Supporting Information
for
Switchable highly regioselective synthesis of 3,4-dihydroquinoxalin-2(1H)ones from o-phenylenediamines and aroylpyruvates

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Additional experimental and characterisation data

Table of Contents
General information.......................................................................................................................................................... S2
Synthesis of compounds................................................................................................................................................. S3
ARIOGRAPHICAL abstract for Supporting Information.............................................................................................. S3
General procedures ..................................................................................................................................................... S3
  General procedure A:................................................................................................................................................. S3
  General procedure B:.................................................................................................................................................... S3
Ethyl 4-chlorobenzoylpyruvate (12a) ......................................................................................................................... S4
4-Chlorobenzoic acid (12b) ......................................................................................................................................... S6
(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-6-methoxy-3,4-dihydroquinoxalin-2(1H)-one (16a (SYN)) .................. S8
(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-7-methoxy-3,4-dihydroquinoxalin-2(1H)-one (17a (ANTI)) .............. S11
(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-6-fluoro-3,4-dihydroquinoxalin-2(1H)-one (16b (SYN)) .................... S15
(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-7-fluoro-3,4-dihydroquinoxalin-2(1H)-one (17b (ANTI)) ................... S18
(Z)-6-Chloro-3-(2-(4-chlorophenyl)-2-oxoethylidene)-3,4-dihydroquinoxalin-2(1H)-one (16c (SYN)) ................. S20
(Z)-7-Chloro-3-(2-(4-chlorophenyl)-2-oxoethylidene)-3,4-dihydroquinoxalin-2(1H)-one (17c (ANTI)) ............... S23
(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-2-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxylic acid (16d (SYN)) .......................................................... S26
(Z)-2-(2-(4-Chlorophenyl)-2-oxoethylidene)-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxylic acid (17d (ANTI)) ........................................................................................................... S30
(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-2-oxo-1,2,3,4-tetrahydroquinoxaline-6-carbonitrile (16e (SYN)) ........................................................................................................... S34
(Z)-2-(2-(4-Chlorophenyl)-2-oxoethylidene)-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carbonitrile (17e (ANTI)) ........................................................................................................... S38
(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-6-nitro-3,4-dihydroquinoxaline-2(1H)-one (16f (SYN)) ........................................................................................................... S41
(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-7-nitro-3,4-dihydroquinoxaline-2(1H)-one (17f (ANTI)) ........................................................................................................... S44

General information

Melting points were measured by Barnstead Electrothermal IA9200 and are uncorrected. $^1$H and $^{13}$C NMR spectra were recorded on Varian Gemini (300 / 600 MHz), chemical shifts are given in parts per million (ppm), tetramethylsilane was used as an internal standard CDCl$_3$ and DMSO-$d_6$ as the solvent, unless otherwise specified. IR spectra were acquired on FTIR-ATR REACT IR 1000 (ASI Applied Systems) with a diamond probe and MTS detector. Mass spectra were performed on a LC-MS apparatus (Agilent Technologies 1200 Series equipped with Mass spectrometer Agilent Technologies 6100 Quadrupole LC-MS). The course of the reactions was followed by TLC analysis (Merck Silica gel 60 F254). UV lamp (254 nm) and iodine vapours were used for the visualization of TLC spots. Starting chemicals not mentioned in the experimental part were purchased from Sigma-Aldrich, Fluorochem, Alfa Aesar or Acros vendors. Explanations: Ar - argon atmosphere, brine (saturated NaCl solution in water), d - day, EA - ethyl acetate, FLC - flash liquid chromatography, H (Hexol or Petroleum ether) is commercial fraction of hexanes, HV - high vacuum (<0.1 Torr), KGR Büchi - Kugelrohr Glass Oven, RVO - Rotary Vacuum Evaporator.

All prepared compounds are characterized by their M.p., NMR diagrams, NMR and IR textural solutions, their spectra and Elemental analysis. NMR diagrams represent compendious and condensed information about assigned $^1$H and $^{13}$C NMR data to a particular structure. $^1$H NMR diagrams allow smart check of both chemical shifts and coupling constants for their completeness and correctness. The numbers in the diagrams mean chemical shift in $\delta$ ppm and number(s) in parenthesis are coupling constant(s) in Hz. The reason to use NMR diagrams is to read and compare the NMR data more conveniently.
Synthesis of compounds

Graphical abstract for Supporting Information

General procedures

General procedure A:

A solution of ethyl 4-chlorobenzoylpyruvate 100 mg (0.39 mmol, 1.00 equiv) 12a, o-phenylenediamine (1.00 equiv) from 11a–f with or without an additive (1.00 equiv) (p-TsOH or DMAP) was stirred in 3.0 ml of DMF (abs) at rt under Ar for 72 h. A low soluble mixture of ANTI/SYN regioisomers slowly precipitated within the reaction. The precipitate was collected by filtration or centrifugation, triturated by 3 ml of Et₂O and crystallized from DMSO (if not otherwise stated) to yield the main solid regioisomer 16 or 17.

General procedure B:

Diisopropylcarbodiimide 82 µl (66.9 mg, 0.53 mmol, 1.20 equiv) DIC was added to a solution of 4-chlorobenzoylpyruvic acid 100 mg (0.44 mmol, 1.00 equiv) 12b and 73.8 mg (0.53 mmol, 1.20 equiv) of HOBT [CAS: 123333-53-9, 97% wetted with ≥ 14 wt % H₂O] in 3.0 ml of DMF (abs) under Ar. The reaction mixture was stirred for 5 min. Then o-phenylenediamine (1.00 mol equiv) from 11a–f was added and the mixture was stirred at rt
under Ar for 72 h. The precipitated product mixture obtained after filtration (or centrifugation) was triturated by 3 ml of Et<sub>2</sub>O and crystallized from DMSO (if not otherwise stated) to yield the main solid regioisomer 16 or 17.

**Ethyl 4-chlorobenzooylpyruvate (12a)**

![Chemical Reaction Diagram]

The ester 12a was prepared according to the procedure described in the literature<sup>1</sup> with 71% yield.

**Novelty:** Compound 12a was previously described in the literature with its M.p., <sup>1</sup>H NMR and <sup>13</sup>C NMR spectrum.<sup>1</sup>

**M.p.:** 62.0 - 63.0 °C [EtOH], yellow solid compound (lit. 62 - 63 °C [EtOH]).<sup>1</sup>

**NMR diagrams:**

![NMR Diagram]

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): δ 7.94 (d, 2H, J(2,3) = 8.6 Hz, 2 x H-C(2)), 7.49 (d, 2H, J(2,3) = 8.6 Hz, 2 x H-C(3)), 7.04 (s, 1H, -CH=), 4.41 (q, 2H, J(CH<sub>2</sub>,CH<sub>3</sub>) = 7.2 Hz, -CH<sub>2</sub>-), 1.42 (t,

3H, \( J(\text{CH}_2\text{CH}_3) = 7.2 \text{ Hz, -CH}_3 \). Enolic hydroxy group has chemical shift out of measured range.

**Figure S1.** \(^1H\)-NMR (300 MHz, CDCl\(_3\)), spectrum of compound 12a.

**FT IR** (solid, cm\(^{-1}\)): 3413 (s, OH), 2986 (m), 1727 (m, C=O), 1718 (m, C=O), 1588 (s, C=O), 1479 (m), 1447 (w), 1397 (w), 1366 (m), 1265 (s), 1175 (m), 1135 (w), 1106 (m), 1088 (s), 1007 (s), 935 (w), 857 (m), 813 (m), 778 (m), 766 (s), 667 (m), 628 (m).

**Figure S2.** IR spectrum of compound 12a.

**MS** (ESI m/z): 253.2 [M-H]\(^-\)

**Anal. calcd for C\(_{12}\)H\(_{11}\)ClO\(_4\) (254.67):** C, 56.59; H, 4.35; Cl, 13.92. Found: C, 56.78; H, 4.55; Cl, 13.74.
4-Chlorobenzoylpyruvic acid (12b)

![Chemical reaction diagram]

The acid 12b was prepared according to the procedure described in the literature. The reaction time was shortened to 10 minutes due to observed 4-chloroacetophenone formation via retro-claisen reaction.

**Novelty:** Compound 12b was described in the literature by M.p. and ¹H-NMR spectrum.

**M.p.:** 163.0 - 165.0 °C [H₂O], white solid compound (lit. 163 - 165 °C [H₂O]).

**NMR diagrams:**

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\( ^1\text{H NMR} \) (300 MHz, DMSO-\( d_6 \)): \( \delta \) 8.09 (d, 2H, \( J(2,3) = 8.6 \text{ Hz} \), 2 x H-C(2)), 7.64 (d, 2H, \( J(2,3) = 8.6 \text{ Hz} \), 2 x H-C(3)), 7.10 (s, 1H, -CH=), -OH and -COOH not seen.

Figure S3 \(^1\text{H NMR} \) (300 MHz, DMSO-\( d_6 \)), spectrum of compound 12b.

\( ^{13}\text{C NMR} \) (75 MHz, DMSO-\( d_6 \)): \( \delta \) 189.4 and 170.7 (\( \beta \)-diketo carbonyls), 163.5 (-COOH), 139.3 (C(4)), 133.9 (C(1)), 130.2 (2 x C(2)), 129.7 (2 x C(3)), 98.4 (-CH=).

Figure S4 \( ^{13}\text{C-NMR} \) (75 MHz, DMSO-\( d_6 \)), spectrum of compound 12b.
**FTIR** (solid, cm\(^{-1}\)): 3501 (s, OH), 1923 (w), 1624 (s, C=O), 1582 (s, C=O), 1492 (m), 1455 (m), 1402 (m), 1319 (m), 1283 (m), 1234 (s), 1187 (m), 1142 (s), 1112 (m), 1095 (s), 1056 (m), 1012 (m), 923 (w), 850 (m), 829 (m), 815 (m), 777 (s), 743 (m), 667 (m), 627 (m).

**Figure S5.** IR spectrum of compound 12b

**MS** (ESI m/z): 225.0 [M-H]

**Anal. calcd for C\(_{10}\)H\(_7\)ClO\(_4\) (226.61):** C, 53.00; H, 3.11. Found: C, 53.09; H, 3.12.

**(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-6-methoxy-3,4-dihydroquinoxalin-2(1H)-one (16a (SYN))**
The 3,4-dihydroquinoxaline-2(1H)-one **16a (SYN)** was prepared according to the general procedure B from acid **12b** diamine **11a**. The crude mixture of ANTI / SYN regioisomers was purified by trituration with boiling ethyl acetate yielding 78.4 mg (0.24 mmol, 54%) of **16a (SYN)**.

**Novelty:** Compound **16a (SYN)** was not described in the literature.

**M.p.:** 269.0 - 272.0 °C [EA], brown solid compound.

**NMR diagrams:**

$^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 13.63 (s, 1H, H-N$_A$(4)), 11.98 (s, 1H, H-N$_A$(1)), 8.00 (d, 2H, $J(B_2,B_3)$ = 8.5 Hz, 2 x H-C$_B$(2)), 7.59 (d, 2H, $J(B_2,B_3)$ = 8.5 Hz, 2 x H-C$_B$(3)), 7.25 (d, 1H, $J(A_5,A_7)$ = 2.5 Hz, H-C$_A$(5)), 7.08 (d, 1H, $J(A_7,A_8)$ = 8.8 Hz, H-C$_A$(8)), 6.80 (s, 1H, -COCH=), 6.77 (dd, 1H, $J(A_7,A_8)$ = 8.8 Hz, $J(A_5,A_7)$ = 2.5 Hz, H-C$_A$(7)), 3.78 (s, 3H, -OMe).

*Figure S6.* $^1$H-NMR (300 MHz, DMSO-$d_6$) spectrum of compound **16a (SYN).*
\[^{13}\text{C NMR}\ (150 \text{ MHz, DMSO-}d_6): \delta\ 187.3 \ (C_{B}(1)C=O),\ 156.3 \ (C_{A}(6)),\ 155.5 \ (C_{A}(2)=O),\ 146.4 \ (C_{A}(3)),\ 137.8 \text{ and } 137.2 \ (C_{B}(1 \text{ and } 4)),\ 129.4 \text{ and } 129.3 \ (2 \times C_{B}(2 \text{ and } 3)),\ 125.2 \ (C_{A}(4a)),\ 121.0 \ (C_{A}(8a)),\ 116.7 \ (C_{A}(8)),\ 112.1 \ (C_{A}(7)),\ 101.5 \ (C_{A}(5)),\ 89.5 \ (-\text{COCH=}),\ 56.1 \ (-\text{OCH}_3).\]

**Figure S7.** \[^{13}\text{C NMR (150 MHz, DMSO-}d_6)\ spectrum of compound 16a (SYN).**

\[^{\text{FTIR (solid, }cm^{-1})}: \ 3063 \ (w, \text{NH}),\ 1741 \ (w),\ 1674 \ (s, \text{C=O}),\ 1600 \ (s, \text{C=O}),\ 1576 \ (s),\ 1526 \ (s),\ 1500 \ (s),\ 1488 \ (m),\ 1456 \ (m),\ 1413 \ (m),\ 1361 \ (s),\ 1304 \ (m),\ 1254 \ (s),\ 1182 \ (m),\ 1161 \ (m),\ 1093 \ (m),\ 1036 \ (m),\ 1012 \ (m),\ 973 \ (w),\ 867 \ (m),\ 790 \ (s),\ 751 \ (s),\ 657 \ (m),\ 621 \ (w).\]

S10
Figure S8. IR spectrum of compound 16a (SYN).

MS (ESI m/z): 327.1 [M-H]^-.

Anal. calcd for C_{17}H_{13}ClN_{2}O_{3} (328.75): C, 62.11; H, 3.99; N, 8.52. Found: C, 62.05; H, 4.07; N, 8.48.

(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-7-methoxy-3,4-dihydroquinoxalin-2(1H)-one (17a (ANTI))
The 3,4-Dihydroquinoxaline-2(1H)-one 17a (ANTI) was prepared according to the general procedure A from ester 12a and diamine 11a with p-TsOH as additive. The crude mixture of ANTI / SYN regioisomers was purified by trituration with acetone and crystalized from EA yielding 59.2 mg (0.18 mmol, 46%) of 17a (ANTI).

**Novelty:** Compound 17a (ANTI) was not described in the literature.

**M.p.:** 288.0 - 291.0 °C [EA], yellow solid compound.

**NMR diagrams:**

\[^1H-NMR\] (300 MHz, DMSO-d_6): δ 13.99 (s, 1H, H-\(N_A(4)\)), 12.06 (s, 1H, H-\(N_A(1)\)), 7.98 (d, 2H, \(J(B_2,B_3) = 8.6\) Hz, 2 x H-\(C_B(2)\)), 7.57 (d, 2H, \(J(B_2,B_3) = 8.6\) Hz, 2 x H-\(C_B(3)\)), 7.53 (d, 1H, \(J(A_5,A_6) = 8.8\) Hz, H-\(C_A(5)\)), 6.79 (dd, 1H, \(J(A_5,A_6) = 8.8\) Hz, \(J(A_6,A_8) = 2.7\) Hz, H-\(C_A(6)\)), 6.73 (s, 1H, -COCH=), 6.72 (d, 1H, \(J(A_6,A_8) = 2.7\) Hz, H-\(C_A(8)\)), 3.77 (s, 3H, -OCH\(_3\)).
**Figure S9.** $^1$H-NMR (300 MHz, DMSO-d$_6$) spectrum of compound 17a (ANTI).

$^{13}$C-NMR (75 MHz, DMSO-d$_6$): $\delta$ 184.9 (C$_B$(1)C=O), 157.0 (C$_A$(2)=O), 156.1 (C$_A$(7)), 146.5 (C$_A$(3)), 137.7 (C$_B$(1)), 136.8 (C$_B$(4)), 129.2 and 129.1 (2 x C$_B$(2 and 3)), 128.8 (C$_A$(8a)), 119.1 and 118.8 (C$_A$(4a) and C$_A$(5)), 111.0 (C$_A$(6)), 100.3 (C$_A$(8)), 88.5 (-COCH=), 55.9 (-OCH$_3$).

**Figure S10.** $^{13}$C-NMR (75 MHz, DMSO-d$_6$) spectrum of compound 17a (ANTI).
**FTIR** (solid, cm⁻¹): 3001 (w, NH), 2837 (w, NH), 1668 (s, C=O), 1632 (s, C=O), 1623 (s), 1524 (m), 1460 (m), 1399 (w), 1358 (m), 1267 (m), 1204 (m), 1170 (m), 1152 (m), 1087 (m), 961 (w), 842 (m), 797 (s), 787 (s), 718 (s), 753 (s), 688 (m), 667 (m), 613 (m).

![IR spectrum of compound 17a (ANTI).](image)

**Figure S11.** IR spectrum of compound 17a (ANTI).

**MS** (ESI m/z): 327.1 [M-H]⁻.

**Anal. calcd for C_{17}H_{13}ClN_{2}O_{3} (328.75):** C, 62.11; H, 3.99; N, 8.52. Found: C, 62.07; H, 4.06; N, 8.36.
\((Z)-3-(2-(4-chlorophenyl)-2-oxoethylidene)-6-fluoro-3,4-dihydroquinoxalin-2(1H)-one (16b (SYN))\)

\[
\begin{array}{c}
\text{1.00 mol eq} \\
\text{F} \\
\text{NH}_2 \\
11b \\
\text{Cl} \\
\text{1.00} \\
\text{HO} \\
\text{C} \\
\text{2} \\
\text{12b} \\
\text{DMF, RT, 72 h} \\
\text{1.20 mol eq DIC} \\
\text{1.20 mol eq HOBt} \\
\text{N} \\
\text{O} \\
\text{F} \\
\text{16b (SYN) (51 %)} \\
\end{array}
\]

The 3,4-Dihydroquinoxaline-2(1H)-one 16b (SYN) was prepared according to the general procedure B from acid 12b diamine 11b. The crude mixture of ANTI / SYN regioisomers was purified by crystallization from DMSO yielding 71.3 mg (0.23 mmol, 51%) of 16b (SYN).

**Novelty:** Compound 16b (SYN) was not described in the literature.

**M.p.:** 310.0 - 314.0 °C [DMSO], yellow solid compound.

**NMR diagrams:**

\[1^H \text{NMR (300 MHz, DMSO-}d_6\text{): } \delta \text{ 13.41 (s, 1H, H-N}_A\text{(4)), 12.05 (s, 1H, H-N}_A\text{(1)), 8.01 (d, 2H, } J(B_2,B_3) = 8.6 \text{ Hz, 2 x H-C}_B\text{(2))}, 7.60 \text{ (d, 2H, } J(B_2,B_3) = 8.6 \text{ Hz, 2 x H-C}_B\text{(3))}, 7.60 \text{ (dd, 1H, } J(A_5,F) = 9.2 \text{ Hz, } J(A_5,A_7) = 2.7 \text{ Hz, H-C}_A\text{(5))}, 7.13 \text{ (dd, 1H, } J(A_7,A_8) = 8.8 \text{ Hz, } J(A_8,F)\text{).} \]
= 5.2 Hz, H-C_A(8)), 7.00 (ddd, 1H, J(A_7,A_8) = 8.8 Hz, J(A_7,F) = 8.8 Hz, J(A_5,A_7) = 2.7 Hz, H-C_A(7)), 6.83 (s, 1H, -COCH=).

**Figure S12.** ^1_H NMR (300 MHz, DMSO-d_6) spectrum of compound 16b (SYN).

**13C NMR** (75 MHz, DMSO-d_6): δ 187.8 (C_B(1)=O), 159.4 (C_A(2)=O), 155.8 (C_A(6)), 145.8 (C_A(3)), 137.6 and 137.4 (C_B(1) and C_B(4)), 129.4 and 129.3 (2 x C_B(2 and 3)), 125.6 (C_A(4a)), 123.8 (C_A(8a)), 117.0 (C_A(8)), 111.3 (C_A(7)), 90.2 (-COCH=).

**Figure S13.** ^13_C NMR (75 MHz, DMSO-d_6) spectrum of compound 16b (SYN).
**FTIR** (solid, cm\(^{-1}\)): 3080 (s, NH), 1684 (s, C=O), 1605 (m, C=O), 1588 (m), 1540 (m), 1523 (s), 1500 (m), 1486 (m), 1456 (m), 1424 (m), 1397 (m), 1362 (m), 1322 (m), 1251 (s), 1238 (s), 1175 (m), 1151 (m), 1115 (m), 1091 (s), 1070 (m), 1012 (m), 984 (w), 915 (w), 880 (m), 870 (m), 842 (m), 794 (s), 780 (s), 751 (m), 719 (m), 668 (s), 629 (m).

![Figure S14. IR spectrum of compound 16b (SYN).](image)

**MS** (ESI m/z): 315.1 [M-H].

**Anal. calcld for C\(_{16}\)H\(_{10}\)ClFN\(_2\)O\(_2\) (316.71):** C, 60.68; H, 3.18; N, 8.85. Found: C, 60.89; H, 3.33; N, 8.90.
(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-7-fluoro-3,4-dihydroquinoxalin-2(1H)-one (17b (ANTI))

The 3,4-dihydroquinoxaline-2(1H)-one 17b (ANTI) was prepared according to the general procedure A from ester 12a and diamine 11b without any additive. The crude mixture of ANTI / SYN regioisomers was purified by FLC (EA / H, 1 / 3) yielding 48.5 mg (0.15 mmol, 39%) of 17b (ANTI).

**Novelty:** Compound 17b (ANTI) was not described in the literature.

**M.p.:** 301.0 - 305.0 °C [EA / H], yellow solid compound.

**NMR diagrams:**

$^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 13.65 (s, 1H, H-N$_A$(4)), 12.13 (s, 1H, H-N$_A$(1)), 7.99 (d, 2H, $J$(B$_2$B$_3$) = 8.6 Hz, 2 x H-C$_B$(2)), 7.64 (dd, 1H, $J$(A$_5$A$_6$) = 8.8 Hz, $J$(A$_5$F) = 5.3 Hz, H-C$_A$(5)), 7.59 (d, 2H, $J$(B$_2$B$_3$) = 8.6 Hz, 2 x H-C$_B$(3)), 7.01 (ddd, 1H, $J$(A$_5$A$_6$) = 8.8 Hz,
$J(A_6,F) = 8.8$ Hz, $J(A_6,A_8) = 2.8$ Hz, H-$C_A(6)$, 6.92 (dd, 1H, $J(A_8,F)) = 9.4$ Hz, $J(A_6,A_8) = 2.8$ Hz, H-$C_A(8)$, 6.77 (s, 1H, -COCH=).

Figure S15. $^1$H NMR (300 MHz, DMSO-$d_6$) spectrum of compound 17b (ANTI).

$^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ 186.4 ($C_B(1)$=O), 156.9 and 155.6 ($C_A(2)$=O and $C_A(7)$), 145.5 ($C_A(3)$), 137.2 and 136.7 ($C_B(1$ and 4)), 2 x 128.8 (2 x $C_B(2$ and 3)), 128.0, 120.0 and 118.6 ($C_A(5$, 4a and 8a)), 110.5 ($C_A(6)$), 101.9 ($C_A(8)$), 88.8 (-COCH=).

Figure S16. $^{13}$C NMR (75 MHz, DMSO-$d_6$) spectrum of compound 17b (ANTI).
**FTIR** (solid, cm⁻¹): 2962 (s, NH), 1684 (w, C=O), 1617 (w, C=O), 1515 (w), 1368 (w), 1257 (m), 1010 (s), 788 (s), 752 (m), 680 (m).

**Figure S17.** IR spectrum of compound 17b (ANTI).

**MS** (ESI m/z): 315.0 [M-H]⁻.

**Anal. calcd for C₁₆H₁₀ClF₃N₂O₂ (316.71):** C, 60.68; H, 3.18; N, 8.85. Found: C, 60.50; H, 3.22; N, 8.71.

(Z)-6-Chloro-3-(2-(4-chlorophenyl)-2-oxoethylidene)-3,4-dihydroquinoxalin-2(1H)-one (16c (SYN))
The 3,4-dihydroquinoxaline-2(1H)-one 16c (SYN) was prepared according to the general procedure B from acid 12b diamine 11c. The crude mixture of ANTI / SYN regioisomers was purified by precipitation from DMSO by H₂O yielding 44.1 mg (0.13 mmol, 30%) of 16c (SYN).

**Novelty:** Compound 16c (SYN) was not described in the literature.

**M.p.:** 285.4 – 286.8 °C [DMSO], yellow solid compound.

**NMR diagrams:**

\[ \text{1H NMR} (300 MHz, DMSO-d₆): } \delta 13.36 \text{ (s, 1H, H-N₄ (4))}, 12.11 \text{ (s, 1H, H-N₅ (1))}, 8.01 \text{ (d, 2H, J(B₂,B₃) = 8.6 Hz, 2 x H-C₆ (2))}, 7.79 \text{ (d, 1H, J(A₅,A₇) = 2.5 Hz, H-C₅ (5))}, 7.60 \text{ (d, 2H, J(B₂,B₃) = 8.6 Hz, 2 x H-C₆ (3))}, 7.18 \text{ (dd, 1H, J(A₇,A₈) = 8.6 Hz, J(A₅,A₇) = 2.5 Hz, H-C₅ (7))}, 7.12 \text{ (d, 1H, J(A₇,A₈) = 8.6 Hz, H-C₅ (8))}, 6.83 \text{ (s, 1H, -COCH=).} \]
**Figure S18.** $^1$H NMR (300 MHz, DMSO-$d_6$) spectrum of compound 16c (SYN).

$^{13}$C NMR (150 MHz, DMSO-$d_6$): $\delta$ 187.8 ($C_B$(1)C=O), 156.0 ($C_A$(2)=O), 145.7 ($C_A$(3)), 137.6 and 137.4 ($C_B$(1 and 4)), 129.5 and 129.3 (2 x $C_B$(2 and 3)), 127.8 ($C_A$(6)), 126.1 ($C_A$(8a)), 125.8 ($C_A$(4a)), 124.1 ($C_A$(7)), 117.1 ($C_A$(8)), 116.7 ($C_A$(5)), 90.3 (-COCH=).

**Figure S19.** $^{13}$C NMR (150 MHz, DMSO-$d_6$) spectrum of compound 16c (SYN).
**FTIR** (solid, cm\(^{-1}\)): 3055 (m, NH), 2961 (s), 2918 (s, NH), 2850 (m), 1690 (s, C=O), 1605 (m), 1578 (m), 1536 (m), 1489 (m), 1459 (m), 1400 (w), 1349 (m), 1256 (m), 1086 (s), 1012 (s), 949 (w), 862 (w), 838 (m), 789 (s), 752 (s), 660 (w).

![IR spectrum of compound 16c (SYN).](image)

**Figure S20.** IR spectrum of compound 16c (SYN).

**MS** (ESI m/z): 331.0 \([M-\text{H}]^\cdot\).

**Anal. calcd for C\(_{16}\)H\(_{10}\)Cl\(_2\)N\(_2\)O\(_2\) (333.17):** C, 57.68; H, 3.03; N, 8.41. Found: C, 57.35; H, 3.10; N, 8.43.

**(Z)-7-Chloro-3-(2-(4-chlorophenyl)-2-oxoethylidene)-3,4-dihydroquinoxalin-2(1H)-one (17c (ANTI))**

![Chemical structures](image)
The 3,4-dihydroquinoxaline-2(1H)-one 17c (ANTI) was prepared according to the general procedure A from ester 12a and diamine 11c without any additive. The crude mixture of ANTI / SYN regioisomers was purified by FLC (EA / H, 1 / 5) yielding 49.7 mg (0.15 mmol, 38 %) of 17c (ANTI).

**Novelty:** Compound 17c (ANTI) was not described in the literature.

**M.p.:** 297.0 - 299.0 °C [EA / H], yellow solid compound.

**NMR diagrams:**

\[
\begin{align*}
\text{\textsuperscript{1}H NMR (300 MHz, DMSO-}d_6\text{): } & \delta 13.51 \text{ (s, 1H, H-N}_A\text{(4))}, 12.11 \text{ (s, 1H, H-N}_A\text{(1))}, 8.00 \text{ (d, 2H, } J(B_2,B_3) = 8.7 \text{ Hz, 2 x H-C}_B\text{(2))}, 7.61 \text{ (d, 1H, } J(A_5,A_6) = 8.5 \text{ Hz, H-C}_A\text{(5))}, 7.59 \text{ (d, 2H, } J(B_2,B_3) = 8.7 \text{ Hz, 2 x H-C}_B\text{(3))}, 7.17 \text{ (dd, 1H, } J(A_5,A_6) = 8.5 \text{ Hz, } J(A_6,A_8) = 2.3 \text{ Hz, H-C}_A\text{(6))}, 7.14 \text{ (d, 1H, } J(A_6,A_8) = 2.3 \text{ Hz, H-C}_A\text{(8))}, 6.80 \text{ (s, 1H, -COCH=).}
\end{align*}
\]
Figure S21. $^1$H NMR (300 MHz, DMSO-$d_6$) spectrum of compound 17c (ANTI).

$^{13}$C NMR (150 MHz, DMSO-$d_6$): δ 187.5 (C$_B$(1)C=O), 156.1 (C$_A$(2)=O), 145.7 (C$_A$(3)), 137.6 and 137.3 (C$_B$(1 and 4)), 130.5 (C$_A$(7)), 129.4 and 129.3 (2 x C$_B$(2 and 3)), 128.5 (C$_A$(8a)), 128.0 (C$_A$(4a)), 123.7 (C$_A$(6)), 118.8 (C$_A$(5)), 115.1 (C$_A$(8)), 89.9 (-COCH=).

Figure S22. $^{13}$C NMR (150 MHz, DMSO-$d_6$) spectrum of compound 17c (ANTI).

FTIR (solid, cm$^{-1}$): 3057 (m, NH), 2920 (s, NH), 2850 (m), 1680 (s, C=O), 1605 (m), 1578 (m), 1536 (m), 1489 (w), 1459 (m), 1399 (w), 1349 (m), 1251 (m), 1223 (m), 1089 (s), 1013 (s), 949 (w), 861 (w), 838 (m), 805 (s), 753 (s), 682 (w), 632 (m).
Figure S23. IR spectrum of compound 17c (ANTI).

MS (ESI m/z): 331.0 [M-H]-.

Anal. calc for C_{16}H_{10}Cl_{2}N_{2}O_{2} (333.17): C, 57.68; H, 3.03; N, 8.41. Found: C, 57.88; H, 3.14; N, 8.35.

(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-2-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxylic acid (16d (SYN))

The 3,4-dihydroquinoxaline-2(1H)-one 16d (SYN) was prepared according to the general procedure A from ester 12a diamine 11d and p-TsOH as additive. The crude mixture of ANTI
SYN regioisomers was purified by crystallization from DMSO yielding 64.6 mg (0.19 mmol, 48%) 16d (SYN).

**Novelty:** Compound 16d (SYN) was not described in the literature.

**M.p.:** 363.0 - 365.0 °C [DMSO], yellow solid compound.

**NMR diagrams:**

\[ \delta 13.48 (s, 1H, H_{-}N_{A}(4)), 12.92 (br s, 1H, -COOH), 12.26 (s, 1H, H-N_{A}(1)), 8.04 (d, 1H, J(A_{5},A_{7}) = 1.5 Hz, H-C_{A}(5)), 7.99 (d, 2H, J(B_{2},B_{3}) = 8.4 Hz, 2 x H-C_{B}(2)), 7.69 (dd, 1H, J(A_{7},A_{8}) = 8.3 Hz, J(A_{5},A_{7}) = 1.5 Hz, H-C_{A}(7)), 7.57 (d, 2H, J(B_{2},B_{3}) = 8.4 Hz, 2 x H-C_{B}(3)), 7.18 (d, 1H, J(A_{7},A_{8}) = 8.3 Hz, H-C_{A}(8)), 6.79 (s, 1H, -COCH=). \]

**Figure S24.** \(^1\)H NMR (600 MHz, DMSO-\(d_6\)) spectrum of compound 16d (SYN).
$^{13}\text{C NMR}$ (150 MHz, DMSO-$d_6$): $\delta$ 187.7 (C$_B$(1)C=O), 167.0 (-COOH), 156.4 (C$_A$(2)), 145.8 (C$_A$(3)), 137.8 (C$_B$(1)), 137.2 (C$_B$(4)), 130.8 (C$_A$(8a)), 129.4 and 129.3 (2 x C$_B$(2 and 3)), 126.4 (C$_A$(6)), 125.6 (C$_A$(7)), 124.4 (C$_A$(4a)), 118.3 (C$_A$(5)), 115.8 (C$_A$(8)), 90.0 (-COCH=).

**Figure S25.** $^{13}\text{C NMR}$ (150 MHz, DMSO-$d_6$) spectrum of compound 16d (SYN).

**Figure S26.** Part of HMBC NMR spectra of compound 16d (SYN) with peak (6.79, 124.34) that confirms regioisomerism.
Figure S27. Part of NOESY NMR spectra of compound 16d (SYN) with peaks (12.26, 7.18; 13.48, 8.02) that confirm regioisomerism.

**FTIR** (solid, cm$^{-1}$): 3184 (s, -OH), 2925 (m), 1732 (w), 1688 (s, C=O), 1615 (s), 1586 (s), 1550 (w), 1486 (w), 1366 (m), 1247 (m), 1218 (m), 1095 (m), 1065 (w), 1011 (w), 787 (w), 750 (m).
Figure S28. IR spectrum of compound 16d.

**MS** (ESI m/z): 341.2 \([M-H]^{-}\).

**Anal. calc**d for C\textsubscript{17}H\textsubscript{11}ClN\textsubscript{2}O\textsubscript{4} (342.73): C, 59.57; H, 3.23; Cl, 10.34; N, 8.17. Found: C, 59.40; H, 3.27; Cl, 10.38; N, 8.04.

(Z)-2-(2-(4-Chlorophenyl)-2-oxoethylidene)-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxylic acid (17d (ANTI))

The 3,4-dihydroquinoxaline-2(1H)-one 17d (ANTI) was prepared according to the general procedure A from diamine 11d, ester 12a and (1.00 equiv) of DMAP as additive. The crude product was crystallized from DMSO and obtained as salt with DMAP. To liberate free acid
**17d** (ANTI), the salt was suspended in 1 M HCl, stirred for 24 h, solid material filtered off, washed with water and dried yielding 48.4 mg (0.14 mmol, 36%) of **17d** (ANTI).

Alternatively **17d** (ANTI) was prepared also by the general procedure B from diamine **11d** and acid **12b**. The crude product crystallized from DMSO to yield 105.9 mg (0.31 mmol, 70%) of **17d** (ANTI).

**Novelty:** Compound **17d** (ANTI) was not described in the literature.

**M.p.:** 391.0 - 392.0 °C [DMSO], yellow solid compound.

**NMR diagrams:**

\[ ^1H \text{ NMR} (300 \text{ MHz}, \text{DMSO-d}_6): \delta \ 13.44 (s, 1H, H-N_A(4)), \ 12.95 (br s, 1H, -COOH), \ 12.14 (s, 1H, H-N_A(1)), \ 8.02 (d, 2H, J(B_2,B_3) = 8.6 \text{ Hz}, 2 \times \text{H-C}_B(2)), \ 7.73 (d, 1H, J(A_6,A_8) = 1.6 \text{ Hz}, H-C_A(8)), \ 7.67 (dd, 1H, J(A_5,A_6) = 8.4 \text{ Hz}, J(A_6,A_8) = 1.6 \text{ Hz}, H-C_A(6)), \ 7.61 (d, 1H, J(A_5,A_6) = 8.4 \text{ Hz}, H-C_A(5)), \ 7.60 (d, 2H, J(B_2,B_3) = 8.6 \text{ Hz}, 2 \times \text{H-C}_B(3)), \ 6.87 (s, 1H, -COCH=). \]
**Figure S29.** $^1$H NMR (300 MHz, DMSO-$d_6$) spectrum of compound 17d (ANTI).

$^{13}$C NMR (150 MHz, DMSO-$d_6$): $\delta$ 188.3 (C$_B$(1)C=O), 167.0 (-COOH), 156.1 (C$_A$(2)=O), 145.6 (C$_A$(3)), 2 x 137.6 (C$_B$(1 and 4)), 129.5 and 129.3 (2 x C$_B$(2 and 3)), 128.1 (C$_A$(4a)), 2 x 126.9 (C$_A$(8a and 7)), 125.2 (C$_A$(6)), 2 x 116.9 (C$_A$(5 and 8)), 90.8 (-COCH=).

**Figure S30.** $^{13}$C NMR (150 MHz, DMSO-$d_6$) spectrum of compound 17d (ANTI).
Figure S31. Part of HMBC NMR spectra of 17d (ANTI) with peak (6.84, 127.78) that confirms regioisomerism.

FTIR (solid, cm\(^{-1}\)): 3486 (m), 3206 (s, -OH), 2634 (w), 1706 (s, C=O), 1661 (w), 1628 (m), 1586 (s, C=O), 1522 (w), 1398 (m), 1374 (w), 1291 (m), 1248 (m), 1184 (m), 1093 (w), 1056 (m), 1009 (w), 899 (w), 781 (w), 764 (w), 721 (w).
Figure S32. IR spectrum of compound 17d (ANTI).

MS (ESI m/z): 341.0 [M-H]-.

Anal. calcd for C_{17}H_{11}ClN_{2}O_{4} (342.73): C, 59.57; H, 3.23; N, 8.17. Found: C, 59.50; H, 3.20; N, 8.20.

(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-2-oxo-1,2,3,4-tetrahydroquinoxaline-6-carbonitrile (16e (SYN))

The 3,4-dihydroquinoxaline-2(1H)-one 16e (SYN) was prepared according to the general procedure A from ester 12a diamine 11e and p-TsOH as additive. The crude mixture of ANTI
/ SYN regioisomers was purified by precipitation from DMSO by H₂O yielding 52.8 mg (0.16 mmol, 37%) 16e (SYN).

**Novelty:** Compound 16e (SYN) was described in the literature by M.p.⁵

**M.p.:** 317.6 – 319.4 °C [DMSO], yellow solid compound (lit. 295 - 296 °C [EtOH]).⁵

**NMR diagrams:**

**¹H NMR** (600 MHz, DMSO-d₆): \( \delta \) 13.31 (s, 1H, H-Nₐ(4)), 12.32 (s, 1H, H-Nₐ(1)), 8.14 (d, 1H, \( J(A₅,A₇) = 1.7 \) Hz, H-Cₐ(5)), 8.02 (d, 2H, \( J(B₂,B₃) = 8.6 \) Hz, 2 x H-Cₐ(3)), 7.61 (d, 2H, \( J(B₂,B₃) = 8.6 \) Hz, 2 x H-Cₐ(3)), 7.54 (dd, 1H, \( J(A₇,A₈) = 8.2 \) Hz, \( J(A₅,A₇) = 1.7 \) Hz, H-Cₐ(7)), 7.22 (d, 1H, \( J(A₇,A₈) = 8.2 \) Hz, H-Cₐ(8)), 6.84 (s, 1H, -COCH=).
Figure S33. $^1$H NMR (600 MHz, DMSO-$d_6$) spectrum of compound 16e (SYN).

$^{13}$C NMR (150 MHz, DMSO-$d_6$): $\delta$ 188.1 ($C_B$(1)=O), 156.4 ($C_A$(2)), 145.3 ($C_A$(3)), 137.6 and 137.5 ($C_B$(1 and 4)), 131.0 ($C_A$(8a)), 129.5 and 129.4 (2 x $C_B$(2 and 3)), 127.9 ($C_A$(7)), 125.3 ($C_A$(4a)), 120.9 ($C_A$(5)), 119.2 (CN), 116.6 ($C_A$(8)), 105.7 ($C_A$(6)), 90.6 (-COCH=).

Figure S34. $^{13}$C NMR (150 MHz, DMSO-$d_6$) spectrum of compound 16e (SYN).
FT IR (solid, cm\(^{-1}\)): 3072 (s), 2231 (s, C=N), 1688 (s, C=O), 1610 (s, C=O), 1575 (s), 1533 (s), 1495 (m), 1456 (w), 1397 (w), 1352 (s), 1260 (m), 1235 (m), 1170 (m), 1139 (w), 1088 (m), 1057 (m), 1014 (m), 973 (m), 906 (m), 782 (s), 753 (s), 680 (m), 655 (m), 615 (s).

Figure S35. IR spectrum of compound 16e (SYN).

MS (ESI m/z): 322.0 [M-H]⁻.

Anal. calcd for C\(_{17}\)H\(_{10}\)ClN\(_3\)O\(_2\) (323.73): C, 63.07; H, 3.11; N, 12.98. Found: C, 63.31; H, 3.19; N, 13.12.
The 3,4-dihydroquinoxaline-2(1H)-one 17e (ANTI) was prepared according to the general procedure B from acid 12b diamine 11e. The crude mixture of ANTI / SYN regioisomers was purified by FLC (EA / H, 1 / 2) yielding 80.0 mg (0.25 mmol, 56%) of 17e (ANTI).

**Novelty:** Compound 17e (ANTI) was described in the literature by its M.p.\(^5\)

**M.p.:** 354.0 – 355.0 °C [MeOH], yellow solid compound (lit. 311 - 312 °C [EtOH]).\(^5\)

**NMR diagrams:**

$^1$H NMR (300 MHz, DMSO-$d_6$): δ 13.27 (s, 1H, H-N$_A$(4)), 12.19 (s, 1H, H-N$_A$(1)), 8.03 (d, 2H, J(B$_2$,B$_3$) = 8.4 Hz, 2 x H-C$_B$(2)), 7.74 (d, 1H, J(A$_5$,A$_6$) = 8.4 Hz, H-C$_A$(5)), 7.62 (d, 2H, J(B$_2$,B$_3$) = 8.4 Hz, 2 x H-C$_B$(3)), 7.56 (dd, 1H, J(A$_5$,A$_6$) = 8.4 Hz, J(A$_6$,A$_8$) = 1.5 Hz, H-C$_A$(6)), 7.40 (d, 1H, J(A$_6$,A$_8$) = 1.5 Hz, H-C$_A$(8)), 6.89 (s, 1H, -COCH=).

Figure S36. $^1$H NMR (300 MHz, DMSO-$d_6$) spectrum of compound 17e (ANTI).

$^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 190.7 (C$_B$(1)C=O), 158.2 (C$_A$(2)), 147.1 (C$_A$(3)), 139.9 and 139.6 (C$_B$(1 and 4)), 131.8, 131.6 and 130.8 (C$_A$(4a, 6 and 8)), 129.9 and 129.7 (2 x C$_B$(2 and 3)), 121.3, 121.0 and 120.1 (C$_A$(5 and 8a) and -CN), 107.6 (C$_A$(7)), 93.7 (-COCH=).
Figure S37. $^{13}$C NMR (75 MHz, DMSO-$d_6$) spectrum of compound 17e (ANTI).

**FTIR** (solid, cm$^{-1}$): 3094 (w, NH), 2912 (m, NH), 2225 (s, CN), 1682 (m, C=O), 1577 (s, C=O), 1549 (s), 1526 (m), 1456 (m), 1399 (m), 1354 (s), 1344 (s), 1269 (m), 1247 (s), 1166 (m), 1085 (m), 1058 (s), 1012 (s), 876 (m), 842 (s), 819 (s), 799 (s), 757 (s), 661 (s), 611 (s).

Figure S38. IR spectrum of compound 17e (ANTI).
MS (ESI m/z): 322.1 [M-H].

**Anal. calcd for C_{17}H_{10}ClN_{3}O_{2} (323.73):** C, 63.07; H, 3.11; N, 12.98. Found: C, 63.11; H, 3.18; N, 12.90.

(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-6-nitro-3,4-dihydroquinoxalin-2(1H)-one (16f (SYN))

The 3,4-dihydroquinoxaline-2(1H)-one 16f (SYN) was prepared according to the general procedure A from ester 12a diamine 11f and p-TsOH as additive. The crude mixture of ANTI / SYN regioisomers was purified by trituration with EA and crystallization from DMSO yielding 48.5 mg (0.14 mmol, 32 %) 16f (SYN).

**Novelty:** Compound 16f (SYN) was not described in the literature.

**M.p.:** 325.0 - 328.0 °C [DMSO], yellow solid compound.

**NMR diagrams:**
**1H NMR** (300 MHz, DMSO-d$_6$): $\delta$ 13.19 (s, 1H, H-N$_A$(4)), 12.38 (s, 1H, H-N$_A$(1)), 8.59 (d, 1H, $J$(A$_5$,A$_7$) = 2.5 Hz, H-C$_A$(5)), 7.96 (d, 2H, $J$(B$_2$,B$_3$) = 8.6 Hz, 2 x H-C$_B$(2)), 7.94 (dd, 1H, $J$(A$_7$,A$_8$) = 8.8, $J$(A$_5$,A$_7$) = 2.5 Hz, H-C$_A$(7)), 7.55 (d, 2H, $J$(B$_2$,B$_3$) = 8.6 Hz, 2 x H-C$_B$(3)), 7.19 (d, 1H, $J$(A$_7$,A$_8$) = 8.8 Hz, H-C$_A$(8)), 6.80 (s, 1H, -COCH=).

![Figure S39](image)

**Figure S39.** $^1$H NMR (300 MHz, DMSO-d$_6$) spectrum of compound 16f (SYN).

**13C NMR** (75 MHz, DMSO-d$_6$): $\delta$ 187.4 (C$_B$(1)C=O), 156.0 (C$_A$(2)), 144.4 (C$_A$(3)), 142.6 (C$_A$(6)), 137.0 and 136.9 (C$_B$(1 and 4)), 132.1 (C$_A$(8a)), 129.0 and 128.8 (2 x C$_B$(2 and 3)), 124.6 (C$_A$(4a)), 119.0 (C$_A$(8)), 115.5 (C$_A$(7)), 112.3 (C$_A$(5)), 90.4 (-COCH=).
**Figure S40.** $^{13}$C NMR (75 MHz, DMSO-$d_6$) spectrum of compound 16f (SYN).

**FTIR** (solid, cm$^{-1}$): 3090 (m, NH), 2855 (m, NH), 1682 (m, C=O), 1601 (s, C=O), 1579 (s), 1541 (m), 1482 (m, NO$_2$), 1433 (w), 1411 (w), 1352 (m), 1316 (s), 1279 (s), 1265 (m), 1245 (m), 1172 (m), 1133 (m), 1087 (m), 1032 (s), 1008 (s), 953 (m), 937 (m), 874 (s), 832 (m), 807 (s), 767 (s), 742 (s), 722 (m), 710 (m), 637 (m).

**Figure S41.** IR spectrum of compound 16f (SYN).
**MS** (ESI m/z): 342.0 [M-H].

**Anal. calcd for C\textsubscript{16}H\textsubscript{10}ClN\textsubscript{3}O\textsubscript{4} (343.72):** C, 55.98; H, 2.93; N, 12.23. Found: C, 56.14; H, 2.90; N, 12.05.

(Z)-3-(2-(4-Chlorophenyl)-2-oxoethylidene)-7-nitro-3,4-dihydroquinoxaline-2(1H)-one (17f (ANTI))

The 3,4-dihydroquinoxaline-2(1H)-one 17f (ANTI) was prepared according to the general procedure B from acid 12b diamine 11f. The crude mixture of ANTI / SYN regioisomers was purified by trituration with boiling CHCl\textsubscript{3} yielding 100.0 mg (0.29 mmol, 66%) of 17f (ANTI).

**Novelty:** Compound 17f (ANTI) was not described in the literature.

**M.p.:** 319.0 - 321.0 °C [CHCl\textsubscript{3}], yellow solid compound.
NMR diagrams:

\[ \delta \text{ (H, DMSO-}d_6) \]

1H NMR (300 MHz, DMSO-\(d_6\)): \(\delta\) 13.21 (s, 1H, H-N\(A(4)\)), 12.19 (s, 1H, H-N\(A(1)\)), 7.98 (d, 2H, \(J(B_2,B_3) = 8.6\ Hz\), 2 x H-C\(B(2)\)), 7.92 (dd, 1H, \(J(A_5,A_6) = 8.9\ Hz\), \(J(A_6,A_8) = 2.4\ Hz\), H-C\(A(6)\)), 7.87 (d, 1H, \(J(A_6,A_8) = 2.4\ Hz\), H-C\(A(8)\)), 7.71 (d, 1H, \(J(A_5,A_6) = 8.9\ Hz\), H-C\(A(5)\)), 7.57 (d, 2H, \(J(B_2,B_3) = 8.6\ Hz\), 2 x H-C\(B(3)\)), 6.86 (s, 1H, -COCH=).

![Figure S42](image_url)  

**Figure S42.** 1H NMR (300 MHz, DMSO-\(d_6\)) spectrum of compound **17f (ANTI)**.
$^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 188.2 (C$_B$(1)C=O), 155.5 (C$_A$(2)=O), 144.0 (C$_A$(3)), 142.1 (C$_A$(7)), 137.3 and 136.7 (C$_B$(1 and 4)), 129.9, 129.1 and 128.9 (C$_A$(4a) and 2 x C$_B$(2 and 3)), 126.7 (C$_A$(8a)), 118.9 (C$_A$(8)), 116.8 (C$_A$(6)), 110.3 (C$_A$(5)), 91.7 (-COCH=).

**Figure S43.** $^{13}$C NMR (75 MHz, DMSO-$d_6$) spectrum of compound 17f (ANTI).

FTIR (solid, cm$^{-1}$): 3036 (m, NH), 2892 (m, NH), 2849 (m), 1693 (s, C=O), 1628 (m), 1605 (m), 1579 (s, NO$_2$), 1551 (m), 1528 (m), 1490 (w), 1458 (w), 1399 (m), 1332 (m), 1281 (m), 1255 (m), 1243 (m), 1182 (w), 1133 (w), 1089 (m), 1056 (m), 1010 (m), 963 (w), 886 (m), 846 (m), 809 (s), 740 (s) 669 (m).
Figure S44. IR spectrum of compound 17f (ANTI).

MS (ESI m/z): 342.1 [M-H]⁻.

**Anal. calcd for C₁₆H₁₀ClN₃O₄ (343.72):** C, 55.91; H, 2.93; N, 12.23. Found: C, 55.99; H, 3.05; N, 12.10.