s, 4H), 3.57 (br. s, 4H). 13C{1H} NMR (100 MHz, DMSO-d6): δ 168.1, 165.0, 160.6, 136.2, 128.6, 128.5, 128.4, 118.3, 71.8, 68.9, 65.5, 56.7, 54.1, 53.2, 50.2. HRMS (ESI) m/z: [M + H]+ calcd. for C19H21N2O5S+ 389.1165; found 389.1164.

Trimethyl 5-morpholino-3-phenylthiophene-2,2,4(3H)-tricarboxylate (5xs)

Product 5xs was obtained according to the general procedure from methyl 2-(morpholine-4-carbonothioyl)-3-phenylacrylate (1x) (58 mg, 1.0 equiv, 0.20 mmol), dimethyl 2-diazomalonate (2s) (47 mg, 1.5 equiv, 0.30 mmol), Rh2(Piv)4 (0.90 mg), chloroform (2.0 mL), 45 °C, reaction time is 1 h. The purification of the crude product by column chromatography on SiO2 (PE/EtOAc, gradient 25:0 to 25:25) with subsequent centrifugation with cold diethyl ether afforded 5xs as a colorless powder (69%, 58 mg), mp 173–176 °C. 1H NMR (400 MHz, CDCl3-d): δ 7.37 (d, J = 7.0 Hz, 2H), 7.29 – 7.24 (m, 3H), 5.25 (s, 1H), 3.87 – 3.75 (m, 7H), 3.67 – 3.59 (m, 2H), 3.55 (s, 3H), 3.40 – 3.35 (m, 2H), 3.29 (s, 3H). 13C{1H} NMR (100 MHz, CDCl3-d): δ 169.1, 166.1, 164.1, 162.9, 138.3, 128.7, 128.2, 127.9, 99.5, 69.2, 66.9, 57.1, 53.9, 53.1, 53.0, 51.1. HRMS (ESI) m/z: [M + H]+ calcd. for C20H24NO7S+ 422.1268; found 422.1271.
Methyl 4-cyano-5-morpholino-2,3-diphenyl-2,3-dihydrothiophene-2-carboxylate (5at)

\[
\begin{align*}
\text{NC} & \quad \equiv \quad \text{S} \\
\text{Ph} & \quad \text{Ph} \\
\text{O} & \quad \text{Me}
\end{align*}
\]

Product 5at was obtained according to the general procedure from 2-(morpholine-4-carbonothioyl)-3-phenylacrylonitrile (1a) (50 mg, 1.0 equiv, 0.19 mmol), methyl 2-diazo-2-phenylacetate (2t) (41 mg, 1.2 equiv, 0.23 mmol), Rh₂(Piv)₄ (0.70 mg), chloroform (2.0 mL), rt, reaction time is 15 min. The purification of the crude product by column chromatography on neutral alumina (PE/EtOAc, gradient 25:0 to 35:15) afforded 5at as a colorless powder (76%, 60 mg), mp 68–70 °C, a mixture of diastereomers (dr 65:35). \(^1\)H NMR (400 MHz, CDCl₃-d): \(\delta\) 7.59 (d, \(J = 7.3\) Hz, 2H), 7.49 (d, \(J = 8.0\) Hz, 2H), 7.45 – 7.30 (m, 7H), 7.12 – 6.93 (m, 6H), 5.24 (s, 0.56H), 4.75 (s, 1H), 3.83 – 3.81 (m, 4H), 3.74 – 3.70 (m, 6H), 3.62 – 3.55 (m, 4H), 3.26 (s, 3H). \(^{13}\)C{\(^1\)H} NMR (100 MHz, CDCl₃-d): \(\delta\) 172.5, 169.5, 162.5, 161.8, 141.8, 137.6, 136.3, 134.5, 129.3, 129.0, 128.6, 128.5, 128.4, 128.4, 128.0, 128.0, 127.8, 127.5, 127.2, 125.6, 119.1, 118.8, 75.2, 74.1, 73.1, 69.9, 66.4, 66.3, 60.0, 59.6, 53.7, 52.8, 50.8, 50.7. HRMS (ESI) m/z: [M + H]^+ calcd. for C₂₃H₂₃N₂O₃S^+ 407.1424; found 407.1423.

Methyl 4-cyano-3-morpholino-1-phenyl-2-thiaspiro[4.7]dodec-3-ene-1-carboxylate (5ot)

\[
\begin{align*}
\text{NC} & \quad \equiv \quad \text{S} \\
\text{Ph} & \quad \text{O} \\
\text{Me}
\end{align*}
\]

Method A. Product 5ot was obtained according to the general procedure from 2-cyclooctylidene-3-morpholino-3-thioxopropanenitrile (1o) (50 mg, 1.0 equiv, 0.14 mmol), methyl 2-diazo-2-phenylacetate (2t) (30 mg, 1.2 equiv, 0.17 mmol), Rh₂(Piv)₄ (0.70 mg), chloroform (2.0 mL), rt, reaction time is 60 min. The purification of the crude product by column chromatography on SiO₂ (PE/EtOAc, gradient 25:0 to 35:15) with subsequent centrifugation with a mixture of diethyl ether:hexane (0.4 mL : 1 mL) afforded 5ot as a colorless powder (85%, 52 mg), mp 179–181 °C. \(^1\)H NMR (400 MHz, CDCl₃-d): \(\delta\) 7.41 – 7.38 (m, 2H), 7.36 – 7.32 (m, 3H), 3.83 – 3.71 (m, 9H), 3.66 – 3.61 (m, 2H), 2.48 – 2.41 (m, 1H), 2.24 – 2.19 (m, 1H), 2.01 – 1.93 (m, 1H), 1.81 – 1.61 (m, 7H), 1.47 – 1.25 (m, 4H). \(^{13}\)C{\(^1\)H} NMR (100 MHz, CDCl₃-d): \(\delta\) 169.8, 163.6, 137.1, 128.5,
128.5, 127.4, 120.3, 80.7, 76.2, 66.7, 60.1, 53.2, 51.1, 30.7, 30.2, 29.7, 28.1, 25.8, 24.3, 22.8. HRMS (ESI) m/z: [M + H]+ calcd. for C$_{24}$H$_{31}$N$_2$O$_3$S$^+$ 427.2050; found 427.2051.

**Method B.** To an oven-dried 50 mL standard screw glass vial (50 mL) [Cu(MeCN)$_4$]CF$_3$SO$_3$ (19 mg, 10 mol %), thioamide (1o) (70 mg, 1.0 equiv, 0.25 mmol), methyl 2-diazo-2-phenylacetate (2t) (88 mg, 2.0 equiv, 0.50 mmol) and dry chloroform (3.5 mL) were added. Then, the reaction mixture was allowed to stir at 90 °C for 24 h. The purification of the crude product by column chromatography on SiO$_2$ (PE/EtOAc, gradient 25:0 to 35:15) with subsequent centrifugation with a mixture diethyl ether:hexane (0.4 mL:1.0 mL) afforded 5ot as a colorless powder (70%, 77 mg), mp 179–181 °C.
General procedure for the synthesis of dihydrothiophenes 6
To an oven-dried 50 mL standard screw glass vial (50 mL) [Cu(MeCN)4]CF3SO3 (10 mol %), thioamides (1i,j,l,o) (1.0 equiv), 2-diazo-3-oxo-\(N\)-phenylbutanamide (2h) (2.0 equiv) and dry chloroform were added. Then, the reaction mixture was allowed to stir at 90 °C for 24 h. Upon completion, the solution was directly subjected to SiO\(_2\) afforded 6.

**2-Acetyl-4-cyano-3-morpholino-\(N\)-phenyl-1-thiaspiro[4.4]non-3-ene-2-carboxamide (6ih)**

![Chemical Structure](image)

Product 6ih was obtained according to the general procedure from 2-cyclopentylidene-3-morpholino-3-thioxopropanenitrile (1i) (203 mg, 1.0 equiv, 0.86 mmol), 2-diazo-3-oxo-\(N\)-phenylbutanamide (2h) (349 mg, 2.0 equiv, 1.72 mmol), [Cu(MeCN)4]OTf (65 mg), chloroform (6.0 mL), 90 °C, reaction time is 24 h. The purification of the crude product by column chromatography on SiO\(_2\) (DCM/EtOAc, gradient 25:0 to 23.5:1.5) afforded 6ih as a yellow oily mass (116 mg). The latter was triturated with hexane:diethyl ether (1:1) and the formed precipitate was centrifugated afforded 6ih as a colorless powder (23%, 80 mg), mp 164–166 °C. The second regioisomer was isolated by column chromatography on SiO\(_2\) (DCM/EtOAc, gradient up to 23:2) as a brown oily mass (144 mg). The trituration with hexane:diethyl ether (1:1) and centrifugation of the formed precipitate afforded 5ih as a colorless powder (31%, 109 mg), mp 154–155 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 9.29 (s, 1H), 7.54 (d, \(J = 7.6\) Hz, 2H), 7.36 (t, \(J = 7.9\) Hz, 2H), 7.17 (t, \(J = 7.4\) Hz, 1H), 3.71 – 3.62 (m, 4H), 3.58 – 3.52 (m, 2H), 3.38 – 3.33 (m, 2H), 2.49 (s, 3H), 2.35 – 2.20 (m, 2H), 2.16 – 2.11 (m, 1H), 2.02 – 1.97 (m, 1H), 1.87 – 1.80 (m, 2H), 1.76 – 1.68. \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\)): \(\delta\) 201.5, 165.7, 156.2, 137.2, 129.3, 125.3, 120.2, 117.4, 91.5, 71.8, 67.5, 66.5, 50.3, 42.4, 41.1, 26.6, 24.3, 24.0. HRMS (ESI) m/z: [M + H]\(^+\) calcd. for C\(_{22}\)H\(_{26}\)N\(_3\)O\(_3\)S\(_2\) 412.1689; found 412.1687.
2-Acetyl-4-cyano-3-morpholino-N-phenyl-1-thiaspiro[4.5]dec-3-ene-2-carboxamide (6jh)

Product 6jh was obtained according to the general procedure from 2-cyclohexylidene-3-morpholino-3-thioxopropanenitrile (1j) (192 mg, 1.0 equiv, 0.77 mmol), 2-diazo-3-oxo-N-phenylbutanamide (2h) (312 mg, 2.0 equiv, 1.53 mmol), [Cu(MeCN)₄]OTf (58 mg), chloroform (6.0 mL), 90 °C, reaction time is 24 h. The purification of the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 25:0 to 23.5:1.5) afforded 6jh as a yellow oily mass (253 mg). The latter was triturated with hexane:diethyl ether (1:1) and the formed precipitate was centrifugated afforded 6jh as a colorless powder (57%, 185 mg), mp 195–196 °C. The second regioisomer was isolated by column chromatography on SiO₂ (DCM/EtOAc, gradient up to 23:2) as a brown gum (30 mg). The trituration with hexane:diethyl ether (1:1) and centrifugation of the formed precipitate afforded 6jh as a colorless powder (5%, 16 mg), mp 198–200 °C. ¹H NMR (400 MHz, CDCl₃): δ 9.35 (s, 1H), 7.54 (d, J = 7.5 Hz, 2H), 7.36 (t, J = 7.5 Hz, 2H), 7.17 (t, J = 6.4 Hz, 1H), 3.67 – 3.62 (m, 4H), 3.57 – 3.51 (m, 2H), 3.37 – 3.32 (m, 2H), 2.49 (s, 3H), 2.04 – 1.96 (m, 3H), 1.88 – 1.79 (m, 3H), 1.67 (d, J = 13.4 Hz, 1H), 1.47 – 1.30 (m, 2H), 1.26 – 1.14 (m, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 201.7, 165.9, 155.8, 137.2, 129.3, 125.3, 120.2, 117.6, 93.9, 71.0, 66.5, 63.8, 50.3, 40.1, 39.0, 26.6, 24.5, 24.4, 23.9. HRMS (ESI) m/z: [M + H]^+ calcd. for C₂₃H₂₈N₃O₃S⁺ 426.1846; found 426.1846.

2-Acetyl-4-cyano-3-morpholino-N-phenyl-1-thiaspiro[4.6]undec-3-ene-2-carboxamide (6lh)

Product 6lh was obtained according to the general procedure from 2-cycloheptylidene-3-morpholino-3-thioxopropanenitrile (1l) (200 mg, 1.0 equiv, 0.76 mmol), 2-diazo-3-oxo-N-phenylbutanamide (2h) (307 mg, 2.0 equiv, 1.51 mmol), [Cu(MeCN)₄]OTf (57 mg), chloroform (6.0 mL), 90 °C, reaction time is 24 h. The purification of the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 25:0 to 23:2) afforded 6lh as a yellow oily mass (281 mg). The latter was triturated with hexane:diethyl ether (1:1) and the formed precipitate was
centrifugated afforded 6lh as a colorless powder (56%, 187 mg), mp 168–170 °C. The second regioisomer was formed in a trace amount. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 9.30 (s, 1H, NH), 7.53 (d, \(J = 8.6\) Hz, 2H), 7.36 (t, \(J = 7.9\) Hz, 2H), 7.17 (t, \(J = 7.4\) Hz, 1H), 3.69 – 3.60 (m, 4H), 3.56 – 3.50 (m, 2H), 3.35 – 3.29 (m, 2H), 2.48 (s, 3H), 2.26 – 2.18 (m, 3H), 2.05 – 2.00 (m, 1H), 1.83 – 1.77 (m, 2H), 1.61 – 1.48 (m, 6H). \(^{13}\)C{\(^1\)H} NMR (100 MHz, CDCl\(_3\)): 201.6, 165.8, 155.4, 137.2, 129.3, 125.3, 120.2, 117.9, 95.3, 71.5, 66.5, 66.0, 50.4, 44.3, 42.6, 27.7, 27.7, 26.6, 24.5, 24.0. HRMS (ESI) m/z: [M + H]\(^+\) calcd. for C\(_{24}\)H\(_{24}\)N\(_3\)O\(_3\)S\(^+\) 440.2002; found 440.1999.

**2-Acetyl-4-cyano-3-morpholino-N-phenyl-1-thiaspiro[4.7]dodec-3-ene-2-carboxamide (6oh)**

![Chemical Structure](image)

Product 6oh was obtained according to the general procedure from 2-cyclooctylidene-3-morpholino-3-thioxopropanenitrile (1o) (200 mg, 1.0 equiv, 0.72 mmol), 2-diazo-3-oxo-N-phenylbutanamide (2h) (292 mg, 2.0 equiv, 1.44 mmol), \([\text{Cu(MeCN)}_4]\)OTf (54 mg), chloroform (6.0 mL), 90 °C, reaction time is 24 h. The purification of the crude product by column chromatography on SiO\(_2\) (DCM/EtOAc, gradient 25:0 to 23.5:1.5) afforded 6oh as a yellow oily mass (276 mg). The latter was triturated with hexane:diethyl ether (1:1) and the formed precipitate was centrifugated afforded 6oh as a colorless powder (67%, 218 mg), mp 241–243 °C. The second regioisomer was formed in a trace amount. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 9.30 (s, 1H, NH), 7.53 (d, \(J = 7.9\) Hz, 2H), 7.36 (t, \(J = 7.7\) Hz, 2H), 7.17 (t, \(J = 7.2\) Hz, 1H), 3.70 – 3.60 (m, 4H), 3.56 – 3.52 (m, 2H), 3.36 – 3.30 (m, 2H), 2.43 (s, 3H), 2.41 – 2.31 (m, 2H), 2.26 – 2.20 (m, 1H), 2.08 – 2.02 (m, 1H), 1.90 – 1.85 (m, 2H), 1.65 – 1.51 (m, 9H). \(^{13}\)C{\(^1\)H} NMR (100 MHz, CDCl\(_3\)): 201.5, 165.9, 156.0, 137.2, 129.3, 125.3, 120.2, 118.2, 94.6, 71.4, 66.6, 65.8, 50.5, 40.8, 38.8, 27.9, 27.8, 26.6, 24.5, 24.1, 24.0. HRMS (ESI) m/z: [M + H]\(^+\) calcd. for C\(_{25}\)H\(_{32}\)N\(_3\)O\(_3\)S\(^+\) 454.2159; found 454.2159.

**Asymmetric Synthesis of Dihydrithiophenes 5**

A 20 mL Schlenk tube was charge with Rh\(_2\)(S-NTTL)_4 (0.5 mol %), thioamide 1 (1.0 equiv) and dry chloroform (1 mL). A solution of diazo compound 2p or 2v (1.5 equiv) in dry chloroform (1 mL) was added slowly to the tube via syringe at 0 °C. Then the reaction solution was allowed to warm to room temperature and stirred for 40 min (for 5hp) or stirred 30 min at 0 °C and 20 min at room temperature (for 5ip, lp, 5op, 5ov), and then the solution was directly subjected to SiO\(_2\).
(S)-3',3',7-Trimethyl-5'-morpholino-2-oxo-3'H-spiro[indoline-3,2'-thiophene]-4'-carbonitrile (5hp)

Product 5hp was obtained according to the general procedure from thioamide 1h (30 mg, 1.0 equiv, 0.14 mmol), diazo compound 2p (37 mg, 1.5 equiv, 0.21 mmol), Rh₂(S-NTTL)₄ (1.3 mg), chloroform (2 mL). The purification of the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 25:0 to 20:5) afforded 5hp as a colorless powder (96%, 49 mg, 1.4:98.6 e.r.), mp 131–133 °C, [α]D²⁰ = +59 (C = 0.89, CHCl₃). The enantiomeric excess was determined by HPLC analysis on a Chiralpak AD column: 5:1 n-hexane/i-PrOH, flow rate 1 mL/min, λ = 220, 230 nm: TR Minor = 8.28 min, TR Major = 9.67 min. ¹H NMR (400 MHz, DMSO-d₆): δ 10.73 (s, 1H, NH), 7.27 (d, J = 7.0 Hz, 1H), 7.11 (d, J = 7.0 Hz, 1H), 6.93 (t, J = 7.4 Hz, 1H), 3.67 (br. s, 4H), 3.53 (br. s, 4H), 2.20 (s, 3H), 1.26 (s, 3H), 1.08 (s, 3H). ¹³C {¹H} NMR (100 MHz, DMSO-d₆): δ 175.9, 161.4, 140.9, 131.3, 123.8, 123.5, 121.7, 119.6, 118.7, 78.2, 65.6, 63.6, 51.6, 50.4, 25.1, 22.1, 16.4. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₁₉H₂₂N₃O₂S⁺ 356.1427; found 356.1433.

(S)-7''-Methyl-5''-morpholino-2''-oxodispiro[cyclopentane-1,3'-thiophene-2',3''-indoline]-4'-carbonitrile (5ip)

Product 5ip was obtained according to the general procedure from thioamide 1i (30 mg, 1.0 equiv, 0.13 mmol), diazo compound 2p (33 mg, 1.5 equiv, 0.19 mmol), Rh₂(S-NTTL)₄ (1.4 mg), chloroform (2 mL). The purification of the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 20:5 to 20:20) afforded 5ip as a colorless powder (83%, 40 mg, 3.9:96.1 e.r.), mp 102–104 °C, [α]D²⁰ = −7.7 (C = 0.77, CHCl₃). The enantiomeric excess was determined by HPLC analysis on a Chiralpak AD column: 5:1 n-hexane/i-PrOH, flow rate 1 mL/min, λ = 220, 230 nm: TR Minor = 11.98 min, TR Major = 12.70 min. ¹H NMR (400 MHz, CDCl₃-d): δ 9.51 (s, 1H, NH), 7.33 (d, J = 7.5 Hz, 1H), 7.11 (d, J = 7.6 Hz, 1H), 6.97 (t, J = 7.6 Hz, 1H), 3.78 – 3.76
(m, 4H), 3.69 – 3.59 (m, 4H), 2.09 – 1.84 (m, 4H), 1.79 – 1.70 (m, 2H), 1.45 – 1.32 (m, 2H). $^{13}$C{1H} NMR (100 MHz, DMSO-d$_6$): $\delta$ 177.6, 162.3, 139.8, 131.5, 125.7, 123.6, 122.9, 120.1, 119.3, 80.8, 66.5, 64.2, 63.9, 51.2, 36.4, 33.6, 24.8, 24.7, 16.5. HRMS (ESI) m/z: [M + H]$^+$ calcd. for C$_{21}$H$_{24}$N$_3$O$_2$S$^+$ 382.1584; found 382.1580.

$(S)$-7''-Methyl-5'-morpholino-2''-oxodispiro[cyclohexane-1,3'-thiophene-2',3''-indoline]-4'-carbonitrile (5jp')

Product 5jp' was obtained according to the general procedure from thioamide 1i (30 mg, 1.0 equiv, 0.12 mmol), diazo compound 2p (31 mg, 1.5 equiv, 0.18 mmol), Rh$_2$(S-NTTL)$_4$ (1.3 mg), chloroform (2 mL). The purification of the crude product by column chromatography on SiO$_2$ (DCM/EtOAc, gradient 20:5 to 20:20) afforded 5jp' as a colorless powder (72%, 34 mg, 4.1:95.9 e.r.), mp 218–219 °C, $[\alpha]_{D}^{20} = +12.0$ (C = 1.07, CHCl$_3$). The enantiomeric excess was determined by HPLC analysis on a Chiralpak AD column: 5:1 n-hexane/i-PrOH, flow rate 1 mL/min, $\lambda$ = 220, 230 nm: TR Minor = 12.33 min, TR Major = 15.82 min. The spectral data are consistent with those reported previously for the racemate 5jp.

$(S)$-7''-methyl-5'-morpholino-2''-oxodispiro[cycloheptane-1,3'-thiophene-2',3''-indoline]-4'-carbonitrile (5lp')

Product 5lp' was obtained according to the general procedure from thioamide 1l (30 mg, 1.0 equiv, 0.11 mmol), diazo compound 2p (29 mg, 1.5 equiv, 0.17 mmol), Rh$_2$(S-NTTL)$_4$ (1.2 mg), chloroform (2 mL). The purification of the crude product by column chromatography on SiO$_2$ (DCM/EtOAc, gradient 20:5 to 20:20) afforded 5lp' as a colorless powder (83%, 38 mg, 4.3:95.7 e.r.), mp 213–215 °C, $[\alpha]_{D}^{20} = +23.0$ (C = 1.27, CHCl$_3$). The enantiomeric excess was determined by HPLC analysis on a Chiralpak AD column: 5:1 n-hexane/i-PrOH, flow rate 1 mL/min, $\lambda$ = 220, 230 nm: TR Minor = 12.87 min, TR Major = 13.70 min. The spectral data are consistent with those reported previously for the racemate 5lp.
(S)-7''-Methyl-5'-morpholino-2''-oxodispiro[cyclooctane-1,3'-thiophene-2',3''-indoline]-4'-carbonitrile (5op)

Product 5op was obtained according to the general procedure from thioamide 1o (30 mg, 1.0 equiv, 0.11 mmol), diazo compound 2p (28 mg, 1.5 equiv, 0.16 mmol), Rh₂(S-NTTL)₄ (1.1 mg), chloroform (2 mL). The purification of the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 20:5 to 20:20) afforded 5op as a colorless powder (91%, 42 mg, 7.0:93.0 e.r.), mp 245–247 °C, [α]D²⁰ = +10.3 (C = 1.17, CHCl₃). The enantiomeric excess was determined by HPLC analysis on a Chiralpak AD column: 5:1 n-hexane/i-PrOH, flow rate 1 mL/min, λ = 220, 230 nm: TR Minor = 28.18 min, TR Major = 12.95 min. The spectral data are consistent with those reported previously for the racemate 5op.

(S)-5''-Methyl-5'-morpholino-2''-oxodispiro[cyclooctane-1,3'-thiophene-2',3''-indoline]-4'-carbonitrile (5ov)

Product 5ov was obtained according to the general procedure from thioamide 1o (30 mg, 1.0 equiv, 0.11 mmol), diazo compound 2v (28 mg, 1.5 equiv, 0.16 mmol), Rh₂(S-NTTL)₄ (1.1 mg), chloroform (2 mL). The purification of the crude product by column chromatography on SiO₂ (DCM/EtOAc, gradient 20:5 to 20:20) afforded 5ov as a pale-red powder (87%, 40 mg, 19:81 e.r.), mp 144–146 °C, [α]D²⁰ = −3.43 (C = 0.67, CHCl₃). The enantiomeric excess was determined by HPLC analysis on a Chiralpak AD column: 5:1 n-hexane/i-PrOH, flow rate 1 mL/min, λ = 220, 230 nm: TR Minor = 23.70 min, TR Major = 11.45 min. ¹H NMR (400 MHz, DMSO-d₆): δ 10.62 (s, 1H, NH), 7.30 (s, 1H), 7.09 (d, J = 7.8 Hz, 1H), 6.75 (d, J = 7.9 Hz, 1H), 3.68 – 3.65 (m, 4H), 3.60 – 3.49 (m, 4H), 2.35 – 2.28 (m, 4H), 2.14 – 1.93 (m, 3H), 1.5 (br. s, 5H), 1.35 – 1.27 (m, 3H), 0.85 (br. s, 1H). ¹³C{¹H} NMR (100 MHz, DMSO-d₆): δ 175.6, 162.9, 139.3, 130.5, 130.3, 119.8, 109.8, 77.8, 65.7, 64.6, 57.3, 50.7, 29.5, 29.4, 28.9, 27.5, 24.8, 22.2, 21.4, 20.8. HRMS (ESI) m/z: [M + H]⁺ calcd. for C₂₄H₃₀N₃O₂S⁺ 424.2053; found 424.2057.
Grame-scale synthesis of dihydrithiophenes 5jh

1-Acetyl-4-cyano-3-morpholino-N-phenyl-2-thiaspiro[4.5]dec-3-ene-1-carboxamide (5jh)

To an oven-dried double neck round bottom flask (100 mL), rhodium (II) pivalate dimer (0.5 mol %, 24.4 mg), thioamide 1j (1000 mg, 1.0 equiv, 3.99 mmol) and dry chloroform (10 mL) were added under an argon atmosphere. After stirring for 15 min at room temperature, a solution of diazoacetamide 2h (811.5 mg, 1.0 equiv, 3.99 mmol) in dry chloroform (20 mL) was added via syringe to the flask. Then, the reaction mixture was allowed to stir at room temperature for 2 h. Two hours later a new portion of a solution of diazoacetamide 2h (811.5 mg, 1.0 equiv, 3.99 mmol) in dry chloroform (20 mL) was added via syringe to the flask. Upon completion (14 h), chloroform was removed under reduced pressure and the product was isolated using column chromatography on SiO2 (Eluent mixture PE/EtOAc, gradient 25:0 to 25:25) afforded 5jh as a colorless powder (74%, 1258 mg), mp 198–200 °C and 6jh as a colorless powder (3%, 51 mg), mp 195–196 °C.
**X-Ray crystallographic data**

A single crystal of 3aa was obtained by crystallization via evaporation at room temperature from its ethyl acetate solution. The deposition number for 3aa at the Cambridge Crystallographic Data Centre is CCDC 2288490.

![Figure S4. X-Ray crystallographic data of 3aa. Thermal ellipsoids are shown at the 50% level.](image_url)

**Crystal Data for 3aa.** C\textsubscript{22}H\textsubscript{20}N\textsubscript{2}O\textsubscript{2}S (M =376.46 g/mol): triclinic, space group P-1 (no. 2), a = 11.9036(6) Å, b = 12.3656(5) Å, c = 13.5444(6) Å, α = 82.460(4)°, β = 80.987(4)°, γ = 79.478(4)°, V = 1925.11(16) Å\textsuperscript{3}, Z = 4, T = 295(2) K, \(\mu(\text{Mo } K\alpha) = 0.187 \text{ mm}^{-1}\), \(D_{\text{calc}} = 1.299 \text{ g/cm}^3\), 21912 reflections measured (7.214° ≤ 2θ ≤ 60.952°), 10398 unique (R\text{int} = 0.0410, R\text{sigma} = 0.0692) which were used in all calculations. The final R\text{1} was 0.0606 (I > 2\(σ(I)\)) and wR\text{2} was 0.1979. GooF 1.007. Largest diff. peak/hole 0.36/-0.40.

A single crystal of 3ad was obtained by crystallization via evaporation at room temperature from its ethyl acetate solution. The deposition number for 3ad at the Cambridge Crystallographic Data Centre is CCDC 2288496.

![Figure S5. X-Ray crystallographic data of 3ad. Thermal ellipsoids are shown at the 50% level.](image_url)
**Crystal Data for 3ad.** \( \text{C}_{20}\text{H}_{22}\text{N}_{2}\text{O}_{2}\text{S} \) (M =354.45 g/mol): orthorhombic, space group Pbc\( \alpha \) (no. 61), \( a = 9.1006(15) \) Å, \( b = 15.187(3) \) Å, \( c = 25.844(6) \) Å, \( V = 3572.0(12) \) Å\(^3\), \( Z = 8 \), \( T = 295.15 \) K, \( \mu(\text{Mo K}\alpha) = 0.197 \) mm\(^{-1}\), \( D_{\text{calc}} = 1.318 \) g/cm\(^3\), 11055 reflections measured (5.364° ≤ 2\( \Theta \) ≤ 58.934°), 4247 unique (\( R_{\text{int}} = 0.0351, R_{\text{sigma}} = 0.0456 \)) which were used in all calculations. The final \( R_1 \) was 0.0485 (I > 2σ(I)) and \( wR_2 \) was 0.1245. GooF 1.038. Largest diff. peak/hole 0.30/-0.29.

A single crystal of \( 3\text{ae} \) was obtained by crystallization via evaporation at room temperature from its ethyl acetate solution. The deposition number for \( 3\text{ae} \) at the Cambridge Crystallographic Data Centre is CCDC 2288498.

![Figure S6](image)

**Figure S6.** X-Ray crystallographic data of \( 3\text{ae} \). Thermal ellipsoids are shown at the 50% level.

**Crystal Data for 3ae.** \( \text{C}_{26}\text{H}_{27}\text{N}_{3}\text{O}_{4}\text{S}_{2} \) (M =509.62 g/mol): orthorhombic, space group Pbc\( \alpha \) (no. 61), \( a = 18.539(3) \) Å, \( b = 11.4393(16) \) Å, \( c = 24.448(4) \) Å, \( V = 5184.6(14) \) Å\(^3\), \( Z = 8 \), \( T = 295.15 \) K, \( \mu(\text{Mo K}\alpha) = 0.242 \) mm\(^{-1}\), \( D_{\text{calc}} = 1.306 \) g/cm\(^3\), 18665 reflections measured (4.504° ≤ 2\( \Theta \) ≤ 58.838°), 6274 unique (\( R_{\text{int}} = 0.0344, R_{\text{sigma}} = 0.0433 \)) which were used in all calculations. The final \( R_1 \) was 0.0579 (I > 2σ(I)) and \( wR_2 \) was 0.1450. GooF 1.034. Largest diff. peak/hole 0.28/-0.51.

A single crystal of \( 3\text{ta} \) was obtained by crystallization via evaporation at room temperature from its ethyl acetate solution. The deposition number for \( 3\text{ta} \) at the Cambridge Crystallographic Data Centre is CCDC 2288497.
**Figure S7.** X-Ray crystallographic data of 3ta. Thermal ellipsoids are shown at the 50% level.

**Crystal Data for 3ta.** \( \text{C}_{14}\text{H}_{13}\text{ClN}_{2}\text{O}_{2}\text{S} \) (M = 308.77 g/mol): monoclinic, space group \( \text{P21/c} \) (no. 14), \( a = 13.453(3) \) Å, \( b = 9.8748(18) \) Å, \( c = 11.570(3) \) Å, \( \beta = 107.97(3)^\circ \), \( V = 1462.0(6) \) Å\(^3\), \( Z = 4 \), \( T = 295(2) \) K, \( \mu(\text{Mo K}\alpha) = 0.406 \text{ mm}\(^{-1}\) \), \( \text{D}_{\text{calc}} = 1.403 \text{ g/cm}\(^3\) \), 7161 reflections measured (5.21° ≤ 2Θ ≤ 58.988°), 3480 unique (\( R_{\text{int}} = 0.0368 \), \( R_{\sigma} = 0.0491 \)) which were used in all calculations. The final \( R_1 \) was 0.0508 (I > 2σ(I)) and \( \text{wR}_2 \) was 0.1446. GooF 1.052. Largest diff. peak/hole 0.46/-0.49.

A single crystal of 4ah was obtained by crystallization via evaporation at room temperature from its mixture of methanol and acetonitrile solution. The deposition number for 4ah at the Cambridge Crystallographic Data Centre is CCDC 2288491.

**Figure S8.** X-Ray crystallographic data of 4ah. Thermal ellipsoids are shown at the 50% level.

**Crystal Data for 4ah.** \( \text{C}_{24}\text{H}_{23}\text{N}_{3}\text{O}_{3}\text{S} \) (M = 433.51 g/mol): orthorhombic, space group \( \text{Pbc}a \) (no. 61), \( a = 13.4556(12) \) Å, \( b = 16.0823(15) \) Å, \( c = 21.045(2) \) Å, \( V = 4554.0(8) \) Å\(^3\), \( Z = 8 \), \( T = 295(2) \) K, \( \mu(\text{Mo K}\alpha) = 0.172 \text{ mm}\(^{-1}\) \), \( \text{D}_{\text{calc}} = 1.265 \text{ g/cm}\(^3\) \), 14386 reflections measured (7.624° ≤ 2Θ ≤ 52.744°), 4622 unique (\( R_{\text{int}} = 0.0648 \), \( R_{\sigma} = 0.0885 \)) which were used in all calculations. The
final $R_1$ was 0.0672 ($I > 2\sigma(I)$) and $wR_2$ was 0.2266. $GooF$ 1.015. Largest diff. peak/hole 0.21/-0.24.

A single crystal of 4ai was obtained by crystallization via evaporation at room temperature from its mixture of methanol, ethyl acetate and acetonitrile solution. The deposition number for 4ai at the Cambridge Crystallographic Data Centre is CCDC 2288493.

![Figure S9. X-Ray crystallographic data of 4ai. Thermal ellipsoids are shown at the 50% level.](image)

**Crystal Data for 4ai.** C$_{32}$H$_{29}$N$_3$O$_3$S (M = 535.64 g/mol): monoclinic, space group P21/n (no. 14), $a = 13.1630(12)$ Å, $b = 11.7627(8)$ Å, $c = 18.6294(17)$ Å, $\beta = 99.090(8)^\circ$, $V = 2848.2(4)$ Å$^3$, $Z = 4$, $T = 295(2)$ K, $\mu$(MoK$\alpha$) = 0.151 mm$^{-1}$, $D_{\text{calc}} = 1.249$ g/cm$^3$, 22624 reflections measured ($7.082^\circ \leq 2\Theta \leq 60.996^\circ$), 7713 unique ($R_{\text{int}} = 0.0677$, $R_{\text{sigma}} = 0.0971$) which were used in all calculations. The final $R_1$ was 0.0670 ($I > 2\sigma(I)$) and $wR_2$ was 0.2342. $GooF$ 1.012. Largest diff. peak/hole 0.28/-0.42.

A single crystal of 4ao was obtained by crystallization via evaporation at room temperature from its methanol solution. The deposition number for 4ao at the Cambridge Crystallographic Data Centre is CCDC 2288492.

![Figure S10. X-Ray crystallographic data of 4ao. Thermal ellipsoids are shown at the 50% level.](image)
Crystal Data for 4ao. C_{17}H_{16}N_{4}O_{2}S (M =340.40 g/mol): orthorhombic, space group Pna21 (no. 33), \(a = 20.677(2) \, \text{Å}, \, b = 10.7808(7) \, \text{Å}, \, c = 15.1131(17) \, \text{Å}, \, V = 3369.0(6) \, \text{Å}^3, \, Z = 8, \, T = 295(2) \, \text{K}, \, \mu(\text{MoK\textalpha}) = 0.209 \, \text{mm}^{-1}, \, D_\text{calc} = 1.342 \, \text{g/cm}^3, \, 11968 \, \text{reflections measured (7.518° \leq 2\Theta \leq 60.962°)}, \, 6726 \, \text{unique (R_{int} = 0.0686, R_{sigma} = 0.1152) which were used in all calculations. The final R_1 was 0.0660 (I > 2\sigma(I)) and wR_2 was 0.1816. GooF 1.002. Largest diff. peak/hole 0.29/-0.34.}

A single crystal of 5in was obtained by crystallization via evaporation at room temperature from its ethyl acetate solution. The deposition number for 5in at the Cambridge Crystallographic Data Centre is CCDC 2288495.

Figure S11. X-Ray crystallographic data of 5in. Thermal ellipsoids are shown at the 50% level.

Crystal Data for 5in. C_{22}H_{24}N_{4}O_{2}S (M =408.51 g/mol): monoclinic, space group C2/c (no. 15), \(a = 19.8227(18) \, \text{Å}, \, b = 8.1430(7) \, \text{Å}, \, c = 26.372(3) \, \text{Å}, \, \beta = 102.977(10)°, \, V = 4148.2(7) \, \text{Å}^3, \, Z = 8, \, T = 295(2) \, \text{K}, \, \mu(\text{MoK\textalpha}) = 0.182 \, \text{mm}^{-1}, \, D_\text{calc} = 1.308 \, \text{g/cm}^3, \, 11495 \, \text{reflections measured (7.526° \leq 2\Theta \leq 56.564°)}, \, 4953 \, \text{unique (R_{int} = 0.0634, R_{sigma} = 0.0960) which were used in all calculations. The final R_1 was 0.0648 (I > 2\sigma(I)) and wR_2 was 0.1999. GooF 1.016. Largest diff. peak/hole 0.30/-0.30.}

A single crystal of 5hp was obtained by crystallization via evaporation at room temperature from its mixture of ethyl acetate and dichloromethane solution. The deposition number for 5hp at the Cambridge Crystallographic Data Centre is CCDC 2288489.
Figure S12. X-Ray crystallographic data of 5hp. Thermal ellipsoids are shown at the 50% level.

Crystal Data for 5hp. C_{19}H_{21}N_{3}O_{2}S (M = 355.45 g/mol): monoclinic, space group P21/n (no. 14), a = 14.247(3) Å, b = 9.0994(10) Å, c = 15.279(4) Å, β = 117.13(3)°, V = 1762.8(8) Å³, Z = 4, T = 295(2) K, μ(MoKα) = 0.201 mm⁻¹, D_{calc} = 1.339 g/cm³, 10192 reflections measured (4.700° ≤ 2Θ ≤ 62.280°), 5831 unique (R_{int} = 0.0271, R_{sigma} = 0.0497) which were used in all calculations. The final R₁ was 0.0770 (I > 2σ(I)) and wR₂ was 0.2509. Good 1.055. Largest diff. peak/hole 0.22/-0.25.

A single crystal of 6jh was obtained by crystallization via evaporation at room temperature from its ethyl acetate solution. The deposition number for 6jh at the Cambridge Crystallographic Data Centre is CCDC 2306789.

Figure S13. X-Ray crystallographic data of 6jh. Thermal ellipsoids are shown at the 50% level.

Crystal Data for 6jh. C_{23}H_{27}N_{3}O_{3}S (M = 425.54 g/mol): monoclinic, space group P2₁/c (no. 14), a = 18.9394(6) Å, b = 9.8877(3) Å, c = 11.9483(3) Å, α = 90°, β = 107.354(3)°, γ = 90°, V = 2135.67(11) Å³, Z = 4, T = 295(2) K, μ(MoKα) = 0.182 mm⁻¹, D_{calc} = 1.324 g/cm³, 9437 reflections
measured (7.378° ≤ 2Θ ≤ 62°), 4252 unique (R_{int} = 0.0407, R_{sigma} = 0.0545) which were used in all calculations. The final R_1 was 0.0510 (I > 2σ(I)) and wR_2 was 0.1397. GooF 1.011. Largest diff. peak/hole 0.29/-0.55.
References


NMR $^1$H, $^{13}$C and $^{19}$F Spectra

$^1$H NMR (400 MHz, DMSO–$d_6$) of 1a

$^{13}$C{H} NMR (100 MHz, DMSO–$d_6$) of 1a
$^1$H NMR (400 MHz, DMSO–$d_6$) of 1b

$^{13}$C{$^1$H} NMR (100 MHz, DMSO–$d_6$) of 1b
$^{1}H$ NMR (400 MHz, DMSO–$d_6$) of 1c

$^{13}C\{^1H\}$ NMR (100 MHz, DMSO–$d_6$) of 1c
$^{1}H$ NMR (400 MHz, DMSO–$d_6$) of 1d

$^{13}C\{1H\}$ NMR (100 MHz, DMSO–$d_6$) of 1d
$^1$H NMR (400 MHz, DMSO–d$_6$) of 1e

$^{13}$C{1H} NMR (100 MHz, DMSO–d$_6$) of 1e
$^1$H NMR (400 MHz, DMSO–$d_6$) of 1f

$^{13}$C{1H} NMR (100 MHz, DMSO–$d_6$) of 1f
$^1$H NMR (400 MHz, CDCl$_3$–d) of 1g

$^{13}$C{1H} NMR (100 MHz, CDCl$_3$–d) of 1g
$^1$H NMR (400 MHz, CDCl$_3$–d) of 1h

$^{13}$C{1H} NMR (100 MHz, CDCl$_3$–d) of 1h
$^1$H NMR (400 MHz, CDCl$_3$–d) of $1i$

$^{13}$C{H} NMR (100 MHz, CDCl$_3$–d) of $1i$
$^1$H NMR (400 MHz, CDCl$_3$–d) of 1j

$^{13}$C{1H} NMR (100 MHz, CDCl$_3$–d) of 1j
$^1$H NMR (400 MHz, CDCl$_3$–$d$) of 11

$^{13}$C{$_1$H} NMR (100 MHz, CDCl$_3$–$d$) of 11
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$\text{13C\{1H\} NMR (100 MHz, CDCl}_3\text{–d) of 1m}$
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$^1$H NMR (400 MHz, CDCl$_3$–$d$) of 1q

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$^1$H NMR (400 MHz, CDCl$_3$–$d$) of 1s

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$^1$H NMR (400 MHz, DMSO–$d_6$) of $1w$

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

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$^1$H NMR (400 MHz, DMSO–$d_6$) of 2p

$^{13}$C{H} NMR (100 MHz, DMSO–$d_6$) of 2p
$^1$H NMR (400 MHz, CDCl$_3$–d) of 2s
$^1$H NMR (400 MHz, CDCl$_3$–$d$) of 2t
$\text{H NMR (400 MHz, CDCl}_3$–$d$) of 2u
$^{1}$H NMR (400 MHz, DMSO–d$_6$) of 2v
$^1$H NMR (400 MHz, DMSO–d$_6$) of L1
$^1$H NMR (400 MHz, CDCl$_3$–d) of $\text{L}_2$

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$^{13}$C{^1}H NMR (100 MHz, CDCl$_3$–d) of Rh$_2$(S-DBPTTL)$_4$
$^{1}H$ NMR (400 MHz, DMSO–$d_6$) of (4RS,5SR)-3aa

$^{13}C\{^1H\}$ NMR (100 MHz, DMSO–$d_6$) of (4RS,5SR)-3aa
$^{1}$H NMR (400 MHz, CDCl$_3$–d) of (4RS,5SR)-3ac

$^{13}$C{1H} NMR (100 MHz, CDCl$_3$–d) of (4RS,5SR)-3ac
$^1$H NMR (400 MHz, DMSO–$d_6$) of (4RS,5SR)-3ba

$^{13}$C{1H} NMR (100 MHz, DMSO–$d_6$) of (4RS,5SR)-3ba
$^1$H NMR (400 MHz, DMSO–$d_6$) of (4RS,5SR)-3ca

$^{13}$C{1H} NMR (100 MHz, DMSO–$d_6$) of (4RS,5SR)-3ca
$^{1}H$ NMR (400 MHz, DMSO–$d_6$) of 3da

$^{13}C\{1H\}$ NMR (100 MHz, DMSO–$d_6$) of 3da
HSQC and HMBC spectra of 3da
$^1$H NMR (400 MHz, DMSO–d$_6$) of 3ga

$^{13}$C{1H} NMR (100 MHz, DMSO–d$_6$) of 3ga
$^1$H NMR (400 MHz, CDCl$_3$–d) of 3wa

$^{13}$C$\{}$1H$\}$ NMR (100 MHz, CDCl$_3$–d) of 3wa
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$^{13}$C{H} NMR (150 MHz, CD$_3$CN–$d_3$) of (4RS, 5RS)-3ad
$^1$H NMR (400 MHz, CDCl$_3$ – $d$) of (2RS,3SR)-3ae

$^{13}$C{1H} NMR (100 MHz, CDCl$_3$–$d$) of (2RS,3SR)-3ae
\(^1\)H NMR (400 MHz, CDCl\(_3\)-d\(_2\)) of 3ha

\(^{13}\)C\{\(1\)H\} NMR (100 MHz, CDCl\(_3\)-d\(_2\)) of 3ha
$^1$H NMR (400 MHz, CDCl$_3$–d) of 3ia

$^{13}$C{1H} NMR (100 MHz, CDCl$_3$–d) of 3ia
$^1$H NMR (400 MHz, CDCl$_3$–d) of 3ja

$^{13}$C{1H} NMR (100 MHz, CDCl$_3$–d) of 3ja
$^1$H NMR (400 MHz, CDCl$_3$–d) of 3ka

$^{13}$C{1H} NMR (100 MHz, CDCl$_3$–d) of 3ka
$^{1}$H NMR (400 MHz, CDCl$_3$–d) of 3la

$^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$–d) of 3la
$^{1}$H NMR (400 MHz, CDCl$_3$–$d$) of 3ma

$^{13}$C{$^{1}$H} NMR (100 MHz, CDCl$_3$–$d$) of 3ma
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$^{13}$C{1H} NMR (100 MHz, CDCl$_3$–d) of 3na
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$^{1}$H NMR (400 MHz, DMSO–$d_6$) of (2RS,3RS)-4‘ah

$^{13}$C{1H} NMR (100 MHz, DMSO–$d_6$) of (2RS,3RS)-4‘ah
$^1$H NMR (400 MHz, DMSO–$d_6$) of (2RS,3SR)-4ai

$^{13}$C{1H} NMR (100 MHz, DMSO–$d_6$) of (2RS,3SR)-4ai
\(^1\)H NMR (400 MHz, DMSO–d\(_6\)) of (2RS, 3RS)-4'ai

\(^{13}\)C\{\(^1\)H\} NMR (100 MHz, DMSO–d\(_6\)) of (2RS, 3RS)-4'ai
$^1$H NMR (400 MHz, DMSO–$d_6$) of (2RS,3SR)-4aj

$^{13}$C{1H} NMR (100 MHz, DMSO–$d_6$) of (2RS,3SR)-4aj
$^1$H NMR (400 MHz, DMSO–$d_6$) of (2RS,3RS)-4’aj

$^{13}$C{¹H} NMR (100 MHz, DMSO–$d_6$) of (2RS,3RS)-4’aj
$^1$H NMR (400 MHz, DMSO–$d_6$) of (2RS,3SR)-4ak

$^{13}$C\{1H\} NMR (150 MHz, DMSO–$d_6$) of (2RS,3SR)-4ak
$^1$H NMR (400 MHz, DMSO–d$_6$) of (2RS,3RS)-4’ak

$^{13}$C{1H} NMR (100 MHz, DMSO–d$_6$) of (2RS,3RS)-4’ak
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$^{19}$F NMR (376 MHz, DMSO–d$_6$) of (2RS,3SR)-4al
$^{13}$C{\textit{H}} NMR (150 MHz, DMSO–d$_6$) of (2RS,3SR)-4al
$^1$H NMR (400 MHz, DMSO–$d_6$) of (2RS,3RS-4′al)

$^{19}$F NMR (376 MHz, DMSO–$d_6$) of (2RS,3RS-4′al)
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$^{13}$C{1H} NMR (100 MHz, DMSO–$d_6$) of (2RS,3RS)-4am
$^1$H NMR (400 MHz, DMSO–d$_6$) of (2RS,3RS)-4an

$^{13}$C{1H} NMR (150 MHz, DMSO–d$_6$) of (2RS,3RS)-4an
$^{1}$H NMR (400 MHz, DMSO–$d_6$) of (2RS,3SR)-4′an

$^{13}$C{1H} NMR (100 MHz, DMSO–$d_6$) of (2RS,3SR)-4′an
$^1$H NMR (400 MHz, DMSO–$d_6$) of \((2RS,3RS)-4\)ao

$^{13}$C\{\(^1\)H\} NMR (150 MHz, DMSO–$d_6$) of \((2RS,3RS)-4\)ao

(2RS,3RS-4ao)

S150
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$^{13}$C{1H} NMR (150 MHz, DMSO–$d_6$) of (2RS,3SR)-4'ao
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$^{13}$C{H} NMR (100 MHz, CDCl$_3$–d) of 5op
$\text{H NMR (400 MHz, CDCl}_3\text{--}d\text{) of 5jq}$

$\text{C\{1H\} NMR (100 MHz, CDCl}_3\text{--}d\text{) of 5jq}$
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$^{13}$C{1H} NMR (100 MHz, CDCl$_3$–d) of 5ot
$^1$H NMR (400 MHz, CDCl$_3$–$d$) of 6ih

$^{13}$C{1H} NMR (100 MHz, CDCl$_3$–$d$) of 6ih
\[1^H \text{NMR (400 MHz, CDCl}_3\text{–d) of 6jh}\]

\[1^3C\{1H\} \text{NMR (100 MHz, CDCl}_3\text{–d) of 6jh}\]
$^1$H NMR (400 MHz, CDCl$_3$–d) of 6lh

$^{13}$C{1H} NMR (100 MHz, CDCl$_3$–d) of 6lh
$^1$H NMR (400 MHz, CDCl$_3$–d) of 6oh

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S181
$^1$H NMR (400 MHz, DMSO-$d_6$) of (S)-5ov

$^{13}$C{$^1$H} NMR (100 MHz, DMSO-$d_6$) of (S)-5ov