Electronic Supplementary Information (ESI) for

A visible-light mediated three-component radical process using dithiocarbamate anion catalysis

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Table of Contents

A. General Information .................................................................S3
B. Experimental Procedure ..........................................................S4
   B.1. Set-up: Temperature-controlled photoreactor and specification of the light source ...............S4
   B.2. General Procedure for the Three-Component Radical Process ........................................S5
   B.3. Characterization of Products ..................................................S5
   B.4. 5 mmol Scale Reaction .........................................................S17
C. Product Modifications ..............................................................S18
   C.1. Assembly Line Synthesis of Difunctionalized Pyrroles ..................................................S18
   C.2. Synthesis of Pyrrolidine 8 ....................................................S19
D. Unsuccessful Substrate Combination ..........................................S20
E. Cyclic Voltammetry Measurements .............................................S21
F. X-ray Crystallographic Data ......................................................S28
G. References ..............................................................................S29
H. $^1$H and $^{13}$C NMR Spectra ......................................................S30
A. General Information

The NMR spectra were recorded at 400 MHz and 500 MHz for $^1$H and 100 or 125 MHz for $^{13}$C. The chemical shift (δ) for $^1$H and $^{13}$C are given in ppm relative to residual signals of the solvents (CHCl$_3$ @ 7.26 ppm $^1$H NMR and 77.16 ppm $^{13}$C NMR, and tetramethylsilane @ 0 ppm). Coupling constants are given in Hertz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; q, quartet; m, multiplet; bs, broad signal; app, apparent.

Infrared (IR) spectra were obtained using a Bruker Alpha FT-IR spectrometer.

High resolution mass spectra (HRMS) were obtained from the ICIQ HRMS unit on MicroTOF Focus and Maxis Impact (Bruker Daltonics) with electrospray ionization (ESI). X-ray data were obtained from the ICIQ X-Ray unit using a Bruker-Nonius diffractometer equipped with an APPEX 2 4K CCD area detector.

Isolated yields refer to materials of >95% purity as determined by $^1$H NMR.

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General Procedures. All reactions were set up under an argon atmosphere in oven-dried glassware using standard Schlenk techniques, unless otherwise stated. Synthesis grade solvents were used as purchased; anhydrous solvents were taken from a commercial SPS solvent dispenser. Chromatographic purification of products was accomplished using forced-flow chromatography (FC) on silica gel (35-70 mesh). For thin layer chromatography (TLC) analysis throughout this work, Merck pre-coated TLC plates (silica gel 60 GF$_{254}$, 0.25 mm) were employed, using UV light as the visualizing agent and an acidic mixture of vanillin or basic aqueous potassium permanganate (KMnO$_4$) stain solutions, and heat as developing agents. Organic solutions were concentrated under reduced pressure on a Büchi rotatory evaporator.

Materials. Most of the starting materials used in this study are commercially available and were purchased in the highest purity available from Sigma-Aldrich, Fluka, Alfa Aesar, Fluorochem, and used as received, without further purifications. The synthesis of the DTC catalyst A is described in our previous work.\textsuperscript{1}
B. Experimental Procedure

B.1. Set-up: Temperature-controlled photoreactor and specifications of the light source

The photoreactor consisted of a 12.5 cm diameter jar, fitted with 4 standard 29 sized ground glass joints arranged in a square and a central 29 sized joint. A commercial 1 meter LED strip was wrapped around the jar, followed by a layer of aluminium foil and cotton for insulation (Figure S1, a). Each of the joints could be used to fit a standard 16 mm or 25 mm diameter Schlenk tube with a Teflon adaptor (Figure S1, b). An inlet and an outlet allow the circulation of liquid from a Huber Minichiller 300 inside the jar. This setup allows to perform reactions at temperatures ranging from -20 ºC to 80 ºC with accurate control of the reaction temperature (± 1ºC) (Figure S1, c). To maintain a consistent illumination during different experiments, only the four external positions were used to perform reactions while the central one was used to monitor the temperature inside a Schlenk tube identical to those used to perform reactions.

Figure S1. (a) Photoreactor used in this study. (b) Teflon adaptors used to accommodate Schlenk tubes in the photoreactor. (c) Fully assembled photoreactor in operation. (d) Emission spectrum of the 465 nm blue LED strip used in this study.
The light source used in this study consisted of a 1 m strip, 14.4W ‘LEDXON MODULAR 9009083 LED, SINGLE 5050’ purchased from Farnell, catalog number 9009083. The emission spectrum of these LEDs was recorded (Figure S1, d).

B.2. General Procedure for the Three-Component Radical Process

In an oven dried Schlenk tube, the DTC catalyst A (31.0 mg, 0.1 mmol, 0.2 equiv.) was dissolved in dichloroethane (0.5 mL), then the alkyl chloride 1 (0.75 mmol, 1.5 equiv.) was added while stirring, followed by 2,6-lutidine (70 µL, 0.6 mmol, 1.2 equiv.), maleimide 2 (0.5 mmol, 1.0 equiv.), and pyrrole 3 (5.0 mmol, 10.0 equiv.). An additional volume of dichloroethane (0.5 mL) was added to the reaction vessel, washing the sides from residual solids. The resulting mixture was degassed via three cycles of freeze-pump-thaw. The Schlenk tube was then placed in the irradiation setup (see section B1, Figure S1), maintained at a temperature of 60 ºC (60-61ºC measured in the central well), and the reaction was stirred for 20 hours under continuous irradiation. After cooling to ambient temperature, the solvent was evaporated and the residue purified by column chromatography to afford the corresponding product 4 in the stated yield with >95% purity according to 1H NMR analysis. The exact conditions for chromatography are reported for each compound.

B.3. Characterization of Products

2'-(1-methyl-4-(1-methyl-1H-pyrrol-2-yl)-2,5-dioxopyrrolidin-3-yl)methylisoindoline-1,3-dione (4a): Synthesized according to the general procedure using N-(chloromethyl)phthalimide 1a (147 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). A single diastereomer was detected by 1H NMR analysis of the crude reaction mixture. Product 4a was purified by column chromatography (gradient from 20% to 35% AcOEt in hexanes as eluent): 100 mg yellow solid, 57% yield. Crystallization from MeOH afforded crystals suitable for X-ray diffraction analysis (CCDC 1894404, see section E), which revealed a trans relative stereochemistry. Product 4a can be synthesized up to a 5 mmol scale using the same photochemical set-up (see Section B.4 for details).

1H NMR (500 MHz, CDCl3) δ 7.73 (dd, J = 5.5, 3.1 Hz, 2H), 7.65 (dd, J = 5.4, 3.1 Hz, 2H), 6.36 (dd, J = 2.5, 2.0 Hz, 1H), 5.78 (dd, J = 3.6, 1.6 Hz, 1H), 5.72 (dd, J = 3.7, 2.8 Hz, 1H), 4.32 (dd, J = 14.0, 5.7 Hz, 1H), 4.07-4.02 (m, 2H), 3.62 (s, 3H), 3.61-3.58 (m, 1H), 2.99 (s, 3H).

13C NMR (126 MHz, CDCl3) δ 175.7, 175.4, 168.5, 134.4, 131.9, 125.3, 124.0, 123.6, 107.3, 106.8, 45.2, 43.7, 38.1, 34.4, 25.5.

IR (thin film) ν 2950, 1773, 1694, 1433, 1395, 1379, 1361, 1304, 1271, 715 cm⁻¹.


TLC: 30:70 EtOAc/hexanes, Rf = 0.14.
3-((1H-benzo[d][1,2,3]triazol-1-yl)methyl)-1-methyl-4-(1-methyl-1H-pyrrol-2-yl)pyrrolidine-2,5-dione (4b): Synthesized according to the general procedure using 1-(chloromethyl)-1H-benzotriazole 1b (126 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). A single diastereomer was detected by ¹H NMR analysis of the crude reaction mixture. Product 4b was purified by column chromatography (gradient from 20% to 35% AcOEt in hexanes as eluent): 91 mg, white foam, 56% yield.

¹H NMR (500 MHz, CDCl₃) δ 8.02-8.00 (m, 1H), 7.62-7.60 (m, 1H), 7.52-7.48 (m, 1H), 7.38-7.35 (m, 1H), 6.60 (dd, J = 2.5, 1.9 Hz, 1H), 6.02 (dd, J = 3.6, 2.8 Hz, 1H), 5.91 (dd, J = 3.7, 1.6 Hz, 1H), 5.21 (dd, J = 14.7, 4.6 Hz, 1H), 4.97 (dd, J = 14.8, 4.3 Hz, 1H), 4.22 (d, J = 6.8 Hz, 1H), 3.65 (s, 3H), 3.64-3.60 (m, 1H), 2.85 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 175.9, 175.2, 146.1, 134.3, 128.4, 125.6, 124.8, 124.4, 120.4, 110.0, 107.6, 106.7, 45.5, 41.4, 34.7, 25.6.

IR (thin film) ν 2924, 1698, 1493, 1483, 1400 cm⁻¹.

HRMS: calculated for C₂₁H₂₁Na₂O₅⁺ (M+Na⁺): 346.1274, found 346.1282.

TLC: 30:70 EtOAc/hexanes, Rₛ = 0.1.

3-((3,5-dimethyl-4,5-dihydro-1H-pyrazol-1-yl)methyl)-1-methyl-4-(1-methyl-1H-pyrrol-2-yl)pyrrolidine-2,5-dione (4c): Synthesized by a two-step procedure. First, the alkyl chloride 1c was synthesized via a variation of a reported procedure:² in a round bottom flask, (3,5-dimethyl-1H-pyrazol-1-yl)methanol (126 mg, 1 mmol, 1 equiv.) was dissolved in dry chloroform (5 mL) and cooled at 0 °C. Thionyl chloride (88 µL, 1.2 mmol, 1.2 equiv.) was added dropwise and the reaction was left stirring at ambient temperature for 30 min. Solvent was removed under vacuum at 25 °C, diethyl ether (5 mL) was added and dried (this was repeated twice) to obtain the crude 1-(chloromethyl)-3,5-dimethyl-1H-pyrazole hydrochloride 1c as a white solid, which was used directly without further purification. The crude product 1c was dissolved in 1,2-dichloroethane giving a stock solution 0.75 M. 1-(chloromethyl)-3,5-dimethyl-1H-pyrazole hydrochloride 1c (0.75 M, 0.75 mmol, 1.5 equiv.) was added in an oven dried Schlenk tube, then the DTC catalyst 3 (31.0 mg, 0.1 mmol, 0.2 equiv.) was added followed by 2,6-lutidine (70 µL, 0.6 mmol, 1.2 equiv.), N-methylmaleimide 2a (57.0 mg, 0.5 mmol, 1 equiv.), and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). The resulting yellow mixture was degassed via three cycles of freeze-pump-thaw. The Schlenk tube was then placed in the irradiation setup at a temperature of 60 °C and irradiated for 20 hours. After cooling to ambient temperature, the solvent was evaporated. Multiple purification by column chromatography (gradient from 10% to 40% AcOEt in hexanes as eluent) resulted in poor separation from several unidentified byproducts, but an analytical amount of the pure major diastereomer was isolated for characterization. The yield (40%) of 4c and the diastereomeric ratio (20:1) were inferred by ¹H NMR analysis of the crude reaction mixture using trichloroethylene as the internal standard.

¹H NMR (500 MHz, CDCl₃) δ 6.60 (dd, J = 2.8, 1.7 Hz, 1H), 6.05 (dd, J = 3.7, 2.7 Hz, 1H), 5.90 (dd, J = 3.8, 1.1 Hz, 1H), 5.73 (s, 1H), 4.54 (dd, J = 14.4, 4.9 Hz, 1H), 4.43 (d, J = 5.7 Hz, 1H), 4.27 (dd, J = 14.4, 4.3 Hz, 1H), 3.68 (s, 3H), 3.34 (m), 2.96 (s, 3H), 2.20 (s, 3H), 2.12 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 176.7, 176.1, 148.4, 140.0, 126.7, 123.7, 107.3, 106.2, 105.6, 48.5, 45.6, 41.1, 34.4, 25.3, 13.6, 11.0.

HRMS: calculated for C₁₈H₂₁Na₂O₅⁺ (M+Na⁺): 323.1478, found 323.1472.

TLC: 40:60 EtOAc/hexanes, Rₛ = 0.25.
3-((3,5-dimethylisoxazol-4-yl)methyl)-1-methyl-4-(1-methyl-1H-pyrrol-2-yl)pyrrolidine-2,5-dione (4d): Synthesized according to the general procedure using 4-(chloromethyl)-3,5-dimethylisoxazole 2d (109 mg, 0.75 µL, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). A single diastereomer was detected by 1H NMR analysis of the crude reaction mixture. Product 4d was purified by column chromatography (gradient from 10% to 30% AcOEt in hexanes as eluent): 96.3 mg pale yellow solid, 64% yield.

1H NMR (500 MHz, CDCl₃) δ 6.61 (dd, J = 2.8, 1.7 Hz, 1H), 6.04 (dd, J = 3.7, 2.8 Hz, 1H), 5.90 (dd, J = 3.8, 0.7 Hz, 1H), 3.59 (s, 3H), 3.58 (d, J = 6.3 Hz, 1H), 3.26 (app q, J = 6.4 Hz, 1H), 2.96 (s, 3H), 2.86 (d, J = 6.3 Hz, 2H), 2.23 (s, 3H), 2.08 (s, 3H).

13C NMR (126 MHz, CDCl₃) δ 177.5, 175.3, 166.6, 159.6, 125.3, 124.2, 109.5, 107.4, 106.6, 46.5, 43.2, 34.3, 25.2, 21.9, 11.2, 10.2.

IR (thin film) ν 2924, 1779, 1701, 1572, 1429, 1377, 1268, 1110, 980, 698 cm⁻¹.

HRMS: calculated for C₁₆H₂₀N₃O₃⁺ (M⁺): 302.1496, found 302.1499

TLC: 30:70 EtOAc/hexanes, Rf = 0.27.

3-(benzo[d]thiazol-2-ylmethyl)-1-methyl-4-(1-methyl-1H-pyrrol-2-yl)pyrrolidine-2,5-dione (4e): Synthesized according to the general procedure using 2-(chloromethyl)-1,3-benzothiazole 1e (138 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). A single diastereomer was detected by 1H NMR analysis of the crude reaction mixture. Product 4e was purified by column chromatography (gradient from 10% to 30% EtOAc in hexanes as eluent, two consecutive purifications): 75.9 mg of a pink oil. The isolated material consisted of a mixture containing 4e an inseparable byproduct in a proportion 6.3:1 (see Figure S2 below), arising from a polar Friedel-Crafts type alkylation of pyrrole with maleimide. Corrected yield of product 4e: 38%.

1H NMR (500 MHz, CDCl₃) δ 7.90 (d, J = 8.1 Hz, 1H), 7.83 (d, J = 7.9 Hz, 1H), 7.45 (ddd, J = 8.3, 7.2, 1.3 Hz, 1H), 7.37 (ddd, J = 8.2, 7.3, 1.2 Hz, 1H), 6.60 (dd, J = 2.7, 1.8 Hz, 1H), 6.06 (dd, J = 3.7, 2.7 Hz, 1H), 5.98 (dd, J = 3.8, 1.7 Hz, 1H), 4.33 (d, J = 5.9 Hz, 1H), 3.78 (dd, J = 15.9, 5.5 Hz, 1H), 3.66 (s, 3H), 3.56 (d, J = 16.0, 4.6 Hz, 1H), 3.51 (app q, J = 5.3 Hz, 1H), 3.04 (s, 3H).

13C NMR (126 MHz, CDCl₃) δ 177.4, 176.1, 166.2, 153.1, 135.4, 126.6, 126.3, 125.4, 123.9, 123.1, 121.7, 107.4, 106.5, 46.6, 42.8, 34.5, 32.4, 25.4.

IR (thin film) ν 2924, 1776, 1695, 1491, 1432, 1381, 1279, 1108, 760, 709 cm⁻¹.

HRMS: calculated for C₁₈H₁₈N₂O₂S⁺ (M⁺): 340.1114, found 340.1113.

TLC: 30:70 EtOAc/hexanes Rf = 0.23.
1-H NMR (500 MHz, CDCl₃) δ 8.69 (d, J = 2.0 Hz, 1H), 7.05 (d, J = 1.5 Hz, 1H), 6.59 (t, J = 2.2 Hz, 1H), 6.05 (dd, J = 3.7, 2.8 Hz, 1H), 5.92 (dd, J = 3.9, 1.7 Hz, 1H), 4.13 (d, J = 5.4 Hz, 1H), 3.64 (s, 3H), 3.47 – 3.39 (m, 2H), 3.36 – 3.27 (m, 1H), 2.95 (s, 3H).

13C NMR (126 MHz, CDCl₃) δ 178.0, 176.3, 153.0, 152.9, 127.0, 126.6, 123.6, 115.8, 107.3, 106.4, 47.4, 42.6, 34.4, 30.0, 25.2.

IR (thin film) ν 3078, 2921, 1691, 1433, 1290, 1067, 993, 731 cm⁻¹.

HRMS: calculated for C₁₄H₁₅N₃Na₂O₇S⁺ (M+Na⁺): 312.0777, found 312.0773.

TLC: 30:70 EtOAc/hexanes, Rᵣ = 0.13.
1-methyl-3-(1-methyl-1H-pyrrol-2-yl)-4-((trifluoromethyl)furan-2-yl)methyl)pyrrolidine-2,5-dione (4g): Synthesized according to the general procedure using 2-(bromomethyl)-5-(trifluoromethyl)furan 1g (172 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). A single diastereomer was detected by $^1$H NMR analysis of the crude reaction mixture. Product 4g was purified by column chromatography (gradient from 0% to 2% acetone in toluene as eluent; two consecutive purifications): 85.0 mg of a brown oil, 50% yield.

$^1$H NMR (500 MHz, CDCl$_3$) δ 6.66 (dd, J = 3.3, 1.4 Hz, 1H), 6.61 (dd, J = 2.7, 1.7 Hz, 1H), 6.15 (d, J = 3.2 Hz, 1H), 6.05 (dd, J = 3.7, 2.8 Hz, 1H), 5.91 (dd, J = 3.8, 1.7 Hz, 1H), 3.81 (d, J = 5.9 Hz, 1H), 3.64 (s, 3H), 3.36 (app q, J = 5.9 Hz, 1H), 3.24 (d, J = 5.9 Hz, 2H), 2.99 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 177.0, 175.4, 154.3 (d, J = 1.5 Hz), 141.4 (q, J = 42.8 Hz), 125.9, 124.0, 119.0 (q, J = 266.8 Hz), 112.6 (q, J = 2.9 Hz), 109.0, 107.3, 106.4, 46.4, 43.2, 34.2, 27.9, 25.2.

$^{19}$F NMR decoupled $^1$H (376 MHz, CDCl$_3$) δ: -64.34

IR (thin film) ν 2950, 1779, 1698, 1616, 1560, 1434, 1382, 1321, 1173, 1122, 1103, 712 cm$^{-1}$.

HRMS: calculated for C$_{13}$H$_{16}$F$_2$N$_2$O$_3$+ (M$^+$): 341.1108, found 341.1105.

TLC: 2:98 acetone/toluene, $R_f$ = 0.35.

1-methyl-3-(1-methyl-1H-pyrrol-2-yl)-4-(thiophen-3-ylmethyl)pyrrolidine-2,5-dione (4h): Synthesized by a two-step procedure. First, the alkyl chloride was synthesized: in an oven dried Schlenk tube, 3-thiophenemethanol (115 mg, 0.75 mmol, 1.5 equiv.) was dissolved in dry dichloromethane (5 mL) and cooled to 0 °C. Thiophenyl chloride (88 µL, 1.2 mmol, 1.2 equiv.) was added dropwise and the reaction was left stirring at ambient temperature for 30 min. Solvent was removed under vacuum at 25 °C, diethyl ether (5 mL) was added and dried (this was repeated twice) to obtain the crude 3-(chloromethyl)thiophene 1h as a colorless oil in quantitative yield, which was used without further purification. The crude adduct 1h was dissolved in 1,2-dichloroethane giving a stock solution 0.75 M. 3-(chloromethyl)thiophene 1h (0.75 M, 0.75 mmol, 1.5 equiv.) was added in an oven dried Schlenk tube, then the DTC catalyst A (31 mg, 0.2 equiv.) was added followed by 2,6-lutidine (157 µL, 1.35 mmol, 2.7 equiv.), N-methylmaleimide 2a (56 µg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). The resulting yellow mixture was degassed via three cycles of freeze-pump-thaw. The Schlenk tube was then placed in the irradiation setup at a temperature of 60 °C and irradiated for 20 hours. After cooling to ambient temperature, the solvent was evaporated and the residue purified by column chromatography (two consecutive purifications; first purification: gradient from 10% to 20% AcOEt in hexanes as eluent; second purification: gradient from 0% to 2% acetone in toluene as eluent): 100.3 mg of 4h isolated as a brown oil, 66% yield. A single diastereomer was detected by $^1$H NMR analysis of the crude reaction mixture.

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.27 – 7.25 (m, 1H), 6.98 – 6.96 (m, 1H), 6.86 (dd, J = 5.0, 1.3 Hz, 1H), 6.60 (dd, J = 2.7, 1.8 Hz, 1H), 6.07 (dd, J = 3.7, 2.7 Hz, 1H), 5.95 (dd, J = 3.7, 1.8, 0.6 Hz, 1H), 3.71 (d, J = 5.5 Hz, 1H), 3.54 (s, 3H), 3.37 – 3.33 (m, 1H), 3.29 (ddd, J = 14.5, 6.3, 0.8 Hz, 1H), 3.12 (dd, J = 14.5, 5.1 Hz, 1H), 2.96 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 178.1, 176.0, 136.8, 128.4, 126.6, 126.5, 123.7, 123.0, 107.3, 106.5, 47.9, 42.5, 34.2, 29.5, 25.1.

IR (thin film) ν 2925, 1776, 1695, 1491, 1432, 1380, 1286, 1119, 1090, 752, 711 cm$^{-1}$.

HRMS: calculated for C$_{13}$H$_{17}$N$_2$O$_3$S$^+$ (M$^+$):289.1005, found 289.1016.

TLC: 30:70 EtOAc/hexanes, $R_f$ = 0.38.
3-benzyl-1-methyl-4-(1-methyl-1H-pyrrol-2-yl)pyrroloidine-2,5-dione (4i): Synthesized according to the general procedure using benzyl bromide (89 µL, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). The diastereomeric ratio (7.6:1) was determined by 1H NMR spectroscopic analysis of the crude reaction mixture by comparison of the resonances at δ 5.95 (minor diastereomer) and δ 5.87 (major diastereomer). Product 4i purified by column chromatography (gradient from 15% to 25% AcOEt in hexanes as eluent): 69 mg of a brown oil, 49% yield.

1H NMR (500 MHz, CDCl3) δ 7.29-7.20 (m, 3H), 7.14-7.11 (m, 2H), 6.55 (dd, J = 2.6, 1.8 Hz, 1H), 6.04 (dd, J = 3.6, 2.9 Hz, 1H), 5.91 (dd, J = 3.6, 1.6 Hz, 1H), 3.70 (d, J = 5.5 Hz, 1H), 3.47 (s, 3H), 3.37 (app q, J = 5.7 Hz, 1H), 3.22 (dd, J = 14.1, 6.5 Hz, 1H), 3.10 (dd, J = 14.1, 5.5 Hz, 1H), 2.94 (s, 3H).

13C NMR (126 MHz, CDCl3) δ 178.2, 176.0, 136.7, 129.5, 128.9, 127.3, 126.6, 123.6, 107.3, 106.7, 48.3, 42.4, 34.3, 34.2, 25.2.

IR (thin film) ν 2926, 1776, 1695, 1494, 1432, 1382, 1287, 1122, 992, 703 cm⁻¹.

HRMS: calculated for C17H19N3O2⁺ (M+H⁺): 283.1441, found 283.1437.

TLC: 20:80 EtOAc/hexanes, Rf = 0.19.

3-(4-fluorobenzyl)-1-methyl-4-(1-methyl-1H-pyrrol-2-yl)pyrroloidine-2,5-dione (4j): Synthesized according to the general procedure using 4-fluorobenzyl bromide (142 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). The diastereomeric ratio (5.3:1) was determined by 1H NMR spectroscopic analysis of the crude reaction mixture by comparison of the resonances at δ 5.92 (major diastereomer) and δ 5.95 (minor diastereomer). Product 4j purified by column chromatography (gradient from 10% to 20% AcOEt in hexanes as eluent): 82.2 mg of a brown oil, 55% yield.

1H NMR (500 MHz, CDCl3) δ 7.13 – 7.08 (m, 2H), 7.00 – 6.94 (m, 2H), 6.59 (dd, J = 2.8, 1.7 Hz, 1H), 6.06 (dd, J = 3.7, 2.7 Hz, 1H), 5.93 (dd, J = 3.7, 1.6 Hz, 1H), 3.68 (d, J = 5.7 Hz, 1H), 3.52 (s, 3H), 3.37 (app q, J = 5.8 Hz, 1H), 3.21 (dd, J = 14.3, 6.3 Hz, 1H), 3.08 (dd, J = 14.3, 5.5 Hz, 1H), 2.96 (s, 3H).

13C NMR (126 MHz, CDCl3) δ 178.0, 175.8, 162.1 (d, J = 246.0 Hz), 132.4 (d, J = 3.3 Hz), 131.0 (d, J = 8.0 Hz), 126.3, 123.9, 115.8 (d, J = 21.3 Hz), 107.3, 106.7, 48.3, 42.4, 34.3, 34.2, 25.2.

19F NMR decoupled 1H (471 MHz, CDCl3) δ -115.32

IR (thin film) ν 2925, 1696, 1508, 1432, 1381, 1286, 1221, 1120, 711 cm⁻¹.

HRMS: calculated for C17H18F3N3O2⁺ (M+H⁺): 301.1347, found 301.1359.

TLC: 20:80 EtOAc/hexanes, Rf = 0.15.

(3S,4R)-3-(4-chlorobenzyl)-1-methyl-4-(1-methyl-1H-pyrrol-2-yl)pyrroloidine-2,5-dione (4k): Synthesized according to the general procedure using 4-chlorobenzyl bromide (154 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). The diastereomeric ratio (6.3:1) was determined by 1H NMR spectroscopic analysis of the crude reaction mixture by comparison of the resonances at δ 5.82 (major diastereomer) and δ 5.77 (minor diastereomer). Product 4k was purified by column chromatography (gradient from 15% to 25% AcOEt in hexanes as eluent): 65 mg of a brown oil,
41% yield. DMSO-d$_6$ was used as a co-solvent in the $^{13}$C NMR spectra to prevent overlap of aliphatic peaks.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.23 (d, $J$ = 8.5 Hz, 2H), 7.06 (d, $J$ = 8.4 Hz, 2H), 6.58 (dd, $J$ = 2.6, 1.8 Hz, 1H), 6.04 (d, $J$ = 3.6, 2.9 Hz, 1H), 5.91 (dd, $J$ = 3.6, 1.6 Hz, 1H), 3.65 (d, $J$ = 5.8 Hz, 1H), 3.51 (s, 3H), 3.36 (app q, $J$ = 5.9 Hz, 1H), 3.20 (dd, $J$ = 14.3, 6.4 Hz, 1H), 3.05 (dd, $J$ = 14.2, 5.6 Hz, 1H), 2.94 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$ + DMSO-d$_6$) $\delta$ 177.0, 175.2, 135.7, 131.5, 130.4, 128.0, 126.1, 122.7, 106.4, 106.1, 47.4, 42.2, 33.8, 33.4, 24.4.

IR (thin film) $\nu$ 2945, 1776, 1697, 1491, 1433, 1382, 1286, 1092, 1015, 716 cm$^{-1}$.

HRMS: calculated for C$_{17}$H$_{18}$ClN$_2$O$_2$ (+M+): 317.1051, found 317.1054.

TLC: 25:75 EtOAc/hexanes, $R_f$ = 0.26.

(3S,4R)-3-(4-bromobenzyl)-1-methyl-4-(1-methyl-1H-pyrrol-2-yl)pyrrolidine-2,5-dione (4l): Synthesized according to the general procedure using 4-bromobenzyl bromide (187 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). Product 4l was purified by column chromatography (gradient from 15% to 25% AcOEt in hexanes as eluent): 104 mg brown oil, 57% yield. A single diastereomer was detected by $^1$H NMR analysis of the crude reaction mixture.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.40 (d, $J$ = 8.4 Hz, 2H), 7.02 (d, $J$ = 8.4 Hz, 2H), 6.59 (dd, $J$ = 2.5, 1.9 Hz, 1H), 6.06 (dd, $J$ = 3.6, 2.9 Hz, 1H), 5.93 (dd, $J$ = 3.6, 1.6 Hz, 1H), 3.66 (d, $J$ = 5.9 Hz, 1H), 3.53 (s, 3H), 3.37 (app q, $J$ = 5.9 Hz, 1H), 3.20 (dd, $J$ = 14.3, 6.3 Hz, 1H), 3.05 (dd, $J$ = 14.3, 5.6 Hz, 1H), 2.95 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 177.7, 175.6, 135.7, 131.9, 131.1, 126.1, 123.8, 121.2, 107.3, 106.6, 47.9, 42.3, 34.3, 34.2, 25.1.

IR (thin film) $\nu$ 2945, 1776, 1694, 1488, 1431, 1381, 1284, 1121, 1090, 714 cm$^{-1}$.

HRMS: calculated for C$_{17}$H$_{17}$BrN$_2$NaO$_2$ (+M+Na$^+$): 383.0366, found 383.0360.

TLC: 25:75 EtOAc/hexanes, $R_f$ = 0.26.

3-(4-iodobenzyl)-1-methyl-4-(1-methyl-1H-pyrrol-2-yl)pyrrolidine-2,5-dione (4m): Synthesized according to the general procedure using 4-iodobenzyl bromide (223 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). Product 4m was purified by column chromatography (gradient from 15% to 25% AcOEt in hexanes as eluent): 128 mg of a pale yellow sticky oil, 63% yield. A single diastereomer was detected by $^1$H NMR analysis of the crude reaction mixture.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.60-7.55 (m, 2H), 6.89-6.84 (m, 2H), 6.87 (dd, $J$ = 2.5, 1.8 Hz, 1H), 6.04 (dd, $J$ = 3.6, 2.5 Hz, 1H), 5.9 (dd, $J$ = 3.6, 1.8 Hz; 1H), 3.64 (d, $J$ = 5.8 Hz; 1H), 3.51 (s, 3H), 3.35 (d, $J$ = 5.9 Hz; 1H), 3.17 (dd, $J$ = 14.7, 6.2 Hz; 1H), 3.01 (dd, $J$ = 14.7, 5.5 Hz; 1H), 2.93 (s, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 178.0, 175.9, 138.2 (x2), 136.6, 131.7 (x2), 126.3, 124.2, 107.6, 106.9, 93.0, 48.2, 42.6, 34.6, 34.6, 25.4.

IR (thin film) $\nu$ 2924, 1775, 1694, 1484, 1430, 1380, 1285, 1120, 1089, 1006, 714 cm$^{-1}$

HRMS: calculated for C$_{17}$H$_{17}$IN$_2$O$_2$ (+M+H$^+$): 409.0708, found 409.0387.
TLC: 20:80 EtOAc/hexanes, \( R_f = 0.2 \).

1-methyl-3-(1-methyl-1H-pyrrol-2-yl)-4-(4-(trifluoromethyl)benzyl)pyrrolidine-2,5-dione (4n): Synthesized according to the general procedure using 4-(trifluoromethyl)benzyl bromide (180 mg, 0.75 mmol, 1.5 equiv.), \( N \)-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and \( N \)-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). The diastereomeric ratio (4:2) was determined by \(^1\)H NMR spectroscopic analysis of the crude reaction mixture by comparison of the resonances at \( \delta 5.92 \) (major diastereomer) and \( \delta 5.95 \) (minor diastereomer). Product 4n was purified by column chromatography (gradient from 10% to 30% AcOEt in hexanes as eluent): 72.4 mg of a brown oil, 41% yield.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta 7.53 \) (d, \( J = 8.0 \) Hz, 2H), 7.26 (d, \( J = 7.8 \) Hz, 2H), 6.58 (dd, \( J = 2.7, 1.8 \) Hz, 1H), 6.04 (dd, \( J = 3.7, 2.7 \) Hz, 1H), 5.92 (dd, \( J = 3.9, 1.7 \) Hz, 1H), 3.64 (d, \( J = 5.9 \) Hz, 1H), 3.51 (s, 3H), 3.42 (app q, \( J = 6.0 \) Hz, 1H), 3.26 (dd, \( J = 14.2, 6.4 \) Hz, 1H), 3.17 (dd, \( J = 14.2, 5.7 \) Hz, 1H), 2.95 (s, 3H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \( \delta 177.6, 175.5, 141.0, 129.9, 129.7 (q, \( J = 32.5 \) Hz), 125.9, 125.8 (q, \( J = 3.8 \) Hz), 124.1 (q, \( J = 272.0 \) Hz), 124.0, 107.4, 106.8, 47.9, 42.6, 34.8, 34.3, 25.2.

\(^{19}\)F NMR decoupled \(^1\)H (471 MHz, CDCl\(_3\)) \( \delta -62.67 \).

IR (thin film) \( \nu 2925, 1778, 1698, 1433, 1382, 1322, 1287, 1162, 1110, 1066, 712 \) cm\(^{-1}\).

HRMS: calculated for C\(_{18}\)H\(_{17}\)F\(_3\)N\(_2\)Na\(_2\)O\(_2\)\(^+\) (M+\(\text{Na}^+\)): 373.1134, found 373.1119.

TLC: 20:80 EtOAc/hexanes, \( R_f = 0.23 \).

1-methyl-3-(1-methyl-1H-pyrrol-2-yl)-4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)pyrrolidine-2,5-dione (4o): Synthesized according to the general procedure using 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl bromide (223 mg, 0.75 mmol, 1.5 equiv.), \( N \)-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and \( N \)-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). Product 4o was purified by column chromatography (gradient from 10% to 30% AcOEt in hexanes as eluent): 39.3 mg pale brown oil, 28% yield. A single diastereomer was detected by \(^1\)H NMR analysis of the crude reaction mixture.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta 7.72 \) (d, \( J = 8.0 \) Hz, 2H), 7.14 (d, \( J = 8.0 \) Hz, 2H), 6.56 (dd, \( J = 2.8, 1.8 \) Hz, 1H), 6.06 (dd, \( J = 3.7, 2.7 \) Hz, 1H), 5.94 (dd, \( J = 3.6, 1.6 \) Hz, 1H), 3.68 (d, \( J = 5.5 \) Hz, 1H), 3.50 (s, 3H), 3.40 (app q, \( J = 5.7 \) Hz, 1H), 3.30 (dd, \( J = 14.0, 6.0 \) Hz, 1H), 3.07 (dd, \( J = 14.1, 5.4 \) Hz, 1H), 2.94 (s, 3H), 1.34 (s, 12H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \( \delta 178.1, 176.0, 139.8, 135.4, 129.0, 126.5, 123.8, 107.3, 106.5, 84.0, 48.2, 42.1, 35.0, 34.3, 25.2, 25.0.

\(^{11}\)B NMR (160 MHz, CDCl\(_3\)) \( \delta 30.76 \).

IR (thin film) \( \nu 3399, 2978, 1696, 1612, 1433, 1359, 1289, 1142, 1090, 1022, 658 \) cm\(^{-1}\).

HRMS: calculated for C\(_{23}\)H\(_{29}\)N\(_2\)O\(_4\)\(^{11}\)B\(^+\) (M+\(\text{Na}^+\)): 431.2113, found 431.2122.

TLC: 20:80 EtOAc/hexanes, \( R_f = 0.31 \).
2-(5-(4-((1,3-dioxoisindolin-2-yl)methyl)-1-methyl-2,5-dioxopyrrolidin-3-yl)thiophen-2-yl)acetonitrile (4p): Synthesized according to the general procedure using (4-(bromomethyl)phenyl)(piperidin-1-yl)methanone (212 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.).

Product 4p was purified by column chromatography (two consecutive purifications. First purification: gradient from 40% to 60% AcOEt in hexanes as eluent. Second purification: 90:10 tol:acetone): 140.3 mg of a pale yellow solid, 71% yield. A single diastereomer was detected by $^1$H NMR analysis of the crude reaction mixture.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.34 – 7.29 (m, 2H), 7.19 – 7.15 (m, 2H), 6.56 (dd, $J = 2.8$, 1.7 Hz, 1H), 6.03 (dd, $J = 3.7$, 2.7 Hz, 1H), 5.91 (ddd, $J = 3.8$, 1.8, 0.6 Hz, 1H), 3.69 (d+bs, $J = 6.0$ Hz, 1H+2H), 3.52 (s, 3H), 3.41 (app q, $J = 5.9$ Hz, 1H), 3.28 (s, 2H), 3.24 (dd, $J = 14.2$, 6.5 Hz, 1H), 3.14 (dd, $J = 14.2$, 5.4 Hz, 1H), 2.96 (s, 3H), 1.67 (bs, 4H), 1.50 (bs, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 177.7, 175.5, 169.8, 138.0, 135.4, 129.4 (x2), 127.3 (x2), 125.9, 123.7, 107.1, 106.5, 48.8 (broad), 47.1, 43.2, 34.2, 26. (broad), 25.5 (broad), 24.5.

HRMS: calculated for C$_{23}$H$_{28}$N$_3$O$_3$ (+) (M+H$^+$): 394.2125, found 394.2131.

IR (thin film) $\nu$ 2932, 2854, 1776, 1696, 1619, 1430, 1274, 1109, 706 cm$^{-1}$.

TLC: 60:40 EtOAc/hexanes, $R_f = 0.16$.

3-(4-(hydroxymethyl)benzyl)-1-methyl-4-(1-methyl-1H-pyrrolo-2-yl)pyrrolidine-2,5-dione (4q): Synthesized according to the general procedure using 4-hydroxymethylbenzyl bromide (150 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). Product 4q was purified by column chromatography (gradient from 40% to 60% AcOEt in hexanes as eluent): 77 mg of a yellowish sticky oil, 49% yield. A single diastereomer was detected by $^1$H NMR analysis of the crude reaction mixture.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.27 – 7.23 (m, 2H), 7.12 – 7.08 (m, 2H), 6.56 (dd, $J = 2.6$, 1.9 Hz, 1H), 6.03 (dd, $J = 3.4$, 2.6 Hz, 1H), 5.9 (ddd, $J = 3.4$, 1.9 Hz, 1H), 4.62 (br s, 2H), 3.68 (d, $J = 5.5$ Hz; 1H), 3.49 (s, 3H), 3.36 (q, $J = 5.7$ Hz; 1H), 3.23 (dd, $J = 14.1$, 6.1 Hz; 1H), 3.05 (dd, $J = 14.1$, 5.4 Hz; 1H), 2.92 (s, 3H), 1.89 (br s, 1H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 178.4; 176.2; 140.2; 136.2; 129.9 (x2); 127.3 (x2); 125.9; 107.5; 106.8; 65.2; 48.5; 42.5; 34.8; 34.5; 25.4.

IR (thin film) $\nu$ 3455, 2924, 1693, 1434, 1382, 1288, 717 cm$^{-1}$.

HRMS: calculated for C$_{18}$H$_{20}$N$_2$NaO$_4$ (+) (M+Na$^+$): 335.1366, found 335.1365.

TLC: 50:50 EtOAc/hexanes, $R_f = 0.25$.

1-methyl-3-(1-methyl-1H-pyrrolo-2-yl)-4(3,4,5-trimethoxybenzyl)pyrrolidine-2,5-dione (4r): Synthesized according to the general procedure using 5-(chloromethyl)-1,2,3-trimethoxybenzene (162 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). A single diastereomer was detected by $^1$H NMR analysis of the crude reaction mixture.

Purification by column chromatography (gradient from 20% to 35% AcOEt in hexanes as eluent) resulted in poor separation, but a clean amount (50 mg) of pure 4r was isolated for
characterization (50 mg). 58% NMR-yield, determined using trichloroethylene as the internal standard. $^1$H NMR (500 MHz, CDCl$_3$) δ 6.57 (dd, $J = 2.6, 1.9$ Hz, 1H), 6.32 (s, 2H), 6.06 (dd, $J = 3.5, 2.9$ Hz, 1H), 5.94 (dd, $J = 3.6, 1.7$ Hz, 1H), 3.80 (s, 3H), 3.74 (s, 6H), 3.71 (d, $J = 5.7$ Hz, 1H), 3.50 (s, 3H), 3.40 (app q, $J = 5.8$ Hz, 1H), 3.15 (dd, $J = 14.5, 6.8$ Hz, 1H), 3.08 (dd, $J = 14.4, 5.5$ Hz, 1H), 2.97 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 178.5, 176.3, 153.7, 137.3, 132.7, 126.9, 124.0, 107.7, 106.8, 106.5, 61.2, 56.4, 48.4, 42.8, 35.6, 34.5, 25.5.

IR (thin film) ν 2939, 2839, 1697, 1589, 1507, 1458, 1431, 1382, 1123, 1006 cm$^{-1}$.

HRMS: calculated for C$_{20}$H$_{24}$N$_2$NaO$_5$+ (M+Na$^+$): 395.1577, found 395.1581.

TLC: 30:70 EtOAc/hexanes, $R_f = 0.11$.

3-((6-chlorobenzo[d][1,3]dioxol-5-yl)methyl)-1-methyl-4-(1-methyl-1H-pyrrol-2-yl)pyrrolidine-2,5-dione (4s): Synthesized according to the general procedure 6-chloropiperonyl chloride (154 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). A single diastereomer was detected by $^1$H NMR analysis of the crude reaction mixture. Product 4s was purified by column chromatography (gradient from 10% to 30% AcOEt in hexanes as eluent): 133 mg of a white foam, 72% yield.

$^1$H NMR (500 MHz, CDCl$_3$) δ 6.8 (s, 1H), 6.7 (s, 1H), 6.6 (dd, $J = 2.7, 1.7$ Hz, 1H), 6.0 (dd, $J = 3.7, 2.7$ Hz, 1H), 5.9 (s, 2H), 5.9 (dd, $J = 3.6, 1.5$ Hz, 1H), 3.8 (d, $J = 5.4$ Hz, 1H), 3.6 (s, 3H), 3.4 (m, 1H), 3.3 (dd, $J = 14.1, 5.7$ Hz, 1H), 3.1 (dd, $J = 14.2, 7.1$ Hz, 1H), 3.0 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 178.0, 175.9, 147.5, 147.1, 127.7, 126.4, 126.0, 123.7, 110.4, 109.9, 107.1, 106.2, 47.5, 42.6, 34.2, 32.7, 25.2.

IR (thin film) ν 2900, 1776, 1696, 1478, 1433, 1381, 1286, 1232, 1118, 1035, 749, 712 cm$^{-1}$.

HRMS: calculated for C$_{18}$H$_{17}$ClN$_2$NaO$_4$+ (M+Na$^+$): 383.0769, found 383.0770.

TLC: 30:70 EtOAc/hexanes, $R_f = 0.33$.

1-methyl-3-((1-methyl-1H-pyrrol-2-yl)-4-(3-methylbut-2-en-1-yl)pyrrolidine-2,5-dione (4t): Synthesized according to the general procedure using 1-chloro-3-methylbut-2-ene chloride (170 µL, 1.50 mmol, 3.0 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). The diastereomeric ratio (2.9:1) was determined by $^1$H NMR spectroscopic analysis of the crude reaction mixture by comparison of the resonances at δ 5.10 (minor diastereomer) and δ 4.87 (major diastereomer). Product 4t was purified by column chromatography (gradient from 15% to 20% AcOEt in hexanes as eluent): 62 mg of a brown oil, 47% yield.

$^1$H NMR (400 MHz, CDCl$_3$) δ 6.62 (dd, $J = 2.6, 1.9$ Hz, 1H), 6.07 (dd, $J = 3.6, 2.9$ Hz, 1H), 5.93 (dd, $J = 3.6, 1.6$ Hz, 1H), 5.05-5.00 (m, 1H), 3.73 (d, $J = 5.3$ Hz, 1H), 3.67 (s, 3H), 3.11 (app q, $J = 5.5$ Hz, 1H), 2.99 (s, 3H), 2.57-2.52 (m, 2H), 1.69 (d, $J = 0.9$ Hz, 1H), 1.62 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 178.5, 176.4, 136.6, 126.9, 123.8, 118.5, 107.3, 106.7, 47.2, 43.0, 34.4, 30.2, 26.0, 25.1, 18.1.

IR (thin film) ν 2918, 1776, 1696, 1492, 1432, 1380, 1285, 1095, 995, 713 cm$^{-1}$.

HRMS: calculated for C$_{15}$H$_{20}$N$_2$NaO$_2$+ (M+Na$^+$): 283.1417, found 283.1415.

TLC: 30:70 EtOAc/hexanes, $R_f = 0.33$.  

S14
2-((4-(1-methyl-1H-pyrrol-2-yl)-2,5-dioxopyrrolidin-3-yl)methyl)isoindoline-1,3-dione (4u): Synthesized according to the general procedure using N-(chloromethyl)phthalimide chloride 1a (147 mg, 0.75 mmol, 1.5 equiv.), unprotected maleimide 2b (48 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). The diastereomeric ratio (1.9:1) was determined by ¹H NMR spectroscopic analysis of the crude reaction mixture by comparison of the resonances at δ 5.96 (minor diastereomer) and δ 5.72 (major diastereomer). Purification by column chromatography (gradient from 15% to 25% AcOEt in hexanes as eluent) resulted in very poor separation, but an analytical amount of the major diastereomer was isolated for characterization. NMR yield of the mixture of diastereoisomers (1.9:1) is 77%. DMSO-d₆ was used either as a solvent or co-solvent in the NMR spectra to promote solubility; in the case of ¹³C NMR, chloroform was required in order to prevent overlap of aromatic peaks.

¹H NMR (500 MHz, DMSO-d₆) δ 11.30 (s, 1H), 7.77 (s, 4H), 6.48 (app t, J = 2.1 Hz, 1H), 5.76 (dd, J = 3.5, 1.8 Hz, 1H), 5.60 (dd, J = 3.5, 2.8 Hz, 1H), 4.22 (d, J = 7.3 Hz, 1H), 4.09 (dd, J = 14.0, 6.0 Hz, 1H), 4.02 (dd, J = 14.1, 9.0 Hz, 1H), 3.53 (s, 3H), 3.52-3.48 (m, 1H).

¹³C NMR (126 MHz, CDCl₃ + DMSO-d₆) δ 176.8, 175.9, 168.4, 134.3, 131.9, 125.4, 123.8, 123.5, 107.2, 106.8, 46.2, 45.0, 38.0, 34.3.

IR (thin film) ν 2976, 1774, 1697, 1436, 1399, 1364, 1263, 1158, 1106, 714 cm⁻¹.

HRMS: calculated for C₁₆H₁₅N₃O₄⁺ (M+H⁺): 394.1761, found 394.1765.

TLC: 50:50 EtOAc/hexanes, Rₚ = 0.31.

2-((1-tert-butyl)-4-(1-methyl-1H-pyrrol-2-yl)-2,5-dioxopyrrolidin-3-yl)methyl)isoindoline-1,3-dione (4v): Synthesized according to the general procedure using N-(chloromethyl)phthalimide chloride 1a (147 mg, 0.75 mmol, 1.5 equiv.), N-tert-butylmaleimide 2c (76 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). A single diastereomer was detected by ¹H NMR analysis of the crude reaction mixture. Product 4v was purified by column chromatography (gradient from 15% to 25% AcOEt in hexanes as eluent): 127 mg of an orange foam, 64% yield.

¹H NMR (500 MHz, CDCl₃) δ 7.73-7.69 (m, 2H), 7.65-7.62 (m, 2H), 6.32 (dd, J = 2.5, 1.9 Hz, 1H), 5.74 (dd, J = 3.6, 1.6 Hz, 1H), 5.68 (dd, J = 3.6, 2.8 Hz, 1H), 4.26 (dd, J = 14.0, 5.7 Hz, 1H), 3.99 (dd, J = 14.0, 9.6 Hz, 1H), 3.88 (d, J = 7.3 Hz, 1H), 3.59 (s, 3H), 3.47-3.42 (m, 1H), 1.55 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 176.7, 176.2, 168.5, 134.3, 132.0, 126.1, 123.8, 123.5, 107.3, 106.4, 59.2, 45.0, 43.9, 38.4, 34.3, 28.7.

IR (thin film) ν 2976, 1774, 1697, 1436, 1396, 1330, 1263, 1158, 1106, 714 cm⁻¹.

HRMS: calculated for C₂₂H₂₃N₃O₄⁺ (M+H⁺): 394.1761, found 394.1765.

TLC: 20:80 EtOAc/hexanes, Rₚ = 0.14.

3-((1H-benzo[d][1,2,3]triazol-1-yl)methyl)-1-benzyl-4-(1-methyl-1H-pyrrol-2-yl)pyrrolidin-2,5-dione (4w): Synthesized according to the general procedure using 1-(chloromethyl)-1H-benzotriazole 1b (126 mg, 0.75 mmol, 1.5 equiv.), N-benzylmaleimide 2d (94 mg, 0.5 mmol, 1 equiv.) and N-methylpyrrole 3a (445 µL, 5 mmol, 10 equiv.). A single diastereomer was detected by ¹H NMR analysis of the crude reaction mixture. Product 4w was purified by column chromatography (gradient from 10% to 30% AcOEt in hexanes as eluent): 112.1 mg of a white foam, 56% yield.
$^1$H NMR (400 MHz, CDCl$_3$) δ 8.02 (dt, $J = 8.4, 0.9$ Hz, 1H), 7.61 (dt, $J = 8.4, 0.9$ Hz, 1H), 7.49 – 7.45 (m, 1H), 7.37 (ddd, $J = 8.1, 6.9, 1.0$ Hz, 1H), 7.20 – 7.15 (m, 1H), 7.14 – 7.09 (m, 2H), 7.03 – 6.98 (m, 2H), 6.62 (dd, $J = 2.7, 1.7$ Hz, 1H), 6.05 (dd, $J = 3.7, 2.7$ Hz, 1H), 5.92 (dd, $J = 3.5, 1.6$ Hz, 1H), 5.24 (dd, $J = 14.7, 4.3$ Hz, 1H), 5.00 (dd, $J = 14.8, 4.1$ Hz, 1H), 4.57 (d, $J = 14.3$ Hz, 1H), 4.48 (d, $J = 14.3$ Hz, 1H), 4.32 (d, $J = 6.7$ Hz, 1H), 3.67 (s, 3H), 3.62 (dt, $J = 6.7, 4.2$ Hz, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 175.4, 174.5, 145.9, 135.0, 133.4, 128.7 (2C), 128.2, 128.1 (2C), 128.0, 125.4, 124.5, 124.2, 120.1, 109.9, 107.4, 106.6, 47.9, 45.3, 42.9, 41.1, 34.6.

HRMS: calculated for C$_{23}$H$_{22}$N$_5$O$_2$: 400.1778, found 400.1768.

TLC: 30:70 EtOAc/hexanes, $R_f = 0.13$.

2-((1-methyl-2,5-dioxo-4-(thiophen-2-yl)pyrrolidin-3-yl)methyl)isoindoline-1,3-dione (4x): Synthesized according to the general procedure using N-(chloromethyl)phthalimide chloride 1a (147 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and thiophene 3b (400 µL, 5 mmol, 10 equiv.). A single diastereomer was detected by $^1$H NMR analysis of the crude reaction mixture. Product 4x was purified by column chromatography (gradient from 10% to 30% AcOEt in hexanes as eluent): 64.6 mg pale brown solid, 36% yield.

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.81 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.73 – 7.69 (m, 2H), 7.08 (dd, $J = 5.1, 1.2$ Hz, 1H), 6.89 (dd, $J = 3.6, 1.1$ Hz, 1H), 6.78 (dd, $J = 5.2, 3.5$ Hz, 1H), 4.32 (dd, $J = 14.1, 6.2$ Hz, 1H), 4.21 (d, $J = 6.3$ Hz, 1H), 4.09 (dd, $J = 14.1, 9.2$ Hz, 1H), 3.66 – 3.56 (m, 1H), 3.07 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 175.0, 175.0, 168.2, 136.9, 134.4, 131.8, 127.1, 126.3, 125.7, 123.6, 47.7, 46.3, 37.9, 25.6.

IR (thin film) ν 2924, 1766, 1693, 1435, 1401, 1365, 1298, 1190, 1107, 1067, 692 cm$^{-1}$.

HRMS: calculated for C$_{18}$H$_{14}$N$_2$NaO$_4$S$^+$ (M+Na$^+$): 377.0566, found 377.0558.

TLC: 30:70 EtOAc/hexanes, $R_f = 0.22$.

2-((1-methyl-2,5-dioxoisoindolin-2-yl)methyl)-1-methyl-2,5-dioxopyrrolidin-3-yl)thiophen-2-yl)acetonitrile (4y): Synthesized according to the general procedure using N-(chloromethyl)phthalimide 1a (147 mg, 0.75 mmol, 1.5 equiv.), N-methylmaleimide 2a (56 mg, 0.5 mmol, 1 equiv.) and thiophene-2-acetonitrile 3sj (615 µL, 5 mmol, 10 equiv.). Product 4y was purified by column chromatography (gradient from 10% to 30% AcOEt in hexanes as eluent): 40 mg of a pale yellow solid, 20% yield. A single diastereomer was detected by $^1$H NMR analysis of the crude reaction mixture.

$^1$H NMR (400 MHz, DMSO-d$_6$) δ 7.83 – 7.80 (m, 4H), 6.82 (dd, $J = 3.6, 0.9$ Hz, 1H), 6.75 (dt, $J = 3.6, 1.1$ Hz, 1H), 4.27 (d, $J = 6.9$ Hz, 1H), 4.14 (dd, $J = 14.1, 6.4$ Hz, 1H), 4.10 (d, $J = 1.0$ Hz, 2H), 4.04 (dd, $J = 14.1, 8.3$ Hz, 1H), 3.54 (dt, $J = 8.2, 6.6$ Hz, 1H), 2.85 (s, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) δ 175.2, 175.0, 167.8 (x2), 137.7, 134.5 (x2), 132.0, 131.3, 126.7, 125.9, 123.1 (CN), 123.1(x2), 118.2, 46.2, 45.6, 36.9, 24.9, 17.4.

IR (thin film) ν 2913, 1767, 1693, 1440, 1399, 1363, 1298, 1190, 1107, 1067, 692 cm$^{-1}$.

HRMS: calculated for C$_{20}$H$_{15}$N$_3$NaO$_4$S$^+$ (M+Na$^+$): 416.0669, found 416.0675.

TLC: 30:70 EtOAc/hexanes, $R_f = 0.43$. 

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Note: The above text contains chemical structures and reactions, which are not fully depicted in the text. The chemical structures and reactions are typically represented in chemical drawings or diagrams in a scientific context.
B.4. 5 mmol Scale Reaction

The model photoinduced multicomponent reaction can be scaled-up up to 5 mmol scale by using the same experimental set-up described in Figure S1. In an oven dried Schlenk tube (length x diameter = 22 x 2 cm), the DTC catalyst $\text{A}$ (310 mg, 1 mmol, 0.2 equiv.) was dissolved in dichloroethane (5 mL), then the $N$-(chloromethyl)phthalimide $1\text{a}$ (1.5 g, 7.5 mmol, 1.5 equiv.) was added, with stirring, followed by 2,6-lutidine (700 µL, 6 mmol, 1.2 equiv.), $N$-methylmaleimide $2\text{a}$ (556 mg, 5 mmol, 1.0 equiv.), and $N$-methylpyrrole $3\text{a}$ (4.4 mL, 50 mmol, 10.0 equiv.). An additional volume of dichloroethane (5 mL) was added to the reaction tube, washing the sides from residual solids. The resulting mixture was degassed via three cycles of freeze-pump-thaw. The Schlenk tube was then placed in the irradiation setup, maintained at a temperature of 60 ºC (60-61ºC measured in the central well), and the reaction was stirred for 30 hours under continuous irradiation.

After cooling to ambient temperature, the solvent was evaporated and the residue purified by column chromatography (gradient from 10% to 30% AcOEt in hexanes as eluent). Peroduct $4\text{a}$ was isolated as a mixture containing about 14% of an inseparable byproduct, arising from a polar Friedel-Crafts type alkylation of pyrrole $3\text{a}$ with maleimide $2\text{a}$: 1.05 g (containing 14% of byproduct). Corrected yield of product $4\text{a}$: 52% (906 mg). The NMR yield of the observed single diastereomer was measured as 62%, using 1,1,2-trichloroethene as the internal standard.
C. Product Modifications

C.1. Assembly Line Synthesis of Difunctionalized Pyrroles

**C2-functionalization.** In an oven dried Schlenk tube, the DTC catalyst A (15.5 mg, 0.05 mmol, 0.1 equiv.) and sodium acetate (49 mg, 0.6 mmol, 1.2 equiv.) were suspended in 1,2-dichloroethane (1 mL), then chloroacetonitrile 5 (32 µL, 0.5 mmol, 1 equiv.) was added followed by N-methylpyrrole 3a (444 µL, 5 mmol, 10 equiv.). The resulting yellow mixture was degassed via three cycles of freeze-pump-thaw. The Schlenk tube was then placed in the irradiation setup (see Figure S1) set at a temperature of 60 ºC (60-61ºC measured in the central well) and irradiated for 24 hours. After cooling to ambient temperature, the volatiles were evaporated and the residue purified by column chromatography on silica gel (toluene as eluent): 55 mg, 92% yield; spectral data matched those reported in the literature.1

**C5-functionalization.** Substrate 7 was synthesized according to the general procedure for the radial MCR reaction using N-(chloromethyl)phthalimide 1a (147 mg, 0.75 mmol, 1.5 equiv.), maleimide 2a (56 mg, 0.5 mmol, 1.0 equiv.) and the C2-functionalized pyrrole 6 (600 mg, 5.0 mmol, 10.0 equiv.). Irradiation time: 24 hours. A single diastereomer was detected by 1H NMR analysis of the crude reaction mixture. Product 7 was purified by column chromatography (gradient from 10% to 40% AcOEt in hexanes as eluent): 61.8 mg of a pale brown solid, 32% yield.

4-((1,3-dioxoisindolin-2-yl)methyl)-1-methyl-2,5-dioxopyrrolidin-3-yl)-1-methyl-1H-pyrrol-2-yl)acetonitrile (7):

1H NMR (500 MHz, CDCl3) δ 7.75 (dd, J = 5.5, 3.0 Hz, 2H), 7.68 (dd, J = 5.5, 3.0 Hz, 2H), 5.74 (d, J = 3.8 Hz, 1H), 5.68 (d, J = 3.8 Hz, 1H), 4.38 (dd, J = 14.0, 5.3 Hz, 1H), 4.12 – 4.01 (m, 2H), 3.61 (ddd, J = 10.2, 7.3, 5.2 Hz, 1H), 3.57 (s, 3H), 3.49 (dd, J = 5.6, 0.8 Hz, 2H), 3.02 (s, 3H).

13C NMR (126 MHz, CDCl3) δ 175.0, 174.7, 168.3, 134.4, 131.5, 126.9, 123.5, 121.6, 116.2, 108.3, 106.0, 44.7, 43.9, 37.8, 31.0, 25.3, 16.4.

IR (thin film) ν 2936, 1778, 1765, 1697, 1498, 1400, 1274, 1094, 725 cm⁻¹.

HRMS: calculated for C21H18N4NaO4⁺ (M+Na⁺): 413.1220, found 413.1215.

TLC: 40:60 EtOAc/hexanes, Rf = 0.23.

Figure S3. Sequential C2 and C5-functionalization of N-methyl pyrrole 3a
C.2. Synthesis of Pyrrolidine 8

A solution of the MCR adduct 4w (80 mg, 0.2 mmol, 1 equiv.) in dry THF (0.5 mL) was added dropwise to a cooled suspension of LiAlH₄ (31 mg, 0.8 mmol, 4 equiv.) in dry THF (0.5 mL) at 0 °C. After completion of the addition, the reaction was stirred at room temperature for 6 h. Complete conversion of 4w was observed after 6 h, as judged by TLC analysis of the reaction mixture. The reaction mixture was then diluted with Et₂O (1 mL), and quenched successively with water (1 mL) and NaOH (1M, 0.5 mL). The aqueous phase was extracted three times with Et₂O, and the collected organic phase was washed successively with brine, water and dried over magnesium sulfate. The volatiles were evaporated and the residue purified by column chromatography on silica gel (98:2, DCM:MeOH): 68 mg, 92% yield, white solid.

**Figure S4.** Reduction of the succinimide core of the MCR product 4w.

1-(((3R,4R)-1-benzyl-4-(1-methyl-1H-pyrrol-2-yl)pyrrolidin-3-yl)methyl)-1H-benzo[d][1,2,3]triazole (8)

1H NMR (500 MHz, CDCl₃) δ 8.00 (dt, J = 8.3, 1.0 Hz, 1H), 7.38 (ddd, J = 8.4, 6.7, 1.0 Hz, 1H), 7.34 – 7.19 (m, 8H), 6.47 (dd, J = 2.7, 1.8 Hz, 1H), 6.01 (dd, J = 3.6, 2.7 Hz, 1H), 5.98 (dd, J = 3.6, 1.8 Hz, 1H), 4.71 (s, 1H), 4.70 (d, J = 1.7 Hz, 1H), 3.64 (d, J = 12.9 Hz, 1H), 3.55 (d, J = 12.9 Hz, 1H), 3.24 – 3.13 (m, 2H), 3.06 – 2.96 (m, 1H), 2.76 (dd, J = 9.7, 4.7 Hz, 1H), 2.63 (dd, J = 9.7, 7.5 Hz, 1H), 2.41 (td, J = 7.1, 1.4 Hz, 1H).

13C NMR (125 MHz, CDCl₃) δ 146.0, 138.8, 133.7, 133.3, 128.8 (x2C), 128.4 (x2C), 127.4, 127.2, 123.9, 122.3, 120.1, 109.3, 107.0, 105.0, 61.0, 60.1, 56.9, 51.1, 45.1, 39.2, 33.9.

TLC: 2:98 MeOH/DCM, Rₜ = 0.15.
D. Unsuccessful Substrate Combinations

The optimised conditions of the model MCR reaction were evaluated with a variety of substrates. Those shown in Figure S5 failed to deliver yields higher than the catalyst loading or any product at all.

**Figure S5.** Substrates that failed to provide synthetically useful yields of MCR products. Unless otherwise noted, yields were determined by $^1$H NMR analysis of the crude mixture using trichloroethylene as the internal standard.
E. Cyclic Voltammetry Measurements

Substrates 1a, 1b, 1d, 1e, 1f, 1g, 1k, 1n, 1o, 1r and 1s were electrochemically characterized. The measured reduction potential values are compiled in Figure S6. The cyclic voltammograms are shown in Figures S7-S17.

Figure S6. Reduction potentials (E^{red}) measured vs. Ag/AgCl (KCl, 3.5 M). *Reported in literature and referenced to Ag/AgCl (KCl saturated), according to reference 6.
**Figure S7.** Cyclic voltammogram for N-(chloromethyl)phtalamide chloride 1a [0.02M] in [0.1 M] TBAPF$_6$ in CH$_3$CN. Sweep rate: 100 mV/s. Pt electrode working electrode, Ag/AgCl (KCl 3.5 M) reference electrode, Pt wire auxiliary electrode. Irreversible reduction, $E^C_p = E^{\text{red}}(1a/1a^-) = -1.48$ V, $E^C_p$ refers to the cathodic peak potential, while the $E^{\text{red}}$ value describes the electrochemical properties of 1a.

**Figure S8.** Cyclic voltammogram for 1-(chloromethyl)-1H-benzotriazole 1b [0.02M] in [0.1 M] TBAPF$_6$ in CH$_3$CN. Sweep rate: 100 mV/s. Pt electrode working electrode, Ag/AgCl (KCl 3.5 M) reference electrode, Pt wire auxiliary electrode. First irreversible reduction, $E^C_p = E^{\text{red}}(1b/1b^-) = -2.15$ V, $E^C_p$ refers to the cathodic peak potential, while the $E^{\text{red}}$ value describes the electrochemical properties of 1b.
**Figure S9.** Cyclic voltammogram for 4-(chloromethyl)3,5-dimehtylisoxazole chloride 1d [0.02M] in [0.1 M] TBAPF₆ in CH₃CN. Sweep rate: 50 mV/s. Glassy carbon electrode working electrode, Ag/AgCl (KCl 3.5 M) reference electrode, Pt wire auxiliary electrode. Reduction of substrate 1d was not observed in the registered potential window (from 0 to -2.70 V).

![Cyclic voltammogram for 4-(chloromethyl)3,5-dimehtylisoxazole chloride 1d](image)

**Figure S10.** Cyclic voltammogram for 2-(chloromethyl)-1,3-benzothiazole chloride 1e [0.02M] in [0.1 M] TBAPF₆ in CH₃CN. Sweep rate: 50 mV/s. Glassy carbon electrode working electrode, Ag/AgCl (KCl 3.5 M) reference electrode, Pt wire auxiliary electrode. Irreversible reduction, \( E_p^C = E_{\text{red}}(1e/1e^+) = -2.18 \) V, \( E_p^C \) refers to the cathodic peak potential, while the \( E_{\text{red}} \) value describes the electrochemical properties of 1e.

![Cyclic voltammogram for 2-(chloromethyl)-1,3-benzothiazole chloride 1e](image)
**Figure S11.** Cyclic voltammogram for 4-(chloromethyl)thiazole $\text{If}$ [0.02M] in [0.1 M] TBAPF$_6$ in CH$_3$CN. Sweep rate: 500 mV/s. Pt electrode working electrode, Ag/AgCl (KCl 3.5 M) reference electrode, Pt wire auxiliary electrode. Reduction of substrate $\text{If}$ was not observed in the registered potential window (from 0 to -2.70 V).

**Figure S12.** Cyclic voltammogram for 2-(bromomethyl)-5-(trifluoromethyl)furan bromide $\text{1g}$ [0.02M] in [0.1 M] TBAPF$_6$ in CH$_3$CN. Sweep rate: 50 mV/s. Glassy carbon electrode working electrode, Ag/AgCl (KCl 3.5 M) reference electrode, Pt wire auxiliary electrode. Irreversible reduction, $E_{pC} = E_{\text{red}}(\text{1g/1g}^-) = -2.19$ V, $E_{pC}$ refers to the cathodic peak potential, while the $E^\text{red}$ value describes the electrochemical properties of $\text{1g}$.
Figure S13. Cyclic voltammogram for 4-chlorobenzyl bromide 1k [0.02M] in [0.1 M] TBAPF₆ in CH₃CN. Sweep rate: 500 mV/s. Pt electrode working electrode, Ag/AgCl (KCl 3.5 M) reference electrode, Pt wire auxiliary electrode. Irreversible reduction, \( E_p^C = E_{red}(1k/1k^-) = -2.42 \text{ V} \), \( E_p^C \) refers to the cathodic peak potential, while the \( E_{red} \) value describes the electrochemical properties of 1k.

Figure S14. Cyclic voltammogram for 4-(trifluoromethyl)benzyl bromide 1n [0.02M] in [0.1 M] TBAPF₆ in CH₃CN. Sweep rate: 500 mV/s. Pt electrode working electrode, Ag/AgCl (KCl 3.5 M) reference electrode, Pt wire auxiliary electrode. Irreversible reduction, \( E_p^C = E_{red}(1n/1n^-) = -2.33 \text{ V} \), \( E_p^C \) refers to the cathodic peak potential, while the \( E_{red} \) value describes the electrochemical properties of 1n.
Figure S15. Cyclic voltammogram for 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl bromide 1o [0.02M] in [0.1 M] TBAPF$_6$ in CH$_3$CN. Sweep rate: 500 mV/s. Pt electrode working electrode, Ag/AgCl (KCl 3.5 M) reference electrode, Pt wire auxiliary electrode. Irreversible reduction, $E_p^c = E_{red}^{red}(1o/1o^-) = -2.27$ V, $E_p^c$ refers to the cathodic peak potential, while the $F_{red}^{red}$ value describes the electrochemical properties of 1o.

Figure S16. Cyclic voltammogram for 5-(chloromethyl)-1,2,3-trimethoxybenzene 1r [0.02M] in [0.1 M] TBAPF$_6$ in CH$_3$CN. Sweep rate: 100 mV/s. Pt electrode working electrode, Ag/AgCl (KCl 3.5 M) reference electrode, Pt wire auxiliary electrode. Reduction of substrate 1r was not observed in the registered potential window (from 0 to -2.70 V).
Figure S17. Cyclic voltammogram for 6-chloropiperonyl chloride 1s [0.02M] in [0.1 M] TBAPF$_6$ in CH$_3$CN. Sweep rate: 50 mV/s. Glassy carbon electrode working electrode, Ag/AgCl (KCl 3.5 M) reference electrode, Pt wire auxiliary electrode. Reduction of substrate 1s was not observed in the registered potential window (from 0 to -2.70 V).

The reduction potential of substrates 1i, 1j, 1l, 1t are reported in literature$^{3,4,5}$. The literature values were referenced to Ag/AgCl. KCl saturated$^6$, and are the following:

$E^{\text{red}}(1i/1i^-) = -1.80$ V (vs. Ag/AgCl, KCl saturated)

$E^{\text{red}}(1j/1j^-) = -1.59$ V (vs. Ag/AgCl, KCl saturated)

$E^{\text{red}}(1l/1l^-) = -1.51$ V (vs. Ag/AgCl, KCl saturated)

$E^{\text{red}}(1t/1t^-) = -2.50$ V (vs. Ag/AgCl, KCl saturated)
F. X-ray Crystallographic Data

Single Crystal X-ray Diffraction Data for Compound 4a

Crystals of the compound 4a were obtained by slow evaporation of a methanol solution. Measurements were made on a Bruker-Nonius diffractometer equipped with an APPEX 2 4K CCD area detector, a FR591 rotating anode with MoKα radiation, Montel mirrors and a Cryostream Plus low temperature device (T = 100K). Full-sphere data collection was used with ω and φ scans.

Table S1. Crystal data and structure refinement for 4a. CCDC 1894404

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H. $^1$H and $^{13}$C NMR Spectra
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**S54**