Pd-Catalysed Suzuki-Miyaura Cross-Coupling of Aryl Chlorides at Low Catalyst Loadings in Water for the Synthesis of Industrial Important Fungicides

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1. General Information

All reactions were performed in flame-dried glassware using an MBraun glove box or conventional Schlenk techniques under a static pressure of argon (glove box) unless otherwise stated. Liquids and solutions were transferred with either syringes or glass pipettes. Solvents for catalyst stock solutions (cyclohexane, THF, ethyl acetate and toluene) were purchased by ACROS Organics with a purity of 99.99% (absolute) and used without further purification. Commercially available chemicals were purchased by Sigma Aldrich, TCI or Apollon Scientific. Commercial liquid substrates were degassed with three freeze-pump-thaw cycles and stored in a glove box over thermally activated 4-Å molecular sieves. Commercial solid substrates were dried under high vacuum prior to being stored in the glove box. 5-(Difluoromethyl)-1methyl-1H-pyrazole-4-carbonyl chloride (11) was synthesised according to previously reported method.^{S1} Analytical thin layer chromatography (TLC) was performed on pre-coated Macherey-Nagel ALUGRAM® SIL G/UV254 aluminium sheets. Standard flash chromatography was performed on an Isolera[™] Spektra Systems automated with high performance flash purification system using BIOTAGE® Cartridge Sfär Silica D10, using petrol ether and ethyl acetate (EtOAc) as eluents. ¹H, ¹³C and ¹⁹F NMR spectra were recorded in CDCl₃, on a Bruker AVANCE III 300 or Bruker AVANCE III 500 spectrometers at the Organisches-Chemie Institut, Ruprecht-Karls-University Heidelberg. Chemical shifts are reported in parts per million (ppm) and are referenced to the residual solvent resonance as the internal standard (CHCl₃: δ = 7.26 ppm for ¹H NMR and CDCl₃: δ = 77.16 ppm for ¹³C NMR). ¹⁹F chemical shifts are referenced in compliance with the unified scale as recommended by the IUPAC stating the chemical shift relative to CCl₃F and Me₄Si.^{S2} Data are reported as follows: chemical shift, multiplicity (br s = broad singlet, s = singlet, d = doublet, dd = doublet of doublets, dt = doublet of triplets, t = triplet, m = multiplet), coupling constants (Hz), and integration. Gas liquid chromatography (GLC) was performed on an Agilent Technologies 6890N gas chromatograph equipped with a DB-5 capillary column (30 m × 0.32 mm, 0.25 μm film thickness) by CS-Chromatographie Service using the following program: He₂ carrier gas, injection temperature 250 °C, detector temperature 300 °C, flow rate: 3.42 mL/min; temperature program: start temperature 60 °C for 1 min, heating rate 5 °C/min, end temperature 120 °C, then heating rate 15 °C/min until 270 °C, end temperature 270 °C for 2 min. High resolution mass spectrometry (HRMS) analysis and X-Ray analysis were performed by the Analytical Facility at the Organisch-Chemisches Institut, Ruprecht-Karls-University Heidelberg. Elemental Analysis measurements were performed by the Mikroanalytisches Laboratorium der Chemischen Institute der Universität Heidelberg. Metal concentration determination by ICP-MS was conducted at the Kompetenzzentrum Analytik at BASF SE.

2. Optimisation study for Suzuki-Miyaura Cross-Coupling in Water

Scheme S1. Catalyst screening with surfactant.



Table S1. Screening of the catalyst systems.^a

| entry | catalytic system | conversion (%) ^b | yield (%) ^b |
|-------|---|-----------------------------|------------------------|
| 1 | Pd(dtbpf)Cl ₂ | - | _ |
| 2 | PEPPSI-Ipr | 70 | 14 |
| 3 | Pd(OAc) ₂ + PAd ₃ | 73 | 15 |
| 4 | Pd(OAc) ₂ + SPhos | >99 | 79 |
| 5 | Pd(OAc) ₂ + XPhos | >99 | 56 |
| 6 | Pd(OAc) ₂ + MePhos | >99 | 86 |
| 7 | Pd(OAc) ₂ + PPh ₃ | >99 | 13 |
| 8 | Pd(OAc) ₂ + P(<i>t</i> -Bu)Cy ₂ | >99 | 95 |
| 9 | Pd(OAc) ₂ + dppe | >99 | 27 |
| 10 | Pd(OAc) ₂ + PCy ₃ | >99 | 52 |
| 11 | Pd(OAc) ₂ + P(o-tolyl) ₃ | >99 | 72 |
| 12 | Pd(OAc) ₂ + P(<i>t</i> -Bu ₂)Ph | 68 | 53 |
| 13° | Pd(PPh ₃)Cl ₂ | 35 | 21 |

^a Unless otherwise noted, all reactions were performed in a glovebox with 0.5 mmol of the aryl halide **4a**, 1.0 equiv of 4-chlorophenylboronic acid (**5a**), K₃PO₄ (3.0 equiv) and 10 μ L of the respective catalytic system (0.05 M in cyclohexane) (0.10 mol%) in 1.0 mL of SPGS-550-M/H₂O (2.0 wt%) at 50 °C for 20 h. ^{*b*} Determined by GC analysis after calibration, using mesitylene as internal standard. ^{*c*} TPGS-750-M/H₂O (2.0 wt%) was used instead of SPGS-550-M/H₂O (2.0 wt%).



Scheme S2. Base screening.

Table S2. Bases used.^a

| entry | base | conversion (%) ^b | yield (%) ^b |
|-------|---------------------------------|-----------------------------|-------------------------|
| 1 | K ₂ CO ₃ | >99 | 88 |
| 2 | Et ₃ N | >99 | quant (97) ^c |
| 3 | NaOH | >99 | quant (95) ^c |
| 4 | KOH | 81 | 46 |
| 5 | Na ₂ CO ₃ | >99 | 88 |
| 6 | DIPEA | >99 | 95 |

^a Unless otherwise noted, all reactions were performed in a glovebox with 0.5 mmol of the aryl chloride **4a**, 1.0 equiv of 4-chlorophenylboronic acid (**5a**), the respective base (2.0 equiv) and 5 μ L of Pd(OAc)₂ + P(*t*-Bu)Cy₂ solution (0.05 M in cyclohexane) (0.05 mol%) in 1.0 mL of H₂O at 60 °C for 20 h. ^{*b*} Determined by GC analysis after calibration, using mesitylene as internal standard. ^{*c*} Isolated yield. [DIPEA = di-*i*-propylethylamine].

Scheme S3. Temperature screening.



| Table S3. Temperature screening. | Fable S3. | Temperature | screening. ^a |
|----------------------------------|-----------|-------------|-------------------------|
|----------------------------------|-----------|-------------|-------------------------|

| entry | T (°C) | conversion (%) ^b | yield (%) ^b |
|----------------|--------|-----------------------------|------------------------|
| 1 | 75 | 20 | 5 |
| 2 | 100 | 38 | 38 |
| 3 | 120 | 56 | 42 |
| 4 ^c | 120 | >99 | 84 |

^a Unless otherwise noted, all reactions were performed in a glovebox with 0.5 mmol of the aryl chloride **4a**, 1.0 equiv of 4-chlorophenylboronic acid (**5a**), Et₃N (2.0 equiv) and 5 μ L of Pd(OAc)₂ + P(*t*-Bu)Cy₂ solution (0.005 M in cyclohexane) (0.005 mol%) in 1.0 mL of H₂O at 60 °C for 20 h. ^{*b*} Determined by GC

analysis after calibration, using mesitylene as internal standard. c The reaction was run with 0.50 mL of H₂O (1.0 M).

Scheme S4. Ligand amount screening.



Table S4. Ligand amount screening.^a

| entry | equiv of L (X) | conversion (%) ^b | yield (%) ^b |
|----------------|----------------|-----------------------------|------------------------|
| 1 | 2.0 | 93 | 77 |
| 2 ^c | 4.0 | 87 | 60 |
| 3 | 4.0 | 98 | 91 (87) ^d |
| 4 ^e | 4.0 | 47 | 31 |
| 5 ^c | 6.0 | 22 | 3 |
| 6 | 6.0 | 98 | 85 (81) ^d |

^a Unless otherwise noted, all reactions were performed in a glovebox with 0.5 mmol of the aryl chloride **4a**, 1.0 equiv of 4-chlorophenylboronic acid (**5a**), Et₃N (2.0 equiv) and 5 μ L of Pd(OAc)₂ + P(*t*-Bu)Cy₂ solution (0.005 M in cyclohexane with different ratio of ligand) (0.005 mol%) in 1.0 mL of H₂O at 60 °C for 20 h. ^{*b*} Determined by GC analysis after calibration, using mesitylene as internal standard. ^{*c*} The reaction was run at 60 °C. ^{*d*} Isolated yield. ^{*e*} The reaction was run with 0.50 mL of H₂O (1.0 M).

Scheme S5. Base screening at higher temperature.



Table S5. Bases screened.^a

| entry | base | conversion (%) ^b | yield (%) ^b |
|-------|---------------------------------|-----------------------------|------------------------|
| 1 | K ₂ CO ₃ | >99 | 93 ^c |
| 2 | Na ₂ CO ₃ | >99 | 97 ^c |
| 3 | K ₃ PO ₄ | 95 | 75 |
| 4 | NaOH | 95 | 80 |

| 5 Et ₃ N 80 63 |
|---------------------------|
|---------------------------|

^a Unless otherwise noted, all reactions were performed in a glovebox with 0.5 mmol of the aryl chloride **4a**, 1.1 equiv of 4-chlorophenylboronic acid (**5a**), the respective base (2.0 equiv) and 5 μL of Pd(OAc)₂ + P(*t*-Bu)Cy₂ solution (0.005 M in cyclohexane) (0.005 mol%) in 1.0 mL of H₂O at 120 °C for 20 h. ^{*b*} Determined by GC analysis after calibration, using mesitylene as internal standard. ^c Isolated yield.

Scheme S6. Temperature screening under optimised conditions.



Table S6. Temperature screening.^a

| entry | T (°C) | conversion (%) ^b | yield (%) ^b |
|-------|--------|-----------------------------|------------------------|
| 1 | 80 | >99 | 81 |
| 2 | 90 | >99 | 84 |
| 3 | 100 | >99 | 96 ^c |
| 4 | 120 | >99 | 78 |
| 5 | 140 | >99 | 80 |

^a Unless otherwise noted, all reactions were performed in a glovebox with 0.5 mmol of the aryl chloride **4a**, 1.1 equiv of 4-chlorophenylboronic acid (**5a**), Na₂CO₃ (1.0 equiv) and 5 μ L of Pd(OAc)₂ + P(*t*-Bu)Cy₂ solution (0.005M in cyclohexane) (0.005 mol%) in 0.50 mL of H₂O at the indicated temperature for 1 h. ^b Determined by GC analysis after calibration, using mesitylene as internal standard. ^c Isolated yield.

Scheme S7. Base screening under optimised conditions.



Table S7. Bases screened.^a

| entry | base | conversion (%) ^b | yield (%) ^b |
|-------|---------------------------------|-----------------------------|------------------------|
| 1 | K ₃ PO ₄ | 89 | 68 |
| 2 | K ₂ CO ₃ | >99 | 83 |
| 3 | Cs ₂ CO ₃ | >99 | 96 |

| 4 | NaOH | 97 | 81 |
|---|------|----|----|
| 5 | КОН | 82 | 64 |

^a Unless otherwise noted, all reactions were performed in a glovebox with 0.5 mmol of the aryl chloride **4a**, 1.1 equiv of 4-chlorophenylboronic acid (**5a**), the respective base (1.0 equiv) and 5 μL of Pd(OAc)₂ + P(*t*-Bu)Cy₂ solution (0.005 M in cyclohexane) (0.005 mol%) in 0.50 mL of H₂O at 100 °C for 1 h. ^{*b*} Determined by GC analysis after calibration, using mesitylene as internal standard.





Table S8. Catalyst loading investigation.^a

| entry | catalyst loading (mol%) | X μL added of 0.0005M solution | conversion (%) ^b | yield (%) ^b |
|----------------|-------------------------|-------------------------------------|-----------------------------|------------------------|
| 1 | 0.0005 | 5 | 65 | 35 |
| 2 | 0.0010 | 10 | 75 | 51 |
| 3 | 0.0025 | 25 | 81 | 67 |
| 4 ^c | 0.0005 | 5 | 55 | 30 |
| 5 ^d | 0.005 | 5 | >99 | 96 ^e |

^a Unless otherwise noted, all reactions were performed in a glovebox with 0.5 mmol of the aryl chloride **4a**, 1.1 equiv of 4-chlorophenylboronic acid (**5a**), Na₂CO₃ (1.0 equiv) and the respective μ L of Pd(OAc)₂ + P(*t*-Bu)Cy₂ solution (0.0005 M in cyclohexane) (0.0005–0.0025 mol%) in 0.50 mL of H₂O at 100 °C for 1 h. ^{*b*} Determined by GC analysis after calibration, using mesitylene as internal standard. ^{*c*} The reaction was run for 72 h. ^{*d*} Comparison experiment with 5 μ L of Pd(OAc)₂ + P(*t*-Bu)Cy₂ solution (0.005 M in cyclohexane). ^{*e*} Isolated yield. Scheme S9. Kinetic experiment under optimised conditions.^a



^a Four different experiments were set at the same time and analyzed by GC respectively after 5, 15, 30, 45 and 60 min.





Scheme S10. Kinetic experiment under optimised conditions in deuterated water.^a



^a Four different experiments were set at the same time and analyzed by GC respectively after 5, 15, 30, 45 and 60 min.



Figure S2. Plot of yield of product 6a vs time.





^a Four different experiments were set at the same time and analyzed by GC respectively after 5, 15, 30, 45 and 60 min. After 60 min, the final product **6a** was isolated in 94% yield as a yellow oil (110.2 mg).







Scheme S12. Removal of cyclohexane solvent.

In a glovebox, a 5.0 mL pressure tube was equipped with a magnetic stir bar, 0.55 mmol of the corresponding aryl boronic acid (**5a**, 86.0 mg, 1.1 equiv) was added with 0.50 mmol of Na₂CO₃ (53.0 mg, 1.0 equiv), 5 μ L of Pd(OAc)₂ and P(*t*-Bu)Cy₂ solution (0.005M in cyclohexane) (0.002 μ mol, 0.005 mol%, Pd:L = 1:4) and 0.50 mmol of 1-chloro-2-nitrobenzene (**4a**, 79.0 mg, 1.0 equiv). The tube was sealed and transferred outside the glovebox and full vacuum was applied to the tube for 10 s in order to remove the volatile cyclohexane. Finally, 0.50 mL of H₂O were added under a flow of Ar and the tube was placed in a preheated 100 °C oil bath for 1 h. After this time, the mixture was diluted with 5.0 mL of brine and extracted with EtOAc (3 x 2.0 mL). The combined organic phases were dried over MgSO₄ and filtered. After concentration under reduce pressure, the crude product was purified by flash column chromatography on silica gel to get the title compound 4'-chloro-2-nitro-1,1'-biphenyl (**6a**, 107 mg, 96%) was obtained as a yellow solid. The spectroscopic data are in accordance with those previously reported.^{S3}

Scheme S13. Control experiments without catalyst.^a



w/o catalyst: no reaction

^a The experiment were done in a used pressure tube and using used stirrer bars according to the procedure described before.

3. Study on the Reaction Phases

3.1 Study on the Reaction Phases after 5 min



In a glovebox, a 5.0 mL pressure tube was equipped with a magnetic stir bar, 0.55 mmol of 4chlorophenylboronic acid (**5a**, 86.0 mg, 1.1 equiv) was added with 0.50 mmol of Na₂CO₃ (53.0 mg, 1.0 equiv), 5 μ L of Pd(OAc)₂ and P(*t*-Bu)Cy₂ solution (0.005 M in cyclohexane) (0.002 μ mol, 0.005 mol%, Pd:L = 1:4) and 2-chloro-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol). The tube was sealed and transferred outside the glovebox, where 0.50 mL of H₂O were added under a flow of Ar. The tube was finally placed in a preheated 100 °C oil bath for 5 min. After this time, the tube was put in an ice bath and 0.50 mL of EtOAc were added. The organic phase was then analyzed by GC and ICP-MS. The remaining water phase was analyzed by ¹¹B NMR spectroscopy and ICP-MS.





3.2 Study on the Reaction Phases after 60 min



In a glovebox, a 5.0 mL pressure tube was equipped with a magnetic stir bar, 0.55 mmol of 4chlorophenylboronic acid (**5a**, 86.0 mg, 1,1 equiv) was added with 0.50 mmol of Na₂CO₃ (53.0 mg, 1.0 equiv), 5 μ L of Pd(OAc)₂ and P(*t*-Bu)Cy₂ solution (0.005 M in cyclohexane) (0.002 μ mol, 0.005 mol%, Pd:L = 1:4) and 2-chloro-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol). The tube was sealed and transferred outside the glovebox, where 0.50 mL of H₂O were added under a flow of Ar. The tube was finally placed in a preheated 100 °C oil bath for 1 h. After this time, the tube was put in an ice bath and 0.50 mL of EtOAc were added. The organic phase was then analyzed by GC and ICP-MS. The remaining water phase was analyzed by ¹¹B NMR spectroscopy and ICP-MS.

Figure S5. ¹¹B NMR of the water phase after 60 min.



3.3 Study on the Water Effect on the Reaction



or conversion 37%; yield 13% w/ 0.1 mL H_2 O: conversion >99%; yield 85% (isolated yield 75%)

In a glovebox, a 5.0 mL pressure tube was equipped with a magnetic stir bar, 0.55 mmol of 4chlorophenylboronic acid (**5a**, 86.0 mg 1.1 equiv) was added with 0.50 mmol of Na₂CO₃ (53.0 mg, 1.0 equiv), 5 μ L of Pd(OAc)₂ and P(*t*-Bu)Cy₂ solution (0.005 M in cyclohexane) (0.002 μ mol, 0.005 mol%, Pd:L = 1:4) and 2-chloro-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol). The tube was sealed and transferred outside the glovebox and placed in a preheated 100 °C oil bath for 1 h. After this time, the mixture was diluted with 2.0 mL of brine, and the solution was extracted with 3 x 2.0 mL EtOAc. The combined organic phases were dried over MgSO₄, filtered and the solution was repeated two times, giving the outcome reported in the scheme.

Similarly, in a glovebox, a 5.0 mL pressure tube was equipped with a magnetic stir bar, 0.55 mmol of 4-chlorophenylboronic acid (**5a**) was added with 0.50 mmol of Na₂CO₃ (53.0 mg, 1.0 equiv), 5 μ L of Pd(OAc)₂ and P(*t*-Bu)Cy₂ solution (0.005 M in cyclohexane) (0.002 μ mol, 0.005 mol%, Pd:L = 1:4) and 2-chloro-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol). The tube was sealed and transferred outside the glovebox, where 0.1 mL of H2O were added under a flow of Ar. The tube was then placed in a preheated 100 °C oil bath for 1 h. After this time, the mixture was diluted with 2.0 mL of brine, and the solution was extracted with 3 x 2.0 mL EtOAc. The combined organic phases were dried over MgSO₄, filtered and then concentrated in vacuo. The title compound 4'-chloro-2-nitro-1,1'-biphenyl (**6a**, 88.0 mg, 75%) was obtained as a yellow solid.

4. Suzuki-Miyaura Cross-Coupling of Aryl Chlorides at ppm Level in Water

4.1 General Procedure for the Preparation of the Catalyst Stock solutions

In a glovebox, a 10.0 mL vial was charged with 6.0 mg of $Pd(OAc)_2$ (0.25 mmol) and 25.0 mg of $P(t-Bu)Cy_2$ (0.10 mmol, Pd:L = 1:4) and diluted in 5.0 mL of the respective solvent, obtaining a 0.005 M solution of the catalytic system. The mixture was left stirring in the glovebox and the desired amount (5 µL, 0.002 µmol) was taken with a micropipette and directly injected in the reaction vessel.

4.2 General Procedure for Suzuki-Miyaura Cross-Coupling of Aryl Chloride with Aryl Boronic Acids (GP1)



In a glovebox, a 5.0 mL pressure tube was equipped with a magnetic stir bar, 0.55 mmol of the corresponding aryl boronic acid (**5a–5j**) was added with 0.50 mmol of Na₂CO₃ (53.0 mg, 1.0 equiv), 5 μ L of Pd(OAc)₂ and P(*t*-Bu)Cy₂ solution (0.005 M in cyclohexane) (0.002 μ mol, 0.005 mol%, Pd:L = 1:4) and 0.50 mmol of 1-chloro-2-nitrobenzene (**4a**, 79.0 mg, 1.0 equiv). The tube was sealed and transferred outside the glovebox, where 0.50 mL of H₂O were added under a flow of Ar. The tube was finally placed in a preheated 100 °C oil bath for 3 h. After this time, the mixture was diluted with 5.0 mL of brine and extracted with EtOAc (3 x 2.0 mL). The combined organic phases were dried over MgSO₄ and filtered. After concentration under reduce pressure, the crude product was purified by flash column chromatography on silica gel using indicated solvents to get spectroscopically pure product.



4.3 General Procedure for Suzuki-Miyaura Cross-Coupling of Aryl Halides (GP2)

In a glovebox, a 5.0 mL pressure tube was equipped with a magnetic stir bar, 0.55 mmol of 4chlorophenylboronic acid (**5a**, 86.0 mg, 1.1 equiv) was added with 0.50 mmol of Na₂CO₃ (53.0 mg, 1.0 equiv), 5 μ L of Pd(OAc)₂ and P(*t*-Bu)Cy₂ solution (0.005 M in cyclohexane) (0.002 μ mol, 0.005 mol%, Pd:L = 1:4) and 0.50 mmol of the corresponding aryl chloride (**4k**-**r**) or aryl bromide (**4s**-**4v**). The tube was sealed and transferred outside the glovebox, where 0.50 mL of H₂O were added under a flow of Ar. The tube was finally placed in a preheated 100 °C oil bath for 5 h. After this time, the mixture was diluted with 5.0 mL of brine and extracted with EtOAc (3 x 2.0 mL). The combined organic phases were dried over MgSO₄ and filtered. After concentration under reduce pressure, the crude product was purified by flash column chromatography on silica gel using indicated solvents to get spectroscopically pure product.

4.4 Substrate Scope for Nucleophiles

4.4.1 4'-Chloro-2-nitro-1,1'-biphenyl (6a)



Prepared from 1-chloro-2-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (**5a**, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP1**. The title compound 4'-chloro-2-nitro-1,1'-biphenyl (**6a**, 112.0 mg, 97%) was obtained as a yellow solid. The spectroscopic data are in accordance with those previously reported.^{S3}

 \mathbf{R}_{f} = 0.36 (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 21.01 min.

¹**H NMR** (500 MHz, CDCl₃): δ = 7.80 (dd, *J* = 8.7, 1.0 Hz, 1 H), 7.55 (td, *J* = 7.6, 1.0 Hz, 1 H), 7.42 (dt, *J* = 8.0, 1.3 Hz, 1 H), 7.32 (dd, *J* = 8.6, 1.9 Hz, 3 H), 7.17 (dd, *J* = 7.6, 1.3 Hz, 2 H) ppm. ¹³**C NMR** (125 MHz, CDCl₃): δ = 149.2, 136.0, 135.4, 134.6, 132.6, 131.9, 129.4, 129.0, 128.7, 124.4 ppm. **HRMS** (EI) for C₁₂H₈CINO₂⁺ [M⁺]: calculated 233.0238, found 233.0234.

4.4.2 4'-Methoxy-2-nitro-1,1'-biphenyl (6b)



Prepared from 1-chloro-2-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol) and 4-methoxy-phenylboronic acid (**5b**, 88.0 mg, 0.55 mmol) according to **GP1**. The title compound 4'-methoxy-2-nitro-1,1'-biphenyl (**6b**, 106.5 mg, 93%) was obtained as a bright yellow oil. The spectroscopic data are in accordance with those previously reported.^{S5}

 $\mathbf{R}_{f} = 0.37$ (petrol ether: EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 21.56 min.

¹H NMR (300 MHz, CDCl₃): δ = 7.74 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.51 (td, *J* = 8.1, 1.3 Hz, 1H), 7.39–7.33 (m, 2H), 7.20–7.15 (m, 2H), 6.91–6.85 (m, 2H), 3.77 (s, 3H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 159.8, 135.9, 132.2, 132.0, 129.6, 129.2, 127.8, 124.1, 114.3, 55.4 ppm. HRMS (EI) for C₁₃H₁₁NO₃⁺ [M⁺]: calculated 229.0733, found 229.0739.

4.4.3 4'-Methyl-2-nitro-1,1'-biphenyl (6c)



Prepared from 1-chloro-2-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol) and *p*-tolylboronic acid (**5c**, 75.0 mg, 0.55 mmol) according to **GP1**. The title compound 4'-methyl-2-nitro-1,1'-biphenyl (**6c**, 94.0 mg, 88%) was obtained as a light yellow oil. The spectroscopic data are in accordance with those previously reported.^{S4}

 \mathbf{R}_{f} = 0.55 (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 20.28 min.

¹H NMR (300 MHz, CDCl₃): δ = 7.74 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.51 (td, *J* = 7.5, 1.3 Hz, 1H) 7.40–7.33 (m, 2H), 7.18–7.11 (m, 4H), 2.32 (s, 3H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 149.5, 138.3, 136.4, 134.5, 132.3, 132.0, 129.6, 128.0, 127.9, 124.1, 21.4 ppm. HRMS (EI) for C₁₃H₁₁NO₂⁺ [M+H⁺]: calculated 213.0784, found 213.0796.

4.4.4 2-Nitro-1,1'-biphenyl (6d)



Prepared from 1-chloro-2-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol) and phenylboronic acid (**5d**, 67.0 mg, 0.55 mmol) according to **GP1**. The title compound 2-nitro-1,1'-biphenyl (**6d**, 83.2 mg, 83%) was obtained as a pale yellow oil. *When the reaction was run with 0.01 mol% catalyst, the title compound 2-nitro-1,1'-biphenyl 6d was obtained in 97% yield (97.0 mg). The spectroscopic data are in accordance with those previously reported.^{S4}*

 $\mathbf{R}_{f} = 0.58$ (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 19.29 min.

¹**H NMR** (300 MHz, CDCl₃): δ = 7.86 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.62 (td, *J* = 7.6, 1.3 Hz, 1H), 7.53–7.40 (m, 5H), 7.36–7.29 (m, 2H) ppm. ¹³**C NMR** (75 MHz, CDCl₃): δ = 137.5, 136.5, 132.4, 132.1, 128.8, 128.4, 128.3, 128.0, 124.2 ppm. **HRMS** (EI) for C₁₂H₉NO₂⁺ [M⁺]: calculated 199.0628, found 199.0645.

4.4.5 4'-Fluoro-2-nitro-1,1'-biphenyl (6e)



Prepared from 1-chloro-2-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol) and 4-fluoro-phenylboronic acid (**5e**, 77.0 mg, 0.55 mmol) according to **GP1**. The title compound 4'-Fluoro-2-nitro-1,1'- biphenyl (**6e**, 104.7 mg, 96%) was obtained as a yellow oil. The spectroscopic data are in accordance with those previously reported.^{S4}

 $\mathbf{R}_{f} = 0.47$ (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 19.21 min.

¹H NMR (400 MHz, CDCl₃): δ = 7.78 (dd, J = 8.1, 1.2 Hz, 1H), 7.54 (td, J = 7.8, 1.2 Hz, 1H), 7.41 (td, J = 7.8, 1.5 Hz, 1H), 7.34 (dd, J = 7.6, 1.5 Hz, 1H), 7.25–7.16 (m, 2H), 7.04 (tt, J = 8.8, 2.2 Hz, 2H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ 162.9 (d, $J_{C,F}$ = 246.9 Hz), 135.4, 136.5 (d, $J_{C,F}$ = 3.4 Hz), 132.5, 132.1, 129.8 (d, $J_{C,F}$ = 8.3 Hz), 128.5, 124.3, 115.8 (d, $J_{C,F}$ = 22.4 Hz) ppm. ¹⁹F NMR (282 MHz, CDCl₃): δ = –113.6 ppm. HRMS (EI) for C₁₂H₈FNO₂⁺ [M⁺]: calculated 217.0522, found 217.0518.

4.4.6 3',4',5'-Trifluoro-2-nitro-1,1'-biphenyl (6f)



Prepared from 1-chloro-2-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol) and 3,4,5-trifluoro-phenylboronic acid (**5f**, 97.0 mg, 0.55 mmol) according to **GP1**. The title compound 3',4',5'-trifluoro-2-nitro-1,1'-biphenyl (**6f**, 115.8 mg, 91%) was obtained as a yellow solid. The spectroscopic data are in accordance with those previously reported.^{S6}

 $\mathbf{R}_{f} = 0.28$ (petrol ether: EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 18.92 min.

¹**H NMR** (500 MHz, CDCl₃): δ = 7.86 (dd, J = 8.1, 1.0 Hz, 1H), 7.58 (td, J = 7.6, 1.1 Hz, 1H), 7.49 (dt, J = 8.0, 1.1 Hz, 1H), 7.31 (dd, J = 7.6, 1.0 Hz, 1H), 6.89-6.83 (m, 2H) ppm. ¹³**C NMR**

(125 MHz, CDCl₃): δ = 151.2 (dq, $J_{C,F}$ = 251.9, 4.6 Hz), 148.8, 139.9 (dt, $J_{C,F}$ = 253.8, 15.1 Hz), 133.7, 133.6, 132.9, 131.8, 129.5, 124.7, 112.7 (dd, $J_{C,F}$ = 17.0, 5.5 Hz) ppm. ¹⁹**F NMR** (471 MHz, CDCl₃): δ = -160.6 (t, $J_{F,F}$ = 20.8 Hz), -133.4 (d, $J_{F,F}$ = 20.8 Hz) ppm. **HRMS** (EI) for C₁₂H₆F₃NO₂⁺ [M⁺]: calculated 253.0345, found 253.0354.

4.4.7 2-Nitro-4'-(trifluoromethyl)-1,1'-biphenyl (6g)



Prepared from 1-chloro-2-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol) and 4-trifluoromethylphenylboronic acid (**5g**, 104.0 mg, 0.55 mmol) according to **GP1**. The title compound 2nitro-4'-(trifluoromethyl)-1,1'-biphenyl (**6g**, 122.6 mg, 92%) was obtained as a yellow oil. The spectroscopic data are in accordance with those previously reported.^{S4}

 $R_{f} = 0.30$ (petrol ether:EtOAc = 95:5). t_{R} (GLC) = 19.21 min.

¹H NMR (300 MHz, CDCl₃): δ = 7.95 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.72–7.64 (m, 3H), 7.55 (td, *J* = 7.8, 1.5 Hz, 1H), 7.47–7.40 (m, 3H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 149.1, 141.4, 135.3, 132.8, 131.9, 130.7, 129.1, 128.5, 125.7 (q, *J*_{C,F} = 3.9 Hz), 124.6 ppm. ¹⁹F NMR (471 MHz, CDCl₃): δ = -62.6 ppm. HRMS (EI) for $C_{13}H_8F_3NO_2^+$ [M⁺]: calculated 267.0502, found 267.0509.

4.4.8 3'-Methyl-2-nitro-1,1'-biphenyl (6h)



Prepared from 1-chloro-2-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol) and 3-methyl-phenylboronic acid (**5h**, 70.0 mg, 0.55 mmol) according to **GP1**. The title compound 3'-methyl-2-nitro-1,1'- biphenyl (**6h**, 97.0 mg, 91%) was obtained as a yellow oil. The spectroscopic data are in accordance with those previously reported.^{S7}

 \mathbf{R}_{f} = 0.55 (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 20.05 min.

¹**H NMR** (500 MHz, CDCl₃): δ = 7.84 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.60 (td, *J* = 7.6, 1.3 Hz, 1H), 7.95–7.42 (m, 2H), 7.34–7.30 (m, 1H), 7.24–7.20 (m, 1H), 7.15–7.10 (m, 2H), 2.39 (s, 3H) ppm. ¹³**C NMR** (125 MHz, CDCl₃): δ = 149.5, 138.5, 137.4, 136.6, 132.3, 132.0, 129.1, 128.7, 128.6, 128.1, 125.1, 124.1, 21.5 ppm. **HRMS** (EI) for C₁₃H₁₁NO₂⁺ [M⁺]: calculated 213.0784, found 213.0799.

4.4.9 2'-Nitro-[1,1'-biphenyl]-4-carbonitrile (6i)



Prepared from 1-chloro-2-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol) and 4-cyanophenylboronic acid (**5i**, 81.0 mg, 0.55 mmol) according to **GP1**. The title compound 2'-nitro-[1,1'-biphenyl]-4-carbonitrile (**6i**, 93.4 mg, 83%) was obtained as a yellowish solid. The spectroscopic data are in accordance with those previously reported.^{S5}

 $\mathbf{R}_{f} = 0.10$ (petrol ether: EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 22.16 min.

¹**H NMR** (300 MHz, CDCl₃): δ = 7.98 (dd, J = 8.1, 1.2 Hz, 1H), 7.75–7.65 (m, 3H), 7.58 (td, J = 7.9, 1.4 Hz, 1H), 7.45–7.39 (m, 3H) ppm. ¹³**C NMR** (75 MHz, CDCl₃): δ = 148.7, 142.6, 134.8, 133.0, 132.4, 131.8, 129.5, 128.9, 124.7, 118.5, 112.2 ppm. **HRMS** (EI) for C₁₃H₈N₂O₂⁺ [M⁺]: calculated 224.0580, found 224.0570.

4.4.10 Methyl 2'-nitro-[1,1'-biphenyl]-4-carboxylate (6j)



Prepared from 1-chloro-2-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol) and 4-methoxycarbonylphenylboronic acid (**5j**, 99.0 mg, 0.55 mmol) according to **GP1**. The title compound methyl 2'-nitro-[1,1'-biphenyl]-4-carboxylate (**6j**, 98.4 mg, 77%) was obtained as a pale yellow solid. The spectroscopic data are in accordance with those previously reported.^{S4}

 $R_{f} = 0.17$ (petrol ether: EtOAc = 95:5). t_{R} (GLC) = 22.86 min.

¹H NMR (300 MHz, CDCl₃): δ = 8.09 (dt, *J* = 8.5, 1.8 Hz, 2H), 7.92 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.65 (td, *J* = 7.4, 1.4 Hz, 1H), 7.53 (td, *J* = 8.1, 1.8 Hz, 1H), 7.45–7.36 (m, 3H), 3.93 (s, 3H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 166.8, 149.1, 142.3, 132.7, 131.9, 130.1, 128.9, 128.2, 124.5, 52.4 ppm. HRMS (EI) for C₁₄H₁₁NO₄⁺ [M⁺]: calculated 257.0683, found 257.0653.

4.5 Substrate Scope for Electrophiles

4.5.1 4'-Chloro-4-nitro-1,1'-biphenyl (6k)



Prepared from 4-chloro-nitrobenzene (**4k**, 79.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (**5a**, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP2** for 1 h. The title compound 4'-chloro-4-nitro-1,1'-biphenyl (**6k**, 106.2 mg, 91%) was obtained as a pale yellow solid. The spectroscopic data are in accordance with those previously reported.^{S10}

 \mathbf{R}_{f} = 0.39 (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 22.34 min.

¹H NMR (300 MHz, CDCl₃): δ = 8.29(d, *J* = 8.7 Hz, 2 H), 7.70 (d, *J* = 8.7 Hz, 2 H), 7.56 (d, *J* = 8.7 Hz, 2 H), 7.46 (d, *J* = 8.7 Hz, 2 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 147.4, 146.4, 137.3, 135.4, 129.5, 128.7, 127.8, 124.3 ppm. HRMS (EI) for $C_{12}H_8CINO_2^+$ [M⁺]: calculated 233.0238, found 233.0232.

4.5.2 4'-Chloro-[1,1'-biphenyl]-2-carbonitrile (6l)



Prepared from 2-chloro-benzonitrile (**4I**, 69.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (**5a**, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP2**. The title compound 4'-chloro-[1,1'-biphenyl]-2-carbonitrile (**6I**, 68.1 mg, 64%) was obtained as a colorless solid. The spectroscopic data are in accordance with those previously reported.^{S9}

 \mathbf{R}_{f} = 0.30 (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 20.62 min.

¹H NMR (500 MHz, CDCl₃) δ = 7.80–7.43 (m, 1H), 7.67–7.62 (m, 1H), 7.53–7.43 (m, 6H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ = 144.4, 136.7, 135.2, 133.9, 133.1, 130.2, 130.0, 129.1, 128.0, 118.6, 111.4 ppm. HRMS (EI) for C₁₃H₈CIN⁺ [M⁺]: calculated 213.0340, found 213.0348.

4.5.3 4'-Chloro-[1,1'-biphenyl]-4-carbonitrile (6m)



Prepared from 4-chloro-benzonitrile (**4m**, 69.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (**5a**, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP2**. The title compound 4'-chloro-[1,1'-biphenyl]-4-carbonitrile (**6m**, 67.2 mg, 63%) was obtained as a colorless solid. The spectroscopic data are in accordance with those previously reported.^{S10}

 \mathbf{R}_{f} = 0.30 (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 21.35 min.

¹H NMR (500 MHz, CDCl₃) δ = 7.76–7.70 (m, 2H), 7.68–7.62 (m, 2H), 7.55–7.49 (m, 2H), 7.48–7.43 (m, 2H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ = 144.5, 137.7, 135.1, 132.8, 129.5, 128.6, 127.7, 118.9, 111.4 ppm. HRMS (EI) for C₁₃H₈CIN⁺ [M⁺]: calculated 213.0340, found 213.0350.

4.5.4 2-(4-Chlorophenyl)pyridine (6n)



Prepared from 2-chloro-pyridine (**4n**, 57.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (**5a**, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP2**. The title compound 2-(4-chlorophenyl)pyridine (**6n**, 52.0 mg, 55%) was obtained as a colorless solid. The spectroscopic data are in accordance with those previously reported.^{S8}

 $\mathbf{R}_{f} = 0.19$ (petrol ether: EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 18.87 min.

¹H NMR (500 MHz, CDCl₃) δ = 8.63–8.59 (m, 1H), 7.89–7.83 (m, 2H), 7.71–7.60 (m, 2H), 7.40–7.33 (m, 2H), 7.18–7.13 (m, 1H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ = 156.4, 149.9, 136.9, 135.2, 129.1, 128.3, 122.5, 120.5 ppm. HRMS (EI) for C₁₁H₈ClN⁺ [M⁺]: calculated 189.0340, found 189.0350.

4.5.5 Methyl 4'-chloro-[1,1'-biphenyl]-4-carboxylate (60)



Prepared from methyl 4-chlorobenzoate (**4o**, 82.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (**5a**, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP2**. The title compound methyl 4'-chloro-[1,1'-biphenyl]-4-carboxylate (**6o**, 68.4 mg, 55%) was obtained as a colorless solid. *When the reaction was run with 0.01 mol% catalyst, the title compound 4'-chloro-[1,1'-biphenyl]-4-carboxylate* **6o** *was obtained in 82% yield (101.1 mg)*. The spectroscopic data are in accordance with those previously reported.^{S11}

 $\mathbf{R}_{f} = 0.33$ (petrol ether: EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 22.12 min.

¹**H NMR** (500 MHz, CDCl₃) δ = 8.14 –8.08 (m, 2H), 7.65–7.59 (m, 2H), 7.58–7.51 (m, 2H), 7.47–7.40 (m, 2H), 3.94 (s, 3H) ppm. ¹³**C NMR** (125 MHz, CDCl₃) δ = 169.9, 144.5, 138.6, 134.5, 130.3, 129.4, 129.2, 128.7, 127.0, 52.3 ppm. **HRMS** (EI) for C₁₄H₁₁ClO₂⁺ [M⁺]: calculated 246.0442, found 246.0441.

4.5.6 1-(4'-Chloro-[1,1'-biphenyl]-4-yl)ethan-1-one (6p)



Prepared from 4-chloro-acetophenone (**4p**, 75.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (**5a**, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP2**. The title compound 1-(4'-chloro-[1,1'-biphenyl]-4-yl)ethan-1-one (**6p**, 75.0 mg, 65%) was obtained as a colorless solid. The spectroscopic data are in accordance with those previously reported.^{S12}

 \mathbf{R}_{f} = 0.33 (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 22.02 min.

¹H NMR (500 MHz, CDCl₃) δ = 8.08 –7.98 (m, 2H), 7.69–7.62 (m, 2H), 7.59–7.52 (m, 2H), 7.48–7.40 (m, 2H), 2.64 (s, 3H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ = 197.7, 144.6, 138.4,

136.3, 134.6, 129.3, 129.1, 128.6, 127.2, 26.8 ppm. **HRMS** (EI) for C₁₄H₁₁ClO⁺ [M⁺]: calculated 230.0493, found 230.0480.

4.5.7 (4'-Chloro-[1,1'-biphenyl]-4-yl)(phenyl)methanone (6q)



Prepared from 4-chlorobenzophenone (**4q**, 108.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (**5a**, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP2**. The title compound (4'-chloro-[1,1'-biphenyl]-4-yl)(phenyl)methanone (**6q**, 103.6 mg, 71%) was obtained as a colorless solid. The spectroscopic data are in accordance with those previously reported.^{S12}

 $\mathbf{R}_{f} = 0.32$ (petrol ether:EtOAc = 95:5).

¹H NMR (500 MHz, CDCl₃) δ = 7.93 –7.88 (m, 2H), 7.86–7.81 (m, 2H), 7.70–7.65 (m, 2H), 7.61–7.57 (m, 2H), 7.55–7.43 (m, 5H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ = 196.4, 144.0, 138.6, 137.8, 136.7, 134.6, 132.6, 131.6, 130.9, 130.1, 130.1, 129.3, 129.8, 128.7, 128.5, 126.9 ppm. HRMS (EI) for C₁₉H₁₃ClO⁺ [M⁺]: calculated 292.0650, found 292.0653.

4.5.8 4'-Chloro-[1,1'-biphenyl]-4-carbaldehyde (6r)



Prepared from 4-chlorobenzaldehyde (**4r**, 70.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (**5a**, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP2**. The title compound 4'-chloro-[1,1'-biphenyl]-4-carbaldehyde (**6r**, 81.7 mg, 75%) was obtained as a colorless solid. The spectroscopic data are in accordance with those previously reported.^{S11}

 \mathbf{R}_{f} = 0.28 (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 21.23 min.

¹H NMR (500 MHz, CDCl₃) δ = 10.06 (s, 1H), 7.98–7.92 (m, 2H), 7.75–7.68 (m, 2H), 7.61–7.53 (m, 2H), 7.49–7.41 (m, 2H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ = 191.9, 145.9, 138.3, 135.5,

134.9, 130.5, 129.3, 128.7, 127.6 ppm. **HRMS** (EI) for $C_{13}H_8CIO^+$ [M⁺]: calculated 216.0336, found 216.0345.

4.5.9 4-Chloro-4'-(trifluoromethyl)-1,1'-biphenyl (6s)



Prepared from 4-chlorotbenzotrifluoride (**4s**, 90.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (**5a**, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP2**. The title compound 4-chloro-4'- (trifluoromethyl)-1,1'-biphenyl (**6s**, 80.0 mg, 62%) was obtained as a colorless solid. The spectroscopic data are in accordance with those previously reported.^{S13}

 $\mathbf{R}_{f} = 0.76$ (petrol ether: EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 18.15 min.

¹H NMR (500 MHz, CDCl₃) δ = 7.66 –7.53 (m, 4H), 7.48–7.40 (m, 2H), 7.39–7.32 (m, 2H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ = 43.6, 138.3, 134.6, 129.8 (d, $J_{C,F}$ = 32.6 Hz), 129.3, 128.6, 127.4, 126.0 (q, $J_{C,F}$ = 3.9 Hz), 122.5 (q, $J_{C,F}$ = 273.4 Hz) ppm. ¹⁹F NMR (471 MHz, CDCl₃): δ = –62.5 ppm. HRMS (EI) for C₁₃H₈ClF₃⁺ [M⁺]: calculated 256.0261, found 256.0270.

4.5.10 4'-Chloro-[1,1'-biphenyl]-2-amine (6t)



Prepared from 2-bromoaniline (**4t**, 90.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (**5a**, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP2**. The title compound 4'-chloro-[1,1'-biphenyl]-2-amine (**6t**, 93.2 mg, 91%) was obtained as a pink solid. The spectroscopic data are in accordance with those previously reported.^{S3}

 \mathbf{R}_{f} = 0.24 (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 20.19 min.

¹H NMR (500 MHz, CDCl₃) δ = 7.44 –7.38 (m, 4H), 7.17 (td, J = 7.8, 1.5 Hz, 1H), 7.09 (dd, J = 7.6, 1.5 Hz, 1H), 6.83 (td, J = 7.6, 0.9 Hz, 1H), 6.77 (dd, J = 7.8, 0.9 Hz, 1H), 3.71 (br s, 2H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ = 143.5, 138.1, 133.2, 130.6, 130.4, 129.1, 128.9, 126.4, 118.9, 115.8 ppm. HRMS (EI) for C₁₂H₁₀ClN⁺ [M⁺]: calculated 203.0496, found 203.0503.

4.5.11 4-Chloro-4'-methyl-1,1'-biphenyl (6u)



Prepared from 4-bromotoluene (**4u**, 85.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (**5a**, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP2**. The title compound 4-chloro-4'-methyl-1,1'- biphenyl (**6u**, 72.0 mg, 71%) was obtained as a colorless solid. The spectroscopic data are in accordance with those previously reported^{S10}

 $\mathbf{R}_{f} = 0.78$ (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 19.25 min.

¹H NMR (300 MHz, CDCl₃) δ = 7.44 –7.35 (m, 4H), 7.34 –7.28 (m, 2H), 7.20 –7.15 (m, 2H), 2.32 (s, 3H) ppm. ¹³C NMR (75 MHz, CDCl₃) δ = 139.7, 137.5, 137.2, 133.1, 129.7, 128.9, 128.3, 126.9, 21.2 ppm. HRMS (EI) for C₁₃H₁₁Cl⁺ [M⁺]: calculated 202.0544, found 202.0537.

4.5.12 4-Chloro-4'-methoxy-1,1'-biphenyl (6v)



Prepared from 4-bromoanisole (4v, 93.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (5a, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP2**. The title compound 4-chloro-4'-methoxy-1,1'-biphenyl (6v, 80.5 mg, 74%) was obtained as a colorless solid. The spectroscopic data are in accordance with those previously reported.^{S10}

 $\mathbf{R}_{f} = 0.46$ (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 20.69 min.

¹H NMR (300 MHz, CDCl₃) δ = 7.52–7.44 (m, 4H), 7.41 –7.35 (m, 2H), 7.02 –6.94 (m, 2H), 3.86 (s, 3H) ppm. ¹³C NMR (75 MHz, CDCl₃) δ = 159.5, 139.4, 132.8, 132.6, 128.9, 128.2, 128.1, 114.4, 55.5 ppm. HRMS (EI) for C₁₃H₁₁ClO⁺ [M⁺]: calculated 218.0493, found 218.0506.

4.5.13 2,4'-Dichloro-1,1'-biphenyl (6w)



Prepared from 1-bromo-2-chlorobenzene (**4w**, 96.0 mg, 0.50 mmol) and 4-chlorophenylboronic acid (**5a**, 86.0 mg, 0.55 mmol, 1.1 equiv) according to **GP2**. The title compound 2,4'-dichloro-1,1'-biphenyl (**6w**, 110.9 mg, 99%) was obtained as a colorless oil. The spectroscopic data are in accordance with those previously reported.^{S14}

 \mathbf{R}_{f} = 0.76 (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 19.32 min.

¹H NMR (300 MHz, CDCl₃) δ = 7.50–7.45 (m, 1H), 7.44 –7.37 (m, 4H), 7.35 –7.29 (m, 3H) ppm. ¹³C NMR (75 MHz, CDCl₃) δ = 139.4, 137.9, 133.8, 132.6, 131.3, 130.9, 130.2, 129.0, 128.4, 127.1 ppm. HRMS (EI) for C₁₂H₈Cl₂⁺ [M⁺]: calculated 221.9998, found 222.0045.

5. Scale-up Experiments

5.1 5.0 mmol experiments

5.1.1 4'-Chloro-2-nitro-1,1'-biphenyl (6a)



In a glovebox, a 25.0 mL pressure tube equipped with a stirrer bar was charged with 4chlorophenylboronic acid (**5a**, 0.86 g, 1.10 equiv, 5.50 mmol), Na₂CO₃ (0.53 g, 1.0 equiv, 5.0 mmol), 50 μ L of a 0.005 M solution of Pd(OAc)₂ + P(*t*-Bu)Cy₂ in cyclohexane (0.25 μ mol, 0.005 mol%, Pd:L = 1:4) and 2-chloro-nitrobenzene (**4a**, 0.79 g, 5.0 mmol). The tube was capped and transferred outside the glovebox, where 5.0 mL of H₂O were added under a flow of Ar. The mixture was heated at 100 °C for 6 h. After this time, the tube was cooled down to rt and the mixture was diluted with 2.0 mL brine and extracted with EtOAc (3 x 5.0 mL), the combined organic extracts were dried over MgSO₄, filtered and concentrate in vacuo. The remaining mixture was purified by column chromatography (petrol ether:EtOAc = 95:5). The title compound 4'-chloro-2-nitro-1,1'-biphenyl (**6a**, 1.07 g, 92%) was obtained as a yellow solid. The spectroscopic data are in accordance with those previously reported.^{S3}



Figure S6. Reaction pictures for 5.0 mmol scale: a) after the reaction; b) upon addition of EtOAc (phase separation).



5.1.2 3',4'-Dichloro-5-fluoro-2-nitro-1,1'-biphenyl (9)

In a glovebox, a 25.0 mL pressure tube equipped with a stirrer bar was charged with 3,4dichlorophenylboronic acid (**9**, 1.05 g, 1.10 equiv, 5.50 mmol), Na₂CO₃ (0.53 g, 1.0 equiv, 5.0 mmol), 50 μ L of a 0.005 M solution of Pd(OAc)₂ + P(*t*-Bu)Cy₂ in cyclohexane (0.25 μ mol, 0.005 mol%, Pd:L = 1:4) and 2-chloro-4-fluoro-nitrobenzene (**10**, 0.88 g, 5.0 mmol). The tube was capped and transferred outside the glovebox, where 5.0 mL of H₂O were added under a flow of Ar. The mixture was heated at 100 °C for 6 h. After this time, the tube was cooled down to rt and the mixture was diluted with 2.0 mL brine and extracted with EtOAc (3 x 5.0 mL), the combined organic extracts were dried over MgSO₄, filtered and concentrate in vacuo. The remaining solid was recrystallised by EtOH, obtaining the title compound 3',4'-dichloro-5-fluoro-2-nitro-1,1'-biphenyl (**11**, 1.06 g, 74%) as a bright yellow solid.

 \mathbf{R}_{f} = 045 (petrol ether:EtOAc = 95:5). \mathbf{t}_{R} (GLC) = 22.03 min.

¹H NMR (500 MHz, CDCl₃): δ = 8.02 (dd, J = 8.7, 5.0 Hz, 1 H), 7.50 (d, J = 8.2 Hz, 1 H), 7.42– 7.40 (m, 1 H), 7.22 (td, J = 8.2, 2.0 Hz, 1 H), 7.11 (ddd, J = 8.7, 5.0, 2.0 Hz, 2 H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 164.1 (d, $J_{C,F}$ = 258.1 Hz), 144.8, 137.4 (d, $J_{C,F}$ = 10.0 Hz), 136.6 (d, $J_{C,F}$ = 1.1 Hz), 133.2 (d, $J_{C,F}$ = 23.8 Hz), 130.8, 129.8, 127.5 (d, $J_{C,F}$ = 10.0 Hz), 127.2, 119.0 (d, $J_{C,F}$ = 23.8 Hz), 116.1 (d, $J_{C,F}$ = 23.2 Hz) ppm. ¹⁹F NMR (471 MHz, CDCl₃): δ = -103.6 ppm. HRMS (EI) for C₁₂H₆Cl₂FNO₂⁺ [M⁺]: calculated 250.0066, found 250.0076. Elemental analysis: calculated C (50.38), H (2.11), N (4.90); found C (50.31), H (2.40), N (4.76).



Figure S7. Reaction pictures for 5.0 mmol scale: a) after the reaction; b) upon addition of EtOAc (phase separation).

5.2 5-g Experiment

5.2.1 4'-Chloro-2-nitro-1,1'-biphenyl (6a)



In a glovebox, a glass autoclave equipped with a spherical stirrer bar was charged with 4chlorophenylboronic acid (**5a**, 5.0 g, 32.0 mmol, 1.1 equiv), Na₂CO₃ (3.4 g, 29.0 mmol, 1.0 equiv), 290 μ L of a 0.005 M solution of Pd(OAc)₂ + P(*t*-Bu)Cy₂ in cyclohexane (1.45 mmol, 0.005 mol%, Pd:L = 1:4) and 2-chloro-nitrobenzene (**4**, 4.56 g, 29.0 mmol). The autoclave was screwed inside the glovebox and transferred outside, where 29.0mL of H₂O were added under a flow of Ar. The glass autoclave was finally sealed and heated in an oil bath at 100 °C for 6 h. After this time the mixture was diluted with 10.0 mL of brine and subsequently extracted with EtOAc (2 x 5.0 mL) and the combined organic phases were dried over MgSO₄, filtered and then concentrated in vacuo. The remaining solid was recrystallised by EtOH (10.0 mL), obtaining the title compound 4'-chloro-2-nitro-1,1'-biphenyl (**6a**, 5.48 g, 84%) as yellow crystals. The spectroscopic data are in accordance with those previously reported.^{S3} **Elemental analysis**: calculated C (61.69), H (3.45), N (5.99); found C (61.80), H (3.70), N (5.82).



Figure S8. Reaction pictures for 5-gram scale: a) reaction stirring; b) after the reaction; c) upon addition of EtOAc (phase separation).

5.3 50-g Experiment

5.3.1 4'-Chloro-2-nitro-1,1'-biphenyl (6a)



A 1-L Schlenk flask equipped with a spherical stirrer bar was charged with was charged with 4-chlorophenylboronic acid (**5a**, 50.0 g, 320 mmol, 1.10 equiv), Na₂CO₃ (30.7 g, 290 mmol, 1.00 equiv). The flask was transferred into a glovebox, where Pd(OAc)₂ (4.0 mg, $1.78 \cdot 10^{-5}$, 0.005 mol%) and the ligand P(*t*-Bu)Cy₂ (16.0 mg, $6.29 \cdot 10^{-5}$, 0.02 mol%, Pd:L = 1:4) were added into the solid aryl chloride **4a**. The flask was then transferred outside, where 290 mL of H₂O were added under a flow of Ar. The flask was finally heated in an oil bath at 100 °C for 8 h. After this time the mixture was diluted with 100 mL of brine and subsequently extracted with EtOAc (2 x 100 mL) and the combined organic phases were dried over MgSO₄, filtered and then concentrated in vacuo. The concentrated EtOAc solution was filtered over a pad of activated charcoal for the removal of Pd-catalyst traces. The mixture was finally concentrated in vacuo and the remaining solid was recrystallised by EtOH (50.0 mL), obtaining the title compound 4'-chloro-2-nitro-1,1'-biphenyl (**6a**, 50.60 g, 75%) as yellow crystals. The spectroscopic data are in accordance with those previously reported.^{S3}

Elemental analysis: calculated C (61.69), H (3.45), N (5.99); found C (61.52), H (3.63), N (6.00).



Figure S9. Reaction pictures for 50-gram scale: a) reaction stirring; b) after the reaction.

The organic extracts in ethyl acetate were placed in a Schlenk flask and connected to a glass trap for the solvent evaporation. Under vacuum there were condensed out circa 30.0 mL of ethyl acetate, which were then analyzed by GC. The GC chromatogram showed a purity of 99.99% for the distilled ethyl acetate and is therefore pure enough to be reused in a subsequent extraction. The GC chromatogram of the distilled ethyl acetate is reported in Figure S12a; for comparison the GC chromatogram of the ethyl acetate is also reported (Figure S12b).



b)



Figure S10. GC chromatogram for the distilled ethyl acetate used for the extraction of the product **6a** (a), and the GC chromatogram of the standard ethyl acetate for comparison (b).

5.3.2 E-Factor calculation for the 50-g experiment

E-Factor = waste (g)/product (g)

Waste^{*} (g) = 11.5 (**1a** left at 75% yield) + 12.5 (**2a** excess at 75% yield) + 30.7 (Na₂CO₃) + 8.22 (by-product salt containing Cl) + 10.23 (by-product salt containing B) + 290.0 (H₂O_{reaction}) + 100 (H₂O_{work-up}) + 180.4 (EtOAc_{extr}) + 49.3 (EtOH_{recrys}) = 692.85

*Pd-catalyst and the ligand were not considered as only very small amount.

Product (g) = 50.60 (75% yield)

E-Factor (without work-up) = 363.15 g/50.6 g = 7.18

E-Factor (with work-up) = 692.85 g/50.6 g = 13.69

E-Factor (without work-up and without considering H_2O) = 73.15 g/50.6 g = 1.44

E-Factor (with work-up and without considering H_2O) = 302.85 g/50.6 g = 5.98

E-Factor (with work-up and recycle of EtOAc)* = 530.85 g/50.6 g = 10.49

*The recycle of EtOAc was approximated to 90% in weight, considering a 10% of loss.

6. Three-Step Synthesis of Fungicides

6.1 Boscalid (1) Synthesis



In a glovebox, a 5.0 mL pressure tube equipped with a spherical stirrer bar was charged with 4-chlorophenylboronic acid (5a, 86.0 mg, 0.55 mmol, 1.10 equiv), Na₂CO₃ (53.0 mg, 0.50 mmol, 1.0 equiv), 5 μ L of a 0.005 M solution of Pd(OAc)₂ + P(*t*-Bu)Cy₂ in cyclohexane (0.002 μ mol, 0.005 mol%, Pd:L = 1:4) and 2-chloro-nitrobenzene (4a, 79.0 mg, 0.50 mmol). The tube was capped and transferred outside the glovebox, where 0.50 mL of H₂O were added under a flow of Ar. The tube was heated in an oil bath at 100 °C for 1 h. After this time, the reaction mixture was cooled down to rt and was filtered through a pad of activated charcoal to remove traces of Pd catalyst. The mixture in the pressure tube was transferred into a 10.0 mL crimp vial equipped with a stirrer bar and a bended needle on the septum. The pressure tube was rinsed with 0.50 mL of water and 0.50 mL of EtOAc for washing it. Finally, the crimp vial was charged with 10.0 mg of Pt/C (10.0 wt%, 1.0 mol%) and the crimp cap was closed. The vial was placed in a PREMEX autoclave and charged with 10 bar of H_2 . The autoclave was then placed at 45 °C for 30 min. After this time, the autoclave was cooled to rt and depressurised. The crimp vial was opened and the containing mixture was filtered over a pad of celite to remove the Pt/C catalyst into a 5.0 mL vial. The crimp vial was rinsed with 0.50 mL of EtOAc for washing it. Subsequently, the 5.0 mL vial was charged with Et₃N (0.14 mL, 1.0 mmol, 2.0 equiv) and the mixture was left stirring gently at rt for 10 min. After this time, the vial was quickly opened and 2-chloronicotinoyl chloride (**10**, 133.0 mg, 0.75 mmol, 1.5 equiv) was added inside and the mixture was left stirring at 60 °C for 18 h. The reaction was monitored by TLC to follow the full consumption of the starting material. The mixture was then cooled down and extracted with EtOAc (3 x 2.0 mL) and brine (5.0 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated in vacuo. Finally, the product was purified by column chromatography (form petrol ether: EtOAc = 95:5 to petrol ether: EtOAc = 60:40). The title compound **Boscalid** (**1**, 130.2 mg, 75%) was obtained as a colourless solid. The spectroscopic data are in accordance with those previously reported.^{S3}

 $\mathbf{R}_{f} = 0.69$ (petrol ether: EtOAc = 60:40).

¹**H NMR** (500 MHz, CDCl₃): δ = 8.41 –8.31 (m, 2H), 8.07 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.38–7.34 (m, 2H), 7.31 –7.25 (m, 3H), 7.21–7.18 (m, 2H) ppm. ¹³**C NMR** (125 MHz, CDCl₃): δ = 162.6, 151.4, 146.8, 140.3, 136.4, 134.6, 134.4, 132.3, 131.1, 130.9, 130.3, 129.4, 129.0, 125.4, 123.0, 122.2 ppm. **HRMS** (EI) for C₁₈H₁₂Cl₂N₂O⁺ [M⁺]: calculated 342.0313, found 342.0316.

The **Boscalid** (1) was further characterised by X-Ray analysis.



6.2 Fluxapyroxad (2) Synthesis

In a glovebox, a 5.0 mL pressure tube equipped with a spherical stirrer bar was charged with 3,4,5-trifluorophenylboronic acid (**5b**, 97.0 mg, 0.55 mmol, 1.1 equiv), Na₂CO₃ (53.0 mg, 0.50 mmol, 1.0 equiv), 5 μ L of a 0.005 M solution of Pd(OAc)₂ + P(*t*-Bu)Cy₂ in cyclohexane (0.002 μ mol, 0.005 mol%, Pd:L = 1:4) and 2-chloro-nitrobenzene (**4a**, 79.0 mg, 0.50 mmol). The tube was capped and transferred outside the glovebox, where 0.50 mL of H₂O were added under a flow of Ar. The tube was heated in an oil bath at 100 °C for 3 h. After this time, the reaction mixture was cooled down to rt and was transferred into a 10.0 mL crimp vial equipped with a stirrer bar and a bended needle on the septum. The pressure tube was charged with 0.50 mL of Pt/C (10.0 wt%, 1.0 mol%) and the crimp cap was closed. The vial was placed in a HEL CAT 7 autoclave and charged with 10 bar of H₂. The autoclave was then placed at 45 °C for 30 min. After this time, the autoclave was cooled to rt and depressurised. The crimp vial was opened and the containing mixture was filtered over a pad of celite to remove the Pt/C catalyst into a 5.0 mL vial. The crimp vial was rinsed with 0.50 mL of EtOAc for washing it. Subsequently, the
5.0 mL vial was charged with Et₃N (0.14 mL, 1.0 mmol, 2.0 equiv) and the mixture was left stirring gently at rt for 10 min. After this time, the vial was quickly opened and 5- (difluoromethyl)-1-methyl-1H-pyrazole-4-carbonyl chloride (**11**, 243.0 mg, 1.25 mmol, 2.5 equiv) was added inside and the mixture was left stirring at 60 °C for 18 h. The reaction was monitored by TLC to follow the full consumption of the starting material. The mixture was then cooled down and extracted with EtOAc ($3 \times 2.0 \text{ mL}$) and brine (5.0 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated in vacuo. Finally, the product was purified by column chromatography (form petrol ether: EtOAc = 95:5 to petrol ether: EtOAc = 60:40). The title compound **Fluxapyroxad** (**2**, 126.0 mg, 66%) was obtained as a colourless solid. The spectroscopic data are in accordance with those previously reported.^{S6}

 $\mathbf{R}_{f} = 0.25$ (petrol ether: EtOAc = 60:40).

¹H NMR (500 MHz, CDCl₃): δ = 8.15 (d, *J* = 8.2 Hz, 1H), 7.94 (s, 1H), 7.84 (br s, 1H), 7.43– 7.39 (m, 1H), 7.24–7.20 (m, 2H), 7.02–6.95 (m, 2H), 6.67 (t, *J* = 54.2 Hz, 1H), 3.89 (s, 3H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 159.5, 151.4 (ddd, $J_{C,F}$ = 251.7, 9.9, 4.2 Hz), 142.4 (t, $J_{C,F}$ = 29.0 Hz), 139.6 (dt, $J_{C,F}$ = 252.9, 15.3 Hz), 136.4, 134.6, 1324.2 (td, $J_{C,F}$ = 7.9, 4.9 Hz), 131.3, 130.1, 129.3, 125.3, 123.6, 116.6, 113.8 (dd, $J_{C,F}$ = 16.2, 5.3 Hz), 111.7 (t, $J_{C,F}$ = 234.1 Hz), 39.6 ppm. ¹⁹F NMR (471 MHz, CDCl₃): δ = –108.9, –133.7 (d, $J_{F,F}$ = 20.2 Hz), –161.5 (t, $J_{F,F}$ = 20.2 Hz) ppm. HRMS (EI) for C₁₈H₁₂F₅N₃O⁺ [M⁺]: calculated 381.0895, found 381.0895.

The Fluxapyroxad (2) was further characterised by X-Ray analysis.

6.3 Bixafen (3) Synthesis



In a glovebox, a 5.0 mL pressure tube equipped with a spherical stirrer bar was charged with 3,4-dichlorophenylboronic acid (**8**, 105.0 mg, 0.55 mmol, 1.1 equiv), Na₂CO₃ (53.0 mg, 0.50 mmol, 1.0 equiv), 10 μ L of a 0.005 M solution of Pd(OAc)₂ + P(*t*-Bu)Cy₂ in cyclohexane (0.004 μ mol, 0.01 mol%, Pd:L = 1:4) and 2-chloro-4-fluoro-nitrobenzene (**7**, 88.0 mg, 0.50 mmol). The tube was capped and transferred outside the glovebox, where 0.50 mL of H₂O were added under a flow of Ar. The tube was heated in an oil bath at 100 °C for 3 h. After this time, the reaction mixture was cooled down to rt and was filtered through a pad of activated charcoal to remove traces of Pd catalyst. The mixture in the pressure tube was transferred into a 10.0 mL crimp vial equipped with a stirrer bar and a bended needle on the septum. The pressure tube

was rinsed with 0.50 mL of water and 0.50 mL of EtOAc for washing it. Finally, the crimp vial was charged with 10.0 mg of Pt/C (10.0 wt%, 1.0 mol%) and the crimp cap was closed. The vial was placed in a HEL CAT 7 autoclave and charged with 10 bar of H₂. The autoclave was then placed at 45 °C for 30 min. After this time, the autoclave was cooled to rt and depressurised. The crimp vial was opened and the containing mixture was filtered over a pad of celite to remove the Pt/C catalyst into a 5.0 mL vial. The crimp vial was rinsed with 0.50 mL of EtOAc for washing it. Subsequently, the 5.0 mL vial was charged with Et₃N (0.14 mL, 1.0 mmol, 2.0 equiv) and the mixture was left stirring gently at rt for 10 min. After this time, the vial was quickly opened and 5-(difluoromethyl)-1-methyl-1H-pyrazole-4-carbonyl chloride (11, 243.0 mg, 1.25 mmol, 2.5 equiv) was added inside and the mixture was left stirring at 60 °C for 18 h. The reaction was monitored by TLC to follow the full consumption of the starting material. The mixture was then cooled down and extracted with EtOAc (3 x 2.0 mL) and brine (5.0 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated in vacuo. Finally, the product was purified by column chromatography (form petrol ether: EtOAc = 95:5 to petrol ether: EtOAc = 60:40). The title compound **Bixafen** (3, 157.8 mg, 76%) was obtained as a colourless solid. The spectroscopic data are in accordance with those previously reported.^{S15}

 $\mathbf{R}_{\mathbf{f}} = 0.19$ (petrol ether:EtOAc = 60:40).

¹**H NMR** (500 MHz, CDCl₃): δ = 8.08 (dd, *J* = 9.1, 5.3 Hz, 1H), 7.91 (s, 1H), 7.73 (br.s, 1H), 7.50 (d, *J* = 8.2 Hz, 1H), 7.46 (d, *J* =2.0 Hz, 1H), 7.19 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.12 (td, *J* = 8.6 Hz, 3.0 Hz, 1H), 6.97 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.68 (t, *J* = 54.2 Hz, 1H), 3.92 (s, 3H) ppm. ¹³**C NMR** (125 MHz, CDCl₃): δ = 159.8 (d, *J*_{C,F} = 247 Hz), 159.7, 142.7 (t, *J*_{C,F} = 28.8 Hz), 137.2 (d, *J*_{C,F} = 1.5 Hz), 135.9, 134.0 (d, *J*_{C,F} = 7.8 Hz), 133.2, 132.8, 131.1, 131.0, 130.6, (d, *J*_{C,F} = 3.0 Hz), 125.8 (d, *J*_{C,F} = 8.2 Hz), 116.9 (d, *J*_{C,F} = 23.2 Hz), 116.5, 115.8 (d, *J*_{C,F} = 21.8 Hz), 111.6 (t, *J*_{C,F} = 233.9 Hz), 39.7 ppm. ¹⁹**F NMR** (471 MHz, CDCl₃): δ = -108.9, -116.6 ppm. **HRMS** (EI) for C₁₈H₁₂Cl₂F₃N₃O⁺ [M⁺]: calculated 413.0304, found 413.0308.

The **Bixafen** (3) was further characterised by X-ray analysis.

7. NMR Spectra

4'-Chloro-2-nitro-1,1'-biphenyl (6a): ¹H NMR spectrum (500 MHz, CDCl₃, 298 K) [50 g-scale reaction, purification via recrystallisation]



4'-Chloro-2-nitro-1,1'-biphenyl (6a): ¹³C{¹H} NMR (125 MHz, CDCl₃, 298 K)



4'-Methoxy-2-nitro-1,1'-biphenyl (6b): ¹H NMR spectrum (300 MHz, CDCl₃, 298 K)



4'-Methoxy-2-nitro-1,1'-biphenyl (6b): ¹³C{¹H} NMR (75 MHz, CDCl₃, 298 K)



4'-Methyl-2-nitro-1,1'-biphenyl (6c): ¹H NMR spectrum (300 MHz, CDCl₃, 298 K)



4'-Methyl-2-nitro-1,1'-biphenyl (6c): ¹³C{¹H} NMR (75 MHz, CDCl₃, 298 K)



2-Nitro-1,1'-biphenyl (6d): ¹H NMR spectrum (300 MHz, CDCI₃, 298 K)



2-Nitro-1,1'-biphenyl (6d): ¹³C NMR spectrum (75 MHz, CDCl₃, 298 K)



4'-Fluoro-2-nitro-1,1'-biphenyl (6e): ¹H NMR spectrum (300 MHz, CDCl₃, 298 K)



4'-Fluoro-2-nitro-1,1'-biphenyl (6e): ¹³C{¹H} NMR (75 MHz, CDCl₃, 298 K)



4'-Fluoro-2-nitro-1,1'-biphenyl (6e): ¹⁹F{¹H} NMR (282 MHz, CDCl₃, 298 K)

| | | | | | | | | | | | | · | | |
|----|----|---|-----|-----|-----|-----|------|------|------|------|------|------|------|-----|
| 40 | 20 | 0 | -20 | -40 | -60 | -80 | -100 | -120 | -140 | -160 | -180 | -200 | -220 | ppm |

3',4',5'-Trifluoro-2-nitro-1,1'-biphenyl (6f): ¹H NMR spectrum (500 MHz, CDCl₃, 298 K)



3',4',5'-Trifluoro-2-nitro-1,1'-biphenyl (6f): ¹³C{¹H} NMR (125 MHz, CDCl₃, 298 K)





3',4',5'-Trifluoro-2-nitro-1,1'-biphenyl (6f): ¹⁹F{¹H} NMR (471 MHz, CDCl₃, 298 K)







2-Nitro-4'-(trifluoromethyl)-1,1'-biphenyl (6g): ¹H NMR spectrum (300 MHz, CDCl₃, 298 K)

2-Nitro-4'-(trifluoromethyl)-1,1'-biphenyl (6g):¹³C{¹H} NMR (75 MHz, CDCl₃, 298 K)



2-Nitro-4'-(trifluoromethyl)-1,1'-biphenyl (6g): ¹⁹F{¹H} NMR (471 MHz, CDCl₃, 298 K)



3'-Methyl-2-nitro-1,1'-biphenyl (6h):¹H NMR spectrum (500 MHz, CDCl₃, 298 K)



3'-Methyl-2-nitro-1,1'-biphenyl (6h): ¹³C{¹H} NMR (125 MHz, CDCl₃, 298 K)



2'-Nitro-[1,1'-biphenyl]-4-carbonitrile (6i): ¹H NMR spectrum (300 MHz, CDCl₃, 298 K)



2'-Nitro-[1,1'-biphenyl]-4-carbonitrile (6i): ¹³C{¹H} NMR (75 MHz, CDCl₃, 298 K)











4'-Chloro-4-nitro-1,1'-biphenyl (6k): ¹H NMR spectrum (300 MHz, CDCl₃, 298 K)



4'-Chloro-4-nitro-1,1'-biphenyl (6k): ¹³C{¹H} NMR (75 MHz, CD₂Cl₂, 298 K)



4'-Chloro-[1,1'-biphenyl]-2-carbonitrile (6I): ¹H NMR spectrum (500 MHz, CDCl₃, 298 K)



4'-Chloro-[1,1'-biphenyl]-2-carbonitrile (6I): ¹³C{¹H} NMR (125 MHz, CD₂Cl₂, 298 K)



4'-Chloro-[1,1'-biphenyl]-4-carbonitrile (6m): ¹H NMR spectrum (500 MHz, CD₂Cl₂, 298 K)



4'-Chloro-[1,1'-biphenyl]-4-carbonitrile (6m): ¹³C{¹H} NMR (125 MHz, CDCl₃, 298 K)



2-(4-Chlorophenyl)pyridine (6n): ¹H NMR spectrum (500 MHz, CDCl₃, 298 K)



2-(4-Chlorophenyl)pyridine (6n): ¹³C{¹H} NMR (125 MHz, CDCl₃, 298 K)



Methyl 4'-chloro-[1,1'-biphenyl]-4-carboxylate (6o): ¹H NMR spectrum (500 MHz, CDCl₃, 298 K)







1-(4'-Chloro-[1,1'-biphenyl]-4-yl)ethan-1-one (6p): ¹H NMR spectrum (500 MHz, CDCl₃, 298 K)


1-(4'-Chloro-[1,1'-biphenyl]-4-yl)ethan-1-one (6p): ¹³C{¹H} NMR (125 MHz, CD₂Cl₂, 298 K)



(4'-Chloro-[1,1'-biphenyl]-4-yl)(phenyl)methanone (6q): ¹H NMR spectrum (500 MHz, CDCl₃, 298 K)



(4'-Chloro-[1,1'-biphenyl]-4-yl)(phenyl)methanone (6q): ¹³C{¹H} NMR (125 MHz, CD₂Cl₂, 298 K)



4'-Chloro-[1,1'-biphenyl]-4-carbaldehyde (6r): ¹H NMR spectrum (500 MHz, CDCl₃, 298 K)



4'-Chloro-[1,1'-biphenyl]-4-carbaldehyde (6r): ¹³C{¹H} NMR (125 MHz, CDCl₃, 298 K)



4-Chloro-4'-(trifluoromethyl)-1,1'-biphenyl (6s): ¹H NMR spectrum (500 MHz, CDCl₃, 298 K)



4-Chloro-4'-(trifluoromethyl)-1,1'-biphenyl (6s): ¹³C{¹H} NMR (125 MHz, CD₂Cl₂, 298 K)





4-Chloro-4'-(trifluoromethyl)-1,1'-biphenyl (6s): ¹⁹F{¹H} NMR (471 MHz, CDCl₃, 298 K)

4'-Chloro-[1,1'-biphenyl]-2-amine (6t): ¹H NMR spectrum (500 MHz, CDCl₃, 298 K)



4'-Chloro-[1,1'-biphenyl]-2-amine (6t): ¹³C{¹H} NMR (125 MHz, CD₂Cl₂, 298 K)

143.6 138.1 138.1 138.1 133.2 133.2 133.2 133.5



4-Chloro-4'-methyl-1,1'-biphenyl (6u): ¹H NMR spectrum (300 MHz, CDCl₃, 298 K)



4-Chloro-4'-methyl-1,1'-biphenyl (6u): ¹³C{¹H} NMR (75 MHz, CD₂Cl₂, 298 K)



4-Chloro-4'-methoxy-1,1'-biphenyl (6v): ¹H NMR spectrum (300 MHz, CDCl₃, 298 K)



4-Chloro-4'-methoxy-1,1'-biphenyl (6v): ¹³C{¹H} NMR (75 MHz, CD₂Cl₂, 298 K)



2,4'-Dichloro-1,1'-biphenyl (6w): ¹H NMR spectrum (300 MHz, CDCl₃, 298 K)



2,4'-Dichloro-1,1'-biphenyl (6w): ¹³C{¹H} NMR (75 MHz, CD₂Cl₂, 298 K)



3',4'-Dichloro-5-fluoro-2-nitro-1,1'-biphenyl (9): ¹H NMR spectrum (500 MHz, CDCI₃, 298 K)



3',4'-Dichloro-5-fluoro-2-nitro-1,1'-biphenyl (9): ¹³C{¹H} NMR (125 MHz, CD₂Cl₂, 298 K)



3',4'-Dichloro-5-fluoro-2-nitro-1,1'-biphenyl (9): ¹⁹F{¹H} NMR (471 MHz, CDCl₃, 298 K)

| 40 | 20 | 0 | -20 | -40 | -60 | -80 | -100 | -120 | -140 | -160 | -180 | -200 | -220 | ppm |
|----|----|---|-----|-----|-----|-----|------|------|------|------|------|------|------|-----|

--103.6

Boscalid (1): ¹H NMR spectrum (500 MHz, CDCl₃, 298 K)







Fluxapyroxad (2): ¹H NMR spectrum (500 MHz, CDCI₃, 298 K)



Fluxapyroxad (2): ¹³C{¹H} NMR (125 MHz, CD₂Cl₂, 298 K)









Bixafen (3): ¹⁹F{¹H} NMR (471 MHz, CDCl₃, 298 K)

| 40 20 | 0 -20 | -40 -60 | -80 -100 | -120 | -140 -160 | -180 -2 | 200 -220 | -240 ppm |
|-------|-------|---------|----------|------|-----------|---------|----------|----------|

8. Crystallographic Data

8.1 Boscalid (1)



Figure S11. Crystallographic structure of product Boscalid (1) (CCDC: 2086181).

Table S9. Crystal data and structure refinement for Boscalid (1).

| Identification code (CCDC) | 2086181 |
|---------------------------------|--|
| Empirical formula | $C_{18}H_{12}CI_2N_2O$ |
| Formula weight | 343.20 |
| Temperature | 200(2) K |
| Wavelength | 0.71073 Å |
| Crystal system | monoclinic |
| Space group | P21/c |
| Z | 8 |
| Unit cell dimensions | a = 14.8126(13) Å α = 90 deg. |
| | b = 11.5893(9) Å β =91.746(2) deg. |
| | c = 18.7010(15) Å γ = 90 deg. |
| Volume | 3208.9(5) Å ³ |
| Density (calculated) | 1.42 g/cm ³ |
| Absorption coefficient | 0.41 mm ⁻¹ |
| Crystal shape | plate |
| Crystal size | 0.180 x 0.078 x 0.032 mm ³ |
| Crystal colour | colourless |
| Theta range for data collection | 2.1 to 24.4 deg. |
| Index ranges | -17 $\leq h \leq$ 17, -13 $\leq k \leq$ 13, -21 $\leq l \leq$ 21 |
| Reflections collected | 28243 |
| Independent reflections | 5283 (R(int) = 0.0851) |
| Observed reflections | 3100 (I > 2σ(I)) |

| Absorption correction | Semi-empirical from equivalents |
|-----------------------------------|---|
| Max. and min. transmission | 0.96 and 0.91 |
| Refinement method | Full-matrix least-squares on F ² |
| Data/restraints/parameters | 5283 / 0 / 423 |
| Goodness-of-fit on F ² | 1.03 |
| Final R indices (I>2sigma(I)) | R1 = 0.054, wR2 = 0.120 |
| | |
| Largest diff. peak and hole | 0.28 and -0.38 eÅ ⁻³ |

Table S10. Atomic coordinates ($x \ 10^4$) and equivalent isotropic displacement parameters (Å²x 10^3) for **Boscalid** (1). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

| atom | х | У | Z | U(eq) |
|------|-----------|------------|------------|------------|
| CI11 | 0.6305(1) | 0.0958(1) | 0.6966(1) | 0.0535(4) |
| Cl21 | 0.8816(1) | -0.1284(1) | 0.7804(1) | 0.0612(4) |
| C101 | 0.6377(2) | 0.3309(3) | 0.7726(2) | 0.0254(9) |
| O101 | 0.6721(2) | 0.3641(2) | 0.7174(1) | 0.0320(6) |
| N111 | 0.6739(2) | 0.3561(3) | 0.8375(2) | 0.0272(8) |
| H111 | 0.650(2) | 0.326(3) | 0.8661(19) | 0.019(12) |
| C111 | 0.5512(2) | 0.2643(3) | 0.7728(2) | 0.0279(9) |
| C121 | 0.5385(3) | 0.1596(3) | 0.7374(2) | 0.0328(10) |
| N131 | 0.4632(2) | 0.1003(3) | 0.7342(2) | 0.0427(9) |
| C141 | 0.3933(3) | 0.1442(4) | 0.7682(2) | 0.0465(12) |
| H141 | 0.3379 | 0.1029 | 0.7666 | 0.056 |
| C151 | 0.3973(3) | 0.2461(4) | 0.8053(2) | 0.0462(12) |
| H151 | 0.3458 | 0.2745 | 0.8287 | 0.055 |
| C161 | 0.4778(3) | 0.3068(3) | 0.8083(2) | 0.0392(10) |
| H161 | 0.4824 | 0.3770 | 0.8343 | 0.047 |
| C211 | 0.7534(3) | 0.4259(3) | 0.8449(2) | 0.0286(9) |
| C221 | 0.8364(2) | 0.3808(3) | 0.8263(2) | 0.0275(9) |
| C231 | 0.9101(3) | 0.4553(4) | 0.8270(2) | 0.0394(11) |
| H231 | 0.9673 | 0.4276 | 0.8129 | 0.047 |
| C241 | 0.9013(3) | 0.5688(4) | 0.8480(2) | 0.0463(12) |
| H241 | 0.9518 | 0.6192 | 0.8470 | 0.056 |
| C251 | 0.8192(3) | 0.6094(4) | 0.8703(2) | 0.0436(11) |
| H251 | 0.8140 | 0.6864 | 0.8872 | 0.052 |
| C261 | 0.7450(3) | 0.5383(3) | 0.8679(2) | 0.0348(10) |
| H261 | 0.6881 | 0.5665 | 0.8822 | 0.042 |
| C311 | 0.8468(2) | 0.2557(3) | 0.8112(2) | 0.0286(9) |
| C321 | 0.8717(3) | 0.2126(3) | 0.7451(2) | 0.0348(10) |
| H321 | 0.8827 | 0.2642 | 0.7069 | 0.042 |
| C331 | 0.8807(3) | 0.0950(4) | 0.7352(2) | 0.0408(11) |
| H331 | 0.8961 | 0.0660 | 0.6896 | 0.049 |
| C341 | 0.8675(3) | 0.0199(3) | 0.7903(2) | 0.0380(10) |
| C351 | 0.8438(3) | 0.0605(4) | 0.8554(2) | 0.0398(11) |

| H351 | 0.8351 | 0.0085 | 0.8939 | 0.048 |
|------|-----------|-----------|-----------|------------|
| C361 | 0.8324(3) | 0.1770(3) | 0.8651(2) | 0.0383(10) |
| H361 | 0.8141 | 0.2042 | 0.9103 | 0.046 |
| CI12 | 0.4680(1) | 0.1254(1) | 0.5276(1) | 0.0831(5) |
| Cl22 | 0.8190(1) | 0.8667(1) | 0.5950(1) | 0.0687(4) |
| O102 | 0.6292(2) | 0.2681(3) | 0.4651(1) | 0.0526(8) |
| C102 | 0.6255(3) | 0.2984(3) | 0.5278(2) | 0.0346(10) |
| N112 | 0.6974(2) | 0.3070(3) | 0.5729(2) | 0.0310(8) |
| H112 | 0.687(3) | 0.330(3) | 0.619(2) | 0.049(13) |
| C112 | 0.5380(3) | 0.3343(3) | 0.5597(2) | 0.0328(10) |
| C122 | 0.4639(3) | 0.2634(4) | 0.5627(2) | 0.0449(11) |
| N132 | 0.3865(3) | 0.2898(4) | 0.5918(2) | 0.0605(11) |
| C142 | 0.3801(4) | 0.3962(5) | 0.6185(3) | 0.0616(14) |
| H142 | 0.3256 | 0.4171 | 0.6407 | 0.074 |
| C152 | 0.4465(4) | 0.4763(4) | 0.6157(2) | 0.0563(13) |
| H152 | 0.4373 | 0.5524 | 0.6328 | 0.068 |
| C162 | 0.5282(3) | 0.4446(4) | 0.5873(2) | 0.0468(12) |
| H162 | 0.5770 | 0.4979 | 0.5867 | 0.056 |
| C212 | 0.7864(3) | 0.2736(3) | 0.5540(2) | 0.0319(10) |
| C222 | 0.8560(3) | 0.3557(3) | 0.5569(2) | 0.0340(10) |
| C232 | 0.9426(3) | 0.3174(4) | 0.5403(2) | 0.0425(11) |
| H232 | 0.9917 | 0.3701 | 0.5430 | 0.051 |
| C242 | 0.9580(3) | 0.2058(4) | 0.5203(2) | 0.0496(12) |
| H242 | 1.0172 | 0.1824 | 0.5086 | 0.059 |
| C252 | 0.8882(3) | 0.1268(4) | 0.5170(2) | 0.0474(12) |
| H252 | 0.8990 | 0.0495 | 0.5025 | 0.057 |
| C262 | 0.8029(3) | 0.1608(4) | 0.5349(2) | 0.0384(10) |
| H262 | 0.7550 | 0.1063 | 0.5341 | 0.046 |
| C312 | 0.8417(3) | 0.4804(3) | 0.5720(2) | 0.0341(10) |
| C322 | 0.7757(3) | 0.5425(4) | 0.5345(2) | 0.0378(10) |
| H322 | 0.7349 | 0.5031 | 0.5028 | 0.045 |
| C332 | 0.7680(3) | 0.6615(4) | 0.5423(2) | 0.0416(11) |
| H332 | 0.7229 | 0.7033 | 0.5161 | 0.050 |
| C342 | 0.8263(3) | 0.7167(4) | 0.5884(2) | 0.0432(11) |
| C352 | 0.8912(3) | 0.6580(4) | 0.6277(2) | 0.0507(12) |
| H352 | 0.9304 | 0.6980 | 0.6603 | 0.061 |
| C362 | 0.8987(3) | 0.5406(4) | 0.6192(2) | 0.0469(12) |
| H362 | 0.9437 | 0.4998 | 0.6462 | 0.056 |
| | | | | |

Table S11. Bond lengths [Å] and angles $[\circ]$ for Boscalid (1).

| CI11-C121 | 1.747(4) |
|-----------|----------|
| Cl21-C341 | 1.742(4) |
| C101-O101 | 1.227(4) |
| C101-N111 | 1.343(5) |
| C101-C111 | 1.497(5) |
| N111-C211 | 1.432(5) |
| N111-H111 | 0.73(3) |
| C111-C161 | 1.381(5) |
| C111-C121 | 1.392(5) |
| C121-N131 | 1.311(5) |
| N131-C141 | 1.332(5) |
| C141-C151 | 1.370(6) |
| C141-H141 | 0.9500 |
| C151-C161 | 1.383(5) |
| C151-H151 | 0.9500 |
| C161-H161 | 0.9500 |
| C211-C261 | 1.379(5) |
| C211-C221 | 1.390(5) |
| C221-C231 | 1.392(5) |
| C221-C311 | 1.486(5) |
| C231-C241 | 1.381(6) |
| C231-H231 | 0.9500 |
| C241-C251 | 1.380(6) |
| C241-H241 | 0.9500 |
| C251-C261 | 1.373(5) |
| C251-H251 | 0.9500 |
| C261-H261 | 0.9500 |
| C311-C361 | 1.381(5) |
| C311-C321 | 1.393(5) |
| C321-C331 | 1.383(5) |
| C321-H321 | 0.9500 |
| C331-C341 | 1.367(5) |
| C331-H331 | 0.9500 |
| C341-C351 | 1.361(5) |
| C351-C361 | 1.373(5) |
| C351-H351 | 0.9500 |
| C361-H361 | 0.9500 |
| CI12-C122 | 1.731(4) |
| Cl22-C342 | 1.746(4) |
| O102-C102 | 1.227(4) |
| C102-N112 | 1.342(5) |
| C102-C112 | 1.501(5) |
| N112-C212 | 1.429(5) |
| N112-H112 | 0.92(4) |
| C112-C122 | 1.374(6) |
| C112-C162 | 1.388(5) |
| C122-N132 | 1.320(5) |
| | |

| N132-C142 | 1.335(6) |
|-------------------|----------|
| C142-C152 | 1.354(7) |
| C142-H142 | 0.9500 |
| C152-C162 | 1.386(6) |
| C152-H152 | 0.9500 |
| C162-H162 | 0.9500 |
| C212-C262 | 1.378(5) |
| C212-C222 | 1.402(5) |
| C222-C232 | 1.401(5) |
| C222-C312 | 1,490(5) |
| C232-C242 | 1.367(6) |
| C232-H232 | 0.9500 |
| C242-C252 | 1.381(6) |
| C242-H242 | 0.9500 |
| C252-C262 | 1 375(6) |
| C252-H252 | 0.9500 |
| C262-H262 | 0.3500 |
| $C_{202} - 11202$ | 0.9300 |
| C312-C322 | 1.300(3) |
| C312-C302 | 1.391(3) |
| 0322-0332 | 1.391(5) |
| C322-H322 | 0.9500 |
| 0332-0342 | 1.361(6) |
| C332-H332 | 0.9500 |
| 0342-0352 | 1.373(6) |
| C352-C362 | 1.375(6) |
| C352-H352 | 0.9500 |
| C362-H362 | 0.9500 |
| 0101 C101 N111 | 101 0/2) |
| | 121.0(3) |
| | 122.8(3) |
| N111-C101-C111 | 115.3(3) |
| C101-N111-C211 | 120.9(3) |
| C101-N111-H111 | 112(3) |
| C211-N111-H111 | 127(3) |
| C161-C111-C121 | 116.2(4) |
| C161-C111-C101 | 120.3(3) |
| C121-C111-C101 | 123.4(3) |
| N131-C121-C111 | 125.6(4) |
| N131-C121-Cl11 | 115.6(3) |
| C111-C121-Cl11 | 118.8(3) |
| C121-N131-C141 | 116.7(4) |
| N131-C141-C151 | 123.3(4) |
| N131-C141-H141 | 118.3 |
| C151-C141-H141 | 118.3 |
| C141-C151-C161 | 118.9(4) |
| C141-C151-H151 | 120.6 |
| C161-C151-H151 | 120.6 |
| C111-C161-C151 | 119.3(4) |
| C111-C161-H161 | 120.4 |
| | |

| C151-C161-H161 | 120.4 |
|----------------|----------|
| C261-C211-C221 | 121.4(4) |
| C261-C211-N111 | 118.9(3) |
| C221-C211-N111 | 119.7(3) |
| C211-C221-C231 | 117.7(4) |
| C211-C221-C311 | 120.7(3) |
| C231-C221-C311 | 121.4(3) |
| C241-C231-C221 | 120.8(4) |
| C241-C231-H231 | 119.6 |
| C221-C231-H231 | 119.6 |
| C251-C241-C231 | 120.2(4) |
| C251-C241-H241 | 119.9 |
| C231-C241-H241 | 119.9 |
| C261-C251-C241 | 119.8(4) |
| C261-C251-H251 | 120.1 |
| C241-C251-H251 | 120.1 |
| C251-C261-C211 | 119.9(4) |
| C251-C261-H261 | 120.1 |
| C211-C261-H261 | 120.1 |
| C361-C311-C321 | 117.5(4) |
| C361-C311-C221 | 119.2(3) |
| C321-C311-C221 | 123.4(3) |
| C331-C321-C311 | 120.2(4) |
| C331-C321-H321 | 119.9 |
| C311-C321-H321 | 119.9 |
| C341-C331-C321 | 120.6(4) |
| C341-C331-H331 | 119.7 |
| C321-C331-H331 | 119.7 |
| C351-C341-C331 | 120.1(4) |
| C351-C341-Cl21 | 118.0(3) |
| C331-C341-Cl21 | 121.8(3) |
| C341-C351-C361 | 119.6(4) |
| C341-C351-H351 | 120.2 |
| C361-C351-H351 | 120.2 |
| C351-C361-C311 | 122.1(4) |
| C351-C361-H361 | 119.0 |
| C311-C361-H361 | 119.0 |
| O102-C102-N112 | 124.3(4) |
| O102-C102-C112 | 121.5(4) |
| N112-C102-C112 | 114.1(3) |
| C102-N112-C212 | 123.1(3) |
| C102-N112-H112 | 117(2) |
| C212-N112-H112 | 119(2) |
| C122-C112-C162 | 116.3(4) |
| C122-C112-C102 | 123.5(4) |
| C162-C112-C102 | 120.3(4) |
| N132-C122-C112 | 125.7(4) |
| N132-C122-Cl12 | 114.3(4) |
| C112-C122-Cl12 | 120.0(3) |
| | · / |

| C122-N132-C142 | 116.1(4) |
|----------------|----------|
| N132-C142-C152 | 123.9(4) |
| N132-C142-H142 | 118.0 |
| C152-C142-H142 | 118.0 |
| C142-C152-C162 | 118.5(5) |
| C142-C152-H152 | 120.7 |
| C162-C152-H152 | 120.7 |
| C152-C162-C112 | 119.2(4) |
| C152-C162-H162 | 120.4 |
| C112-C162-H162 | 120.4 |
| C262-C212-C222 | 121.2(4) |
| C262-C212-N112 | 119.5(4) |
| C222-C212-N112 | 119.3(3) |
| C232-C222-C212 | 117.0(4) |
| C232-C222-C312 | 119.1(4) |
| C212-C222-C312 | 123.8(4) |
| C242-C232-C222 | 121.4(4) |
| C242-C232-H232 | 119.3 |
| C222-C232-H232 | 119.3 |
| C232-C242-C252 | 120.6(4) |
| C232-C242-H242 | 119.7 |
| C252-C242-H242 | 119.7 |
| C262-C252-C242 | 119.4(4) |
| C262-C252-H252 | 120.3 |
| C242-C252-H252 | 120.3 |
| C252-C262-C212 | 120.4(4) |
| C252-C262-H262 | 119.8 |
| C212-C262-H262 | 119.8 |
| C322-C312-C362 | 117.7(4) |
| C322-C312-C222 | 120.7(4) |
| C362-C312-C222 | 121.3(4) |
| C312-C322-C332 | 121.3(4) |
| C312-C322-H322 | 119.4 |
| C332-C322-H322 | 119.4 |
| C342-C332-C322 | 118.7(4) |
| C342-C332-H332 | 120.6 |
| C322-C332-H332 | 120.6 |
| C332-C342-C352 | 121.8(4) |
| C332-C342-Cl22 | 118.2(4) |
| C352-C342-Cl22 | 120.0(4) |
| C342-C352-C362 | 119.1(4) |
| C342-C352-H352 | 120.5 |
| C362-C352-H352 | 120.5 |
| C352-C362-C312 | 121.4(4) |
| C352-C362-H362 | 119.3 |
| C312-C362-H362 | 119.3 |
| | |

Symmetry transformations used to generate equivalent atoms.

| | U11 | U22 | U33 | U23 | U13 | U ¹² |
|------|------------|------------|------------|-------------|-------------|-----------------|
| CI11 | 0.0554(7) | 0.0387(7) | 0.0679(8) | -0.0163(6) | 0.0241(6) | -0.0063(5) |
| Cl21 | 0.0854(10) | 0.0346(7) | 0.0646(8) | -0.0014(6) | 0.0193(7) | 0.0066(6) |
| C101 | 0.027(2) | 0.023(2) | 0.026(2) | -0.0017(17) | 0.0002(18) | 0.0039(17) |
| O101 | 0.0400(16) | 0.0377(16) | 0.0185(14) | 0.0003(12) | 0.0049(12) | -0.0074(13) |
| N111 | 0.0262(19) | 0.032(2) | 0.0239(19) | 0.0040(16) | 0.0050(16) | -0.0056(15) |
| C111 | 0.027(2) | 0.032(2) | 0.026(2) | 0.0039(17) | 0.0004(17) | 0.0029(17) |
| C121 | 0.037(3) | 0.031(2) | 0.031(2) | 0.0006(18) | 0.0022(19) | 0.0002(19) |
| N131 | 0.040(2) | 0.042(2) | 0.045(2) | -0.0046(17) | 0.0025(18) | -0.0134(18) |
| C141 | 0.034(3) | 0.048(3) | 0.057(3) | 0.005(2) | -0.005(2) | -0.013(2) |
| C151 | 0.029(3) | 0.053(3) | 0.057(3) | 0.003(2) | 0.009(2) | -0.002(2) |
| C161 | 0.037(3) | 0.030(2) | 0.050(3) | -0.004(2) | 0.005(2) | -0.002(2) |
| C211 | 0.035(2) | 0.032(2) | 0.019(2) | 0.0007(17) | -0.0024(17) | -0.0001(18) |
| C221 | 0.029(2) | 0.033(2) | 0.021(2) | -0.0005(17) | -0.0001(17) | 0.0003(18) |
| C231 | 0.030(2) | 0.043(3) | 0.045(3) | -0.006(2) | 0.004(2) | -0.004(2) |
| C241 | 0.046(3) | 0.038(3) | 0.055(3) | -0.004(2) | -0.001(2) | -0.013(2) |
| C251 | 0.054(3) | 0.030(3) | 0.047(3) | -0.008(2) | 0.000(2) | -0.004(2) |
| C261 | 0.034(2) | 0.036(3) | 0.034(2) | -0.0002(19) | 0.0010(19) | 0.005(2) |
| C311 | 0.022(2) | 0.034(2) | 0.029(2) | -0.0019(18) | 0.0003(17) | -0.0023(17) |
| C321 | 0.040(2) | 0.034(3) | 0.031(2) | 0.0020(19) | 0.0078(19) | 0.0052(19) |
| C331 | 0.046(3) | 0.043(3) | 0.034(2) | -0.010(2) | 0.009(2) | 0.010(2) |
| C341 | 0.039(2) | 0.029(2) | 0.046(3) | 0.000(2) | 0.006(2) | 0.0036(19) |
| C351 | 0.044(3) | 0.042(3) | 0.034(2) | 0.005(2) | 0.005(2) | 0.000(2) |
| C361 | 0.048(3) | 0.038(3) | 0.029(2) | -0.0043(19) | 0.007(2) | 0.001(2) |
| CI12 | 0.0756(10) | 0.0573(9) | 0.1179(13) |)-0.0312(8) | 0.0274(9) | -0.0194(7) |

Table S12. Anisotropic displacement parameters ($Å^2x \ 10^3$) for **Boscalid** (1). The anisotropic displacement factor exponent takes the form: $-2p^2[h^2a^{*2}U^{11} + ... + 2hka^*b^*U^{12}]$

| Cl22 | 0.0883(10) | 0.0413(8) | 0.0766(9) | -0.0040(6) | 0.0035(8) | -0.0095(7) |
|------|------------|-----------|------------|--------------|-------------|-------------|
| O102 | 0.055(2) | 0.080(2) | 0.0225(17) |)-0.0159(15) | 0.0023(14) | 0.0094(17) |
| C102 | 0.042(3) | 0.031(2) | 0.032(2) | -0.0028(18) | 0.005(2) | -0.0022(19) |
| N112 | 0.035(2) | 0.039(2) | 0.0195(18 |)-0.0030(15) | 0.0043(16) | -0.0045(16) |
| C112 | 0.042(3) | 0.038(3) | 0.018(2) | -0.0039(18) | 0.0007(18) | 0.006(2) |
| C122 | 0.042(3) | 0.047(3) | 0.046(3) | -0.006(2) | 0.004(2) | 0.002(2) |
| N132 | 0.037(2) | 0.080(3) | 0.065(3) | -0.008(2) | 0.002(2) | 0.002(2) |
| C142 | 0.050(3) | 0.089(4) | 0.046(3) | -0.010(3) | 0.001(2) | 0.030(3) |
| C152 | 0.067(4) | 0.058(3) | 0.043(3) | -0.018(2) | -0.006(3) | 0.024(3) |
| C162 | 0.060(3) | 0.048(3) | 0.032(2) | -0.007(2) | 0.001(2) | 0.003(2) |
| C212 | 0.042(3) | 0.037(3) | 0.017(2) | 0.0029(17) | 0.0025(18) | 0.005(2) |
| C222 | 0.039(3) | 0.039(3) | 0.024(2) | 0.0048(18) | -0.0011(18) | 0.003(2) |
| C232 | 0.038(3) | 0.051(3) | 0.039(3) | 0.004(2) | -0.001(2) | 0.003(2) |
| C242 | 0.045(3) | 0.053(3) | 0.051(3) | 0.012(2) | 0.008(2) | 0.020(3) |
| C252 | 0.061(3) | 0.040(3) | 0.041(3) | 0.005(2) | 0.010(2) | 0.016(2) |
| C262 | 0.051(3) | 0.037(3) | 0.027(2) | 0.0055(19) | 0.007(2) | 0.001(2) |
| C312 | 0.033(2) | 0.040(3) | 0.029(2) | 0.0012(19) | 0.0038(19) | -0.004(2) |
| C322 | 0.043(3) | 0.040(3) | 0.031(2) | 0.0008(19) | -0.001(2) | -0.005(2) |
| C332 | 0.049(3) | 0.038(3) | 0.038(3) | 0.004(2) | -0.001(2) | 0.003(2) |
| C342 | 0.049(3) | 0.038(3) | 0.043(3) | -0.004(2) | 0.006(2) | -0.002(2) |
| C352 | 0.051(3) | 0.049(3) | 0.051(3) | -0.007(2) | -0.013(2) | -0.012(2) |
| C362 | 0.044(3) | 0.049(3) | 0.046(3) | 0.000(2) | -0.005(2) | -0.003(2) |
| | | | | | | |
8.2 Fluxapyroxad (2)



Figure S12. Crystallographic structure of product Fluxapyroxad (2) (CCDC: 2086182).

 Table S13. Crystal data and structure refinement for Fluxapyroxad (2).

| Identification code (CCDC) | 2086182 | |
|---------------------------------|---|----------------------------|
| Empirical formula | $C_{18}H_{12}F_5N_3O$ | |
| Formula weight | 381.31 | |
| Temperature | 200(2) K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Orthorhombic | |
| Space group | Pbca | |
| Z | 8 | |
| Unit cell dimensions | a = 12.8826(6) Å | α = 90 deg. |
| | b =9.2515(5) Å | β = 90 deg. |
| | c = 28.4963(12) Å | $\gamma = 90 \text{ deg.}$ |
| Volume | 3396.3(3) Å ³ | |
| Density (calculated) | 1.49 g/cm ³ | |
| Absorption coefficient | 1.16 mm ⁻¹ | |
| Crystal shape | needle | |
| Crystal size | 0.110 x 0.055 x 0.02 | 24 mm ³ |
| Crystal colour | colourless | |
| Theta range for data collection | 6.1 to 66.7 deg. | |
| Index ranges | -15 \leq h \leq 7, -9 \leq k \leq | 10, -33 \leq I \leq 32 |
| Reflections collected | 10749 | |
| Independent reflections | 2929 (R(int) = 0.052 | 29) |
| Observed reflections | 1728 (I > 2\s(I)) | |

| Absorption correction | Semi-empirical from equivalents |
|--|---|
| Max. and min. transmission | 0.98 and 0.44 |
| Refinement method | Full-matrix least-squares on F ² |
| Data/restraints/parameters | 2929 / 0 / 288 |
| Goodness-of-fit on F ² | 1.02 |
| Final R indices (I>2σ(I)) | R1 = 0.051, wR2 = 0.100 |
| Largest diff. peak and hole | 0.26 and -0.18 eÅ ⁻³ |
| Refinement method Data/restraints/parameters Goodness-of-fit on F^2 Final R indices (I>2 σ (I)) Largest diff. peak and hole | Full-matrix least-squares on F ² 2929 / 0 / 288 1.02 R1 = 0.051, wR2 = 0.100 0.26 and -0.18 eÅ ⁻³ |

Table S14. Atomic coordinates ($x \ 10^4$) and equivalent isotropic displacement parameters (Å²x 10³) for **Fluxapyroxad** (2). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

| atom | х | у | Z | U(eq) |
|------|------------|------------|------------|-----------|
| C1 | 0.1933(2) | 0.7062(3) | 0.6124(1) | 0.0368(7) |
| C2 | 0.2591(2) | 0.6701(3) | 0.5752(1) | 0.0406(7) |
| C3 | 0.2140(3) | 0.6283(4) | 0.5325(1) | 0.0511(8) |
| H3 | 0.256(3) | 0.606(4) | 0.5032(12) | 0.077 |
| C4 | 0.1069(3) | 0.6271(4) | 0.5271(1) | 0.0531(9) |
| H4 | 0.079(3) | 0.599(4) | 0.4956(13) | 0.080 |
| C5 | 0.0436(3) | 0.6651(4) | 0.5638(1) | 0.0499(8) |
| H5 | -0.032(3) | 0.673(4) | 0.5598(12) | 0.075 |
| C6 | 0.0865(2) | 0.7040(3) | 0.6067(1) | 0.0446(8) |
| H6 | 0.042(3) | 0.730(4) | 0.6330(12) | 0.067 |
| N7 | 0.2331(2) | 0.7495(3) | 0.6569(1) | 0.0393(6) |
| H7 | 0.216(2) | 0.830(4) | 0.6654(11) | 0.059 |
| O8 | 0.3223(2) | 0.5443(2) | 0.6734(1) | 0.0423(5) |
| C8 | 0.2919(2) | 0.6658(3) | 0.6847(1) | 0.0349(6) |
| C9 | 0.3205(2) | 0.7292(3) | 0.7305(1) | 0.0337(6) |
| C10 | 0.4043(2) | 0.6902(3) | 0.7596(1) | 0.0393(7) |
| N11 | 0.4068(2) | 0.7676(3) | 0.7990(1) | 0.0456(6) |
| N12 | 0.3234(2) | 0.8553(3) | 0.7956(1) | 0.0420(6) |
| C13 | 0.2708(2) | 0.8355(3) | 0.7554(1) | 0.0403(7) |
| H13 | 0.210(2) | 0.891(3) | 0.7488(10) | 0.060 |
| C14 | 0.4861(2) | 0.5806(4) | 0.7504(1) | 0.0587(9) |
| H14 | 0.4805 | 0.5414 | 0.7178 | 0.070 |
| F15A | 0.4742(7) | 0.4704(6) | 0.7838(3) | 0.091(3) |
| F16A | 0.5790(3) | 0.6331(7) | 0.7583(4) | 0.086(3) |
| F15B | 0.5435(17) | 0.544(2) | 0.7847(5) | 0.125(10) |
| F16B | 0.5640(9) | 0.6646(12) | 0.7197(10) | 0.125(7) |
| C17 | 0.3009(3) | 0.9578(4) | 0.8329(1) | 0.0609(9) |
| H17A | 0.3569 | 1.0293 | 0.8348 | 0.091 |
| H17B | 0.2955 | 0.9062 | 0.8629 | 0.091 |
| H17C | 0.2352 | 1.0070 | 0.8263 | 0.091 |
| C21 | 0.3744(2) | 0.6773(3) | 0.5789(1) | 0.0428(7) |
| C22 | 0.4337(3) | 0.5613(4) | 0.5631(1) | 0.0493(8) |
| H22 | 0.402(3) | 0.468(4) | 0.5518(12) | 0.074 |

| F23 | 0.5996(2) | 0.4574(2) | 0.5513(1) | 0.0785(6) | |
|-----|-----------|-----------|------------|-----------|--|
| C23 | 0.5402(3) | 0.5699(4) | 0.5656(1) | 0.0548(9) | |
| F24 | 0.6941(1) | 0.6948(2) | 0.5849(1) | 0.0829(7) | |
| C24 | 0.5890(2) | 0.6887(4) | 0.5831(1) | 0.0582(9) | |
| F25 | 0.5800(2) | 0.9199(2) | 0.6152(1) | 0.0891(8) | |
| C25 | 0.5300(3) | 0.8023(4) | 0.5985(1) | 0.0572(9) | |
| C26 | 0.4240(2) | 0.7989(4) | 0.5968(1) | 0.0507(8) | |
| H26 | 0.387(3) | 0.881(4) | 0.6071(12) | 0.076 | |
| | | | | | |

| C1-C6 | 1.386(4) |
|----------|-----------|
| C1-C2 | 1.398(4) |
| C1-N7 | 1.426(3) |
| C2-C3 | 1.402(4) |
| C2-C21 | 1.490(4) |
| C3-C4 | 1.388(4) |
| C3-H3 | 1.02(3) |
| C4-C5 | 1.371(5) |
| C4-H4 | 1.00(4) |
| C5-C6 | 1.390(4) |
| C5-H5 | 0.98(3) |
| C6-H6 | 0.98(3) |
| N7-C8 | 1.342(4) |
| N7-H7 | 0.82(3) |
| O8-C8 | 1.233(3) |
| C8-C9 | 1.477(4) |
| C9-C13 | 1.372(4) |
| C9-C10 | 1.408(4) |
| C10-N11 | 1.332(4) |
| C10-C14 | 1.486(4) |
| N11-N12 | 1.350(3) |
| N12-C13 | 1.342(3) |
| N12-C17 | 1.455(4) |
| C13-H13 | 0.96(3) |
| C14-F15B | 1.271(9) |
| C14-F16A | 1.311(5) |
| C14-F15A | 1.403(5) |
| C14-F16B | 1.542(15) |
| C14-H14 | 1.0000 |
| C17-H17A | 0.9800 |
| C17-H17B | 0.9800 |
| C17-H17C | 0.9800 |
| C21-C26 | 1.390(4) |
| C21-C22 | 1.394(4) |
| C22-C23 | 1.376(5) |
| C22-H22 | 1.01(4) |
| F23-C23 | 1.355(4) |
| C23-C24 | 1.361(5) |
| F24-C24 | 1.355(4) |
| C24-C25 | 1.369(5) |
| F25-C25 | 1.351(4) |
| C25-C26 | 1.367(4) |
| C26-H26 | 0.94(4) |
| C6-C1-C2 | 120.7(3) |
| C6-C1-N7 | 117.7(3) |
| C2-C1-N7 | 121.6(3) |

 Table S15. Bond lengths [Å] and angles [°] for Fluxapyroxad (2).

| C1-C2-C3 | 118.2(3) |
|---------------|----------------------|
| C1-C2-C21 | 122.7(3) |
| C3-C2-C21 | 119.2(3) |
| C4-C3-C2 | 120.7(3) |
| C4-C3-H3 | 116(2) |
| C2-C3-H3 | 123(2) |
| C5-C4-C3 | 120.3(3) |
| C5-C4-H4 | 123(2) |
| C3-C4-H4 | 117(2) |
| C4-C5-C6 | 120 0(3) |
| | 120.0(3) |
| | 149(2) |
| | 110(2) |
| | 120.1(3) |
| C1-C6-H6 | 120(2) |
| C5-C6-H6 | 120(2) |
| C8-N7-C1 | 124.5(2) |
| C8-N7-H7 | 121(2) |
| C1-N7-H7 | 115(2) |
| 08-C8-N7 | 123.4(3) |
| O8-C8-C9 | 120.9(2) |
| N7-C8-C9 | 115.6(2) |
| C13-C9-C10 | 103.7(2) |
| C13-C9-C8 | 128.7(3) |
| C10-C9-C8 | 127.6(2) |
| N11-C10-C9 | 112.2(2) |
| N11-C10-C14 | 119.8(3) |
| C9-C10-C14 | 128.0(3) |
| C10-N11-N12 | 104.0(2) |
| C13-N12-N11 | 112.5(2) |
| C13-N12-C17 | 127.7(3) |
| N11-N12-C17 | 119.8(2) |
| N12-C13-C9 | 107.6(2) |
| N12-C13-H13 | 120.7(19) |
| C9-C13-H13 | 131 7(19) |
| F16A-C14-F15A | 104 7(4) |
| F15B-C14-C10 | 117 3(5) |
| F16A-C14-C10 | 111 A(3) |
| F15A-C14-C10 | 107 A(3) |
| E15B_C14-E16B | 107.4(3) 101.1(0) |
| | 107.6(5) |
| | 102.0(3) |
| | 111.1 |
| | 111.1 |
| C10-C14-H14 | 111.1 |
| N12-017-H17A | 109.5 |
| N12-UT/-H1/B | 109.5 |
| H1/A-C1/-H1/B | 109.5 |
| N12-C1/-H17C | 109.5 |
| H17A-C17-H17C | 109.5 |
| H17B-C17-H17C | 109.5 |

| C26-C21-C22 | 119.4(3) |
|-------------|-----------|
| C26-C21-C2 | 121.4(3) |
| C22-C21-C2 | 119.3(3) |
| C23-C22-C21 | 119.0(3) |
| C23-C22-H22 | 118.4(19) |
| C21-C22-H22 | 122(2) |
| F23-C23-C24 | 118.0(3) |
| F23-C23-C22 | 120.2(3) |
| C24-C23-C22 | 121.8(3) |
| F24-C24-C23 | 120.6(4) |
| F24-C24-C25 | 120.7(4) |
| C23-C24-C25 | 118.7(3) |
| F25-C25-C26 | 120.5(3) |
| F25-C25-C24 | 117.8(3) |
| C26-C25-C24 | 121.7(3) |
| C25-C26-C21 | 119.4(3) |
| C25-C26-H26 | 118(2) |
| C21-C26-H26 | 122(2) |
| | |

Symmetry transformations used to generate equivalent atoms.

| | U11 | U22 | U33 | U23 | U13 | U12 |
|------|------------|------------|------------|-------------|--------------|------------|
| C1 | 0.0479(17) | 0.0263(15) | 0.0363(15) | -0.0021(12 |)-0.0034(13) | -0.0014(13 |
| C2 | 0.0477(17) | 0.0371(18) | 0.0369(16) | 0.0022(14) |) 0.0002(14) | -0.0015(14 |
| C3 | 0.063(2) | 0.054(2) | 0.0356(17) | 0.0007(16) |) 0.0012(16) | -0.0039(18 |
| C4 | 0.066(2) | 0.053(2) | 0.0406(19) | 0.0025(16) |)-0.0106(17) | -0.0088(18 |
| C5 | 0.0512(18) | 0.047(2) | 0.051(2) | 0.0042(16) |)-0.0078(16) | -0.0047(17 |
| C6 | 0.0489(19) | 0.0380(18) | 0.0468(18) | 0.0008(14) |)-0.0029(15) | 0.0005(15) |
| N7 | 0.0499(15) | 0.0317(14) | 0.0364(13) | -0.0065(12) |)-0.0048(11) | 0.0047(12) |
| O8 | 0.0563(12) | 0.0268(11) | 0.0437(11) | -0.0030(9) | 0.0012(10) | 0.0029(10) |
| C8 | 0.0381(15) | 0.0287(16) | 0.0381(15) | 0.0002(13) |) 0.0037(12) | -0.0032(14 |
| C9 | 0.0352(15) | 0.0284(15) | 0.0376(15) | -0.0009(12) |) 0.0000(12) | -0.0021(13 |
| C10 | 0.0351(15) | 0.0371(17) | 0.0458(17) | -0.0039(14 |)-0.0006(13) | -0.0009(14 |
| N11 | 0.0392(14) | 0.0473(16) | 0.0503(15) | -0.0058(12) |)-0.0062(11) | 0.0015(13) |
| N12 | 0.0427(14) | 0.0447(16) | 0.0385(13) | -0.0095(12) |)-0.0021(11) | 0.0009(12) |
| C13 | 0.0409(17) | 0.0394(18) | 0.0404(17) | -0.0066(14 |)-0.0044(13) | 0.0013(14) |
| C14 | 0.046(2) | 0.060(2) | 0.070(2) | -0.010(2) | -0.0087(19) | 0.0121(18) |
| F15A | 0.089(4) | 0.060(3) | 0.123(4) | 0.024(3) | 0.008(3) | 0.027(3) |
| F16A | 0.0301(19) | 0.077(4) | 0.151(8) | -0.028(4) | -0.012(3) | 0.005(2) |
| F15B | 0.132(19) | 0.132(16) | 0.111(9) | -0.047(8) | -0.068(10) | 0.084(16) |
| F16B | 0.056(6) | 0.119(8) | 0.200(19) | -0.007(9) | 0.047(8) | 0.004(5) |
| C17 | 0.060(2) | 0.072(2) | 0.0506(19) | -0.0261(18) |)-0.0038(16) | 0.0038(19) |

Table S16. Anisotropic displacement parameters (Å 2x 10 $^3)$ for Fluxapyroxad (2). The anisotropic

| displacement factor exponent takes the form: | -2p ² [h ² a* ² U ¹¹ + + | - 2 h k a* b* U ¹²] |
|--|---|---------------------------------|
|--|---|---------------------------------|

| C21 | 0.0496(18) | 0.0430(19) | 0.0358(16) | 0.0073(14) 0.002 | 3(13) | -0.0004(16) |
|-----|------------|------------|------------|-------------------|-------|-------------|
| C22 | 0.057(2) | 0.053(2) | 0.0376(18) | 0.0042(15) 0.003 | 8(15) | 0.0083(18) |
| F23 | 0.0726(13) | 0.0944(17) | 0.0686(13) | -0.0043(12) 0.014 | 2(10) | 0.0291(13) |
| C23 | 0.060(2) | 0.064(3) | 0.0398(18) | 0.0110(17) 0.009 | 4(16) | 0.018(2) |
| F24 | 0.0477(11) | 0.1076(19) | 0.0934(15) | 0.0319(13) 0.002 | 8(10) | 0.0035(12) |
| C24 | 0.045(2) | 0.069(3) | 0.060(2) | 0.0259(19) 0.001 | 9(17) | 0.001(2) |
| F25 | 0.0607(13) | 0.0643(14) | 0.142(2) | 0.0105(14)-0.022 | 5(13) | -0.0155(11) |
| C25 | 0.051(2) | 0.050(2) | 0.070(2) | 0.0129(18)-0.006 | 2(17) | -0.0090(19) |
| C26 | 0.047(2) | 0.048(2) | 0.057(2) | 0.0093(17)-0.002 | 1(15) | -0.0019(17) |

8.2 Bixafen (3)



Figure S13. Crystallographic structure of product Bixafen (3) (CCDC: 2086183).

Table S17. Crystal data and structure refinement for Bixafen (3).

| Identification code (CCDC) | 2086183 | |
|---------------------------------|-------------------------------|-------------------------------------|
| Empirical formula | $C_{18}H_{12}CI_2F_3N_3O$ | |
| Formula weight | 414.21 | |
| Temperature | 200(2) K | |
| Wavelength | 0.71073 Å | |
| Crystal system | monoclinic | |
| Space group | P21/c | |
| Z | 4 | |
| Unit cell dimensions | a = 11.8929(7) Å | α = 90 deg. |
| | b = 18.0476(11) Å | $\beta = 110.0924(15) \text{ deg.}$ |
| | c = 8.6239(5) Å | $\gamma = 90 \text{ deg.}$ |
| Volume | 1738.37(18) Å ³ | |
| Density (calculated) | 1.58 g/cm ³ | |
| Absorption coefficient | 0.42 mm ⁻¹ | |
| Crystal shape | plank | |
| Crystal size | 0.143 x 0.070 x 0.0 | 21 mm³ |
| Crystal colour | colourless | |
| Theta range for data collection | 1.8 to 26.4 deg. | |
| Index ranges | $-14 \le h \le 14, -22 \le 1$ | k ≤ 22, -10 ≤ l ≤ 10 |

| Reflections collected | 17929 |
|-----------------------------------|---|
| Independent reflections | 3545 (R(int) = 0.0695) |
| Observed reflections | 2247 (l > 2σ(l)) |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.96 and 0.93 |
| Refinement method | Full-matrix least-squares on F ² |
| Data/restraints/parameters | 3545 / 0 / 248 |
| Goodness-of-fit on F ² | 1.02 |
| Final R indices (I>2sigma(I)) | R1 = 0.052, wR2 = 0.104 |
| Largest diff. peak and hole | 0.30 and -0.33 eÅ ⁻³ |

Table S18. Atomic coordinates ($x \ 10^4$) and equivalent isotropic displacement parameters (Å²x 10³) for **Bixafen** (3). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

| atom | Х | У | Z | U(eq) |
|------|-----------|------------|-----------|------------|
| C1 | 0.5690(3) | 0.5680(2) | 0.7531(4) | 0.0237(7) |
| O1 | 0.4683(2) | 0.5519(1) | 0.7495(3) | 0.0339(6) |
| N1 | 0.5901(2) | 0.6210(1) | 0.6543(3) | 0.0268(6) |
| H1 | 0.655(3) | 0.6348(19) | 0.676(4) | 0.040 |
| C2 | 0.6734(3) | 0.5289(2) | 0.8670(4) | 0.0223(7) |
| C3 | 0.7939(3) | 0.5206(2) | 0.8781(4) | 0.0247(7) |
| N4 | 0.8539(2) | 0.4757(1) | 1.0009(3) | 0.0310(6) |
| N5 | 0.7734(2) | 0.4555(1) | 1.0708(3) | 0.0297(6) |
| C6 | 0.6658(3) | 0.4851(2) | 0.9949(4) | 0.0266(7) |
| H6 | 0.5963 | 0.4776 | 1.0235 | 0.032 |
| C7 | 0.8600(3) | 0.5468(2) | 0.7704(4) | 0.0380(9) |
| H7 | 0.9452 | 0.5299 | 0.8155 | 0.046 |
| F8 | 0.8068(2) | 0.5210(1) | 0.6135(3) | 0.0569(6) |
| F9 | 0.8554(2) | 0.6219(1) | 0.7569(3) | 0.0598(7) |
| C10 | 0.8091(3) | 0.4050(2) | 1.2113(5) | 0.0492(10) |
| H10A | 0.7443 | 0.4010 | 1.2567 | 0.074 |
| H10B | 0.8813 | 0.4241 | 1.2964 | 0.074 |
| H10C | 0.8259 | 0.3560 | 1.1753 | 0.074 |
| C11 | 0.5011(3) | 0.6581(2) | 0.5234(4) | 0.0245(7) |
| C12 | 0.5172(3) | 0.7323(2) | 0.4866(4) | 0.0230(7) |
| C13 | 0.4287(3) | 0.7659(2) | 0.3542(4) | 0.0267(7) |
| H13 | 0.4374 | 0.8160 | 0.3264 | 0.032 |
| C14 | 0.3291(3) | 0.7262(2) | 0.2643(4) | 0.0285(7) |
| C15 | 0.3115(3) | 0.6544(2) | 0.3004(4) | 0.0300(8) |
| H15 | 0.2409 | 0.6286 | 0.2376 | 0.036 |
| C16 | 0.3985(3) | 0.6201(2) | 0.4303(4) | 0.0281(7) |
| H16 | 0.3879 | 0.5700 | 0.4562 | 0.034 |
| F18 | 0.2457(2) | 0.7598(1) | 0.1340(2) | 0.0417(5) |
| C21 | 0.6257(3) | 0.7765(2) | 0.5807(4) | 0.0245(7) |
| C22 | 0.7370(3) | 0.7592(2) | 0.5726(4) | 0.0328(8) |

| H22 | 0.7448 | 0.7182 | 0.5080 | 0.039 |
|-----|-----------|-----------|-----------|-----------|
| C23 | 0.8370(3) | 0.8009(2) | 0.6573(4) | 0.0354(8) |
| C24 | 0.8264(3) | 0.8609(2) | 0.7524(4) | 0.0336(8) |
| C25 | 0.7156(3) | 0.8801(2) | 0.7584(4) | 0.0345(8) |
| H25 | 0.7079 | 0.9219 | 0.8209 | 0.041 |
| C26 | 0.6153(3) | 0.8381(2) | 0.6725(4) | 0.0291(7) |
| H26 | 0.5391 | 0.8515 | 0.6765 | 0.035 |
| Cl1 | 0.9734(1) | 0.7769(1) | 0.6414(2) | 0.0614(3) |
| Cl2 | 0.9514(1) | 0.9121(1) | 0.8619(1) | 0.0544(3) |
| | | | | |

 Table S19.
 Bond lengths [Å] and angles [°] for Bixafen (3).

| C1-O1 | 1.222(3) |
|----------|----------|
| C1-N1 | 1.361(4) |
| C1-C2 | 1.471(4) |
| N1-C11 | 1.421(4) |
| N1-H1 | 0.77(3) |
| C2-C6 | 1.385(4) |
| C2-C3 | 1.411(4) |
| C3-N4 | 1.330(4) |
| C3-C7 | 1.485(4) |
| N4-N5 | 1.346(3) |
| N5-C6 | 1.333(4) |
| N5-C10 | 1.458(4) |
| C6-H6 | 0.9500 |
| C7-F9 | 1.359(4) |
| C7-F8 | 1.364(4) |
| C7-H7 | 1.0000 |
| C10-H10A | 0.9800 |
| C10-H10B | 0.9800 |
| C10-H10C | 0.9800 |
| C11-C16 | 1.389(4) |
| C11-C12 | 1.406(4) |
| C12-C13 | 1.398(4) |
| C12-C21 | 1.497(4) |
| C13-C14 | 1.373(4) |
| C13-H13 | 0.9500 |
| C14-F18 | 1.359(3) |
| C14-C15 | 1.366(4) |
| C15-C16 | 1.382(4) |
| C15-H15 | 0.9500 |
| C16-H16 | 0.9500 |
| C21-C22 | 1.385(4) |
| C21-C26 | 1.394(4) |
| C22-C23 | 1.385(4) |
| C22-H22 | 0.9500 |

| C23-C24 | 1.390(5) |
|---------------|----------|
| C23-Cl1 | 1.729(3) |
| C24-C25 | 1.381(5) |
| C24-Cl2 | 1.729(3) |
| C25-C26 | 1.394(4) |
| C25-H25 | 0.9500 |
| C26-H26 | 0.9500 |
| 01-C1-N1 | 122.7(3) |
| 01-C1-C2 | 119 9(3) |
| N1-C1-C2 | 117 4(3) |
| C1-N1-C11 | 125 5(3) |
| C1-N1-H1 | 117(3) |
| | 117(3) |
| | 102 1(2) |
| 00-02-03 | 103.1(3) |
| | 122.3(3) |
| 03-02-01 | 134.5(3) |
| N4-C3-C2 | 112.0(3) |
| N4-C3-C7 | 115.9(3) |
| C2-C3-C7 | 131.9(3) |
| C3-N4-N5 | 104.6(2) |
| C6-N5-N4 | 112.5(2) |
| C6-N5-C10 | 128.0(3) |
| N4-N5-C10 | 119.5(3) |
| N5-C6-C2 | 107.8(3) |
| N5-C6-H6 | 126.1 |
| C2-C6-H6 | 126.1 |
| F9-C7-F8 | 105.3(3) |
| F9-C7-C3 | 110.9(3) |
| F8-C7-C3 | 110.3(3) |
| F9-C7-H7 | 110.1 |
| F8-C7-H7 | 110.1 |
| C3-C7-H7 | 110.1 |
| N5-C10-H10A | 109.5 |
| N5-C10-H10B | 109.5 |
| H10A-C10-H10B | 109.5 |
| N5-C10-H10C | 109.5 |
| H10A-C10-H10C | 109.5 |
| H10B-C10-H10C | 100.0 |
| C16-C11-C12 | 120.0(3) |
| C16-C11-N1 | 120.0(3) |
| C12 C11 N1 | 120 4(2) |
| C12-C11-IN1 | 120.4(3) |
| | 110.4(3) |
| | 118.6(3) |
| | 1∠3.U(3) |
| 014-013-012 | 119.8(3) |
| 014-013-H13 | 120.1 |
| C12-C13-H13 | 120.1 |
| F18-C14-C15 | 119.0(3) |
| F18-C14-C13 | 118.5(3) |

| C15-C14-C13 | 122.4(3) |
|-------------|----------|
| C14-C15-C16 | 118.6(3) |
| C14-C15-H15 | 120.7 |
| C16-C15-H15 | 120.7 |
| C15-C16-C11 | 120.8(3) |
| C15-C16-H16 | 119.6 |
| C11-C16-H16 | 119.6 |
| C22-C21-C26 | 118.7(3) |
| C22-C21-C12 | 120.9(3) |
| C26-C21-C12 | 120.3(3) |
| C23-C22-C21 | 121.0(3) |
| C23-C22-H22 | 119.5 |
| C21-C22-H22 | 119.5 |
| C22-C23-C24 | 119.9(3) |
| C22-C23-Cl1 | 118.8(3) |
| C24-C23-Cl1 | 121.3(3) |
| C25-C24-C23 | 120.0(3) |
| C25-C24-Cl2 | 119.8(3) |
| C23-C24-Cl2 | 120.3(3) |
| C24-C25-C26 | 119.8(3) |
| C24-C25-H25 | 120.1 |
| C26-C25-H25 | 120.1 |
| C21-C26-C25 | 120.6(3) |
| C21-C26-H26 | 119.7 |
| C25-C26-H26 | 119.7 |

Symmetry transformations used to generate equivalent atoms.

Table S20. Anisotropic displacement parameters ($Å^2x \ 10^3$) for **Bixafen** (3). The anisotropic displacement factor exponent takes the form: $-2p^2[h^2a^{*2}U^{11} + ... + 2hka^*b^*U^{12}]$

| | U ¹¹ | U ²² | U33 | U ²³ | U13 | U12 |
|----|-----------------|-----------------|------------|-----------------|------------|-------------|
| C1 | 0.0237(17) | 0.0239(16) | 0.0239(17) | -0.0005(13) | 0.0087(13) | 0.0005(13) |
| O1 | 0.0232(12) | 0.0426(13) | 0.0381(14) | 0.0139(11) | 0.0134(10) | 0.0058(10) |
| N1 | 0.0203(14) | 0.0283(14) | 0.0300(15) | 0.0054(12) | 0.0063(12) | -0.0015(11) |
| C2 | 0.0225(16) | 0.0197(15) | 0.0236(16) | -0.0014(13) | 0.0066(13) | -0.0012(12) |
| C3 | 0.0197(16) | 0.0266(16) | 0.0246(16) | 0.0023(14) | 0.0036(13) | -0.0032(13) |
| N4 | 0.0213(14) | 0.0363(15) | 0.0317(16) | 0.0114(13) | 0.0044(12) | -0.0014(12) |
| N5 | 0.0239(14) | 0.0356(15) | 0.0278(15) | 0.0115(12) | 0.0067(12) | -0.0016(12) |

| C6 | 0.0202(16) | 0.0308(17) | 0.0283(17) | 0.0049(14) | 0.0077(13) | -0.0004(13) |
|-----|------------|------------|------------|-------------|------------|-------------|
| C7 | 0.0232(18) | 0.044(2) | 0.045(2) | 0.0122(18) | 0.0089(16) | 0.0008(15) |
| F8 | 0.0486(13) | 0.0911(17) | 0.0353(12) | 0.0110(12) | 0.0199(11) | 0.0056(12) |
| F9 | 0.0381(12) | 0.0528(13) | 0.0863(18) | 0.0293(13) | 0.0185(12) | -0.0112(10) |
| C10 | 0.0307(19) | 0.065(3) | 0.047(2) | 0.034(2) | 0.0077(17) | -0.0007(18) |
| C11 | 0.0234(16) | 0.0258(16) | 0.0235(16) | 0.0013(13) | 0.0071(13) | 0.0043(13) |
| C12 | 0.0223(15) | 0.0255(16) | 0.0240(16) | -0.0004(13) | 0.0114(13) | -0.0001(13) |
| C13 | 0.0270(17) | 0.0245(16) | 0.0319(18) | 0.0033(14) | 0.0143(14) | 0.0010(13) |
| C14 | 0.0256(17) | 0.0322(18) | 0.0259(17) | 0.0034(14) | 0.0065(14) | 0.0060(14) |
| C15 | 0.0264(17) | 0.0313(18) | 0.0285(18) | -0.0065(15) | 0.0044(14) | -0.0039(14) |
| C16 | 0.0312(18) | 0.0220(16) | 0.0296(18) | 0.0000(14) | 0.0085(15) | -0.0026(14) |
| F18 | 0.0377(11) | 0.0391(11) | 0.0366(11) | 0.0069(9) | -0.0022(9) | 0.0056(9) |
| C21 | 0.0273(16) | 0.0228(15) | 0.0217(16) | 0.0045(13) | 0.0060(13) | -0.0032(13) |
| C22 | 0.0292(18) | 0.0266(17) | 0.044(2) | -0.0002(16) | 0.0142(16) | -0.0034(14) |
| C23 | 0.0264(18) | 0.0370(19) | 0.042(2) | 0.0099(17) | 0.0106(16) | -0.0038(15) |
| C24 | 0.0329(19) | 0.0359(19) | 0.0263(18) | 0.0046(15) | 0.0028(15) | -0.0122(15) |
| C25 | 0.044(2) | 0.0327(18) | 0.0280(19) | -0.0030(15) | 0.0136(16) | -0.0068(16) |
| C26 | 0.0322(18) | 0.0290(17) | 0.0262(17) | -0.0005(14) | 0.0100(14) | -0.0013(14) |
| Cl1 | 0.0294(5) | 0.0605(7) | 0.0971(9) | -0.0028(6) | 0.0252(5) | -0.0050(5) |
| Cl2 | 0.0476(6) | 0.0624(6) | 0.0450(6) | -0.0040(5) | 0.0056(5) | -0.0267(5) |
| | | | | | | |

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