Supporting Information

for

A Brønsted base-promoted diastereoselective dimerization of azlactones

Danielle L. J. Pinheiro, Gabriel M. F. Batista, Pedro P. de Castro, Leonã S. Flores, Gustavo F. S. Andrade and Giovanni W. Amarante*

Address: Chemistry Department, Federal University of Juiz de Fora, Cidade Universitária, São Pedro, Juiz de Fora, MG, CEP 36036-900, Brazil

Email: Giovanni W. Amarante - giovanni.amarante@ufjf.edu.br

*Corresponding author

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1- Experimental section

General information

Unless otherwise noted, all reagents were obtained commercially and used without further purification. Unless otherwise noted, all reaction mixtures were carried out in flame-dried flask under a positive pressure of dry nitrogen. Analytical thin layer chromatography (TLC) was performed on precoated glass-backed TLC plates (silica gel 60 F254) and visualized by UV lamp (254 nm). Yields refer to chromatographically purified or by recrystallization and spectroscopically pure compounds, unless stated otherwise. $^1$H and $^{13}$C spectra were recorded on a 500 MHz spectrometer. Chemical shifts are reported in ppm. $^1$H NMR spectra were referenced to CDCl$_3$ (7.26 ppm) and $^{13}$C NMR spectra were referenced to CDCl$_3$ (77.0 ppm). All $^{13}$C spectra were measured with complete proton decoupling. Peak multiplicities are designated by the following abbreviations: s, singlet; d, doublet; dd, double doublet; t, triplet; m, multiplet; br, broad; and $J$, coupling constant in Hz. High-resolution mass spectra were acquired in the positive ion mode using a mass spectrometer equipped with an electrospray ionization source. Azlactones, were prepared according to literature procedure [1].

General procedure and characterization data for the dimerization of azlactones 2a–i

In a flamed-dried screw-cap vial, with 4 Å molecular sieves as additive, under nitrogen atmosphere, was added CH$_3$CN (to provide a solution 0.06 mol L$^{-1}$ in azlactone), and azlactone (0.3 mmol). To this solution, potassium or sodium trichloroacetate salts (0.09 mmol) were added. The reaction was kept at room temperature for 1 h and monitored by thin layer chromatography. The crude reaction mixture was diluted with CH$_2$Cl$_2$ (10 mL) and washed with water (5 mL). The organic layer was dried over anhydrous Na$_2$SO$_4$, filtered off and concentrated under reduced pressure. At this point, an aliquot was dissolved in CDCl$_3$ and directly analyzed by $^1$H NMR in order to see the corresponding dr. Then the major diastereomer was obtained after recrystallization or purification through column chromatography (hexanes/ethyl acetate 3:1).
**(+/-) N-((3S,5S)-1-Benzoyl-3,5-dimethyl-2,4-dioxopyrrolidin-3-yl)benzamide (2a)**

Diastereomeric ratio (dr) from 1H NMR analysis of crude reaction mixture: 6/1 (trans/cis). The product was purified by recrystallization (EtOH/H2O 5:1) to afford 2a (major diastereomer, 22 mg, 84%) as a white solid (m.p. 226°C). 1H NMR (500 MHz, CDCl3) δ: 7.74-7.72 (m, 2H), 7.70-7.68 (m, 2H), 7.56 (tt, 1H, J = 1.3 Hz, J = 5.0 Hz), 7.53 (tt, 1H, J = 1.3 Hz, J = 5.0 Hz), 7.47-7.44 (m, 2H), 7.42-7.39 (m, 2H), 6.85 (s, 1H), 5.18 (q, 1H, J = 7.0 Hz), 1.70 (s, 3H), 1.67 (d, 3H, J = 7.1 Hz); 13C NMR (125 MHz, CDCl3) δ: 205.7, 172.3, 169.7, 167.4, 134.4, 132.7, 132.5, 130.9, 128.8, 128.7, 128.1, 127.5, 60.8, 60.5, 19.6, 16.9. 2a (minor diastereomer, 3.5 mg, 14%). 1H NMR (500 MHz, CDCl3) δ: 7.83-7.79 (m, 4H), 7.58-7.53 (m, 2H), 7.48-7.41 (m, 4H), 6.69 (s, 1H), 4.94 (q, 1H, J = 8.0 Hz), 1.77 (d, 3H, J = 7.0 Hz), 1.57 (s, 3H); 13C NMR (125 MHz, CDCl3) δ: 206.0, 170.8, 170.3, 167.3, 134.2, 132.9, 132.7, 131.3, 129.8, 128.8, 128.0, 127.5, 60.1, 59.1, 19.1, 14.6. For IR and HRMS data, see reference [2].

**(+/-) N-((3S,5S)-1-Benzoyl-3,5-diisobutyl-2,4-dioxopyrrolidin-3-yl)benzamide (2b)**

Diastereomeric ratio (dr) from 1H NMR analysis of crude reaction mixture: 4/1 (trans/cis). The product was purified by recrystallization (EtOH/H2O 5:1) to afford 2b (major diastereomer, 23 mg, 71%) as a white solid (m.p. 124°C). 1H NMR (500 MHz, CDCl3) δ: 7.72-7.70 (m, 2H), 7.69-7.67 (m, 2H), 7.56 (tt, 1H, J = 1.2 Hz, J = 5.0 Hz), 7.52 (tt, 1H, J = 1.2 Hz, J = 5.0 Hz), 7.47-7.44 (m, 2H), 7.42-7.39 (m, 2H), 6.89 (s, 1H), 5.15 (dd, 1H, J = 4.7 Hz, J = 9.1 Hz), 2.10-2.02 (m, 2H), 1.94-1.92 (m, 2H), 1.85-1.71 (m, 2H), 1.14 (d, 3H, J = 6.6 Hz), 1.10-1.09 (m, 6H), 1.02 (d, 3H, J = 6.6 Hz); 13C NMR (125 MHz, CDCl3) δ: 204.3, 171.9, 169.9, 167.13, 134.7, 132.6, 132.5, 128.9, 128.7, 128.6, 128.1, 127.4, 64.5, 62.7, 41.8, 41.4, 25.1, 24.4, 24.2, 24.1, 23.1, 21.7. For IR and HRMS data, see reference [2].

**(+/-) N-((3S,5S)-1-Benzoyl-3,5-dibenzyl-2,4-dioxopyrrolidin-3-yl)benzamide (2c)**

Diastereomeric ratio (dr) from 1H NMR analysis of crude reaction mixture: >19/1 (trans/cis). The product was purified by recrystallization (EtOH/H2O 5:1) to afford 2c (major diastereomer, 34 mg, 92%) as a white solid (m.p. 150°C). 1H NMR (500 MHz, CDCl3) δ 7.75-7.73 (m, 2 H), 7.61 (tt, 1H, J = 1.3 Hz, J = 5.0 Hz), 7.52-7.46 (m, 5H), 7.43-7.38 (m, 3H), 7.36-7.33 (m, 4H), 7.30-7.28 (m, 1H), 7.23-7.21 (m, 2H), 7.19-7.17 (m, 2H), 6.72 (s, 1H), 5.52 (dd, 1H, J = 3.6 Hz, J = 5.7 Hz), 3.40 (dd, 1H, J = 5.7 Hz, J = 14.0 Hz), 3.28 (dd, 1H, J = 3.6 Hz, J = 14.0 Hz), 2.43 (d, 1H, J = 14.0 Hz), 2.26 (d, 1H, J = 14.0 Hz); 13C NMR (125 MHz, CDCl3) δ: 204.3, 171.8, 170.0, 167.0, 135.9,
Diastereomeric ratio (dr) from \(^1\)H NMR analysis of crude reaction mixture: >19/1 (trans/cis). The product was purified by column chromatography on silica gel (hexanes/EtOAc 3:1) to afford 2d (major diastereomer, 36 mg, 93%) as a white solid (m.p. 140ºC). IR (TlBr-TlI): 1720, 1683, 1508, 1468, 1258. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta:\) 7.73-7.71 (m, 2H), 7.53-7.46 (m, 6H), 7.36-7.27 (m, 2H) 7.21-7.20 (m, 2H), 7.14-7.04 (m, 6H), 6.51 (s, 1H), 5.46 (dd, 1H, \(J = 3.5\) Hz, \(J = 5.6\) Hz), 3.32 (dd, 2H, \(J = 5.7\) Hz, \(J = 14.4\) Hz), 3.23 (dd, 2H, \(J = 3.5\) Hz, \(J = 14.4\) Hz), 2.35 (s, 3H), 2.29 (s, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta:\) 204.4, 171.9, 170.1, 167.0, 138.4, 137.3, 134.5, 132.7, 132.6, 132.5, 131.1, 130.5, 130.2, 129.9, 129.7, 129.5, 129.3, 129.2, 129.0, 128.8, 128.6, 128.1, 127.5, 127.3, 66.9, 62.2, 35.9, 33.5, 21.1, 21.0; HRMS: calcd for [C34H30N2O4]\(^+\) ([M+Na]\(^+\)) \(m/z\) 553.2103, found 553.2092.

\((+/-)N-(3S,5S)-1-Benzoyl-3,5-bis(4-methylbenzyl)-2,4-dioxopyrrolidin-3-yl)benzamide (2e)

Diastereomeric ratio (dr) from \(^1\)H NMR analysis of crude reaction mixture: 4/1 (trans/cis). The product was purified by column chromatography on silica gel (hexanes/EtOAc 3:1) to afford 2e (major diastereomer, 36 mg, 60%) as a white oil. IR (TlBr-TlI): 1749, 1650, 1635, 1521, 1461, 1283. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta:\) 8.32 (d, 2H, \(J = 8.8\) Hz), 8.30 (d, 2H, \(J = 8.8\) Hz), 7.90 (d, 2H, \(J = 8.9\) Hz), 7.80 (d, 2H, \(J = 8.9\) Hz), 6.79 (s, 1H), 5.10 (dd, 1H, \(J = 4.7, J = 9.6\) Hz), 2.09-2.04 (m, 2H), 2.01-1.99 (m, 2H), 1.97-1.91 (m, 2H), 1.19 (d, 3H, \(J = 6.0\) Hz), 1.15-1.14 (m, 6H), 1.05 (d, 3H, \(J = 6.6\) Hz); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta:\) 203.0, 171.4, 168.0, 165.4, 150.3, 149.7, 149.3, 136.5, 129.4, 128.6, 124.0, 64.6, 62.8, 41.9, 41.2, 29.7, 25.0, 24.5, 24.2, 23.2, 21.5; HRMS: calcd for [C26H28N4O8]\(^+\) ([M+H]\(^+\)) \(m/z\) 525.1985, found 525.1971.

\((+/-)N-(3S,5S)-3,5-Diallyl-1-benzoyl-2,4-dioxopyrrolidin-3-yl)benzamide (2f)

Diastereomeric ratio (dr) from \(^1\)H NMR analysis of crude reaction mixture: 4/1 (trans/cis). The product was purified by column chromatography on silica gel (hexanes/EtOAc 3:1) to afford 2f (mixture of diastereomer, 13 mg, 78%) as a white oil. IR (TlBr-TlI): 1743, 1688, 1642, 1524, 1283. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta:\) 7.87-7.85 (m, 2H minor), 7.80-7.78 (m, 2H minor), 7.72-7.68 (m, 3H major + 4H minor), 7.59-7.55 (m, 1H major + 2H minor), 7.52 (tt, \(J = 1.0\) Hz, \(J = 7.5\) Hz, 1H major), 7.48-7.39 (m, 5H major), 7.26-7.12 (m, 2H minor), 3.48 (dd, 2H, \(J = 6.5\) Hz, \(J = 11.2\) Hz), 2.40-2.31 (m, 2H), 2.25-2.19 (m, 2H), 1.97-1.91 (m, 2H), 1.19 (d, 3H, \(J = 6.0\) Hz), 1.15-1.14 (m, 6H), 1.05 (d, 3H, \(J = 6.6\) Hz); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta:\) 203.0, 171.4, 168.0, 165.4, 150.3, 149.7, 149.3, 136.5, 129.4, 128.6, 124.0, 64.6, 62.8, 41.9, 41.2, 29.7, 25.0, 24.5, 24.2, 23.2, 21.5; HRMS: calcd for [C26H28N4O8]\(^+\) ([M+H]\(^+\)) \(m/z\) 525.1985, found 525.1971.
(+/−)-N-((3S,5S)-1-Benzoyl-3,5-bis(2-(methylthio)ethyl)-2,4-dioxopyrrolidin-3-yl)benzamide (2g)

Diastereomeric ratio (dr) from 1H NMR analysis of crude reaction mixture: 4/1 (trans/cis). The product was purified by column chromatography on silica gel (hexanes/EtOAc 4:1) to afford 2g (major diastereomer, 23 mg, 66%) as a white oil. IR (TlBr-Tli): 1743, 1704, 1634, 1508, 1283. 1H NMR (500 MHz, CDCl3) δ: 8.66 (s, 1H), 7.79 (d, 2H, J = 8.0 Hz), 7.71 (d, 2H, J = 8.0 Hz), 7.58-7.52 (m, 2H), 7.48-7.42 (m, 4H), 5.29 (dd, 1H, J = 4.0 Hz, J = 8.0 Hz), 2.96 (t, 2H, J = 6.0 Hz), 2.77-2.76 (m, 1H), 2.66-2.63 (m, 1H), 2.44-2.39 (m, 4H), 2.29 (s, 3H), 2.15 (s, 3H); 13C NMR (125 MHz, CDCl3) δ: 204.3, 171.4, 169.9, 167.2, 134.3, 132.6, 130.9, 128.9, 128.7, 128.2, 127.5, 127.4, 127.33, 123.08, 122.53, 119.04, 65.11, 62.72, 61.66, 37.81, 35.94, 34.06, 33.12; HRMS: calcd for [C24H22N2O4]⁺ ([M+H]⁺): m/z 425.1477, found 425.1470.

(+/−) 4-Bromo-N-((3S,5S)-3,5-dibenzyl-1-(4-bromobenzoyl)-2,4-dioxopyrrolidin-3-yl)benzamide (2h)

Diastereomeric ratio (dr) from 1H NMR analysis of crude reaction mixture: >19/1 (trans/cis). The product was purified by column chromatography on silica gel (hexanes/EtOAc 3:1) to afford 2h (major diastereomer, 40 mg, 88%) as a yellow solid (m.p. 163°C). IR (TlBr-Tli): 3263, 1749, 1678, 1622, 1587, 1520, 1266, 1230, 743. 1H NMR (500 MHz, CDCl3) δ: 8.80 (s, 1H), 7.59 (t, 1H, J = 6.6 Hz), 7.55-7.46 (m, 5H), 7.39 (d, 1H, J = 8.4 Hz), 7.33-7.19 (m, 8H), 7.08-7.03 (m, 3H), 5.36 (dd, 1H, J = 3.9 Hz, 7.5 Hz), 5.00 (q, 1H, J = 7.5 Hz), 2.77 (t, 2H, J = 7.5 Hz), 1.32 (s, 3H), 1.31 (s, 3H); HRMS: calcd for [C24H26N2O4S2]⁺ ([M+Na]+): m/z 481.1442, found 481.1437.
$J = 5.6$ Hz), 3.25 (dd, 1H, $J = 6.9$ Hz, $J = 14.3$ Hz), 3.06 (dd, 1H, $J = 4.3$ Hz, $J = 14.3$ Hz), 2.36 (d, 1H, $J = 14.0$ Hz), 2.19 (d, 1H, $J = 14.1$ Hz); $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 204.2, 171.9, 169.2, 166.3, 135.9, 133.3, 132.1, 131.8, 131.6, 130.9, 130.7, 130.5, 130.0, 129.8, 129.4, 129.2, 128.9, 128.8, 128.4, 127.9, 127.7, 126.9, 67.0, 62.3, 36.6, 34.2; HRMS: calcd for [C32H25Br2N2O4]$^+$ ([M+H]$^+$): $m/z$ 659.0181, found 659.0181.

(+/-) $N$-((3S,5S)-1-Benzoyl-3,5-diphenyl-2,4-dioxopyrrolidin-3-yl)benzamide (2i)

Diastereomeric ratio (dr) from $^1$H NMR analysis of crude reaction mixture: >19/1 (trans/cis). The product was purified by column chromatography on silica gel (hexanes/EtOAc 3:1) to afford 2i (major diastereomer, 19 mg, 63%) as a yellow oil. $^1$H NMR (500 MHz, CDCl$_3$) δ: 8.35-8.29 (m, 1H), 8.17-8.11 (m, 1H), 8.02-7.97 (m, 1H), 7.93 (d, 1H, $J = 7.3$ Hz), 7.86 (t, 1H, $J = 7.4$ Hz), 7.82-7.80 (m, 1H), 7.70-7.68 (m, 2H), 7.44-7.51 (m, 8H), 7.37-7.34 (m, 5H), 5.77 (d, 1H, $J = 6.8$ Hz); $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 199.4, 170.3, 167.3, 166.4, 134.3, 133.7, 133.4, 133.4, 133.1, 132.7, 130.6, 129.9, 129.0, 128.9, 128.8, 128.7, 128.2, 128.1, 128.0, 127.5, 126.7, 68.7, 67.0; HRMS: calcd for [C30H23N2O4]$^+$ ([M+H]$^+$): $m/z$ 475.1658, found 475.1636. For IR and HRMS data, see reference [2].

4-Isopropyl-2-phenyloxazol-5-ol (2j)

The product was purified by column chromatography on silica gel (hexanes/EtOAc 3:1) to afford 2j (53 mg, 79%) as a white solid (m.p. 125°C). IR (TlBr-TlI): 3255, 2957, 2918, 1723, 1670, 1495, 1483, 1450, 1269, 1138. $^1$H NMR (500 MHz, CDCl$_3$) δ: 8.44 (s, 1H), 7.92-7.81 (m, 2H), 7.66-7.59 (m, 1H), 7.57-7.48 (m, 2H), 3.67 (hept, 1H, $J = 6.9$ Hz), 1.29 (d, 6H, $J = 6.8$ Hz); $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 179.9, 165.2, 133.3, 133.2, 129.2, 127.7, 35.1, 18.9; HRMS: calcd for [C24H25N2O4]$^+$ ([dimer+H]$^+$): $m/z$ 405.1814, found 405.1797.

(S)-4-sec-Butyl-2-phenyloxazol-5-ol (2k)

The product was purified by column chromatography on silica gel (hexanes/EtOAc 3:1) to afford 2k (48 mg, 76%) as a green solid (m.p. 116°C). IR (TlBr-TlI): 3269, 2970, 2924, 2872, 1723, 1670, 1646, 1509, 1483, 1450, 1261, 1138. $^1$H NMR (500 MHz, CDCl$_3$) δ: 8.76 (s, 1H), 7.92-7.80 (m, 2H), 7.59 (td, 1H, $J = 0.9$ Hz, $J = 7.7$ Hz), 7.48 (t,
2H, \( J = 7.7 \) Hz), 3.49 (h, 1H, \( J = 6.8 \) Hz), 1.90-1.76 (m, 1H), 1.57-1.43 (m, 1H), 1.23 (dd, 3H, \( J = 0.6 \) Hz, \( J = 6.8 \) Hz), 0.97 (t, 3H, \( J = 7.2 \) Hz); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \): 179.7, 165.6, 133.2, 129.0, 128.7, 127.8, 127.5, 41.7, 26.6, 16.4, 11.7; HRMS: calcd for [C\(_{26}\)H\(_{29}\)N\(_2\)O\(_4\)]\(^+\) ([dimer+H]): \( m/z \) 433.2127, found 433.2110.

**Preparation and characterization of product 6**

Product 2c (40 mg, 0.12 mmol) was dissolved in acetic acid/dichloromethane (242.4:3.5, 0.24 mL), cooled to 0 °C, and NaBH\(_4\) (5.5 mg, 0.14 mmol) was added. The reaction mixture was stirred for 3 h. The crude reaction mixture was diluted with CH\(_2\)Cl\(_2\) (5 mL) and washed with water (10 mL). The organic layer was dried over anhydrous Na\(_2\)SO\(_4\), filtered off and concentrated under reduced pressure. At this point, the crude reaction mixture was dissolved in CDCl\(_3\) and directly send to \(^1\)H NMR in order to see the corresponding dr.

Diastereomeric ratio from \(^1\)H NMR analysis of crude reaction mixture: >19:1 (trans/cis). The crude product was subjected to flash column chromatography (hexanes/AcOEt 3:1) and the compound 6 was obtained as a white solid, 28 mg, 70% yield (m.p. 140°C). IR (TlBr-TII): 3352, 1719, 1680, 1648, 1618, 1266. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \): 7.62-7.60 (m, 2H), 7.56 (tt, 1H, \( J = 1.2 \) Hz, \( J = 7.5 \) Hz), 7.51-7.49 (m, 3H), 7.45-7.42 (m, 4H), 7.37-7.34 (m, 2H), 7.29-7.26 (m, 3H), 7.25-7.24 (m, 2H), 7.19 (tt, 1H, \( J = 1.2 \) Hz, \( J = 7.3 \) Hz), 7.13-7.11 (m, 2H), 6.68 (s, 1H), 5.56 (d, 1H, \( J = 1.7 \) Hz), 5.20 (dt, 1H, \( J = 6.2 \) Hz, \( J = 9.3 \) Hz), 4.84 (dd, 1H, \( J = 1.6 \) Hz, \( J = 9.3 \) Hz), 3.89 (d, 1H, \( J = 14.5 \) Hz), 3.68 (dd, 1H, \( J = 6.6 \) Hz, \( J = 14.0 \) Hz), 3.15 (d, 1H, \( J = 14.4 \) Hz), 3.09 (dd, 1H, \( J = 5.9 \) Hz, \( J = 14.0 \) Hz); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \): 173.3, 170.0, 168.7, 138.4, 134.7, 134.2, 133.1, 132.8, 132.4, 130.5, 130.1, 128.8, 128.5, 128.4, 128.2, 127.5, 127.0, 126.9, 73.7, 67.4, 58.9, 37.0, 36.2; HRMS: calcd for [C\(_{32}\)H\(_{28}\)N\(_2\)O\(_4\)]\(^+\) ([M+H]): \( m/z \) 505.2127, found 505.2112.
2- $^1$H and $^{13}$C NMR spectra of dimerization products:

$^1$H NMR of 2a (CDCl$_3$, 500 MHz).

$^{13}$C NMR of 2a (CDCl$_3$, 125 MHz).
$^1$H NMR of 2a' (CDCl$_3$, 500 MHz).

$^{13}$C NMR of 2a' (CDCl$_3$, 125 MHz).
$^1$H NMR of 2b (CDCl$_3$, 500 MHz).

$^{13}$C NMR of 2b (CDCl$_3$, 125 MHz).
$^1$H NMR of 2c (CDCl$_3$, 500 MHz).

$^{13}$C NMR of 2c (CDCl$_3$, 125 MHz).
$^1$H NMR of 2d (CDCl$_3$, 500 MHz).

$^{13}$C NMR of 2d (CDCl$_3$, 125 MHz).
$^1$H NMR of 2e (CDCl$_3$, 500 MHz).

$^{13}$C NMR of 2e (CDCl$_3$, 125 MHz).
$^1$H NMR of 2f (CDCl$_3$, 500 MHz).

$^{13}$C NMR of 2f (CDCl$_3$, 125 MHz).
$^{1}$H NMR of $2g$ (CDCl$_3$, 500 MHz).

$^{13}$C NMR of $2g$ (CDCl$_3$, 125 MHz).
$^1$H NMR of 2h (CDCl$_3$, 500 MHz).

$^{13}$C NMR of 2h (CDCl$_3$, 125 MHz).
$^1$H NMR of 2i (CDCl$_3$, 500 MHz).

$^{13}$C NMR of 2i (CDCl$_3$, 125 MHz).
$^1$H NMR of 2j (CDCl$_3$, 500 MHz).

$^{13}$C NMR of 2j (CDCl$_3$, 125 MHz).
$^1$H NMR of 2k (CDCl$_3$, 500 MHz).

$^{13}$C NMR of 2k (CDCl$_3$, 125 MHz).
DEPT135 of 2k (CDCl₃, 125 MHz).
3- $^1$H and $^{13}$C NMR spectra of product 6:

$^1$H NMR of 6 (CDCl$_3$, 500 MHz).

$^{13}$C NMR of 6 (CDCl$_3$, 125 MHz).
DEPT135 of 6 (CDCl₃, 125 MHz).

HSQC of 6
HMBC of 6

NOESY of 6
4- Crude NMR data employed for dr calculation

Crude NMR data of compound 2a

Crude NMR data of compound 2b
Crude NMR data of compound 2c

Crude NMR data of compound 2d
Crude NMR data of compound 2e

Crude NMR data of compound 2f
Crude NMR data of compound 2g

Crude NMR data of compound 2h
Crude NMR data of compound 2i
5- Mechanism and kinetic experiments by NMR monitoring:

Reactions were carried out using NMR technique on a 500 MHz spectrometer. Solutions of azlactone 1a (10.5 mg; 0.06 mmol) and sodium trichloroacetate salt (30 mol %; 1.6 mg) were prepared individually in deuterated acetonitrile (1 mL). The solutions were added to a NMR tube and the reaction was maintained at 25 °C and monitored by a single pulse $^1$H NMR for 15 min. A plot of $1/\sqrt{[A]}$ vs time showed that the reaction exhibited a 3/2 order behavior in azlactone such as was suggested by Mazurkiewicz et al. [4]. Results based on average of three runs.

$^1$H NMR spectra copies which show the formation of CHCl$_3$. The corresponding trichloroacetate salts are freshly prepared, which we believe a little bit of water remains:
Kinetic graphics:

A plot of $1/\sqrt{[A]}$ vs time showed that the reaction exhibited a 3/2 order behavior in azlactone such as was suggested by Mazurkiewick et al. [4]. Results based on average of three runs.

$$\frac{1}{[A]^{1/2}} = (0.0450\pm0.0013) - (0.225\pm0.014)t$$

$R^2 = 0.99047$

Graphic using initial rates technique. Results based on average of three runs:
- Demonstration of reaction order equations for the proposed mechanism:

To obtain the expected reaction order based on the proposed mechanism, one may assume, to simplify notation, in the proposed mechanism in Figure 3 of the main text:

\[
\frac{d[A^-]}{dt} = k_1[A][B] - k_{-1}[A^-][BH] - k_2[A][A^-] \quad \text{(S1)}
\]

Considering the equilibrium for the formation of \( A^- \) in the first step is quickly achieved, so that \( k_{-1}[A][B] \gg k_2[A][A^-] \), the second step may be considered the rate determining step, and one may write down the approximation:

\[-\frac{d[A^-]}{dt} = k_2[A][A^-] \quad \text{(S2)}\]

Considering \( A^- \) as a steady-state, so that only a small concentration of the anion will be present (due to the high value of \( k_{-1} \)), then \( d[A^-]/dt = 0 \), so that:
\[ k_1[A][B] = k_{-1}[A^-][BH] + k_2[A][A^-] \quad (S3) \]

Additionally, because \( k_{-1}[A][B] \gg k_2[A][A^-] \), then \( k_2[A][A^-] \) may be considered negligibly small; and, also due to the same relation above, it may be assumed that only a small fraction of the basis B will exist in the protonated state BH, so that \([B]=[B]_0\), where \([B]_0\) is the initial concentration of the basis added to the reaction vessel, and also that \([A^-] \approx [BH]\). Applying the above considerations, eq. (S3) becomes:

\[ k_1[A][B]_0 = k_{-1}[A^-]^2 \]

Or:

\[ [A^-] = \left( \frac{k_1}{k_{-1}} [A][B]_0 \right)^{1/2} \quad (S4) \]

Substituting (S4) in (S2):

\[ -\frac{d[A^-]}{dt} = k_2 \left( \frac{k_1}{k_{-1}} \right)^{1/2} [A]^{3/2}[B]_0^{1/2} \quad (S5) \]

Equation (S5) indicates that the reaction order for compound 1a would be 3/2 if the reaction mechanism is correct.

Isolating the terms containing \([A^-]\) and \(t\), and integrating in both sides:

\[ \frac{1}{[A]^{1/2}} - \frac{1}{[A]_{t=0}^{1/2}} = \frac{k_2}{2} \left( \frac{k_1}{k_{-1}} \right)^{1/2} [B]_0^{1/2} t \quad (S6) \]

Or

\[ [A]^{-1/2} = [A]_{t=0}^{-1/2} + \frac{k_2}{2} \left( \frac{k_1}{k_{-1}} \right)^{1/2} [B]_0^{1/2} t \quad (S7) \]

Setting \([A]_{t=0}^{-1/2} \equiv a\) and \(\frac{k_2}{2} \left( \frac{k_1}{k_{-1}} \right)^{1/2} [B]_0^{1/2} \equiv b\) and rearranging, one may get equation (1) in the main text.

Finally, from equation S6 one may state that a plot of \([A]^{-1/2}\) v. time should result in a linear relationship if the reaction order was actually \(3/2\) for compound 1a. It was taken into consideration the possibility of other reaction orders resulting in better description of the experimental data of \([A]\) versus time, and fits to different order using the corresponding integrated rate laws were performed, as presented in Table S1.
Table S1. Reaction order most probable possibilities, fitted equation to data and the obtained correlation factor ($R^2$).

| Reaction order | Fitted equation       | $R^2$  |
|----------------|-----------------------|--------|
| 1              | $\ln([A]/[A]_0) \ v. \ t$ | 0.94154|
| 2              | $1/[A] \ v. \ t$     | 0.97506|
| $3/2$          | $1/[A]^{1/2} \ v. \ t$ | 0.99047|

One may observe in Table S1 that the integrated rate law that results in the best fit for the experimental data, measured by the $R^2$, is the one that corresponds to the $3/2$ reaction order (in comparison to the expected relations for other reaction orders). The adjusted data for the $3/2$ reaction order is presented in Figure 4 of the main text.
6. Reaction reversibility evaluation

Reversibility study was carried out by adding the purified product 2h in the optimized reaction conditions (30 mol % of NaTCA, acetonitrile as solvent, room temperature for 1h). The crude reaction mixture was diluted with CH₂Cl₂ and washed with water. The organic layer was dried over anhydrous Na₂SO₄, filtered off and concentrated under reduced pressure. An aliquot was dissolved in CDCl₃ and analyzed by ¹H NMR in order to evaluate the corresponding d.r. No reaction takes place (the reaction isn’t reversible) and no differences were detected in the diastereomeric ratio (only one diastereomer could be detected, the same that the original product 2h).

Reaction reversibility study.

NMR data of product 2h after the reversibility test.
7- X-ray data

Figure 1. ORTEP representation of asymmetric unit of 2a crystal structure.
Figure 2. ORTEP representation showing (a) the asymmetric unit that contains two independents molecules of 6 and in which one of them have a disordered phenylic ring and (b) the independent molecule non-disordered emphasizing the chiral center formed.

(a)  

(b)  

Obs: Some hydrogen atoms had been omitted for more clarification and the anisotropic displacement ellipsoids are drawn at the 30% of probability level.
Table S2. Crystal data, data collection and structure refinement details

| Formula | C_{160.66}H_{142.85}N_{16.10}O_{32.23} – 2a | C_{256}H_{224}N_{16}O_{32} – 6 |
|---------|----------------------------------------|----------------------------------|
| Formula weight/g mol⁻¹ | 351.47 | 1009.18 |
| Temperature/K | 293 | 150 |
| Crystal system | Orthorhombic | Monoclinic |
| Space group | Pbca | P2₁/n |
| a/Å | 16.6696 (5) | 14.4834 (7) |
| b/Å | 9.8327 (3) | 14.1638 (6) |
| c/Å | 22.2624 (7) | 26.2185 (14) |
| β (°) | 90 | 94.314 (5) |
| V/Å³ | 3648.97 (19) | 5363.2 (4) |
| Z | 8 | 4 |
| Radiation type | Mo Kα | Cu Kα |
| Crystal size/mm | 0.98 x 0.15 x 0.11 | 0.33 x 0.12 x 0.08 |
| d_cal/g cm⁻³ | 1.276 | 1.250 |
| No. of measured, independent and observed [I > 2σ(I)] reflections | 65705, 5009, 3780 | 48269, 10392, 8163 |
| R_int | 0.046 | 0.065 |
| Observed reflections | 5009 | 10392 |
| N°. of parameters refined | 251 | 704 |
| R[F²>2σ(F²)] | 0.056 | 0.106 |
| wR(F²) | 0.136 | 0.306 |
| S | 1.06 | 1.03 |
| RMS e. Å⁻³ | 0.033 | 0.083 |

Table S3. Selected geometrical parameters in 2a crystal structure.

| Geometric parameters |
|----------------------|
| Bond distance / Å    |
| O₁—C₁₄ | 1.2390 (16) | N₁—C₁₄ | 1.3382 (18) |
| N₁—C₁₁ | 1.4445 (19) | O₂—C₈ | 1.1986 (19) |
| C₁₄—C₁₅ | 1.488 (2) | N₂—C₈ | 1.3948 (19) |
| N₂—C₇ | 1.409 (2) | N₂—C₉ | 1.476 (2) |
| C₁₅—C₁₇ | 1.384 (2) | C₁₅—C₁₆ | 1.390 (2) |
Bond angles / °

| Bond          | Angle       | Bond          | Angle       |
|---------------|-------------|---------------|-------------|
| C14—N1—C11   | 117.91 (12) | O4—C10—C9    | 124.86 (17) |
| O1—C14—N1    | 118.60 (13) | O4—C10—C11   | 124.87 (16) |
| O1—C14—C15   | 121.48 (13) | C9—C10—C11   | 110.22 (14) |
| C8—N2—C7     | 124.64 (14) | C8—N2—C9     | 113.67 (12) |
| C7—N2—C9     | 119.12 (13) | C17—C15—C16  | 118.69 (15) |
| C17—C15—C14  | 117.80 (13) | C16—C15—C14  | 123.51 (14) |
| N1—C11—C10   | 112.23 (13) | N1—C11—C8    | 111.61 (12) |
| C10—C11—C8   | 102.94 (12) | N1—C11—C13   | 110.51 (13) |
| C10—C11—C13  | 110.16 (15) | C8—C11—C13   | 109.13 (14) |
| O2—C8—N2     | 126.34 (14) | O2—C8—C11    | 125.54 (14) |
| N2—C8—C11    | 108.12 (13) | O3—C7—N2     | 119.03 (17) |
| O3—C7—C6     | 122.38 (16) | N2—C7—C6     | 118.48 (15) |
| C4—C6—C5     | 119.6 (2)   | C4—C6—C7     | 121.41 (17) |
| C5—C6—C7     | 118.67 (19) | C18—C16—C15  | 120.22 (17) |
| N2—C9—C10    | 102.69 (13) | N2—C9—C12    | 113.09 (15) |
| C10—C9—C12   | 112.58 (17) | C19—C17—C15  | 120.28 (17) |
| C20—C18—C16  | 120.52 (18) | C6—C4—C2     | 119.6 (2)   |
| C18—C20—C19  | 119.84 (18) | C20—C19—C17  | 120.42 (19) |
| C3—C5—C6     | 120.1 (2)   | C1—C2—C4     | 119.7 (3)   |
| C1—C3—C5     | 120.25 (15) | C3—C1—C2     | 120.7 (2)   |

Torsion angles / °

| Torsion       | Angle       | Torsion       | Angle       |
|---------------|-------------|---------------|-------------|
| C11—N1—C14—O1| −2.2 (2)    | C8—N2—C9—C10| 8.59 (19)   |
| C11—N1—C14—C15| 176.35 (13) | C7—N2—C9—C10| 171.25 (14) |
| O1—C14—C15—C17| 12.4 (2)   | C8—N2—C9—C12| 130.17 (18) |
| N1—C14—C15—C17| −166.07 (15)| C7—N2—C9—C12| −67.2 (2)   |
| O1—C14—C15—C16| −168.00 (16)| C16—C15—C17—C19| −1.3 (3) |
C9—N2—C8—C11 −15.47 (18)  N1—C11—C10—C9 −130.17 (15)
N1—C11—C8—O2 −45.2 (2)  C8—C11—C10—C9 −10.02 (18)
C10—C11—C8—O2 −165.78 (16)  C13—C11—C10—C9 106.23 (17)
C13—C11—C8—O2 77.2 (2)  C15—C16—C18—C20 1.3 (3)
N1—C11—C8—N2 135.63 (13)  C5—C6—C4—C2 0.1 (3)
C10—C11—C8—N2 15.06 (16)  C7—C6—C4—C2 −173.32 (18)
C13—C11—C8—N2 −101.94 (16)  C16—C18—C20—C19 −1.6 (3)
C8—N2—C7—O3 145.53 (18)  C18—C20—C19—C17 0.5 (4)
C9—N2—C7—O3 −15.1 (2)  C15—C17—C19—C20 1.0 (3)
C8—N2—C7—C6 −38.2 (2)  C4—C6—C5—C3 1.1 (3)
C9—N2—C7—C6 161.15 (15)  C7—C6—C5—C3 174.68 (16)
O3—C7—C6—C4 131.9 (2)  C6—C4—C2—C1 −0.8 (3)
N2—C7—C6—C4 −44.2 (2)  C6—C5—C3—C1 −1.6 (3)
O3—C7—C6—C5 −41.6 (3)  C5—C3—C1—C2 0.8 (3)
N2—C7—C6—C5 142.32 (18)  C4—C2—C1—C3 0.4 (4)
C17—C15—C16—C18 0.2 (3)  C8—N2—C9—C10 8.59 (19)
C14—C15—C16—C18 −179.39 (16)  C7—N2—C9—C10 171.25 (14)

Hydrogen bonds

| D—H···A | D—H | H···A | D···A | D—H···A |
|---------|-----|------|------|--------|
| C12—H12A···O3 | 0.96 | 2.65 | 3.157 (3) | 113 |
| N1—H1A···O1 | 0.878 (19) | 1.95 (2) | 2.8071 (15) | 164.3 (16) |

Symmetry code: (i) −x+3/2, y−1/2, z.

Table S4. Selected geometrical parameters in 6 crystal structure.

Geometric parameters

| Bond distance / Å | | | |
|-------------------|-------------------|------------------|------------------|
| O1—C3 | 1.226 (4) | C27—C35 | 1.546 (8) |
| O2—C5 | 1.232 (5) | O3—C6 | 1.231 (4) |
| C28—C38 | 1.385 (7) | O4—C30 | 1.258 (5) |
| C28—C31 | 1.396 (7) | O5—C12 | 1.418 (4) |
| C29—C41 | 1.402 (8) | N1—C6 | 1.362 (4) |
| N1—C04 | 1.476 (4) | C32—C51 | 1.400 (6) |
| O6—C8 | 1.214 (5) | N2—C3 | 1.379 (4) |
| C33—C39 | 1.400 (7) | N2—C8 | 1.430 (4) |
| N2—C1 | 1.490 (4) | C34—C43 | 1.372 (10) |
| N3—C30 | 1.347 (5) | N3—C010 | 1.454 (6) |
| C36—C41 | 1.389 (7) | C04—C3 | 1.533 (5) |
| Bond          | Distance (Å) | Bond          | Distance (Å) |
|--------------|--------------|--------------|--------------|
| C04—C15      | 1.564 (5)    | C04—C12      | 1.573 (5)    |
| O11—C35      | 1.434 (5)    | C39—C47      | 1.374 (8)    |
| N6—C5        | 1.384 (5)    | N6—C23       | 1.420 (7)    |
| C40—C47      | 1.385 (7)    | N6—C27       | 1.509 (7)    |
| C1—C10       | 1.539 (4)    | C1—C12       | 1.550 (4)    |
| C42—C54      | 1.405 (7)    | C2—C9        | 1.393 (6)    |
| C2—C16       | 1.405 (5)    | C45—C55      | 1.395 (5)    |
| C2—C15       | 1.530 (5)    | C4—C20       | 1.398 (5)    |
| C46—C10A     | 1.545 (8)    | C4—C22       | 1.400 (5)    |
| C4—C8        | 1.490 (5)    | C5—C010      | 1.549 (6)    |
| C6—C14       | 1.512 (5)    | C48—C55      | 1.374 (7)    |
| C7—C40       | 1.401 (6)    | C48—C54      | 1.389 (9)    |
| C7—C18       | 1.409 (6)    | C7—C30       | 1.494 (6)    |
| C49—C56      | 1.393 (9)    | C9—C31       | 1.404 (6)    |
| C10—C21      | 1.524 (5)    | C51—C53      | 1.389 (8)    |
| C52—C59      | 1.360 (11)   | C11—C26      | 1.395 (6)    |
| C52—C57      | 1.390 (9)    | C11—C34      | 1.404 (8)    |
| C11—C23      | 1.488 (8)    | C53—C58      | 1.397 (7)    |
| C010—C37     | 1.560 (5)    | C010—C35     | 1.568 (6)    |
| C14—C45      | 1.384 (6)    | C56—C59      | 1.468 (10)   |
| C14—C42      | 1.396 (6)    | C16—C38      | 1.404 (5)    |
| C10A—C102    | 1.325 (13)   | C17—C21      | 1.396 (6)    |
| C10A—C11A    | 1.353 (15)   | C17—C58      | 1.405 (6)    |
| C10A—C14A    | 1.374 (10)   | C10A—C200    | 1.404 (12)   |
| C18—C33      | 1.379 (7)    | C201—C12A    | 1.335 (17)   |
| C201—C15A    | 1.346 (15)   | O10—C23      | 1.223 (6)    |
| C201—C300    | 1.360 (13)   | C20—C29      | 1.390 (6)    |
| C201—C400    | 1.373 (14)   | C21—C32      | 1.403 (6)    |
| C200—C400    | 1.384 (14)   | C22—C36      | 1.393 (5)    |
| C24—C50      | 1.383 (8)    | C102—C300    | 1.377 (13)   |
| C24—C43      | 1.402 (9)    | C25—C57      | 1.389 (10)   |
| C14A—C15A    | 1.414 (13)   | C25—C37      | 1.521 (8)    |
| C11A—C12A    | 1.446 (16)   | C26—C50      | 1.377 (8)    |
| C27—C46      | 1.541 (7)    |               |              |

Bond angles / °

| Bond         | Angle (°) |
|--------------|-----------|
| C6—N1—C04   | 120.8 (3) |
| C51—C32—C21 | 121.2 (4) |
C3—N2—C8  123.0 (3)  C3—N2—C1  113.7 (3)
C18—C33—C39  119.4 (5)  C8—N2—C1  117.7 (3)
C30—N3—C010  120.7 (4)  C43—C34—C11  120.4 (5)
N1—C04—C3  110.5 (3)  N1—C04—C15  107.2 (3)
O11—C35—C27  118.8 (5)  C3—C04—C15  109.2 (3)
O11—C35—C010  113.1 (4)  N1—C04—C12  110.1 (3)
C27—C35—C010  106.5 (4)  C3—C04—C12  105.0 (2)
C15—C04—C12  114.8 (3)  C5—N6—C23  122.9 (4)
C41—C36—C22  119.6 (4)  C5—N6—C27  113.0 (4)
C23—N6—C27  119.5 (4)  N2—C1—C10  111.4 (3)
C25—C37—C010  119.1 (4)  N2—C1—C12  104.3 (3)
C10—C1—C12  114.6 (3)  C9—C2—C16  118.2 (3)
C28—C38—C16  120.7 (4)  C9—C2—C15  119.8 (3)
C16—C2—C15  121.9 (4)  O1—C3—N2  125.9 (3)
C47—C39—C33  120.6 (5)  O1—C3—C04  125.6 (3)
N2—C3—C04  108.4 (3)  C20—C4—C22  119.6 (3)
C47—C40—C7  120.1 (4)  C20—C4—C8  117.9 (4)
C22—C4—C8  122.1 (3)  O2—C5—N6  126.0 (4)
C36—C41—C29  120.7 (4)  O2—C5—C010  125.4 (3)
O2—C5—C010  125.4 (3)  N6—C5—C010  108.6 (4)
O3—C6—N1  120.8 (3)  C14—C42—C54  120.2 (5)
O3—C6—C14  121.6 (3)  N1—C6—C14  117.5 (3)
C40—C7—C18  119.0 (4)  C34—C43—C24  120.0 (6)
C40—C7—C30  117.5 (4)  C18—C7—C30  123.5 (4)
O6—C8—N2  119.1 (3)  C14—C45—C55  120.3 (4)
O6—C8—C4  122.8 (3)  N2—C8—C4  117.9 (3)
C2—C9—C31  121.5 (4)  C27—C46—C10A  115.2 (5)
C21—C10—C1  111.4 (3)  C39—C47—C40  120.4 (5)
C26—C11—C34  118.7 (5)  C55—C48—C54  119.8 (4)
C26—C11—C23  121.3 (5)  C34—C11—C23  119.5 (4)
O5—C12—C1  111.9 (3)  C56—C49—C25  122.0 (7)
O5—C12—C04  114.1 (3)  C1—C12—C04  106.1 (3)
C26—C50—C24  120.0 (5)  N3—C010—C5  110.4 (3)
C53—C51—C32  119.9 (4)  N3—C010—C37  105.8 (3)
C5—C010—C37  109.5 (3)  N3—C010—C35  110.0 (4)
C59—C52—C57  120.4 (7)  C5—C010—C35  105.0 (4)
| Bond          | Angle (°) |
|--------------|-----------|
| C7—C10—C35  | 116.1 (3) |
| C51—C53—C58 | 119.9 (4) |
| C42—C14—C6  | 117.4 (4) |
| C48—C54—C42 | 119.7 (5) |
| C38—C16—C2  | 120.4 (4) |
| C21—C17—C58 | 121.2 (4) |
| C33—C18—C7  | 120.5 (4) |
| C29—C20—C4  | 120.3 (4) |
| C17—C21—C32 | 118.1 (4) |
| C17—C21—C10 | 119.6 (3) |
| C32—C21—C10 | 122.3 (4) |
| C36—C22—C4  | 120.3 (4) |
| C14A—C10A—C46 | 120.3 (6) |
| O10—C23—N6  | 119.0 (5) |
| O10—C23—C11 | 122.3 (5) |
| N6—C23—C11  | 118.6 (4) |
| C400—C200—C10A | 116.5 (14) |
| C57—C25—C37 | 121.0 (7) |
| C49—C25—C37 | 118.6 (6) |
| C10A—C102—C300 | 118.7 (14) |
| N6—C27—C35  | 105.0 (4) |
| C46—C27—C35 | 111.8 (5) |
| C38—C28—C31 | 119.7 (4) |
| C20—C29—C41 | 119.5 (4) |
| O4—C30—N3   | 119.8 (4) |
| C201—C15A—C14A | 121.0 (9) |
| C28—C31—C9  | 119.6 (4) |

Torsion angles / °

| Bond           | Torsion Angle (°) |
|----------------|-------------------|
| C6—N1—C04—C3  | −51.1 (4)         |
| C5—N6—C27—C35 | 10.4 (5)          |
| C6—N1—C04—C15 | −170.0 (3)        |
| C23—N6—C27—C35 | 167.1 (4)       |
| C6—N1—C04—C12 | 64.5 (4)          |
| C4—C20—C29—C41 | −0.7 (6)       |
| C3—N2—C1—C10  | 139.3 (3)         |
| C010—N3—C30—O4 | 4.2 (6)         |
| C8—N2—C1—C10  | −66.1 (4)         |
| C010—N3—C30—C7 | −176.2 (3)      |
| C3—N2—C1—C12  | 15.2 (3)          |
| C40—C7—C30—O4 | −21.4 (5)        |
| C8—N2—C1—C12  | 169.8 (3)         |
| C18—C7—C30—O4 | 156.9 (4)        |
C8—N2—C3—O1 12.9 (5)  C40—C7—C30—N3 158.9 (4)
C1—N2—C3—O1 166.0 (3)  C18—C7—C30—N3 −22.8 (5)
C8—N2—C3—C04 −169.8 (3)  C38—C28—C31—C9 0.8 (6)
C1—N2—C3—C04 −16.7 (4)  C2—C9—C31—C28 −1.3 (6)
N1—C04—C3—O1 −53.2 (4)  C17—C21—C32—C51 −0.5 (6)
C15—C04—C3—O1 64.4 (4)  C10—C21—C32—C51 −179.6 (4)
C12—C04—C3—O1 −171.9 (3)  C7—C18—C33—C39 −1.8 (7)
N1—C04—C3—N2 129.5 (3)  C26—C11—C34—C43 −0.7 (7)
C15—C04—C3—N2 −112.9 (3)  C23—C11—C34—C43 172.3 (4)
C12—C04—C3—N2 10.8 (3)  N6—C27—C35—O11 127.2 (5)
C23—N6—C5—O2 10.5 (6)  C46—C27—C35—O11 6.0 (7)
C27—N6—C5—O2 166.2 (4)  N6—C27—C35—C010 −1.8 (5)
C23—N6—C5—C010 −170.5 (4)  C46—C27—C35—C010 −123.0 (4)
C27—N6—C5—C010 −14.7 (4)  N3—C010—C35—O11 102.9 (5)
C04—N1—C6—O3 7.7 (5)  C5—C010—C35—O11 −138.3 (4)
C04—N1—C6—C14 −172.1 (3)  C37—C010—C35—O11 −17.2 (7)
C3—N2—C8—O6 130.5 (4)  N3—C010—C35—C27 −124.9 (4)
C1—N2—C8—O6 −21.6 (5)  C5—C010—C35—C27 −6.1 (5)
C3—N2—C8—C4 −54.6 (4)  C37—C010—C35—C27 115.0 (4)
C1—N2—C8—C4 153.3 (3)  C4—C22—C36—C41 −0.7 (6)
C20—C4—C8—O6 −24.5 (5)  C57—C25—C37—C010 92.3 (6)
C22—C4—C8—O6 148.8 (4)  C49—C25—C37—C010 −94.2 (6)
C20—C4—C8—N2 160.8 (3)  N3—C010—C37—C25 158.4 (5)
C22—C4—C8—N2 −25.9 (5)  C5—C010—C37—C25 39.4 (6)
C16—C2—C9—C31 0.4 (6)  C35—C010—C37—C25 −79.2 (6)
C15—C2—C9—C31 −178.2 (4)  C31—C28—C38—C16 0.6 (6)
N2—C1—C10—C21 162.0 (3)  C2—C16—C38—C28 −1.5 (6)
C12—C1—C10—C21 −79.9 (4)  C18—C33—C39—C47 2.3 (8)
N2—C1—C12—O5 117.8 (3)  C18—C7—C40—C47 0.3 (6)
C10—C1—C12—O5 −4.3 (4)  C30—C7—C40—C47 178.7 (4)
N2—C1—C12—C04 −7.2 (3)  C22—C36—C41—C29 −0.1 (6)
| Bond           | Angle (deg)      | Bond           | Angle (deg)      |
|----------------|------------------|----------------|------------------|
| C10-C1-C12-C04 | -129.3 (3)       | C20-C29-C41-C36 | 0.9 (7)          |
| N1-C04-C12-O5  | 115.8 (3)        | C45-C14-C42-C54 | -0.9 (8)         |
| C3-C04-C12-O5  | -125.3 (3)       | C6-C14-C42-C54 | -178.7 (5)       |
| C15-C04-C12-O5 | -5.3 (4)         | C11-C34-C43-C24 | -1.8 (8)         |
| N1-C04-C12-C1  | -120.6 (3)       | C50-C24-C43-C34 | 2.4 (8)          |
| C3-C04-C12-C1  | -1.6 (3)         | C42-C14-C45-C55 | 0.5 (7)          |
| C15-C04-C12-C1 | 118.4 (3)        | C6-C14-C45-C55 | 178.1 (4)        |
| C30-N3-C010-C5 | -53.1 (5)        | N6-C27-C46-C10A | 150.9 (6)        |
| C30-N3-C010-C37| -171.5 (4)       | C35-C27-C46-C10A| -91.8 (7)        |
| C30-N3-C010-C35| 62.4 (5)         | C33-C39-C47-C40 | -1.6 (8)         |
| O2-C5-C010-N3  | -49.8 (5)        | C7-C40-C47-C39 | 0.2 (7)          |
| N6-C5-C010-N3  | 131.2 (3)        | C57-C25-C49-C56 | -0.4 (9)         |
| O2-C5-C010-C37 | 66.4 (5)         | C37-C25-C49-C56 | -174.1 (5)       |
| N6-C5-C010-C37 | -112.7 (4)       | C11-C26-C50-C24 | -1.1 (7)         |
| O2-C5-C010-C35 | -168.3 (4)       | C43-C24-C50-C26 | -0.9 (8)         |
| N6-C5-C010-C35 | 12.6 (4)         | C21-C32-C51-C53 | 1.2 (7)          |
| O3-C6-C14-C45  | 179.2 (4)        | C32-C51-C53-C58 | -0.5 (8)         |
| N1-C6-C14-C45  | -1.0 (5)         | C55-C48-C54-C42 | 2.7 (10)         |
| O3-C6-C14-C42  | -3.0 (5)         | C14-C42-C54-C48 | -0.7 (10)        |
| N1-C6-C14-C42  | 176.7 (4)        | C54-C48-C55-C45 | -3.1 (9)         |
| C9-C2-C15-C04  | -105.2 (4)       | C14-C45-C55-C48 | 1.6 (7)          |
| C16-C2-C15-C04 | 76.3 (4)         | C25-C49-C56-C59 | -0.7 (8)         |
| N1-C04-C15-C2  | 154.7 (3)        | C49-C25-C57-C52 | 1.2 (9)          |
| C3-C04-C15-C2  | 34.9 (4)         | C37-C25-C57-C52 | 174.7 (5)        |
| C12-C04-C15-C2 | -82.7 (4)        | C59-C52-C57-C25 | -0.9 (9)         |
| C9-C2-C16-C38  | 1.0 (5)          | C51-C53-C58-C17 | -0.9 (8)         |
| C15-C2-C16-C38 | 179.5 (3)        | C21-C17-C58-C53 | 1.6 (7)          |
| C40-C7-C18-C33 | 0.5 (6)          | C57-C52-C59-C56 | -0.3 (9)         |
| C30-C7-C18-C33 | -177.8 (4)       | C49-C56-C59-C52 | 1.0 (8)          |
| C22-C4-C20-C29 | -0.1 (5)         | C27-C46-C10A-C102| -87.7 (11)       |
| C8-C4-C20-C29  | 173.4 (3)        | C27-C46-C10A-C11A| 27.0 (14)        |
C58—C17—C21—C32  -0.9 (6)  C27—C46—C10A—C14A  -143.6 (8)
C1—C10—C21—C17  -75.9 (4)  C102—C10A—C200—C400  6 (2)
C1—C10—C21—C32  103.2 (4)  C46—C10A—C200—C400  -178.5 (14)
C20—C4—C22—C36  0.9 (5)  C300—C201—C400—C200  3 (3)
C8—C4—C22—C36  -172.4 (3)  C10A—C200—C400—C201  -7 (3)
C5—N6—C23—O10  133.1 (5)  C200—C10A—C102—C300  -1.8 (17)
C27—N6—C23—O10  -21.2 (6)  C46—C10A—C102—C300  -176.9 (13)
C5—N6—C23—C11  -51.5 (6)  C400—C201—C300—C102  2 (3)
C27—N6—C23—C11  154.3 (4)  C10A—C102—C300—C201  -3 (3)
C26—C11—C23—O10  140.5 (5)  C11A—C10A—C14A—C15A  15.6 (16)
C34—C11—C23—O10  -31.9 (7)  C46—C10A—C14A—C15A  -173.2 (9)
C26—C11—C23—N6  -34.8 (6)  C14A—C10A—C11A—C12A  -8.1 (15)
C34—C11—C23—N6  152.8 (4)  C46—C10A—C11A—C12A  -179.1 (11)
C34—C11—C26—C50  1.7 (6)  C15A—C201—C12A—C11A  11 (2)
C23—C11—C26—C50  -170.7 (4)  C10A—C11A—C12A—C201  -5.2 (17)
C5—N6—C27—C46  131.8 (5)  C12A—C201—C15A—C14A  -4 (2)
C23—N6—C27—C46  -71.6 (6)  C10A—C14A—C15A—C201  -10.3 (17)

### Hydrogen bonds

| D—H···A | D—H | H···A | D····A | D-H···A |
|---------|------|-------|--------|--------|
| N1—H1A···O2 | 0.87 (4) | 2.23 (4) | 3.077 (4) | 165 (3) |
| N3—H3A···O1\(^i\) | 0.83 (5) | 2.11 (5) | 2.933 (4) | 169 (4) |
| O5—H5O···O4 | 0.88 (6) | 1.85 (6) | 2.719 (4) | 172 (5) |
| O11—H11···O3\(^i\) | 0.8200 | 2.1900 | 2.911 (5) | 148.00 |
| C10—H10A···O5 | 0.9700 | 2.3700 | 2.720 (5) | 100.00 |
| C15—H15A···O5 | 0.9700 | 2.4400 | 2.815 (5) | 103.00 |
| C16—H16···O5 | 0.9300 | 2.4400 | 3.157 (5) | 134.00 |
| C35—H35···O4 | 0.9800 | 2.4700 | 2.936 (6) | 108.00 |
| C37—H37A···O11 | 0.9700 | 2.4600 | 2.848 (6) | 104.00 |
| C42—H42···O3 | 0.9300 | 2.5000 | 2.808 (5) | 100.00 |
| C45—H45···O2 | 0.9300 | 2.5300 | 3.410 (5) | 159.00 |
| C46—H46B···O11 | 0.9700 | 2.3900 | 2.818 (9) | 106.00 |

Symmetry code: \( (i) = x + 3/2, y + 1/2, z + 1/2. \)
8- References:

(1) Melhado, A. D.; Amarante, G. W.; Wang, Z. J.; Luparia, M.; Toste, F. D. J. *Am. Chem. Soc.* **2011**, *133*, 3517.

(2) Kobayashi, S.; Bryant, L. L.; Tsukamoto, Y.; Saegusa, T. *Macromolecules* **1986**, *19*, 1547.

(3) Ewenson, A.; Cohen-Suissa, R.; Levian-Teitelbaum, D.; Selinger, Z.; Chorev, M.; Gilon, C. *Int. J. Peptide Protein Res.* **1988**, *31*, 269.

(4) Mazurkiewicz, R.; Pierwocha, A. W.; Fryczkowska, B. *J Polish. Chem.* **1998**, *72*, 113.