Supporting Information

Enantioselective Vinylogous-Mukaiyama-Dearomatisation by Anion-Binding Catalysis

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1. General Information and Materials

1H- and 13C-NMR spectra were recorded in CDCl3 or DMSO-d6 (reference signal:\[^{11}\] 1H = 7.26 ppm, 13C = 77.16 ppm for CDCl3; 1H = 2.50 ppm, 13C = 39.52 ppm for DMSO-d6) on a Bruker Advance 300,400, 500 or 600 MHz. Chemical shifts (δ) are given in ppm and spin-spin coupling constants (J) are given in Hz. X-Ray diffraction data sets for a compound 4j were collected with a Bruker D8 Venture PHOTON III diffractometer. Programs used: data collection: APEX3 V2016.1-0[^{2}] (Bruker AXS Inc., 2016); cell refinement: SAINT V8.37A (Bruker AXS Inc., 2015); data reduction: SAINT V8.37A (Bruker AXS Inc., 2015); absorption correction, SADABS V2014/7 (Bruker AXS Inc., 2014); structure solution SHELXT-2015[^{3}] (Sheldrick, G. M. Acta Cryst., 2015. A71, 3-8); structure refinement SHELXL-2015[^{4}] (Sheldrick, G. M. Acta Cryst., 2015, C71, 3-8) and graphics, XP[^{5}] (Version 5.1, Bruker AXS Inc., Madison, Wisconsin, USA, 1998). R-values are given for observed reflections, and wR2 values are given for all reflections. Analytical thin layer chromatography was performed using silica gel 60 F254 and a solution of KMnO4 or phosphomolybdic acid served as staining agent. Column chromatography was performed on silica gel 60 (0.040-0.063 mm). Preparative TLC plates were prepared using silica gel 60PF254 containing gypsum. Exact masses (HRMS) were performed using electrospray ionization techniques (ESI+) and recorded on an Agilent Q-TOF 6540 UHD or a Bruker Daltonics MicroTof spectrometer. The enantiomeric ratios were determined by supercritical fluid chromatography (SFC) on an Agilent SFC-LC 1260 series using a chiral chiralpak Daicel IG, IC, IA, OD-H or OJ-H column. Tetrasatriazoles 1a–d were synthesised according to procedures already described by our research group[^{6}] The quinazoline derivatives 2h–2l[^{7}] 2n–2q[^{8}] and 2r[^{9}] were synthesised following described procedures reported in the literature. The silyl vinylketene acetalts 3a, 3b, 3e, 3f and 3g were synthesised following described procedures reported in the literature[^{10}] while the synthesis of 3c and 3d is described in the following document. The employed solvents such as methyl-tert-butylether (MTBE), diethyl ether (Et2O), and toluene were distilled in a solvent purification system (SPS) and dried over 3 or 4 Å molecular sieve (MS).
2. Synthesis and Analytical Data of S-Methyl (E)-But-2-enethioate

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{C}==\text{C} & \quad \text{Cl} \quad \text{NaSMe} \quad \text{MeCN}, 0 \degree \text{C} \quad \text{r.t.} \\
\text{Cl} & \quad \text{S} \quad \text{MeCN} 
\end{align*}
\]

In a round-bottom flask, crotonyl chloride (3.19 mL, 30 mmol, 1.5 equiv.) was dissolved in dry MeCN. The solution was cooled to 0 °C in an ice-bath and sodium methylthioacetate (1.557 g, 20 mmol, 1 equiv.) was added portion-wise. The reaction was then warmed up to room temperature and stirred overnight. The acetonitrile was removed under reduce pressure and the crude was dissolved in diethyl ether. The organic phase was washed with water, NaHCO₃ (sat) and brine. The organic phase was dried over MgSO₄, filtered and concentrated under reduced pressure. The residue was purified by vacuum distillation using a Kugelrohr apparatus.

Observe boiling point: 42-45 °C (2.3 mbar). The product was obtained as a colourless oil (yield 61%). ¹H NMR (300 MHz, CDCl₃) δ 6.91 (dq, J = 15.5, 6.9 Hz, 1H), 6.16 (dd, J = 15.5, 1.7 Hz, 1H), 2.34 (s, 3H), 1.88 (dd, J = 6.9, 1.7 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 190.4, 140.6, 130.2, 18.0, 11.4.

3. General Procedure for the Synthesis and Analytical Data of 3c and 3d

In a flame-dry Schlenk flask, diisopropylamine (1.1 equiv., 11 mmol, 1.5 mL) was dissolved in dry THF (2 mL/mmol of ester, 20 mL) under Ar atmosphere. The reaction was cooled to -78 °C. Then, nBuLi 2.5 M (1.1 equiv., 11 mmol, 4.4 mL) was added dropwise at -78 °C. The reaction was stirred for 30 min. Subsequently, DMPU (1.2 equiv., 12 mmol, 1.45 mL) was added and some turbidity was appreciated. The reaction was stirred for another 30 min at -78 °C. After this time, the corresponding ester (or thioester) (1 equiv., 10 mmol) was added dropwise, and the reaction was stirred for 30 min observing loss of the turbidity. Then, TBSCI (1.1 equiv., 11 mmol, 1.658 g) was added in one portion. The reaction was then stirred for 2-3 h while reaching room temperature. After this time, pentane was added to the reaction and the organic phase was washed three times with cold water to remove the insoluble salts. The organic phase was dried over MgSO₄ and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and the residue is purified by vacuum distillation using a Kugelrohr apparatus.

** tert-Butyldimethyl((1-phenoxybuta-1,3-dien-1-yl)oxy)silane (3c)**

Following the general procedure, the phenyl (E)-but-2-enoate (10 mmol, 1.62 g) gave the corresponding dienolate as a colourless oil. Observed boiling point: 106 °C (1.7 mbar). Yield 34%. E/Z ratio: 4:1. ¹H NMR (500 MHz, CDCl₃) δ 7.34 (app. t, J = 7.9 Hz, 2H major), 7.31 – 7.27 (app. t, J = 7.9 Hz, 2H minor), 7.23 (app. t, J = 7.9 Hz, 1H minor), 7.14 (app. d, J = 8.0 Hz, 1H major), 7.05 (app. d, J = 7.5, 1.0 Hz, 2H major), 7.00 (app. d, J = 7.7 Hz, 2H minor), 6.56 – 6.41 (m, 1H major+1H minor), 5.03 (d, J = 10.6 Hz, 1H minor), 4.98 (dd, J = 17.1, 2.1 Hz, 1H minor), 4.81 (dd, J = 17.2, 1.9 Hz, 1H major), 4.74 (dd, J = 10.5, 2.2 Hz, 1H minor), 4.69 (dd, J = 10.5, 1.7 Hz, 1H major), 4.54 (d, J = 10.4 Hz, 1H major), 0.98 (s, 9H major), 0.81 (s, 9H minor), 0.23 (s, 6H major), 0.12 (s, 6H minor). ¹³C NMR (125 MHz, CDCl₃) δ 156.2, 154.5, 131.7, 131.5, 129.7, 129.5, 124.3, 122.9, 121.8, 119.8, 117.3, 110.8, 109.5, 95.0, 88.7, 25.8, 25.4, 18.3, -4.1, -4.8; ESI-HRMS: m/z calculated for [C₈H₇OSSi]⁺: 231.1624; found 231.1623.

** tert-Butyldimethyl((1-methylthio)buta-1,3-dien-1-yl)oxy)silane (3d)**

Following the general procedure, the S-methyl (E)-but-2-enethioate (10 mmol, 1.16 g) gave the corresponding dienolate as a yellowish oil. Observed boiling point: 88-93 °C (2.4 mbar). Yield 50%. E/Z ratio: 3:1. ¹H NMR (300 MHz, CDCl₃) δ 6.71 – 6.50 (m, 1H major+1H minor), 5.63 minor (d, J = 10.7 Hz, 1H minor), 5.43 (d, J = 10.6, 1H major), 5.01 (ddd, J = 16.9, 2.0, 0.8 Hz, 1H minor), 4.99 (ddd, J = 17.2, 2.0, 0.7 Hz, 1H major), 4.87 (ddd, J = 10.4, 2.0, 0.8 Hz, 1H minor), 4.81 (ddd, J = 10.3, 2.0, 0.8 Hz, 1H major), 2.27 (s, 3H major), 2.24 (s, 3H minor), 0.99 (s, 9H major), 0.97 (s, 9H minor), 0.24 (s, 6H major+6H minor). ¹³C NMR (75 MHz, CDCl₃) δ 150.0, 150.0, 133.4, 131.0, 114.0, 112.8, 111.7, 111.1, 77.6, 77.2, 76.7, 25.9, 25.8, 18.4, 15.8, 14.1, -4.1, -4.5; ESI-HRMS: m/z calculated for [C₉H₈OSSi]⁺: 231.1239; found 231.1240.
4. Reaction conditions screening for the different N- and O-heteroarenes

Employed H-donor catalysts:

Table S1: Screening of the vinylogous addition reaction with quinazoline

| Entry | Catalyst (mol%) | Solvent | Conc. | T (°C) | Yield (%) | e.r.| [a] |
|-------|----------------|---------|-------|-------|----------|----|-----|
| 1     | 1a (10)        | MTBE    | 0.1 M | -78   | 69       | 84:16 |
| 2     | 1b (10)        | MTBE    | 0.1 M | -78   | 69       | 82:18 |
| 3     | 1c (10)        | MTBE    | 0.1 M | -78   | 46       | 77:23 |
| 4     | 1d (10)        | MTBE    | 0.1 M | -78   | 58       | 75:25 |
| 5     | 1e (10)        | MTBE    | 0.1 M | -78   | 48       | 52:48 |
| 6     | 1f (10)        | MTBE    | 0.1 M | -78   | 50       | 51:49 |
| 7     | 1a (15)        | MTBE    | 0.1 M | -78   | 75       | 82:18 |
| 8     | 1a (5)         | MTBE    | 0.1 M | -78   | 70       | 86:14 |
| 9     | 1a (3)         | MTBE    | 0.1 M | -78   | 73       | 90:10 |
| 10    | 1a (1)         | MTBE    | 0.1 M | -78   | 63       | 88:12 |
| 11    | 1a (3)         | Et₂O    | 0.1 M | -78   | 54       | 87:13 |
| 12    | 1a (3)         | C₆F₆    | 0.1 M | 6     | 35       | 54:46 |
| 13    | 1a (3)         | Et₂O:C₆F₆ (3:1) | 0.1 M | -30   | 66       | 69:31 |
| 14    | 1d (3)         | Et₂O:C₆F₆ (3:1) | 0.1 M | -30   | 70       | 70:30 |
| 15    | 1a (3)         | Toluene | 0.1 M | -78   | 57       | 95:5:4:5 |
| 16    | 1a (1)         | Toluene | 0.1 M | -78   | 71       | 93:7 |
| 17    | 1a (3)         | Toluene | 0.1 M | -78   | 36[b]   | 97:5:3:5 |
| 18    | 1a (3)         | Toluene | 0.2 M | -78   | 81[b]   | 96:4 |
| 19    | 1a (3)         | Toluene | 0.2 M | -78   | 83[b]   | 96:4 |

Conditions: i) Quinazoline (0.1 mmol, 1 equiv.) and TrocCl (1 equiv.) in the appropriate solvent at 0 °C, 30 min; ii) at the corresponding temperature, catalyst 1 (10 mol%) and 3a (2 equiv.) were added and the reaction stirred for 18 h. [a] Isolated yield after column chromatography. [b] E.r. determined by chiral SFC. [c] 0.5 mmol scale reaction. [d] 1.0 mmol scale reaction.
Table S2: Screening of the reaction with quinoline

| Entry | Catalyst | Dienolate 3 | Solvent | T (°C) | Yield (%) | e.r.\[^{[a]}\] |
|-------|----------|-------------|---------|--------|-----------|-----------|
| 1     | 1a       | OMe        | EtO     | -78    | 56        | 76:24     |
| 2     | 1b       | 3a         | EtO     | -78    | 49        | 77:23     |
| 3     | 1c       | 3a         | EtO     | -78    | 47        | 60:20     |
| 4     | 1d       | 3a         | EtO     | -78    | 53        | 80:20     |
| 5     | 1e       | 3a         | EtO     | -78    | 16        | 45:55     |
| 6     | 1f       | 3a         | EtO     | -78    | 76        | 54:46     |
| 7     | 1g       | 3a         | EtO     | -78    | 11        | 46:54     |
| 8     | 1d       | 3a         | toluene | -78    | 53        | 65:35     |
| 9     | 1d       | 3a         | C\(_6\)F\(_6\) | 6     | n.d.      | 75:25     |
| 10    | 1d       | 3a         | EtO:C\(_6\)F\(_6\) (3:1) | -30 | 81        | 82:18     |
| 11    | 1d       | 3a         | EtO:C\(_6\)F\(_6\) (3:1) \[^{[b]}\] | -30 | 86        | 76:24     |
| 12    | 1d\[^{[d]}\] | 3a         | EtO:C\(_6\)F\(_6\) (3:1) | -30 | 65        | 78:22     |
| 13    | 1d       | 3a         | EtO:C\(_6\)F\(_6\) (3:1) + 5 mol% H\(_2\)O | -30 | 58        | 82:18     |
| 14    | 1d       | OTIPS\[^{[c]}\] | EtO:C\(_6\)F\(_6\) (3:1) | -30 | 86        | 75:25     |
| 15    | 1d       | OTBS\[^{[c]}\] | EtO:C\(_6\)F\(_6\) (3:1) | -30 | n.d.      | 78:22     |
| 16    | 1d       | OTBS\[^{[c]}\] | EtO:C\(_6\)F\(_6\) (3:1) | -30 | 80        | 84:16     |
| 17    | 1d       | OTBS\[^{[c]}\] | EtO:C\(_6\)F\(_6\) (3:1) | -30 | 32        | 50:50     |

Conditions: i) Quinoline (0.1 mmol, 1 equiv.) and TrocCl (1 equiv.) in the appropriate solvent (0.1 M) at 0 °C, 30 min; ii) at the corresponding temperature, catalyst 1 (10 mol%) and 3 (2 equiv.) were added and the reaction stirred for 18 h.\[^{[a]}\] Isolated yield after column chromatography.\[^{[b]}\] E.r. determined by chiral SFC.\[^{[c]}\] 0.3 M concentration.\[^{[d]}\] 5 mol% of 1d was used.

Table S3: Screening of the reaction with picoline

| Entry | Catalyst (mol%) | Solvent | T (°C) | Yield (%)\[^{[a]}\] | e.r.\[^{[b]}\] |
|-------|-----------------|---------|--------|---------------------|-----------|
| 1     | OMe-TetraTri    | EtO     | -78    | 39                  | 55:45     |
| 2     | CF\(_3\)-TetraTri isomer | EtO | -78    | 47                  | 56:44     |
| 3     | CF\(_3\)-TetraTri isomer | toluene | -78    | 30                  | 56:44     |
| 4     | CF\(_3\)-TetraTri isomer | EtO:C\(_6\)F\(_6\) 2:1 | -30 | 41                  | 68:32     |
| 5     | CF\(_3\)-TetraTri isomer | C\(_6\)F\(_6\) | 6       | 46                  | 70:30     |
| 6     | –                | C\(_6\)F\(_6\) | –      | –                   | –         |

Conditions: i) Picoline (0.1 mmol, 1 equiv.) and TrocCl (1 equiv.) in the appropriate solvent (0.1 M) at 0 °C, 30 min; ii) at the corresponding temperature, catalyst 1 (10 mol%) and 3a (2 equiv.) were added and the reaction stirred for 18 h.\[^{[a]}\] Isolated yield after column chromatography.\[^{[b]}\] E.r. determined by chiral SFC.
Table S4: Screening of the reaction with 4-chromonenone

| Entry | Catalyst (mol%) | Solvent | T (°C) | Yield [%] | e.r.[c] |
|-------|-----------------|---------|--------|-----------|--------|
| 1     | –               | EtO/CHF (2:1)[d] | –30    | 69        | 50-50  |
| 2     | 1d (10)         | EtO/CHF (2:1)[d] | –30    | 65        | 68-32  |
| 3     | 1d (10)         | CHF    | 6      | 58        | 54-46  |
| 4     | 1a (10)         | toluene | –78    | 70        | 79-21  |
| 5     | 1a (5)          | toluene | –78    | 66        | 79-21  |
| 6     | 1a (2)          | toluene | –78    | 46        | 78-22  |
| 7     | 1a (5)          | toluene [b] | –78    | n.d.    | 76-24  |
| 8     | 1a (5)          | EtO    | –78    | 61        | 65-35  |
| 9     | 1c (5)          | toluene | –78    | 77        | 61-39  |

Conditions: i) Chromonenone (0.1 mmol, 1 equiv.), TBSOTf (1.1 equiv.), collidine (0.3 equiv.) and catalyst 1 in the appropriate solvent (0.25 M at 60 °C, 1 h); ii) at the corresponding temperature, 3a (2 equiv.) was added and the reaction stirred for 18 h. [a] Isolated yield after column chromatography. [b] E.r. determined by chiral SFC. [c] 0.1 M solution. [d] 0.5 M solution.

5. General Procedures for the Anion-Binding Catalysed Vinylogous-Mukaiyama Dearomatisation Reaction

General procedure A: Reaction with quinazoline derivatives

In a flame-dried 5 mL Schlenk pressure tube, the quinazoline derivative 2 (0.10 mmol, 1.0 equiv.) was dissolved in anhydrous toluene (1 mL) and cooled to 0 °C. 2,2,2-Trichloroethoxy carbonyl chloride (14 µL, 0.10 mmol, 1.0 equiv.) was added and the reaction was stirred at 0 °C for 30 min. Subsequently, catalyst 1a (3.36 mg, 3.00 µmol, 3 mol%) was added and the reaction was cooled to –78 °C. Dienolate 3 (0.20 mmol, 2.0 equiv.) was added and the reaction was stirred at –78 °C overnight. The solvent was then removed under reduced pressure and the desired product was obtained after purification by flash column chromatography on silica gel using n-pentane/EtOAc.

The racemic versions were prepared without catalyst, following the general procedure described above. Both possible regioisomers (C-2 and C-4 substitution) were formed in the racemic reactions. In some cases, the C-2 regioisomer could not be completely separated from the C-4 isomer and appear in the SFC chromatograms.

General procedure B: Reaction with quinoline derivatives

In a flame-dry Schlenk flask, the quinoline derivative (0.10 mmol, 1.0 equiv.) was dissolved in a 3:1 mixture of anhydrous EtO/CHF (1 mL) and cooled to 0 °C. TrocCl (14 µL, 0.10 mmol, 1.0 equiv.) was added and the reaction was stirred at 0 °C for 30 min. Subsequently, catalyst 1d (10.6 mg, 0.10 mmol, 10 mol%) was added and the reaction cooled to –30 °C. Then, dienolate 3 (0.2 mmol, 2 equiv.) was added and the reaction was stirred at –30 °C overnight. The solvent was then removed under reduced pressure and the crude was purified by flash column chromatography on silica gel using n-pentane or cyclohexane/EtOAc.

6. Analytical Data for 4a–4s

(R,E)-2,2,2-Trichloroethyl 4-(4-methoxy-4-oxobut-2-en-1-yl)quinazoline-3(4H)-carboxylate (4a)

According to the general procedure A, the reaction of quinazoline (2a) (13.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3a (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pentane/EtOAc 10:1) the desired product 4a (23.1 mg, 0.057 mmol, 57%) as a white solid. The enantiomeric ratio was determined as 95.5:4.5 e.r. by chiral SFC (Chiralcel IG, CH3OH/MeOH (98:2 → 65:35), 2.0 mL/min, (λ = 290 nm); fR (major): 14.1 min, fR (minor): 15.1 min). 1H NMR (500 MHz, CDCl3, 90 °C, DMSO-d6): δ = 7.96 (s, 1H), 7.36–7.32 (m, 1H), 7.30–7.26 (m, 2H), 7.25 (d, 3J = 7.1 Hz, 1H), 6.70 (dt, 3J = 15.3 Hz, 3J = 7.6 Hz, 1H), 5.78 (d, 3J = 15.5 Hz, 1H), 5.48 (t, 3J = 5.7 Hz, 1H), 5.08 (d, 3J = 12.2 Hz, 1H), 5.04 (d, 3J = 12.2 Hz, 1H), 3.63 (s, 3H), 2.74–2.67 (m, 1H), 2.63–2.57 (m, 1H) ppm; 13C NMR (125 MHz, CDCl3, 90 °C, DMSO-d6): δ = 164.9, 150.4, 141.9, 140.0, 138.5, 128.3, 126.9, 125.9, 125.1, 124.9, 124.0, 94.5, 74.8, 54.2, 52.1, 50.6 ppm; ESI-HRMS: m/z calculated for [C19H18Cl2N2O4]+: 405.0170; found 405.0169.

The same reaction with the TIPS-dienolate 3a’ provided the product 4a in 96.4 e.r. (26.5 mg, 0.065 mmol, 65%).

The reaction with 3a’ was also successfully scaled up to 1.0 mmol, leading to 4a in 96:4 e.r. (334.7 mg, 0.825 mmol, 83%).
2.2.2-Trichloroethyl (E)-2-(4-methoxy-4-oxobut-2-en-1-yl)quinazoline-1(2H)-carboxylate (rac-4a')

According to the general procedure A without catalyst for the preparation of the racemic sample, the reaction of quinazoline (2a) (26.0 mg, 0.200 mmol, 1.0 equiv.) with dienolate 3a (94.2 μL, 0.400 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 10:1) the desired product rac-4a (25.3 mg, 0.062 mmol, 31%) and its regioisomer rac-4a' (14.5 mg, 0.036 mmol, 18%) as white solids. The separation of the enantiomers was conducted by chiral SFC (Chiralcel IG, CO₂/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm): 4a' tr (1): 12.4 min, tr (2): 14.2 min; 4a tr (1): 17.7 min, tr (2): 18.2 min).

rac-4a': 'H NMR (500 MHz, 90 °C, DMSO-d₆): δ = 7.95 (s, 1H), 7.36 (td, J = 7.6, 1.4 Hz, 1H), 7.25 (t, J = 7.5 Hz, 2H), 7.10 (d, J = 7.5 Hz, 1H), 5.76 (d, J = 5.0 Hz, 1H), 5.59 (dt, J = 17.6, 9.9 Hz, 1H), 5.14 – 5.04 (m, 4H), 3.67 (s, 3H), 3.50 (dd, J = 9.7, 5.0 Hz, 1H) ppm; 'C NMR (125 MHz, 90 °C, DMSO-d₆): δ = 169.4, 150.2, 140.4, 139.0, 130.0, 128.8, 126.8, 126.4, 125.1, 121.8, 120.7, 94.5, 74.9, 55.1, 54.4, 51.5 ppm; ESI-HRMS: m/z calculated for [C₁₆H₁₄Cl₃N₂O₄Na]+: 426.9990; found 426.9988.

Chiral-phase SFC: Chiralcel IG, CO₂/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm)

Racemic:

![Graph](image1.png)

Mixture of regioisomers rac-4a and rac-4a':

![Graph](image2.png)

Enantioselective:

![Graph](image3.png)

With OTBS-dienolate 3a

![Graph](image4.png)
COSY-spectrum of 4a: measurement in MeCN-d$_3$ @ 25 °C (instead of DMSO-d$_6$ @ 90 °C)

1D-NOESY-spectrum of 4a: saturation of peak @ 5.48 ppm (H$^\beta$)
(R,E)-2,2,2-Trichloroethyl 4-(4-(tert-butoxy)-4-oxobut-2-en-1-yl)quinazoline-3(4H)-carboxylate (4b)

According to the general procedure A, the reaction of quinazoline (2a) (13.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3b (60.3 μL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 5:1) the desired product 4b (36.6 mg, 0.082 mmol, 82%) as a colourless viscous liquid. The enantiomeric ratio was determined as 96:4 e.r. by chiral SFC (Daicel IC, CO₂/MeOH (90:10), 2.0 mL/min, (λ = 290 nm); tr (major): 7.5 min, tr (minor): 9.8 min).

**1H NMR** (500 MHz, 363 K, DMSO-d₆): δ = 7.95 (s, 1H), 7.38–7.30 (m, 1H), 7.30–7.23 (m, 3H), 6.60 (dt, 3Jtrans = 15.4 Hz, 3J = 7.2 Hz, 1H), 5.67 (t, 3Jtrans = 15.4 Hz, 1H), 5.46 (t, 3J = 5.7 Hz, 1H), 5.09 (d, 2J = 12.2 Hz, 1H), 5.02 (d, 2J = 12.2 Hz, 1H), 2.66 (dt, 2J = 13.9 Hz, 3J = 7.2 Hz, 1H), 2.55 (dt, 2J = 13.9 Hz, 3J = 7.2 Hz, 1H), 1.41 (s, 9H) ppm;

**13C NMR** (125 MHz, 90 °C, DMSO-d₆): δ = 163.9, 150.4, 140.7, 139.9, 138.5, 128.3, 126.9, 126.1, 125.9, 125.1, 125.0, 94.5, 79.3, 74.8, 52.2, 38.8, 27.4 ppm;

**ESI-HRMS:** m/z calculated for [C₂₁H₁₇Cl₃N₂O₄Na]⁺: 469.0465; found 469.0463.

**Chiral-phase SFC:** Daicel IC, CO₂/MeOH (90:10) 2.0 mL/min, (λ= 290 nm)

**Racemic:**

![Racemic SFC Peak](image)

**Enantioselective:**

![Enantioselective SFC Peak](image)
(R,E)-2,2,2-Trichloroethyl 4-(4-oxo-4-phenoxybut-2-en-1-yl)quinazoline-3(4H)-carboxylate (4c)

According to the general procedure A, the reaction of quinazoline (2a) (13.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3c (57.0 μL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 5:1) the desired product 4c (30.3 mg, 0.065 mmol, 65%) as a colourless viscous liquid. The enantiomeric ratio was determined as 94:6 e.r. by chiral SFC (Chiralcel OJ-H, CO₂/MeOH (80:20), 2.0 mL/min, (λ = 290 nm): tr (major): 10.1 min, tr (minor): 10.9 min). ¹H NMR (500 MHz, 90 °C, DMSO-d₆): δ = 8.00 (s, 1H), 7.41 (t, ³J = 7.8 Hz, 3H), 7.36 (td, J = 7.2 Hz, 2.4 Hz, 1H), 7.32 (d, J = 2.4 Hz, 1H), 7.27 (dt, J = 14.2 Hz, ³J = 7.5 Hz, 2H), 7.10 (d, ³J = 7.8 Hz, 2H), 6.93 (dt, ³Jtrans = 15.5 Hz, ²J = 7.0 Hz, 1H), 6.01 (d, ³Jtrans = 15.5 Hz, 1H), 5.54 (t, ³J = 5.8 Hz, 1H), 5.11 (d, ³J = 12.2 Hz, 1H), 5.06 (d, ³J = 12.1 Hz, 1H), 2.79 (dt, ²J = 13.9 Hz, ³J = 7.0 Hz, 1H), 2.70 (dt, ²J = 13.9 Hz, ³J = 7.0 Hz, 1H) ppm; ¹³C NMR (125 MHz, 90 °C, DMSO-d₆): δ = 163.0, 150.4, 150.1, 144.4, 140.0, 138.5, 128.9, 128.4, 127.0, 126.0, 125.2, 125.1, 124.9, 123.4, 121.0, 94.6, 74.8, 52.1, 40.1 ppm; ESI-HRMS: m/z calculated for [C₂₁H₁₇Cl₃N₂O₄Na⁺]: 489.0152; found 489.0145.

Chiral-phase SFC: Chiralcel OJ-H, CO₂/MeOH (80:20) 2.0 mL/min, (λ = 290 nm)

Racemic:

Enantioselective:
(R,E)-2,2,2-trichloroethyl 4-(4-(methylthio)-4-oxobut-2-en-1-yl)quinazoline-3(4H)-carboxylate (4d)

According to the general procedure A, the reaction of quinazoline (2a) (13.0 mg, 0.100 mmol, 1.0 equiv.) with thioester dienolate 3d (54.2 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 5:1) the desired product 4d (27.0 mg, 0.064 mmol, 64%) as a colourless oil. The enantiomeric ratio was determined as 82:18 e.r. by chiral SFC (Chiralcel IC, CO2/MeOH (90:10), 2.0 ml/min, (λ = 290 nm); tR(m): 8.0 min, tR(major): 8.8 min). 1H NMR (500 MHz, CD3CN): δ = 7.98 (s, 1H), 7.34 (td, 3J = 7.5 Hz, 4J = 1.6 Hz, 1H), 7.30−7.24 (m, 2H), 7.19 (d, 3J = 7.1 Hz, 1H), 6.67 (dt, 3Jtrans = 15.5 Hz, 3J = 7.8 Hz, 1H), 6.06 (dt, 3Jtrans = 15.4 Hz, 3J = 1.3 Hz, 1H), 5.49 (l, 3J = 5.6 Hz, 1H), 5.00 (s, 2H), 2.68 (brs, 1H), 2.57 (brs, 1H), 2.28 (brs, 2H) ppm; 13C NMR (125 MHz, 90 °C, DMSO-d6): δ = 189.4, 151.3, 140.9, 139.0, 132.1, 129.3, 127.9, 126.9, 126.1, 125.7, 95.5, 75.7, 53.0, 39.8, 11.2 ppm; ESI-HRMS: m/z calculated for [C21H17Cl3N3O3NaS]+: 422.9912; found 422.9903.

Chiral-phase SFC: Chiralcel IC, CO2/MeOH 90:10, 2.0 ml/min, (λ = 290 nm)

Racemic:

Enantioselective:
According to the general procedure A, the reaction of quinazoline (2a) (13.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3e (51.9 μL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 5:1) the desired product 4e (24.7 mg, 0.059 mmol, 59%) as a colourless viscous liquid. The enantiomeric ratio was determined as 90:10 e.r. by chiral SFC (Chiralcel OD-H, CO₂/MeOH (90:10), 2.0 mL/min, (λ = 290 nm): tr (minor): 5.0 min, tr (major): 5.8 min).

**1H NMR** (500 MHz, 90 °C, DMSO-d₆): 7.97 (s, 1H), 7.34 (t, 3J = 7.4 Hz, 1H), 7.26 (t, 3J = 7.4 Hz, 2H), 7.21 (d, 3J = 7.4 Hz, 1H), 5.49–5.44 (m, 2H), 5.08 (d, 2J = 12.2 Hz, 1H), 5.01 (d, 2J = 12.2 Hz, 1H), 3.59 (s, 3H), 2.55–2.50 (m, 1H), 2.09 (s, 3H) ppm; **13C NMR** (125 MHz, 90 °C, DMSO-d₆): δ = 165.1, 152.8, 150.3, 139.9, 138.4, 128.3, 126.75, 125.9, 125.2, 125.0, 118.6, 94.5, 74.8, 51.7, 50.0, 46.5, 18.5 ppm; **ESI-HRMS**: m/z calculated for [C₁₇H₁₇Cl₃N₂O₄Na]⁺: 441.0146; found 441.0142.

**Chiral-phase SFC**: Chiralcel OD-H, CO₂/MeOH (90:10) 2.0 mL/min, (λ= 290 nm)

**Racemic**:

![Racemic SFC](image)

**Enantioselective**:

![Enantioselective SFC](image)
(R,E)-2,2,2-Trichloroethyl 4-(4-methoxy-3-methyl-4-oxobut-2-en-1-yl)quinazoline-3(4H)-carboxylate (4f)

According to the general procedure A, the reaction of quinazoline (2a) (13.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3f (53.1 μL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 5:1) the desired product 4f (16.2 mg, 0.039 mmol, 39%) as a colourless viscous liquid. The enantiomeric ratio was determined as 78:22 e.r. by chiral SFC (Chiralcel OD-H, CO2/MeOH (92:8), 2.0 mL/min, (λ = 290 nm): tr (minor): 7.1 min, tr (major): 8.1 min). 1H NMR (500 MHz, 90 °C, DMSO-d6): δ = 7.96 (s, 1H), 7.36–7.32 (m, 1H), 7.28–7.23 (m, 3H), 6.57 (t, J = 7.6 Hz, 1H), 5.45 (t, J = 6.2 Hz, 1H), 5.08 (d, J = 12.2 Hz, 1H), 5.05 (d, J = 12.2 Hz, 1H), 3.65 (s, 3H), 2.69 (dt, J = 14.3 Hz, J = 7.6 Hz, 1H), 2.59 (dt, J = 14.3 Hz, J = 6.2 Hz, 1H), 1.59 (s, 3H) ppm; 13C NMR (125 MHz, 90 °C, DMSO-d6): δ = 166.6, 150.4, 139.9, 138.5, 134.3, 130.2, 128.2, 126.8, 125.9, 125.0, 124.9, 94.5, 74.8, 52.0, 51.0, 35.2, 11.5 ppm; ESI-HRMS: m/z calculated for [C17H17Cl3N2O4Na]+: 441.0146; found 441.0146.

Chiral-phase SFC: Chiralcel OD-H, CO2/MeOH (92:8) 2.0 mL/min, (λ= 290 nm)

Racemic:

Enantioselective:
(R,E)-2,2,2-Trichloroethyl 4-(5-methoxy-5-oxopent-3-en-2-yl)quinazoline-3(4H)-carboxylate (4g)

According to the general procedure A, the reaction of quinazoline (2a) (13.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3g (49.7 µL, 0.200 mmol, 2.0 equiv.) led to the desired product 4g as a mixture of two diastereomers (d.r.: 6/1, 77% combined NMR yield). The major isomer (26.8 mg, 0.064 mmol, 64%) was isolated after flash column chromatography (n-pent/EtOAc 10:1) as a colourless viscous liquid. The enantiomeric ratio of the major product 4g was determined as 97.5:2.5 e.r. by chiral SFC (Chiralcel OD-H, CO₂/MeOH (92:8), 2.0 mL/min, (λ = 290 nm): tr (minor): 12.1 min, tr (major): 15.2 min).

^1H NMR (500 MHz, 90 °C, DMSO-d₆): δ = 7.98 (s, 1H), 7.39 – 7.35 (m, 1H), 7.30 – 7.23 (m, 3H), 6.61 (dd, Jtrans = 15.6 Hz, J = 8.5 Hz, 1H), 5.72 (d, Jtrans = 15.6 Hz, 1H), 5.33 (d, J = 4.6 Hz, 1H), 5.09 (d, J = 12.2 Hz, 2H), 5.05 (d, J = 12.2 Hz, 2H), 3.62 (s, 3H), 2.86 – 2.77 (m, 1H).

^13C NMR (125 MHz, 90 °C, DMSO-d₆): δ = 165.1, 150.5, 147.5, 140.5, 139.2, 128.5, 126.9, 126.6, 125.0, 122.6, 121.7, 94.6, 74.8, 56.6, 50.6, 42.6, 14.5 ppm; ESI-HRMS: m/z calculated for [C₁₇H₁₇Cl₃N₂O₄Na]⁺: 441.0146; found 441.0146.

Chiral-phase SFC: Chiralcel OD-H, CO₂/MeOH (92:8) 2.0 mL/min, (λ = 290 nm)

Racemic:

Enantioselective:
(R,E)-2,2,2-Trichloroethyl 4-(4-methoxy-4-oxobut-2-en-1-yl)-7-methylquinazoline-3(4H)-carboxylate (4h)

According to the general procedure A, the reaction of 7-methylquinazoline (2h) (14.4 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3a (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 4:1) the desired product 4h (27.2 mg, 0.065 mmol, 65%) as a white solid. The enantiomeric ratio was determined as 95.5:4.5 e.r. by chiral SFC (Chiralcel IG, CO₂/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 290 nm): tr (major): 14.2 min, tr (minor): 16.4 min.).

\[ {^1}H \text{ NMR} \ (500 MHz, 90 °C, DMSO-d₆): \delta = 7.94 \ (s, 1H), 7.14 \ (d, ^3J = 7.5 Hz, 1H), 7.09 \ (d, ^3J = 8.8 Hz, 2H), 6.69 \ (dt, ^3J_{trans} = 15.4 Hz, ^3J = 7.6 Hz, 1H), 5.79 \ (d, ^3J_{trans} = 15.6 Hz, 1H), 5.43 \ (t, ^3J = 5.6 Hz, 1H), 5.08 \ (d, ^2J = 12.2 Hz, 1H), 5.04 \ (d, ^2J = 12.2 Hz, 1H), 3.63 \ (s, 3H), 2.68 \ (dt, ^2J = 13.8 Hz, ^3J = 7.0 Hz, 1H), 2.58 \ (dt, ^2J = 14.1 Hz, ^3J = 6.5 Hz, 1H), 2.32 \ (s, 3H) \text{ ppm; } {^{13}}\text{C NMR} \ (125 MHz, 90 °C, DMSO-d₆): \delta = 164.9, 150.4, 142.0, 139.9, 138.3, 137.8, 127.6, 125.7, 125.6, 123.9, 121.9, 94.5, 74.8, 52.0, 50.6, 39.0, 20.0 \text{ ppm; ESI-HRMS: } m/z \text{ calculated for } [C_{17}H_{17}N_{2}O_{4}Cl_{3}Na]^+: 441.0146; \text{ found 441.0144.}

Chiral-phase SFC: Chiralcel IG, CO₂/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm)

Racemic:

Enantioselective:
(R,E)-2,2,2-Trichloroethyl 4-(4-methoxy-4-oxobut-2-en-1-yl)-7-phenylquinazoline-3(4H)-carboxylate (4i)

According to the general procedure A, the reaction of 7-phenylquinazoline (2i) (20.6 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3a (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 4:1) the desired product 4i (46.3 mg, 0.096 mmol, 96%) as a slightly yellow solid. The enantiomeric ratio was determined as 94:6 e.r. by chiral SFC (Chiralcel IG, CO₂/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 280 nm): tᵣ (major): 13.6 min, tᵣ (minor): 15.3 min).

**¹H NMR** (500 MHz, 90 °C, DMSO-d₆): δ = 8.02 (s, 1H), 7.68 (d, 3J = 7.7 Hz, 2H), 7.58 (dd, 3J = 7.9 Hz, 4J = 2.0 Hz, 1H), 7.52 (d, 4J = 1.9 Hz, 1H), 7.47 (t, 3J = 7.6 Hz, 2H), 7.38 (td, 3J = 7.8 Hz, 4J = 1.9 Hz, 2H), 6.75 (dt, 3J = 15.4 Hz, 5J = 7.6 Hz, 1H), 5.83 (d, 4J = 15.5 Hz, 1H), 5.53 (t, 3J = 5.7 Hz, 1H), 5.10 (d, 4J = 12.2 Hz, 1H), 5.06 (d, 3J = 12.1 Hz, 1H), 3.63 ppm; **¹³C NMR** (125 MHz, 90 °C, DMSO-d₆): δ = 165.0, 150.4, 142.0, 140.6, 140.4, 139.0, 138.8, 128.4, 127.2, 126.5, 126.1, 125.2, 124.0, 124.0, 123.1, 94.5, 74.8, 52.0, 50.6, 38.9 ppm; **ESI-HRMS**: m/z calculated for [C₂₂H₁₉N₂O₄Cl₃Na]⁺: 503.0303; found 503.0302.

**Chiral-phase SFC**: Chiralcel IG, CO₂/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 280 nm)

**Racemic**:

**Enantioselective**:

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S15
(R,E)-2,2,2-Trichloroethyl 4-(4-methoxy-4-oxobut-2-en-1-yl)-7-(4-methoxyphenyl)-quinazoline-3(4H)-carboxylate (4j)

According to the general procedure A, the reaction of 7-(4-methoxyphenyl)quinazoline (2j) (23.6 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3a (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 2:1) the desired product 4j (54.1 mg, 0.99 mmol, 99%) as a slightly yellow solid. The enantiomeric ratio was determined as 95:5 e.r. by chiral SFC (Chiralcel IC, CO2/MeOH (98.2 → 65:35), 2.0 ml/min, (λ = 254 nm): tr (major): 16.7 min, tr (minor): 19.5 min).

**1H NMR** (500 MHz, 90 °C, DMSO-d6): δ = 8.01 (s, 1H), 7.64–7.60 (m, 2H), 7.52 (dd, 3J = 7.9 Hz, 4J = 1.9 Hz, 1H), 7.47 (d, 4J = 1.7 Hz, 1H), 7.32 (d, 3J = 7.9 Hz, 1H), 7.03 (d, 3J = 8.7 Hz, 2H), 6.74 (dt, 3Jtrans = 15.4 Hz, 3J = 7.6 Hz, 1H), 5.83 (dd, 3Jtrans = 15.6 Hz, 1H), 5.51 (t, 3J = 5.7 Hz, 1H), 5.09 (d, 3J = 12.2 Hz, 1H), 5.05 (d, 4J = 12.1 Hz, 1H), 3.82 (s, 3H), 3.63 (s, 3H), 2.74 (dt, 2J = 13.8 Hz, 3J = 6.8 Hz, 1H), 2.64 (dt, 2J = 13.8 Hz, 3J = 6.5 Hz, 1H) ppm; **13C NMR** (125 MHz, 90 °C, DMSO-d6): δ = 165.0, 158.9, 150.4, 142.0, 140.3, 138.9, 131.3, 127.2, 126.4, 124.7, 124.0, 123.2, 122.7, 114.1, 94.5, 74.8, 54.9, 52.0, 50.6, 39.0 ppm; **ESI-HRMS**: m/z calculated for [C23H21N2O5Cl3Na]+: 533.0408; found 533.0411.

**Chiral-phase SFC**: Chiralcel IC, CO2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 254 nm)

**Racemic**:

**Enantioselective**:

Chiralcel IC, CO2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 254 nm)
(R,E)-2,2,2-Trichloroethyl 7-(4-fluorophenyl)-4-(4-methoxy-4-oxobut-2-en-1-yl)-quinazoline-3(4H)-carboxylate (4k)

According to the general procedure A, the reaction of 7-(4-fluorophenyl)quinazoline (2k) (22.4 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3a (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 3:1) the desired product 4k (22.1 mg, 0.044 mmol, 44%) as a white solid. The enantiomeric ratio was determined as 96:4 e.r. by chiral SFC (Chiralcel IC, CO\textsubscript{2}/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 254 nm); tr (major): 12.9 min, tr (minor): 14.1 min. \textsuperscript{1}H NMR (500 MHz, 90 °C, DMSO-\textit{d}\textsubscript{6}): δ = 8.01 (s, 1H), 7.74–7.70 (m, 2H), 7.55 (dd, \textit{\textit{J}} = 7.9 Hz, \textit{\textit{J}} = 1.9 Hz, 1H), 7.50 (d, \textit{\textit{J}} = 1.7 Hz, 1H), 7.36 (d, \textit{\textit{J}} = 7.9 Hz, 1H), 7.29–7.23 (m, 2H), 6.74 (dt, \textit{\textit{J}} = 15.3 Hz, \textit{\textit{J}} = 7.7 Hz, 1H), 6.52 (l, \textit{\textit{J}} = 5.7 Hz, 1H), 5.10 (d, \textit{\textit{J}} = 12.2 Hz, 1H), 5.06 (d, \textit{\textit{J}} = 12.1 Hz, 1H), 3.63 (s, 3H), 2.75 (dt, \textit{\textit{J}} = 13.7 Hz, \textit{\textit{J}} = 6.8 Hz, 1H), 2.64 (dt, \textit{\textit{J}} = 14.2 Hz, \textit{\textit{J}} = 6.6 Hz, 1H) ppm; \textsuperscript{13}C NMR (125 MHz, 90 °C, DMSO-\textit{d}\textsubscript{6}): δ = 164.9, 161.7 (d, \textit{\textit{J}}_{C,F} = 245.1 Hz), 150.4, 141.9, 140.5, 139.5, 139.0, 135.3 (d, \textit{\textit{J}}_{C,F} = 3.0 Hz), 128.2 (d, \textit{\textit{J}}_{C,F} = 8.2 Hz), 126.6, 125.1, 124.0, 124.0, 123.1, 115.2 (d, \textit{\textit{J}}_{C,F} = 21.5 Hz), 94.5, 74.8, 52.0, 50.6, 38.9 ppm; \textsuperscript{19}F NMR (600 MHz, 25 °C, DMSO-\textit{d}\textsubscript{6}): -113.79, -114.89 ppm; ESI-HRMS: m/z calculated for \([\text{C}_{22}\text{H}_{18}\text{N}_{2}\text{O}_{4}\text{Cl}_{3}\text{Na}]^{+}\): 521.0208; found 521.0214.

Chiral-phase SFC: Chiralcel IC, CO\textsubscript{2}/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 254 nm)

\textit{Racemic}:

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{racerb.png}
\caption{Chiral-phase SFC: Chiralcel IC, CO\textsubscript{2}/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 254 nm)}
\end{figure}

\textit{Enantioselective}:

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{enabc.png}
\caption{Chiral-phase SFC: Chiralcel IC, CO\textsubscript{2}/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 254 nm)}
\end{figure}
(R)-2,2,2-Trichloroethyl 4-((E)-4-methoxy-4-oxobut-2-en-1-yl)-7-((E)-styryl)quinazoline-3(4H)-carboxylate (4l)

According to the general procedure A, the reaction of 7-((E)-styryl)quinazoline (2l) (23.2 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3a (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 3:1) the desired product 4l (37.8 mg, 0.074 mmol, 74%) as a slightly yellow solid. The enantiomeric ratio was determined as 92:8 e.r. by chiral SFC (Chiralcel IC, CO2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm): tr (major): 17.4 min, tr (minor): 18.8 min).

1H NMR (500 MHz, 90 °C, DMSO-d6): δ = 8.00 (s, 1H), 7.60 (d, J = 8.1 Hz, 2H), 7.50 (dd, J = 7.9 Hz, J = 1.8 Hz, 1H), 7.47 (d, J = 1.7 Hz, 1H), 7.38 (t, J = 7.7 Hz, 2H), 7.27 (dd, J = 12.2 Hz, J = 4.5 Hz, 3H), 7.21 (d, J = 6.4 Hz, 1H), 6.72 (dt, J = 16.3 Hz, J = 7.6 Hz, 1H), 5.81 (d, J = 5.6 Hz, 1H), 5.48 (t, J = 5.6 Hz, 1H), 5.09 (d, J = 12.2 Hz, 1H), 5.05 (d, J = 12.0 Hz, 1H), 3.63 (s, 3H), 2.73 (dt, J = 13.8 Hz, J = 8.7 Hz, 1H), 2.62 (dt, J = 14.2 Hz, J = 6.8 Hz 1H) ppm; 13C NMR (125 MHz, 90 °C, DMSO-d6): δ = 165.3, 150.4, 141.9, 140.3, 138.8, 137.6, 136.5, 129.0, 128.1, 127.3, 127.2, 126.3, 126.1, 125.0, 124.0, 124.0, 123.0, 94.5, 73.6, 52.1, 50.6, 38.9 ppm; ESI-HRMS: m/z calculated for [C24H21N2O4Cl3Na]+: 529.0459; found 529.0465.

Chiral-phase SFC: Chiralcel IC, CO2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm)

Racemic:

Enantioselective:
(R,E)-2,2,2-Trichloroethyl 4-(4-methoxy-4-oxobut-2-en-1-yl)-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinazoline-3(4H)-carboxylate (4m)

According to the general procedure A, the reaction of benzo[f]quinazoline (2m) (25.6 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3a (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 3:1) the desired product 4m (32.3 mg, 0.061 mmol, 61%) as a slightly yellow solid. The enantiomeric ratio was determined as 96:4 e.r. by chiral SFC (Chiralcel IC, CO\textsubscript{2}/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 230 nm): tr (major): 11.0 min, tr (minor): 12.6 min). \textsuperscript{1}H NMR (500 MHz, 90 °C, DMSO-\textsubscript{d}6): δ = 7.97 (s, 1H), 7.56 (d, \textsuperscript{3}J = 7.5 Hz, 1H), 7.51 (s, 1H), 7.28 (d, \textsuperscript{3}J = 7.5 Hz, 1H), 6.69 (dt, \textsuperscript{3}J\textsubscript{trans} = 15.3 Hz, \textsuperscript{3}J\textsubscript{cis} = 7.6 Hz, 1H), 5.79 (d, \textsuperscript{3}J\textsubscript{trans} = 15.5 Hz, 1H), 5.49 (t, \textsuperscript{3}J = 5.6 Hz, 1H), 5.08 (d, \textsuperscript{3}J = 12.1 Hz, 1H), 5.04 (d, \textsuperscript{2}J = 12.1 Hz, 1H), 3.63 (s, 2H), 2.71 (dt, \textsuperscript{2}J\textsubscript{trans} = 13.9 Hz, \textsuperscript{2}J\textsubscript{cis} = 6.7 Hz, 1H), 2.60 (dt, \textsuperscript{2}J = 14.1 Hz, \textsuperscript{3}J = 6.5 Hz, 1H) ppm; \textsuperscript{13}C NMR (125 MHz, 90 °C, DMSO-\textsubscript{d}6): δ = 164.9, 150.4, 141.8, 140.2, 138.0, 132.8, 130.9, 127.9, 125.6, 124.0, 94.5, 83.4, 74.8, 52.2, 50.6, 38.8, 24.2 ppm; ESI-HRMS: m/z calculated for [C\textsubscript{22}H\textsubscript{26}N\textsubscript{2}O\textsubscript{6}BCl\textsubscript{3}Na]+: 533.0846; found 553.0850.

Chiral-phase SFC: Chiralcel IC, CO\textsubscript{2}/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 230 nm)

**Racemic:**

**Enantioselective:**
(R,E)-2,2,2-Trichloroethyl 7-bromo-4-(4-methoxy-4-oxobut-2-en-1-yl)quinazoline-3(4H)-carboxylate (4o)

According to the general procedure A, the reaction of 7-bromoquinazoline (2o) (20.9 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3a (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 5:1) the desired product 4o (38.2 mg, 0.079 mmol, 79%) as a white solid. The enantiomeric ratio was determined as 94:6 e.r. by chiral SFC (Chiralcel IG, CO2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 290 nm)): tr (major): 10.8 min, tr (minor): 11.8 min. $^1$H NMR (500 MHz, 90 °C, DMSO-$d_6$): $\delta$ = 8.00 (s, 1H), 7.45 (dd, $^3$J = 8.1 Hz, $^4$J = 1.9 Hz, 1H), 7.41 (d, $^4$J = 2.1 Hz, 1H), 7.26 (d, $^3$J = 8.1 Hz, 1H), 6.70 (dt, $^3$Jtrans = 15.3 Hz, $^3$J = 7.6 Hz, 1H), 5.80 (d, $^4$Jtrans = 15.6 Hz, 1H), 5.49 (l, $^4$J = 5.7 Hz, 1H), 5.08 (d, $^3$J = 12.2 Hz, 1H), 5.05 (d, $^3$J = 12.2 Hz, 1H), 3.63 (s, 3H), 2.70 (dt, $^3$J = 13.8 Hz, $^3$J = 6.7 Hz, 1H), 2.60 (dt, $^3$J = 14.3 Hz, $^3$J = 6.6 Hz, 1H) ppm; $^{13}$C NMR (125 MHz, 90 °C, DMSO-$d_6$): $\delta$ = 164.9, 150.2, 141.6, 141.5, 140.2, 129.5, 127.9, 127.5, 124.2, 120.7, 94.4, 74.9, 51.8, 50.6, 38.7 ppm; ESI-HRMS: m/z calculated for [C_{16}H_{14}BrClN_2O_4Na]^+: 506.9072; found 506.9071.

The same reaction with the TIPS-dienolate 3a’ led to the product 4o in a 97:3 e.r. (27.9 mg, 0.058 mmol, 58%).

Chiral-phase SFC: Chiralcel IC, CO2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm)

Racemic:

Enantioselective:

With OTBS-dienolate 3a

With OTIPS-dienolate 3a’
(R,E)-2,2,2-Trichloroethyl 6-bromo-4-(4-methoxy-4-oxobut-2-en-1-yl)quinazoline-3(4H)-carboxylate (4p)

According to the general procedure A, the reaction of 6-bromoquinazoline (2p) (20.9 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3a (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 5:1) the desired product 4p (36.5 mg, 0.075 mmol, 75%) as a white solid. The enantiomeric ratio was determined as 80:20 e.r. by chiral SFC (Chiralcel IG, CO2/MeOH (70:30), 2.0 ml/min, (λ = 290 nm): tr (major): 8.6 min, tr (minor): 10.6 min).

**1H NMR** (500 MHz, 90 °C, DMSO-d6): δ = 7.98 (s, 1H), 7.55 (d, 3J = 2.2 Hz, 1H), 7.50 (dd, 3J = 8.4 Hz, 4J = 2.1 Hz, 1H), 7.18 (d, 3J = 8.3 Hz, 1H), 6.70 (dt, 3Jtrans = 15.4 Hz, 3J = 7.6 Hz, 1H), 5.80 (d, 3Jtrans = 15.5 Hz, 1H), 5.52 (t, 3J = 5.7 Hz, 1H), 5.08 (d, 3J = 12.2 Hz, 1H), 5.04 (d, 3J = 12.1 Hz, 1H), 3.63 (s, 3H). 2.74–2.66 (m, 1H), 2.70 (dt, 3J = 12.8 Hz, 3J = 6.4 Hz, 1H), 2.61 (dt, 3J = 14.0 Hz, 3J = 6.4 Hz, 1H) ppm; **13C NMR** (125 MHz, 90 °C, DMSO-d6): δ = 164.9, 150.3, 141.7, 140.7, 137.8, 131.3, 128.8, 127.2, 127.0, 124.2, 119.1, 94.4, 74.9, 51.5, 50.6, 38.8 ppm; **ESI-HRMS**: m/z calculated for [C16H14BrClNO4Na]+: 506.9072; found 506.9071.

**Chiral-phase SFC**: Chiralcel IC, CO2/MeOH 70:30, 2.0 ml/min, (λ = 290 nm)

**Racemic**:  

**Enantioselective**:  

S21
(R,E)-2,2,2-Trichloroethyl 7-fluoro-4-(4-methoxy-4-oxobut-2-en-1-yl)quinazoline-3(4H)-carboxylate (4q)

According to the general procedure A, the reaction of 7-fluoroquinazoline (2q) (14.8 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3a (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 4:1) the desired product 4q (30.1 mg, 0.071 mmol, 71%) as a white solid. The enantiomeric ratio was determined as 94:6 e.r. by chiral SFC (Chiralcel IC, CO₂/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 280 nm): tr (major): 8.6 min, tr (minor): 9.3 min). ^1H NMR (500 MHz, 90 °C, DMSO-d6): δ = 8.01 (s, 1H), 7.33 (dd, 3J = 8.4 Hz, 4J = 6.0 Hz, 1H), 7.10 (td, 3J = 8.6 Hz, 4J = 2.7 Hz, 1H), 7.03 (dd, 3J = 9.8 Hz, 4J = 2.7 Hz, 1H), 6.70 (dt, 3Jtrans = 15.4 Hz, 3J = 7.6 Hz, 1H), 5.78 (dd, 3Jtrans = 15.6 Hz, 1H), 5.50 (t, 3J = 5.6 Hz, 1H), 5.08 (dd, 3J = 12.1 Hz, 1H), 5.05 (d, 3J = 12.2 Hz, 1H), 3.63 (s, 3H), 2.69 (dt, 2J = 14.2 Hz, 3J = 6.9 Hz, 1H), 2.59 (dt, 2J = 14.1 Hz, 3J = 6.9 Hz, 1H) ppm; ^13C NMR (125 MHz, 90 °C, DMSO-d6): δ = 164.9, 161.7 (d, 1JC,F = 243.9 Hz), 149.4, 141.7, 141.3, 140.2 (d, 3JCF = 11.2 Hz), 127.7 (d, 2JC,F = 9.3 Hz), 124.1, 121.1 (d, 4JC,F = 3.3 Hz), 113.6 (d, 3JCF = 21.9 Hz), 111.5 (d, 2JC,F = 22.4 Hz), 94.5, 74.9, 51.7, 50.6, 38.9 ppm; ^19F NMR (600 MHz, 25 °C, DMSO-d6): -112.50, -112.93 ppm; ESI-HRMS: m/z calculated for [C₁₆H₁₄N₂O₄Cl₃FNa]⁺: 444.9895; found 444.9893.

Chiral-phase SFC: Chiralcel IC, CO₂/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 280 nm)

Racemic:

![Racemic SFC](image)

| Signal | DAD1E.Sign=280.4 Ref=300.100 |
|--------|-------------------------------|
| RT [min] | Type | Width [min] | Area | Height | Area% |
| 9.351 MM m | 0.0970 | 2203.2209 | 351.9599 | 48.837 |
| 10.182 MM m | 0.1094 | 2308.6100 | 322.8540 | 51.106 |
| Sum | 4511.0820 |

Enantioselective:

![Enantioselective SFC](image)

| Signal | DAD1E.Sign=280.4 Ref=300.100 |
|--------|-------------------------------|
| RT [min] | Type | Width [min] | Area | Height | Area% |
| 8.591 MM m | 0.0200 | 8378.4026 | 1359.4815 | 93.803 |
| 9.349 MM m | 0.1118 | 553.4724 | 73.5797 | 6.1966 |
| Sum | 8931.8749 |

p = 192 bar
(R,E)-2,2,2-Trichloroethyl 4-(4-methoxy-4-oxobut-2-en-1-yl)-7-nitroquinazoline-3(4H)-carboxylate (4r)

According to the general procedure A, the reaction of 7-nitroquinazoline (2r) (17.5 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3a (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 3:1) the desired product 4r (26.3 mg, 0.058 mmol, 58%) as a yellow solid. The enantiomeric ratio was determined as 77:23 e.r. by chiral SFC (Chiralcel IA, CO2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 290 nm): tr (major): 17.5 min, tr (minor): 19.4 min).

\[ ^{1}H\text{ NMR (500 MHz, DMSO-}d_6)\delta=8.12-8.09 (m, 2H), 7.95 (d, ^{4}J=2.4 \text{ Hz}, 1H), 7.60 (d, ^{3}J=8.4 \text{ Hz}, 1H), 6.71 (dt, ^{3}J_{\text{trans}}=15.4 \text{ Hz}, ^{3}J=7.6 \text{ Hz}, 1H), 5.81 (d, ^{3}J_{\text{trans}}=15.5 \text{ Hz}, 1H), 5.68-5.64 (m, 1H), 5.49 (t, ^{3}J=5.7 \text{ Hz}, 1H), 5.10 (d, ^{2}J=12.1 \text{ Hz}, 1H) 5.07 (d, ^{2}J=12.3 \text{ Hz}, 1H), 3.63 (s, 3H), 2.76 (dt, ^{2}J=13.6 \text{ Hz}, ^{3}J=6.7 \text{ Hz}, 1H), 2.65 (dt, ^{2}J=14.5 \text{ Hz}, ^{3}J=7.1 \text{ Hz}, 1H) \text{ ppm; } ^{13}C\text{ NMR (125 MHz, DMSO-}d_6)\delta=164.8, 150.1, 147.8, 142.5, 141.2, 139.6, 131.9, 127.6, 124.5, 121.3, 119.2, 94.4, 75.0, 51.9, 50.7, 38.6 \text{ ppm; ESI-HRMS: } m/z \text{ calculated for [C}_{16}H_{14}N_{3}O_{6}Cl_{3}Na]+: 471.9840; \text{ found 471.9842.} \]

Chiral-phase SFC: Chiralcel IA, CO2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm)

**Racemic:**

**Enantioselective:**
(R,E)-2,2,2-Trichloroethyl 1-(4-methoxy-4-oxobut-2-en-1-yl)benzo[f]quinazoline-2(1H)-carboxylate (4s)

According to the general procedure A, the reaction of benzo[f]quinazoline (2s) (18.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate 3a (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (n-pent/EtOAc 3:1) the desired product 4s (38.5 mg, 0.084 mmol, 84%) as a brown solid. The enantiomeric ratio was determined as 84:16 e.r. by chiral SFC (Chiralcel IC, CO₂/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 260 nm): tr (major): 12.2 min, tr (minor): 13.1 min). 

$^1$H NMR (500 MHz, 90 °C, DMSO-d$_6$): δ = 8.09 (s, 1H), 8.04 (d, $^3$J = 8.5 Hz, 1H), 7.95 (d, $^3$J = 8.1 Hz, 1H), 7.92 (d, $^2$J = 8.6 Hz, 1H), 7.63 (t, $^2$J = 7.7 Hz, 1H), 7.54 (t, $^3$J = 7.5 Hz, 1H), 7.45 (d, $^3$J = 8.6 Hz, 1H), 6.79 (dt, $^3$J$_{trans}$ = 15.5 Hz, $^2$J = 7.7 Hz, 1H), 6.18 (t, $^3$J = 5.6 Hz, 1H), 5.78 (d, $^3$J$_{trans}$ = 15.5 Hz, 1H), 5.13 (d, $^2$J = 12.2 Hz, 1H), 5.05 (d, $^2$J = 12.1 Hz, 1H), 3.61 (s, 2H), 2.76 (dt, $^2$J = 14.5 Hz, $^2$J = 6.6 Hz, 1H), 2.69 (dt, $^2$J = 14.6 Hz, $^2$J = 7.4 Hz, 1H) ppm; $^{13}$C NMR (125 MHz, 90 °C, DMSO-d$_6$): δ = 164.9, 150.4, 142.2, 140.6, 136.8, 132.3, 128.6, 128.2, 128.1, 126.8, 125.3, 124.2, 123.9, 121.8, 118.4, 94.5, 74.9, 50.6, 49.2, 37.1 ppm; ESI-HRMS: m/z calculated for [C$_{20}$H$_{17}$N$_2$O$_4$Cl$_3$Na]$^+$: 477.0146; found 477.0145.

Chiral-phase SFC: Chiralcel IC, CO₂/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 260 nm)

Racemic:

Enantioselective:
(R,E)-2,2,2-Trichloroethyl 2-(4-methoxy-4-oxobut-2-en-1-yl)quinoline-1(2H)-carboxylate (5a)

According to the general procedure B, the reaction of quinoline (12.3 µL, 0.10 mmol, 1.0 equiv.) with dienolate 3a (47.1 µL, 0.20 mmol, 2.0 equiv.) gave after flash column chromatography (n-pent/EtOAc 20:1) the desired product 5a as a colourless oil (32.8 mg, 0.081 mmol, 81%). The enantiomeric ratio was found to be 82:18 by chiral SFC (Daicel IG, CO₂/MeOH (gradient 98:2 → 65:35) 2.0 mL/min, λ = 290 nm, tr (major): 8.1 min, tr (minor): 8.5 min).

**1H NMR** (400 MHz, CDCl₃): δ 7.66 (bs, 1H), 7.30 – 7.22 (m, 1H), 7.15 – 7.09 (m, 2H), 6.88 (dt, J = 15.4, 7.6 Hz, 1H), 6.55 (d, J = 9.2 Hz, 1H), 6.06 (dd, J = 8.9, 6.0 Hz, 1H), 5.76 (dt, J = 15.4, 1.3 Hz, 1H), 5.27 – 5.14 (m, 1H), 4.82 (bs, 1H), 4.49 (bs, 1H), 3.69 (s, 3H), 2.52 – 2.15 (m, 2H);

**13C NMR** (100 MHz, CDCl₃): δ 166.4, 152.6, 143.4, 133.0, 128.1, 128.0, 127.1, 126.5, 125.8, 125.2, 124.0, 95.2, 75.4, 52.0, 51.5, 35.8 ppm; **ESI-HRMS**: m/z calculated for [C₁₇H₁₆Cl₃NO₄Na⁺]: 426.0037; found 426.0035.

**Chiral-phase SFC**: Chiralpak IG, CO₂/MeOH 95:5 → 65:35, 2.0 ml/min, (λ = 254 nm)

**Racemic:**

![Chiral-phase SFC: Chiralpak IG, CO₂/MeOH 95:5 → 65:35, 2.0 ml/min, (λ = 254 nm)](image)

**Enantioselective:**

![Chiral-phase SFC: Chiralpak IG, CO₂/MeOH 95:5 → 65:35, 2.0 ml/min, (λ = 254 nm)](image)

(R,E)-2,2,2-Trichloroethyl 2-(4-(methylthio)-4-oxobut-2-en-1-yl)quinoline-1(2H)-carboxylate (5b)

According to the general procedure B, the reaction of quinoline (12.3 µL, 0.10 mmol, 1.0 equiv.) with dienolate 3d (54.2 µL, 0.20 mmol, 2.0 equiv.) gave after flash column chromatography (cyclohexane/EtOAc 20:1) the desired product 5b as a white oil (33.6 mg, 0.08 mmol, 80% yield). The enantiomeric ratio was determined as 84:16 e.r. by chiral SFC (Chiralpak IG, CO₂/MeOH (95:5 → 65:35), 2.0 ml/min in 15 min, (λ = 254 nm); tr (major): 11.8 min, tr (minor): 12.6 min).

**1H NMR** (300 MHz, CDCl₃): δ 7.66 (bs, 1H), 7.32 – 7.20 (m, 1H), 7.12 (m, 2H), 6.80 (dt, J = 15.4, 8.3 Hz 1H), 6.55 (d, J = 10.2 Hz, 1H), 6.14 – 5.95 (m, 2H), 5.22 (app. q, J = 6.7 Hz, 1H), 4.67 (bs, 2H), 2.47 – 2.23 (m, 5H) ppm; **13C NMR** (75 MHz, CDCl₃) δ 190.0, 152.6, 139.2, 133.4, 131.4 (2C), 128.2, 127.2, 126.6 (2C), 126.0, 125.3, 95.3, 75.6, 52.2, 51.5, 35.8 ppm; **ESI-HRMS**: m/z calculated for [C₁₇H₁₆Cl₃NO₂SNa⁺]: 437.0255; found 437.0256.

S25
Chiral-phase SFC: Chiralpak IG, CO₂/MeOH 95:5 → 65:35, 2.0 ml/min, (λ = 254 nm)

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
# & Time & Type & Area & Height & Width & Area% & Symmetry \\
\hline
1 & 11.714 & BB & 4222.8 & 582.9 & 0.1125 & 49.924 & 0.874 \\
2 & 12.305 & BB & 4235.6 & 513.6 & 0.1282 & 50.076 & 0.809 \\
\hline
\end{tabular}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
# & Time & Type & Area & Height & Width & Area% & Symmetry \\
\hline
1 & 11.794 & BB & 5178.5 & 697.5 & 0.1166 & 81.104 & 0.811 \\
2 & 12.537 & BB & 978.7 & 126.3 & 0.1184 & 15.896 & 0.877 \\
\hline
\end{tabular}
\end{table}

\((R,E)-2,2,2\text{-Trichloroethyl 6-fluoro-2-(4-(methylthio)-4-oxobut-2-en-1-yl)quinoline-1(2H)-carboxylate (5c)}\)

According to the general procedure B, the reaction of 6-fluorquinoline (12.2 µL, 0.10 mmol, 1.0 equiv.) with dienolate 3d (54.2 µL, 0.20 mmol, 2.0 equiv.) gave after flash column chromatography (cyclohexane/EtOAc 20:1) the desired product 5b as a yellowish oil (25.1 mg, 0.057 mmol, 57% yield).

The enantiomeric ratio was determined as 91:9 e.r. by chiral SFC (Chiralpak IA, CO₂/MeOH (95:5 → 60:40), 3.0 ml/min in 15 min, (λ = 254 nm): tr (major): 5.7 min, tr (minor): 6.0 min). \(^1\)H NMR (300 MHz, CDCl₃): \(\delta\) 7.61 (bs, 1H), 6.96 (td, \(J = 8.6, 3.1\) Hz, 1H), 6.84 (dd, \(J = 8.4, 3.1\) Hz, 1H), 6.81 – 6.69 (m, 1H), 6.51 (d, \(J = 9.6\) Hz, 1H), 6.12 (dd, \(J = 9.6, 5.9\) Hz, 1H), 6.04 (d, \(J = 15.5\) Hz, 1H), 5.30 – 5.18 (m, 1H), 4.84 (bs, 1H), 4.49 (bs, 1H), 2.53 – 2.16 (m, 2H), 2.33 (s, 3H) ppm; \(^{13}\)C NMR (75 MHz, CDCl₃) \(\delta\) 190.0, 160.0 (d, \(^{1}\)J\(_{C,F}\) = 242.3 Hz), 152.6, 138.9, 131.5, 130.0, 128.9 (d, \(^{2}\)J\(_{C,F}\) = 7.5 Hz), 127.3, 125.4, 125.3, 114.8 (d, \(^{2}\)J\(_{C,F}\) = 23.3 Hz), 112.9 (d, \(^{2}\)J\(_{C,F}\) = 23.2 Hz), 95.2, 75.6, 52.2, 35.5, 11.5 ppm; \(^{19}\)F NMR (282 MHz, CDCl₃): -116.88, -117.34; ESI-HRMS: \(m/z\) calculated for \([\text{C}_{17}\text{H}_{19}\text{Cl}_3\text{FN}_{2}\text{O}_3\text{S}\text{NH}_4]^+\): 455.0161; found 455.0106.

Chiral-phase SFC: Chiralpak IA, CO₂/MeOH 95:5 → 60:40, 3.0 ml/min, (λ = 254 nm)

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
# & Time & Type & Area & Height & Width & Area% & Symmetry \\
\hline
1 & 5.6 & BB & 13471.6 & 2466.6 & 0.0877 & 48.390 & 0.655 \\
2 & 5.893 & BB & 14368.4 & 2371.3 & 0.0947 & 51.610 & 0.563 \\
\hline
\end{tabular}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
# & Time & Type & Area & Height & Width & Area% & Symmetry \\
\hline
1 & 5.715 & BB & 9031.9 & 1952.7 & 0.072 & 91.044 & 0.727 \\
2 & 6.039 & BB & 888.5 & 213.3 & 0.0666 & 8.556 & 0.96 \\
\hline
\end{tabular}
\end{table}
(R,E)-2,2,2-Trichloroethyl 2-(4-methoxy-4-oxobut-2-en-1-yl)-6-methylpyridine-1(2H)-carboxylate (6)

In a flame-dried 5 mL Schlenk pressure tube, 2-picoline (9.88 µL, 0.10 mmol, 1.0 equiv.) was dissolved in hexafluorobenzene (1 mL) and cooled to 6 °C. 2,2,2-Trichloroethoxycarbonyl chloride (14 µL, 0.10 mmol, 1.0 equiv.) was added and the reaction was stirred at 6 °C for 30 min. Subsequently, catalyst 1d (10.6 mg, 0.01 mmol, 10 mol%) and dienolate 3a (47.1 µL, 0.20 mmol, 2.0 equiv.) were added and the reaction was stirred at 6 °C overnight. The solvent was then removed under reduced pressure and the desired product was obtained as a colourless oil (17.0 mg, 0.046 mmol, 46%) after purification by column chromatography (n-pent/EtOAc 10:1). The enantiomeric ratio was determined as 70:30 e.r. by chiral SFC (Chiralcel IG, CO2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 290 nm): tr (minor): 6.5 min, tr (major): 7.7 min).

1H NMR (400 MHz, CDCl3) δ 6.89 (dt, 3Jtrans = 15.5 Hz, 3J = 7.7 Hz, 1H), 5.95 (dd, 3J = 9.3 Hz, 3J = 5.3 Hz, 1H), 5.81 (dt, 3Jtrans = 15.6 Hz, 3J = 1.4 Hz, 1H), 5.68 (dd, 3J = 9.4 Hz, 3J = 5.9 Hz, 1H), 5.50 (dp, 3J = 5.2 Hz, 3J = 1.2 Hz, 1H), 5.04 – 4.96 (m, 1H), 4.94 (bs, 1H), 4.68 (bs, 1H), 3.70 (s, 3H), 2.44 – 2.33 (m, 2H), 2.19 (s, 3H) ppm;

13C NMR (100 MHz, CDCl3) δ 166.6, 152.6, 144.0, 133.8, 123.7, 123.13, 123.0, 112.6, 93.0, 75.5, 52.3, 51.6, 35.3, 21.7 ppm;

ESI-HRMS: m/z calculated for [C14H16NO4Cl3Na]+: 390.0037; found 390.0054.

Chiral-phase SFC: Chiralcel IC, CO2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm)

Racemic:

Enantioselective:
(R,E)-Methyl 4-(4-oxochroman-2-yl)but-2-enoate (7)

In a flame-dried 5 mL Schlenk pressure tube, 4H-chromenone (15 mg, 0.10 mmol, 1.0 equiv.) and catalyst 1a (5.6 mg, 0.005 mmol, 5.0 mol%) were dissolved in anhydrous toluene (0.4 mL). 2,4,6-Collidine (4.0 µL, 0.03 mmol, 0.30 equiv.) and TBSOTf (25 µL, 0.11 mmol, 1.1 equiv.) were added and the mixture was stirred at 60 °C for 1 h. Subsequently, the reaction was cooled to ~78 °C and dienolate 3a (47.1 µL, 0.20 mmol, 2.0 equiv.) was added. After stirring for 18 h at ~78 °C, the reaction was quenched with aq. HCl (6.0 equiv., 3 M) and was allowed to warm to room temperature for 1 h. The solution was diluted with water (5 mL), the aq. phase extracted with EtOAc (3 x 3 mL) and the combined organic phases dried over MgSO₄. After removing the solvent under reduced pressure, the residue was purified via column chromatography (SiO₂, n-pent/EtOAc 5:1) to give the desired product as a white solid (16 mg, 0.066 mmol, 66%). The enantiomeric ratio was determined as 79:21 e.r. by chiral SFC (Chiralcel IG, CO₂/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 250 nm): tr (minor): 10.4 min, tr (major): 12.6 min).

1H NMR (400 MHz, CDCl₃): δ = 7.87 (dd, 3J = 7.9 Hz, 4J = 1.7 Hz, 1H), 7.48 (ddd, 3J = 8.3 Hz, 3J = 7.2 Hz, 4J = 1.8 Hz, 1H), 7.08–6.96 (m, 3H), 5.99 (dt, 3J = 15.7 Hz, 4J = 1.5 Hz, 1H), 4.63–4.55 (m, 1H), 3.75 (s, 3H), 2.80–2.63 (m, 4H) ppm; 13C NMR (100 MHz, CDCl₃): δ = 190.7, 166.5, 161.3, 143.2, 135.6, 127.1, 124.6, 121.8, 121.0, 116.7, 73.8, 50.7, 41.8, 38.5 pm; ESI-HRMS: calculated for [C₁₄H₁₀O₄Na]: 269.0795; found 269.0784.

Chiral-phase SFC: Chiralcel IC, CO₂/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 250 nm)

Racemic:

Enantioselective:
7. Derivatization of 4a: Synthesis of 8

In a vial, 4a (202.8 mg, 0.5 mmol, 1 equiv.), activated Zn powder (326.9 mg, 5.0 mmol, 10 equiv.) and NH₄OAc (385.4 mg, 5.0 mmol, 10 equiv.) were dissolved in 1.5 mL of a mixture 3:1 of THF:H₂O and stirred overnight at r.t. Then, a 5 mL of a saturated aqueous solution of Na₂CO₃ was added, followed by an extraction with CHCl₃ (4x3 mL). The organic phases were combined, dried over MgSO₄, filtered and concentrated under reduced pressure. The crude was used in the next step without further purifications.

In a flame-dry sealed vial, Pd/C (5.4 mg, 0.05 mmol, 0.1 equiv.) was suspended in 0.5 mL of dry toluene and the suspension was purged with a H₂ balloon for 15 min. Subsequently, a solution of the previous crude mixture (0.5 mmol, 1 equiv.) in 0.5 mL of dry toluene was added to the suspension and the reaction was stirred overnight. Then, EtOAc was added and the crude was filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and purified by flash chromatography using silica gel (cyclohexane/EtOAc, 1:3), affording the tricyclic product 8 as a white solid (470.6 mg, 2.35 mmol, 47% overall yield). [α]20 D = 59.1 (c 6.9, CHCl₃).

The enantiomeric ratio was determined as 94:6 e.r. by chiral SFC (Chiralcel IA, CO₂/MeOH (95:5 → 60:40), 3.0 ml/min, (λ = 280 nm): tr (minor): 5.4 min, tr (major): 5.8 min). ¹H NMR (300 MHz, CDCl₃): δ 8.41 (s, 1H), 7.35 (d, J = 7.6 Hz, 1H), 7.32 (t, J = 7.5 Hz, 1H), 7.25 – 7.19 (m, 1H), 7.16 (d, J = 7.8 Hz, 1H), 4.94 (dd, J = 10.6, 4.1 Hz, 1H), 2.84 – 2.50 (m, 3H), 2.28 – 1.82 (m, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 170.2, 142.2, 140.1, 129.0, 127.6, 126.6, 126.2, 123.4, 53.9, 32.2, 27.3, 18.9; ESI-HRMS: m/z calculated for [C₁₂H₁₃N₂O]: 201.1022; found: 201.1020.

Chiral-phase SFC: Chiralcel IA, CO₂/MeOH 95:5 → 60:40, 3.0 ml/min, (λ = 280 nm)

Racemic:

| #  | Time | Type | Area  | Height | Width  | Area%  | Symmetry |
|----|------|------|-------|--------|--------|--------|----------|
| 1  | 5.416| BB   | 1916.9| 397.3  | 0.0743 | 49.781 | 0.816    |
| 2  | 5.854| BB   | 1933.7| 317.7  | 0.083  | 50.219 | 0.71     |

Enantioselective:

| #  | Time | Type | Area  | Height | Width  | Area%  | Symmetry |
|----|------|------|-------|--------|--------|--------|----------|
| 1  | 5.423| BB   | 634.1 | 132.8  | 0.0737 | 6.081  | 0.875    |
| 2  | 5.782| BB   | 9793.4| 1343.7 | 0.109  | 93.919 | 0.475    |
8. Kinetic Study

The kinetic study was carried out for the model reaction between quinazoline (2a) (130.0 mg, 1.00 mmol, 1.0 equiv.) and dienolate 3a (471.0 µL, 2.00 mmol, 2.0 equiv.) in presence and absence of catalyst 1a (33.6 mg, 0.03 mmol, 3 mol%). The aliquots were quenched by addition of aq. HCl (1 M), extracted with EtOAc and dried over MgSO₄. After removal of the solvent under reduced pressure, the yield was determined by ¹H NMR analysis using 1,3,5-trimethoxybenzene as internal standard, and the enantiomeric excess was determined by chiral SFC using Chiralcel IG, CO₂/MeOH (98.2 → 65.35), 2.0 ml/min.

![Kinetic Study Diagram]

9. X-Ray Crystal Structure Analysis of 4k

CCDC Nr.: 2069596

A colourless plate-like specimen of C₂₂H₁₈Cl₂FN₃O₄, approximate dimensions 0.053 mm x 0.102 mm x 0.192 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker D8 Venture Bruker D8 Venture Photon III Diffractometer system equipped with a micro focus tube MoKα (MoKα, λ = 0.71073 Å) and a MX mirror monochromator. A total of 510 frames were collected. The total exposure time was 3.54 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 20681 reflections to a maximum θ angle of 26.78° (0.79 Å resolution), of which 4559 were independent (average redundancy 4.536,
completeness = 99.6\%, \ R_{int} = 3.92\%, \ R_{sh} = 2.97\% \) and 4388 (96.25\%) were greater than 2\( \sigma(F^2) \). The final cell constants of \( a = 6.0314(3) \) Å, \( b = 7.4369(3) \) Å, \( c = 23.9241(10) \) Å, \( \beta = 92.818(2) \)^\circ, volume = 1071.82(8) Å³, are based upon the refinement of the XYZ-centroids of 9738 reflections above 20 \( \sigma(I) \) with 5.114 \(^\circ<2\theta<53.52\(^\circ\). Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.939. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9150 and 0.9760.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group \( P2_1_2_1_2 \), with \( Z = 2 \) for the formula unit, \( \text{C}_{22}\text{H}_{18}\text{Cl}_3\text{FN}_{2}\text{O}_4 \). The final anisotropic full-matrix least-squares refinement on \( F^2 \) with 290 variables converged at \( R1 = 2.44\% \), for the observed data and \( wR^2 = 5.67\% \) for all data. The goodness-of-fit was 1.031. The largest peak in the final difference electron density synthesis was 0.207 e/Å³ and the largest hole was -0.195 e/Å³ with an RMS deviation of 0.039 e/Å³. On the basis of the final model, the calculated density was 1.548 g/cm³ and \( F(000) = 512 \) e⁻.

Flack parameter was refined to -0.026(19).

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11. NMR Collection

![NMR Spectrum](image-url)
Due to the presence of Troc-rotamers, broad signals in $^1$H NMR and $^{13}$C NMR were observed, which hampered the characterization of the products. In order to get more defined signals, most of the NMRs were later on measured and given in DMSO-$d_6$ at 90 °C ($^1$H NMR residual solvent peaks DMSO $\sim$ 2.50 ppm, H$_2$O $\sim$ 3.00 ppm), unless a strong and/or fast decomposition of the products takes place at this temperature during the NMR measurements. However, in some cases rotamer species are still present at 90 °C, leading to low intensity signals, in particular in $^{13}$C NMR for the Troc C=O group at $\sim$ 150-152 ppm, and the side chain and Ar$_{C=H}$ bonds close to this group.
4a (DMSO-d$_6$, 90 °C):
4a' (DMSO-d$_6$, 90 °C):
4b (DMSO-d$_6$, 90 °C):
4c (DMSO-d$_6$, 90 °C):
**4d** (MeCN-\textsubscript{d3}, 25 °C): broad signals due Troc-rotamers
4e (DMSO-d$_6$, 90 °C):
4f (DMSO-d$_6$, 90 °C):
4g (DMSO-\text{d}_6, 90 \degree \text{C}):
4h (DMSO-d$_6$, 90 °C):
4i (DMSO-d$_6$, 90 °C):
4j (DMSO-\text{d}_{6}, 90^\circ \text{C}):
4k (DMSO-d$_6$, 90 °C):

\[ \text{[Chemical Structure Image]} \]
$^{1}H$ NMR spectrum of 4l (DMSO-$d_6$, 90 °C):
4m (DMSO-d$_6$, 90 °C):
4o (DMSO-d$_6$, 90 °C):
4p (DMSO-d$_6$, 90 °C):
$4q$ (DMSO-$d_6$, 90 °C):

19F-NMR
4r (DMSO-d$_6$, 90 °C):
4s (DMSO-d$_6$, 90 °C):
$5a$ (CDCl$_3$, 25 °C): broad signals due Troc-rotamers

![NCO$_2$Me](image-url)
5b (CDCl₃, 25 °C): broad signals due Troc-rotamers
5c (CDCl₃, 25 °C): broad signals due Troc-rotamers
6 (CDCl₃, 25 °C): broad signals due to Troc-rotamers (compound unstable in solution; it decomposes partially in the NMR tube within the time)
7 (CDCl₃, 25 °C):
$8$ (CDCl$_3$, 25 °C):