[4+2] Annulation of Arylmethylphosphonochloridates with Dibenzo[b,f][1,4]oxazepines: A Practical Approach to Polycyclic Benzo-δ-phosphonolactams

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1. Experimental

1.1. General information

Unless otherwise noted, all materials were purchased from commercial suppliers. PhCl and MeCN were refluxed over CaH2 and freshly distilled prior to use. Toluene, THF, and 1,4-dioxane were refluxed over sodium with benzophenone as an indicator and freshly distilled prior to use. Flash column chromatography was performed using silica gel (normal phase, 200–300 mesh) from Branch of Qingdao Haiyang Chemicals. The thin layer chromatography silica gel preparative plates were purchased from Anhui Liangchen Silicon Material Co. Ltd. Petroleum ether used for column chromatography was 60–90 °C fraction, and the removal of residue solvent was accomplished under rotovap with repeated azeotrope with chloroform, and then evaporation under vacuum (< 1 mmHg pressure). Reactions were monitored by thin-layer chromatography on silica gel 60–F254 coated 0.2 mm plates from Institute of Yantai Chemical Industry. The plates were visualized under UV light. Melting points were obtained on a melting point apparatus and are uncorrected.

1H (400 MHz), 13C (101 MHz), 31P (162 MHz), and 19F NMR (376 MHz) spectra were recorded on a Bruker 400 NMR spectrometer usually with TMS as an internal standard for 1H NMR, CDCl3 as an internal standard (77.16) for 13C NMR, 85% H3PO4 as an external standard (0.0) for 31P NMR, and CF3CO2H as an external standard (-76.55) for 19F NMR in CDCl3 solution and the chemical shifts (δ) were reported in parts per million (ppm). HRMS measurements were carried out on an LC/MSD TOF mass spectrometer.

All ethyl hydrogen arylmethylphosphonic acids were prepared referring our previous method. All dibenzo[b,f][1,4]oxazepines were synthesized following our previous procedure.

1.2. Optimization of reaction conditions

Table S1: Optimization of reaction conditions

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<tr>
<th>entry</th>
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<th>solvent</th>
<th>T (°C)</th>
<th>x</th>
<th>Yield (%)b</th>
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<td>-</td>
<td>-</td>
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11 KHMDS PhMe -78 °C, 10 min; 110 °C, 24 h 0.8 63 59:41
12 KHMDS PhMe -78 °C, 10 min; 60 °C, 24 h 0.8 42 58:42
13 KHMDS PhMe -78 °C, 10 min; 80 °C 12 h 0.8 61 67:33
14 KHMDS PhMe -78 °C, 10 min; 80 °C 48 h 0.8 80 62:38
15 KHMDS PhMe 80 °C, 24 h 0.8 19 60:40
16 KHMDS PhMe -78 °C, 10 min; 80 °C 24 h with 4Å MS (125 mg) 0.8 80 62:38
17 KHMDS PhMe -78 °C, 10 min; 80 °C 24 h with 3Å MS (125 mg) 0.8 56 70:30
18 KHMDS PhMe -78 °C, 10 min; 80 °C 24 h with TiCl₄ (10 mol%) 0.8 96 70:30
19 KHMDS PhMe -78 °C, 10 min; 80 °C 24 h with AlCl₃ (10 mol%) 0.8 73 58:42

*aAll of the reactions were carried out using dibenzo[8f][1,4]oxazepine 2a (0.2 mmol), phosphonochloridate 1a (x mmol), and KHMDS (0.5 M in toluene solution, x mmol), 2 mL of solvent. bIsolated yields after column chromatography. c The dr ratio (trans/cis) was determined by ³¹P NMR spectrum of crude reaction mixture.

1.3. General procedure for the synthesis of δ-phosphonolactams 3

Ethyl hydrogen aryilmethylphosphonic acid (4 mmol) and thionyl chloride (2 mL) were added in a predried 25 mL round-bottom flask under nitrogen atmosphere. The mixture was refluxed at 80°C in an oil bath for 12 h. After concentrated, the residue was repeated azeotrope with alcohol-free dry chloroform to give yellowish oily product ethyl aryilmethylphosphonochloridate 1.

The prepared ethyl aryilmethylphosphonochloridate 1 was dissolved in toluene (4 mL). To the solution was added dibenzo[8f][1,4]oxazepine 2 (1 mmol). The resulting solution was stirred and cooled to -78°C under nitrogen atmosphere and was added dropwise a solution of 0.5 mol/L KHMDS in toluene (8 mL, 4 mmol). The mixture was kept stirring at the same temperature for 10 min. and then was heated to 80°C in an oil bath and stirred at 80°C for 24 h. After cooled to room temperature and quenched with saturated aqueous ammonium chloride solution (5 mL), the solution was extracted with dichloromethane (20 mL×3). The combined organic phase was dried over sodium sulfate and concentrated under rotovap. The residue was purified on silica gel column chromatography with a mixture of petroleum ether (PE) and ethyl acetate (EA) (PE:EA 2:1 to 1:2, v/v) as eluent to give diastereomeric δ-phosphonolactams 3. Trans-3 is less polar than the corresponding cis-3.

**rel-(4bR,15S)-15-Ethoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[8f]benzo[4,5][1,2]aza-phosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3a)**

Light yellow oil, 115 mg, 26%. Rᵣ = 0.19 (PE/EtOAc = 1/1, v/v). ¹H NMR (400 MHz, CDCl₃): 7.61 (d, J = 7.9 Hz, 1H), 7.52–7.43 (m, 1H), 7.38 (d, J = 7.9 Hz, 1H), 7.23–7.15 (m, 4H), 7.09 (td, J = 8.0, 1.4 Hz, 1H), 6.93 (td, J = 7.9, 1.5 Hz, 1H), 6.81–6.73 (m, 1H), 6.23 (d, J = 7.4 Hz, 1H), 6.06 (d, J = 20.9 Hz, 1H), 4.07–3.89 (m, 2H), 3.15 (dd, J = 16.4, 23.2 Hz, 1H), 3.15 (dd, J = 16.4, 11.2 Hz, 1H), 1.18 (t, J = 7.0 Hz, 3H). ³¹P NMR (162 MHz, CDCl₃): 23.48. ¹³F NMR (376 MHz, CDCl₃): -62.48. ¹³C NMR (101 MHz, CDCl₃): 155.3, 151.2 (d, J = 4.1 Hz), 136.3 (d, J = 9.1 Hz), 131.3, 130.6 (d, J = 9.9 Hz), 130.2, 123.0, 129.9, 129.4, 127.1,
rel-(4bR,15R)-15-Ethoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3a)

Yellow crystals, 312 mg, 70%. M.p.: 167–169 °C. Rₜ = 0.26 (PE/EtOAc = 1/1, v/v). ¹H NMR (400 MHz, CDCl₃): 7.68 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.3 Hz, 2H), 7.34–7.24 (m, 3H), 7.20 (td, J = 8.05, 1.2 Hz, 1H), 7.03 (td, J = 8.1, 1.4 Hz, 1H), 6.92 (td, J = 14.7, 7.6 Hz, 1H), 6.40 (d, J = 7.6 Hz, 1H), 6.24 (d, J = 22.8 Hz, 1H), 3.85–3.73 (m, 1H), 3.60–3.47 (m, 1H), 3.34 (dd, J = 20.8, 16.1 Hz, 1H), 3.20 (dd, J = 19.2, 16.1 Hz, 1H), 0.90 (t, J = 7.0 Hz, 3H). ³¹P NMR (162 MHz, CDCl₃): 22.72. ¹³C NMR (376 MHz, CDCl₃): -62.55. ¹⁹F NMR (377 MHz, CDCl₃): -446.1128, found 446.1132. HRMS (ESI) calcd. for C₂₃H₂₉F₃NO₃P⁺ (M + H⁺) m/z 446.1128, found 446.1132.

rel-(4bR,15S)-15-Ethoxy-7-methyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3b).

Light yellow oil, 95 mg, 21%. Rₜ = 0.18 (PE/EtOAc = 1/1, v/v). ¹H NMR (400 MHz, CDCl₃): 7.67 (d, J = 7.9 Hz, 1H), 7.59–7.50 (m, 2H), 7.44 (d, J = 7.8 Hz, 1H), 7.24 (dd, J = 8.2, 1.6 Hz, 1H), 7.19–7.13 (m, 1H), 7.08 (s, 1H), 7.00 (td, J = 7.9, 1.6 Hz, 1H), 6.64 (d, J = 7.8 Hz, 1H), 6.17 (d, J = 7.9 Hz, 1H), 6.09 (d, J = 21.1 Hz, 1H), 4.12–3.95 (m, 2H), 3.24–3.16 (m, 2H), 2.29 (s, 3H), 1.26 (t, J = 7.0 Hz, 3H). ³¹P NMR (162 MHz, CDCl₃): 23.48. ¹⁹F NMR (377 MHz, CDCl₃): -62.44. ¹³C NMR (101 MHz, CDCl₃): 154.9, 151.3 (d, J = 4.4 Hz), 140.2, 136.4 (d, J = 9.0 Hz), 131.2, 130.4 (d, J = 10.1 Hz), 126.9, 126.3 (d, J = 5.4 Hz), 125.8, 125.4, 123.6 (q, Jₜ,C₉,F = 272.4 Hz), 123.5, 123.3, 122.1, 121.7, 65.1 (d, J = 4.2 Hz), 62.5 (d, J = 5.8 Hz), 30.3 (d, J = 112.8 Hz), 20.9, 16.5 (d, J = 6.0 Hz). HRMS (ESI) calcd. for C₂₃H₂₉F₃NO₃P⁺ (M + H⁺) m/z 460.1284, found 460.1285.

rel-(4bR,15R)-15-Ethoxy-7-methyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3b).

Light yellow oil, 203 mg, 44%. Rₜ = 0.26 (PE/EtOAc = 1/1, v/v). ¹H NMR (400 MHz, CDCl₃): 7.64 (d, J = 7.9 Hz, 1H), 7.59 (d, J = 7.9 Hz, 1H), 7.50–7.44 (m, 2H), 7.25–7.11 (m, 2H), 7.07 (s, 1H), 7.03–6.94 (m, 1H), 6.68 (d, J = 7.7 Hz, 1H), 6.24 (d, J = 7.8 Hz, 1H), 6.14 (d, J = 22.7 Hz, 1H), 3.78–3.76 (m, 1H), 3.59–3.55 (m, 1H), 3.29 (dd, J = 20.8, 16.0 Hz, 1H), 3.16 (dd, J = 20.8, 16.0 Hz, 1H), 2.32 (s, 3H), 0.88 (t, J = 7.0 Hz, 3H). ³¹P NMR (162 MHz, CDCl₃): 22.89. ¹⁹F NMR (377 MHz, CDCl₃): -62.53. ¹³C NMR (101 MHz, CDCl₃): 154.9, 150.9, 140.1, 136.0 (d, J = 7.9 Hz), 135.2, 131.3 (d, J = 11.9 Hz), 131.1, 127.9 (d, J = 8.7 Hz), 126.8 (d, J = 8.0 Hz), 126.2, 125.6 (d, J = 3.5 Hz), 125.3 (d, J = 2.7 Hz).
rel-(4bR,15S)-7-Chloro-15-ethoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f][benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3c).

Light yellow oil, 89 mg, 19%. Rf = 0.16 (PE/EtOAc = 1/1, v/v). ¹H NMR (400 MHz, CDCl₃): 7.71 (d, J = 7.8 Hz, 1H), 7.60–7.52 (m, 2H), 7.48 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 7.6 Hz, 1H), 7.34–7.27 (m, 1H), 7.24–7.18 (m, 1H), 7.05 (td, J = 7.6, 1.7 Hz, 1H), 6.83 (ddd, J = 8.6, 2.4 Hz, 1H), 6.24 (d, J = 8.3 Hz, 1H), 6.04 (d, J = 20.9 Hz, 1H), 4.18–3.94 (m, 2H), 3.24–3.10 (m, 2H), 1.28 (t, J = 7.0 Hz, 3H). ³¹P NMR (162 MHz, CDCl₃): 23.10. ¹⁹F NMR (376 MHz, CDCl₃): -62.47. ¹³C NMR (101 MHz, CDCl₃): 155.4, 151.3 (d, J = 3.9 Hz), 136.0 (d, J = 12.3 Hz), 135.0, 131.2, 130.7, 130.6, 130.1 (d, J = 5.5 Hz), 127.7, 127.4, 127.1, 126.7, 126.1 (d, J = 3.9 Hz), 125.4 (d, J = 4.7 Hz), 123.9, 123.5 (q, J_C,F = 270.2 Hz), 122.8, 121.9, 121.7, 65.1 (d, J = 3.6 Hz), 62.6 (d, J = 5.8 Hz), 30.3 (d, J = 112.7 Hz), 16.5 (d, J = 6.1 Hz). HRMS (ESI) calcd. for C₂₃H₁₉ClF₃NO₃P⁺ (M + H⁺) m/z 480.0738, found 480.0738.

rel-(4bR,15R)-7-Chloro-15-ethoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f][benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3c).

Yellow oil, 151 mg, 31%. Rf = 0.25 (PE/EtOAc = 1/1, v/v). ¹H NMR (400 MHz, CDCl₃): 7.67 (d, J = 8.1 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 7.6 Hz, 2H), 7.28 (d, J = 2.1 Hz, 1H), 7.23–7.16 (m, 2H), 7.03 (ddd, J = 8.6, 6.7, 2.2 Hz, 1H), 6.86 (dd, J = 8.3, 2.1 Hz, 1H), 6.28 (d, J = 8.3 Hz, 1H), 6.09 (d, J = 22.9 Hz, 1H), 3.83 (dq, J = 9.8, 7.0 Hz, 1H), 3.69–3.54 (m, 1H), 3.31 (dd, J = 20.9, 16.1 Hz, 1H), 3.11 (t, J = 19.4, 16.1 Hz, 1H), 0.92 (t, J = 7.1 Hz, 3H). ³¹P NMR (162 MHz, CDCl₃): 22.55. ¹⁹F NMR (377 MHz, CDCl₃): -62.56. ¹³C NMR (101 MHz, CDCl₃): 155.5, 150.7, 136.1, 135.4 (d, J = 3.4 Hz), 134.9, 134.1, 131.6 (d, J = 11.8 Hz), 130.9, 128.3, 127.3 (d, J = 8.6 Hz), 125.9 (d, J = 2.3 Hz), 125.3, 123.6, 122.8, 121.3, 121.1, 64.6 (d, J = 2.9 Hz), 62.7 (d, J = 7.1 Hz), 30.7 (d, J = 118.2 Hz), 16.1 (d, J = 5.2 Hz) [C in CF₃ was not observed, but the group was conform by ¹⁹F]. HRMS (ESI) calcd. for C₂₃H₁₉ClF₃NO₃P⁺ (M + H⁺) m/z 480.0738, found 480.0738.

rel-(4bR,15S)-15-Ethoxy-3,12-bis(trifluoromethyl)-4b,16-dihydrodibenzo[b,f][benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3d).

Yellow oil, 99 mg, 19%. Rf = 0.15 (PE/EtOAc = 1/1, v/v). Pure product was not obtained due to some very closely polar impurity.

rel-(4bR,15R)-15-Ethoxy-3,12-bis(trifluoromethyl)-4b,16-dihydrodibenzo[b,f][benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3d).
Light yellow oil, 134 mg, 26%. Rf = 0.25 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.71 (d, J = 7.9 Hz, 1H), 7.61–7.59 (m, 2H), 7.53 (d, J = 9.9 Hz, 2H), 7.36 (d, J = 8.4 Hz, 1H), 7.29–7.20 (m, 2H), 7.06 (td, J = 7.7, 7.2, 1.8 Hz, 1H), 6.61 (s, 1H), 6.18 (d, J = 22.8 Hz, 1H), 3.85–3.81 (m, 1H), 3.61–3.59 (m, 1H), 3.39 (dd, Jd = 21.0, 16.3 Hz, 1H), 3.11 (dd, J = 19.7, 16.3 Hz, 1H), 0.90 (t, J = 7.1 Hz, 3H). 31P NMR (162 MHz, CDCl3): 22.48. 19F NMR (377 MHz, CDCl3): -62.00, -62.63. 13C NMR (101 MHz, CDCl3): 157.6, 150.6 (d, J = 3.1 Hz), 135.1 (d, J = 7.3 Hz), 134.7 (d, J = 7.5 Hz), 127.0 (d, J = 3.6 Hz), 130.9, 130.4, 130.1, 129.8, 128.4, 128.0, 127.3, 126.99, 126.95 126.1 (d, J = 3.6 Hz), 125.5 (d, J = 3.7 Hz), 125.4, 125.0, 124.6, 123.7, 123.5 (d, J = 3.7 Hz), 122.3, 121.5, 121.1, 164.8 (d, J = 2.4 Hz), 62.6 (d, J = 7.0 Hz), 30.6 (d, J = 119.8 Hz), 16.0 (d, J = 5.5 Hz) [2C in 2CF3 were not observed, but the groups were conform by 19F]. HRMS (ESI) calcd. for C23H16F3NO3P+ (M + H+): m/z 514.1002, found 514.1005.

rel-(4bR,15S)-15-Ethoxy-13-methyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3e). Light yellow oil, 45 mg, 10%. Rf = 0.20 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.66 (d, J = 7.8 Hz, 1H), 7.60 (s, 1H), 7.37 (d, J = 7.8 Hz, 1H), 7.31 (dd, Jd = 8.2, 1.1 Hz, 1H), 7.23–7.16 (m, 3H), 7.06 (dd, J = 6.2, 2.8 Hz, 1H), 6.83 (dd, J = 7.9, 1.1 Hz, 1H), 6.48 (d, J = 7.8 Hz, 1H), 5.52 (d, J = 23.3 Hz, 1H), 4.08–3.91 (m, 2H), 3.18–3.07 (m, 1H), 3.09–2.96 (m, 1H), 2.34 (s, 3H), 1.19 (t, J = 7.0 Hz, 3H). 31P NMR (162 MHz, CDCl3): 23.42. 19F NMR (376 MHz, CDCl3): -62.20. 13C NMR (101 MHz, CDCl3): 154.6, 151.5, 138.8 (d, J = 1.7 Hz), 132.2, 130.8 (d, J = 3.9 Hz), 130.7, 129.1, 128.8 (d, J = 1.3 Hz), 128.7, 127.2 (d, J = 3.4 Hz), 126.9, 126.7, 125.7 (d, J = 7.5 Hz), 125.0 (d, J = 4.0 Hz), 122.9, 122.2, 119.2, 66.0 (d, J = 5.1 Hz), 62.2 (d, J = 5.1 Hz), 30.9 (d, J = 111.9 Hz), 17.7, 16.4 (d, J = 6.0 Hz) [C in CF3 was not observed, but the group was conform by 19F]. HRMS (ESI) calcd. for C23H32F3NO3P+(M + H+): m/z 460.1284, found 460.1282.

rel-(4bR,15R)-15-Ethoxy-13-methyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3e). Light yellow oil, 221 mg, 48%. Rf = 0.35 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.83 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 8.6 Hz, 1H), 7.69–7.54 (m, 1H), 7.49–7.38 (m, 2H), 7.27–7.26 (m, 1H), 7.15–7.13 (m, 1H), 7.05 (d, J = 7.0 Hz, 1H), 6.86–6.82 (m, 1H), 6.38 (d, J = 8.2 Hz, 1H), 5.72 (d, J = 24.8 Hz, 1H), 4.11–0.98 (m, 1H), 3.77–3.68 (m, 1H), 3.24 (dd, J = 22.4, 16.8 Hz, 1H), 3.11 (dd, J = 19.8, 16.8 Hz, 1H), 2.38 (s, 3H), 0.98 (t, J = 7.2 Hz, 3H). 31P NMR (162 MHz, CDCl3): 22.41. 19F NMR (376 MHz, CDCl3): -62.33. 13C NMR (101 MHz, CDCl3): 156.0 (d, J = 2.6 Hz), 154.3, 139.6 (d, J = 2.0 Hz), 138.00, 137.98, 131.7, 131.6, 129.3, 128.5, 127.9, 127.8, 126.7 (d, J = 1.4 Hz), 126.3, 125.6 (d, J = 3.3 Hz), 125.0 (d, J = 5.7 Hz), 122.1, 122.8 (q, Jc,F = 272.7 Hz), 121.1, 118.7, 66.4 (d, J = 3.5 Hz), 62.4 (d, J = 7.2 Hz), 31.1 (d, J = 118.1 Hz), 29.7, 16.2 (d, J = 5.5 Hz). HRMS (ESI) calcd. for C23H32F3NO3P+(M + H+): m/z 460.1284, found 460.1282.
rel-(4bR,15S)-15-Ethoxy-12-methyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3f).

Light yellow oil, 92 mg, 20%. Rf = 0.21 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.69 (d, J = 7.8 Hz, 1H), 7.56–7.48 (m, 1H), 7.28 (d, J = 7.2 Hz, 1H), 7.27–7.24 (m, 1H), 7.18–7.14 (m, 1H), 7.13–7.09 (m, 1H), 7.03–7.02 (m, 1H), 6.99–6.96 (m, 1H), 6.84 (dd, J = 6.6, 2.6 Hz, 1H), 6.28 (d, J = 8.4 Hz, 1H), 6.04 (d, J = 23.2 Hz, 1H), 4.14–4.02 (m, 2H), 3.19 (dd, J = 21.2, 16.4 Hz, 1H), 3.06 (dd, J = 20.2, 16.4 Hz, 1H), 2.28 (s, 3H), 1.18 (t, J = 7.2 Hz, 3H). 31P NMR (162 MHz, CDCl3): 23.41. 19F NMR (377 MHz, CDCl3): -62.46. 13C NMR (101 MHz, CDCl3): 155.2, 149.2 (d, J = 4.3 Hz), 136.4 (d, J = 9.2 Hz), 136.2 (d, J = 9.8 Hz), 133.0, 130.8, 130.5 (d, J = 9.9 Hz), 130.1 (d, J = 5.8 Hz), 129.8, 129.0, 127.7, 126.7, 126.1, 125.9 (d, J = 3.4 Hz), 125.4, 122.6, 121.5, 121.4, 65.4 (d, J = 4.0 Hz), 62.5 (d, J = 5.9 Hz), 30.4 (d, J = 112.8 Hz), 20.6, 16.5 (d, J = 6.0 Hz) [C in CF3 was not observed, but the group was confirm by 19F]. HRMS (ESI) calced. for C24H25F3NO3P+(M + H+) m/z 460.1284, found 460.1286.

rel-(4bR,15R)-15-Ethoxy-12-methyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3f).

Light yellow oil, 149 mg, 33%. Rf = 0.36 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.70 (d, J = 7.8 Hz, 1H), 7.48–7.46 (m, 2H), 7.42–7.31 (m, 1H), 7.29–7.24 (m, 1H), 7.15–7.13 (m, 1H), 7.08 (d, J = 7.8 Hz, 1H), 6.69–6.88 (m, 1H), 6.82 (t, J = 7.6 Hz, 1H), 6.42 (d, J = 8.2 Hz, 1H), 6.08 (d, J = 23.2 Hz, 1H), 3.79–3.68 (m, 1H), 3.54–3.46 (m, 1H), 3.28 (dd, J = 21.2, 15.8 Hz, 1H), 3.18 (dd, J = 20.8, 15.8 Hz, 1H), 2.26 (s, 3H), 1.01 (t, J = 7.2 Hz, 3H). 31P NMR (162 MHz, CDCl3): 22.62. 19F NMR (377 MHz, CDCl3): -62.54. 13C NMR (101 MHz, CDCl3): 155.2, 148.8 (d, J = 3.5 Hz), 135.9 (d, J = 7.8 Hz), 135.3 (d, J = 7.1 Hz), 132.9, 131.4, 131.3, 130.7, 129.7, 129.6, 128.2, 127.6, 126.4, 125.6, 125.4, 125.1 (q, JCF = 272.3 Hz), 122.6, 120.9, 120.7, 65.0 (d, J = 3.0 Hz), 62.4 (d, J = 7.1 Hz), 30.6 (d, J = 119.1 Hz), 20.5, 16.1 (d, J = 5.7 Hz). HRMS (ESI) calced. for C24H23F3NO3P+(M + H+) m/z 460.1284, found 460.1292.

rel-(4bR,155S)-15-Ethoxy-12-methoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3g).

Light yellow oil, 126 mg, 27%. Rf = 0.20 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.68 (d, J = 7.8 Hz, 1H), 7.54 (s, 1H), 7.45 (d, J = 7.9 Hz, 1H), 7.23 (d, J = 5.9 Hz, 2H), 7.17 (d, J = 9.0 Hz, 1H), 6.86–6.80 (m, 2H), 6.73 (dd, J = 9.0, 2.9 Hz, 1H), 6.32 (d, J = 7.7 Hz, 1H), 6.11 (d, J = 21.0 Hz, 1H), 4.35–3.84 (m, 2H), 3.75 (s, 3H), 3.29–3.21 (m, 1H), 3.20–3.12 (m, 1H), 1.27 (t, J = 7.0 Hz, 3H). 31P NMR (162 MHz, CDCl3): 23.53. 19F NMR (377 MHz, CDCl3): -62.44. 13C NMR (101 MHz, CDCl3): 155.4 (d, J = 5.5 Hz), 145.6 (d, J = 4.0 Hz), 136.5 (d, J = 9.0 Hz), 136.2 (d, J = 10.0 Hz), 131.8, 130.6 (d, J = 9.8 Hz), 129.9, 129.1, 126.3, 126.0 (d, J = 2.9 Hz), 125.6, 123.5 (q, J = 271.4 Hz), 122.8, 122.2, 121.6, 112.8, 111.4, 65.3 (d, J = 3.9 Hz), 62.6 (d, J = 5.6 Hz), 55.7, 30.4 (d, J = 112.7 Hz), 16.7 (d, J = 5.9 Hz). HRMS (ESI) calced. for C24H23F3NO3P+(M + H+) m/z 476.1233, found 476.1239.
rel-(4bR,15R)-15-Ethoxy-12-methoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5] [1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3g).

Yellow oil, 227 mg, 48%. Rf = 0.29 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.64 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 7.9 Hz, 1H), 7.48 (s, 1H), 7.38 (d, J = 7.7 Hz, 1H), 7.23–7.16 (m, 2H), 7.13 (d, J = 9.0 Hz, 1H), 6.86 (t, J = 8.2 Hz, 1H), 6.71 (dd, J = 9.0, 2.9 Hz, 1H), 6.37 (dd, J = 7.2 Hz, 1H), 6.20 (d, J = 22.5 Hz, 1H), 3.79–3.76 (m, 1H), 3.74 (s, 3H), 3.64–3.47 (m, 1H), 3.30 (dd, J = 20.8, 16.1 Hz, 1H), 3.16 (dd, J = 20.8, 16.1 Hz, 1H), 0.90 (t, J = 7.1 Hz, 3H). 31P NMR (162 MHz, CDCl3): 22.79. 19F NMR (377 MHz, CDCl3): -62.54. 13C NMR (101 MHz, CDCl3): 155.4, 155.0, 144.7 (d, J = 3.6 Hz), 135.9 (d, J = 7.6 Hz), 135.2 (d, J = 6.6 Hz), 131.6, 131.3 (d, J = 11.9 Hz), 130.1 (d, J = 5.9 Hz), 129.8, 126.4, 125.6 (d, J = 3.4 Hz), 125.4 (d, J = 2.4 Hz), 123.4 (q, J = 271.8 Hz), 122.7, 121.6, 120.9, 113.3, 111.6, 64.6 (d, J = 2.7 Hz), 62.5 (d, J = 7.2 Hz), 55.7, 30.6 (d, J = 118.9 Hz), 16.1 (d, J = 5.7 Hz). HRMS (ESI) calcd. for C22H22F3NO4P+ (M + H+) m/z 476.1233, found 476.1239.


Yellow oil, 82 mg, 17%. Rf = 0.18 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.72 (d, J = 7.9 Hz, 1H), 7.57 (s, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.31 (dd, J = 10.1, 1.5 Hz, 2H), 7.25 (dd, J = 8.1, 1.4 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 7.15 (dd, J = 8.8, 2.4 Hz, 1H), 6.89 (td, J = 7.3, 1.5 Hz, 1H), 6.33 (d, J = 7.7 Hz, 1H), 6.16 (d, J = 20.7 Hz, 1H), 4.23–4.09 (m, 1H), 4.13–3.99 (m, 1H), 3.33–3.13 (m, 2H), 1.32 (t, J = 7.1 Hz, 3H). 31P NMR (162 MHz, CDCl3): 23.67. 19F NMR (377 MHz, CDCl3): -62.50. 13C NMR (101 MHz, CDCl3): 154.9, 149.6 (d, J = 4.1 Hz), 135.9 (d, J = 8.9 Hz), 135.7 (d, J = 9.3 Hz), 132.0, 130.5 (d, J = 10.2 Hz), 130.1, 129.3, 127.9, 126.7, 126.0 (d, J = 14.6 Hz), 125.5, 123.2, 122.7, 121.6, 65.1 (d, J = 4.0 Hz), 62.8 (d, J = 5.6 Hz), 30.3 (d, J = 113.0 Hz), 16.5 (d, J = 5.7 Hz) [C in CF3 was not observed, but the group was conform by 19F]. HRMS (ESI) calcd. for C23H16ClF3NO4P+ (M + H+) m/z 480.0738, found 480.0743.


Yellow oil, 220 mg, 46%. Rf = 0.26 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.68 (d, J = 7.8 Hz, 1H), 7.58–7.47 (m, 2H), 7.44–7.26 (m, 1H), 7.24 (d, J = 7.8 Hz, 1H), 7.20–7.18 (m, 1H), 7.06 (d, J = 7.6 Hz, 1H), 7.02 (dd, J = 7.8, 2.6 Hz, 1H), 6.90–6.84 (m, 1H), 6.38 (d, J = 8.2 Hz, 1H), 6.18 (d, J = 23.2 Hz, 1H), 3.88–3.72 (m, 1H), 3.58–3.48 (m, 1H), 3.36 (dd, J = 21.2, 15.8 Hz, 1H), 3.28 (dd, J = 20.2, 15.8 Hz, 1H), 0.88 (t, J = 7.1 Hz, 3H). 31P NMR (162 MHz, CDCl3): 22.70. 19F NMR (376 MHz, CDCl3): -62.58. 13C NMR (101 MHz, CDCl3): 155.0, 149.1, 135.1 (d, J = 8.0 Hz), 132.0, 131.5, 131.4, 130.2, 129.9, 127.8, 127.3 (d, J = 1.5 Hz), 126.6, 126.3, 125.7 (d, J = 4.0 Hz), 125.4 (d, J = 3.7 Hz), 123.2, 122.1, 120.9, 64.4 (d, J = 3.0 Hz), 62.6 (d, J = 7.2 Hz), 30.6 (d, J = 120.2 Hz), 16.1 (d, J = 5.6
Hz) [C in CF₃ was not observed, but the group was conform by ^{19}F]. HRMS (ESI) calcd. for C₂₃H₁₇ClF₅NO₃P⁺ (M + H⁺) m/z 480.0738, found 480.0734.

**rel-(4bR,15S)-12-Bromo-15-ethoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3i).**

Yellow oil, 85 mg, 16%. Rf = 0.19 (PE/EtOAc = 1/1, v/v). ^{1}H NMR (400 MHz, CDCl₃): 7.72 (d, J = 7.9 Hz, 1H), 7.57 (s, 1H), 7.52–7.45 (m, 2H), 7.32–7.29 (m, 1H), 7.26 (dd, J = 8.0, 6.5 Hz, 2H), 7.15 (d, J = 8.7 Hz, 1H), 6.89 (td, J = 7.6, 1.5 Hz, 1H), 6.32 (d, J = 7.7 Hz, 1H), 6.14 (d, J = 20.8 Hz, 1H), 4.16 (ddq, J = 10.4, 9.0, 7.1 Hz, 1H), 4.11–3.98 (m, 1H), 3.33–3.12 (m, 2H), 1.33 (t, J = 7.1 Hz, 3H). ^{31}P NMR (162 MHz, CDCl₃): 23.68. ^{19}F NMR (377 MHz, CDCl₃): -62.50. ^{13}C NMR (101 MHz, CDCl₃): ^{13}C NMR (101 MHz, CDCl₃): 154.8, 150.3 (d, J = 4.4 Hz), 135.9 (d, J = 8.3 Hz), 135.7 (d, J = 8.9 Hz), 132.3, 131.9, 130.5 (d, J = 10.0 Hz), 130.1, 129.8, 129.2, 129.0, 126.1 (d, J = 3.2 Hz), 125.9, 125.4 (d, J = 3.3 Hz), 123.1 (d, J = 11.4 Hz), 121.5, 115.2, 65.2 (d, J = 3.6 Hz), 62.8 (d, J = 5.3 Hz), 30.3 (d, J = 113.2 Hz), 16.5 (d, J = 5.8 Hz) [C in CF₃ was not observed, but the group was conform by ^{19}F]. HRMS (ESI) calcd. for C₂₅H₁₈BrF₅NO₃P⁺ (M + H⁺) m/z 524.0233, found 524.0234.

**rel-(4bR,15R)-12-Bromo-15-ethoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3i).**

Light yellow oil, 182 mg, 35%. Rf = 0.27 (PE/EtOAc = 1/1, v/v). ^{1}H NMR (400 MHz, CDCl₃): ^{1}H NMR (400 MHz, CDCl₃): 7.77 (dd, J = 2.3, 1.1 Hz, 1H), 7.65 (d, J = 8.2 Hz, 1H), 7.52–7.45 (m, 2H), 7.32–7.27 (m, 1H), 7.27–7.19 (m, 2H), 7.09 (d, J = 8.7 Hz, 1H), 6.91 (td, J = 7.5, 1.1 Hz, 1H), 6.38 (d, J = 7.5 Hz, 1H), 6.21 (d, J = 22.1 Hz, 1H), 3.81 (m, 1H), 3.52 (m, 1H), 3.33 (dd, J = 20.9, 16.2 Hz, 1H), 3.18 (dd, J = 19.8, 16.2 Hz, 1H), 0.91 (t, J = 7.0 Hz, 3H). ^{31}P NMR (162 MHz, CDCl₃): 22.65. ^{19}F NMR (377 MHz, CDCl₃): -62.56. ^{13}C NMR (101 MHz, CDCl₃): 154.9, 149.7 (d, J = 3.5 Hz), 135.1 (d, J = 7.8 Hz), 132.4, 131.5, 131.4, 130.1 (d, J = 4.5 Hz), 129.9, 129.6, 128.0, 126.3, 125.6 (d, J = 33.1 Hz), 122.5, 123.3 (q, J = 273.7 Hz), 120.9, 115.0, 64.5 (d, J = 2.0 Hz), 62.6 (d, J = 7.0 Hz), 30.6 (d, J = 120.3 Hz), 16.1 (d, J = 5.6 Hz). HRMS (ESI) calcd. for C₂₅H₁₈BrF₅NO₃P⁺ (M + H⁺) m/z 524.0233, found 524.0229.

**rel-(4bR,15S)-11-Chloro-15-ethoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3k).**

Yellow oil, 75 mg, 16%. Rf = 0.18 (PE/EtOAc = 1/1, v/v). ^{1}H NMR (400 MHz, CDCl₃): 7.72 (d, J = 7.7 Hz, 1H), 7.57 (s, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.32–7.27 (m, 3H), 7.25–7.21 (m, 1H), 7.00 (dd, J = 8.6, 2.3 Hz, 1H), 6.90 (t, J = 6.9 Hz, 1H), 6.33 (d, J = 7.6 Hz, 1H), 6.15 (d, J = 20.7 Hz, 1H), 4.17–3.99 (m, 2H), 3.24 (dd, J = 20.1, 16.6 Hz, 1H), 3.23 (d, J = 19.7 Hz, 16.1 Hz, 1H), 1.28 (t, J = 7.0 Hz, 3H). ^{31}P NMR (162 MHz, CDCl₃): 23.68. ^{19}F NMR (377 MHz, CDCl₃): -62.48. ^{13}C NMR (101 MHz, CDCl₃): 154.8, 151.1 (d, J = 3.7 Hz), 136.0 (d, J = 9.5 Hz), 135.8 (d, J = 9.2 Hz).

Yellow oil, 175 mg, 37%. \( R_f = 0.26 \) (PE/EtOAc = 1/1, v/v). \(^1\)H NMR (400 MHz, CDCl\(_3\)): 7.65 (d, \( J = 7.8 \) Hz, 1H), 7.54 (d, \( J = 8.6 \) Hz, 1H), 7.47 (d, \( J = 9.4 \) Hz, 2H), 7.29 (td, \( J = 7.9, 1.7 \) Hz, 1H), 7.25–7.19 (m, 2H), 6.95 (dd, \( J = 8.7, 2.4 \) Hz, 1H), 6.91 (t, \( J = 7.7 \) Hz, 1H), 6.37 (d, \( J = 7.5 \) Hz, 1H), 6.21 (d, \( J = 22.6 \) Hz, 1H), 3.75 (tq, \( J = 9.6, 7.0 \) Hz, 1H), 3.55–3.40 (m, 1H), 3.32 (dd, \( J = 21.0, 16.2 \) Hz, 1H), 3.17 (dd, \( J = 19.8, 16.3 \) Hz, 1H), 0.88 (t, \( J = 7.0 \) Hz, 3H). \(^{31}\)P NMR (162 MHz, CDCl\(_3\)): 22.77. \(^{19}\)F NMR (377 MHz, CDCl\(_3\)): -62.56. \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): 154.8, 150.6 (d, \( J = 3.5 \) Hz), 135.2 (d, \( J = 8.7 \) Hz), 135.0 (d, \( J = 10.1 \) Hz), 131.52, 131.48 (d, \( J = 9.4 \) Hz), 130.3, 130.0, 129.7, 128.5, 128.0, 126.3, 125.7 (d, \( J = 2.4 \) Hz), 125.4, 123.8 (q, \( J_{C,F} = 270.8 \) Hz), 123.4, 123.0, 121.2, 121.0, 64.4 (d, \( J = 1.4 \) Hz), 62.5 (d, \( J = 6.9 \) Hz), 30.6 (d, \( J = 119.7 \) Hz), 16.1 (d, \( J = 5.6 \) Hz). HRMS (ESI) calcd. for C\(_{23}\)H\(_{19}\)Cl\(_3\)F\(_3\)NO\(_3\)P\(^+\) (M + H\(^+\)) \( m/z \) 480.0738, found 480.0733.


Yellow oil, 97 mg, 20%. \( R_f = 0.20 \) (PE/EtOAc = 1/1, v/v). \(^1\)H NMR (400 MHz, CDCl\(_3\)): 7.70 (d, \( J = 7.9 \) Hz, 1H), 7.59 (dd, \( J = 9.0, 3.2 \) Hz, 1H), 7.54 (s, 1H), 7.47 (d, \( J = 7.8 \) Hz, 1H), 7.17 (d, \( J = 7.8 \) Hz, 1H), 7.09 (s, 1H), 6.91–6.84 (m, 1H), 6.82 (dd, \( J = 8.3, 2.1 \) Hz, 1H), 6.24 (d, \( J = 8.3 \) Hz, 1H), 5.96 (d, \( J = 21.2 \) Hz, 1H), 4.13–4.01 (m, 2H), 3.22–3.11 (m, 2H), 2.35 (s, 3H), 1.27 (t, \( J = 7.0 \) Hz, 3H). \(^{31}\)P NMR (162 MHz, CDCl\(_3\)): 22.90. \(^{19}\)F NMR (376 MHz, CDCl\(_3\)): -62.44. \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): 155.4, 151.3 (d, \( J = 4.2 \) Hz), 137.8, 136.2 (d, \( J = 8.7 \) Hz), 136.1 (d, \( J = 8.0 \) Hz), 134.9, 130.7, 130.6, 130.1 (d, \( J = 6.0 \) Hz), 128.4, 127.5, 127.3, 126.5 (d, \( J = 1.4 \) Hz), 126.0 (d, \( J = 3.3 \) Hz), 125.4 (d, \( J = 4.0 \) Hz), 124.7, 122.9, 122.0, 121.9, 65.3 (d, \( J = 4.5 \) Hz), 62.5 (d, \( J = 5.9 \) Hz), 30.3 (d, \( J = 112.7 \) Hz), 16.5 (d, \( J = 6.0 \) Hz) [C in CF\(_3\) was not observed, but the group was conform by \(^{19}\)F]. HRMS (ESI) calcd. for C\(_{23}\)H\(_{19}\)Cl\(_3\)F\(_3\)NO\(_3\)P\(^+\) (M + H\(^+\)) \( m/z \) 494.0894, found 494.0890.


Light yellow oil, 110 mg, 22%. \( R_f = 0.30 \) (PE/EtOAc = 1/1, v/v). \(^1\)H NMR (400 MHz, CDCl\(_3\)): 7.65 (d, \( J = 7.8 \) Hz, 1H), 7.54–7.37 (m, 3H), 7.24 (d, \( J = 2.4 \) Hz, 1H), 7.03 (s, 1H), 6.83 (d, \( J = 8.3 \) Hz, 2H), 6.26 (d, \( J = 8.3 \) Hz, 1H), 6.03 (d, \( J = 23.1 \) Hz, 1H), 3.89–3.75 (m, 1H), 3.67–3.49 (m, 1H), 3.30 (dd, \( J = 20.8, 16.0 \) Hz, 1H), 3.09 (dd, \( J = 19.9, 16.1 \) Hz, 1H), 2.33 (s, 3H), 0.92 (t, \( J = 7.0 \) Hz, 3H). \(^{31}\)P NMR (162 MHz, CDCl\(_3\)): 22.38. \(^{19}\)F NMR (377 MHz, CDCl\(_3\)): -62.54. \(^{13}\)C NMR (101 MHz,
CDCl₃): 155.5, 150.4 (d, J = 3.7 Hz), 137.5, 135.6 (d, J = 7.3 Hz), 135.2 (d, J = 8.7 Hz), 134.8, 131.6 (d, J = 11.9 Hz), 128.2 (d, J = 9.3 Hz), 128.0, 127.4, 125.8, 125.3, 124.4, 122.6, 121.3 (d, J = 12.3 Hz), 64.8 (d, J = 2.8 Hz), 62.6 (d, J = 7.2 Hz), 30.6 (d, J = 119.2 Hz), 20.8, 16.2 (d, J = 5.5 Hz) [C in CF₃ was not observed, but the group was conform by ¹⁹F]. HRMS (ESI) calcd. for C₂₅H₂₇ClF₃NO₃P⁺ (M + H⁺) m/z 494.0894, found 494.0898.

rel-(4bR,15S)-15-Ethoxy-7,11-dimethyl-3-(trifluoromethyl)-4b,16-dihydriodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3m).

Light yellow oil, 128 mg, 27%. Rₛ = 0.23 (PE/EtOAc = 1/1, v/v).
³¹P NMR (400 MHz, CDCl₃): 7.68 (d, J = 7.8 Hz, 1H), 7.57 (d, J = 8.2 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.17 (d, J = 8.2 Hz, 1H), 7.08 (s, 2H), 6.83 (d, J = 9.2 Hz, 1H), 6.65 (d, J = 7.7 Hz, 1H), 6.19 (d, J = 7.9 Hz, 1H), 6.03 (d, J = 21.5 Hz, 1H), 4.12–3.97 (m, 2H), 3.26–3.10 (m, 2H), 2.33 (s, 3H), 2.31 (s, 3H), 1.27 (t, J = 6.6 Hz, 3H). 
¹³C NMR (101 MHz, CDCl₃): 154.9, 151.3 (d, J = 4.2 Hz), 140.0, 137.3, 136.7 (d, J = 8.8 Hz), 136.3 (d, J = 9.4 Hz), 130.4 (d, J = 9.9 Hz), 128.4, 126.2 (d, J = 1.6 Hz), 126.1, 126.0, 125.7 (d, J = 3.8 Hz), 125.3 (d, J = 3.6 Hz), 124.2, 123.4, 122.1 (d, J = 1.6 Hz), 65.3 (d, J = 4.5 Hz), 62.4 (d, J = 5.9 Hz), 30.3 (d, J = 120.5 Hz), 20.81, 20.77, 16.5 (d, J = 6.1 Hz) [C in CF₃ was not observed, but the group was conform by ¹⁹F]. HRMS (ESI) calcd. for C₂₅H₂₇ClF₃NO₃P⁺ (M + H⁺) m/z 474.1440, found 474.1445.

rel-(4bR,15R)-15-Ethoxy-7,11-dimethyl-3-(trifluoromethyl)-4b,16-dihydriodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3m).

Light yellow oil, 163 mg, 34%. Rₛ = 0.37 (PE/EtOAc = 1/1, v/v).
³¹P NMR (400 MHz, CDCl₃): 7.66 (d, J = 7.9 Hz, 1H), 7.58 (d, J = 8.2 Hz, 1H), 7.47 (t, J = 6.8 Hz, 1H), 7.41 (d, J = 8.1 Hz, 1H), 7.06 (d, J = 9.0 Hz, 2H), 6.82 (dd, J = 8.1, 1.4 Hz, 1H), 6.69 (d, J = 7.6 Hz, 1H), 6.25 (d, J = 7.8 Hz, 1H), 6.11 (d, J = 23.0 Hz, 1H), 3.85–3.73 (m, 1H), 3.66–3.47 (m, 1H), 3.30 (dd, J = 20.8, 16.0 Hz, 1H), 3.17 (dd, J = 20.8, 16.0 Hz, 1H), 2.35 (s, 3H), 2.34 (s, 3H), 0.92 (t, J = 7.0 Hz, 3H). 
¹³C NMR (101 MHz, CDCl₃): 154.9, 150.5, 140.0, 137.0, 136.2 (d, J = 8.2 Hz), 131.4, 131.3, 130.1, 130.1, 128.3, 127.6 (d, J = 1.5 Hz), 126.7, 126.2, 125.5 (d, J = 4.1 Hz), 125.3 (d, J = 3.3 Hz), 123.9, 123.4, 121.4, 64.8 (d, J = 3.8 Hz), 62.4 (d, J = 7.1 Hz), 30.6 (d, J = 119.0 Hz), 20.9, 20.8, 16.1 (d, J = 5.7 Hz) [C in CF₃ was not observed, but the group was conform by ¹⁹F]. HRMS (ESI) calcd. for C₂₅H₂₇ClF₃NO₃P⁺ (M + H⁺) m/z 474.1440, found 474.1449.

rel-(4bR,15S)-15-Ethoxy-4b,16-dihydriodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4] oxazepine 15-oxide (cis-3p).

Colorless crystals, 15 mg, 4%. M.p. 172–173 °C. Rₛ = 0.30 (PE/EtOAc = 1/1, v/v).
³¹P NMR (400 MHz, CDCl₃): 7.49–7.36 (m, 1H), 7.33–7.24 (m, 6H), 7.18 (td, J = 7.7, 1.6 Hz, 1H), 7.03 (td, J = 7.7, 1.6 Hz, 1H), 6.87 (ddd, J = 8.2, 6.0, 2.6 Hz, 1H), 6.40 (d, J = 7.9 Hz, 1H), 6.06 (d, J = 20.5 Hz, 1H), 4.13–3.97 (m, 2H), 3.14 (dd, J = 20.0, 16.0 Hz, 1H), 3.12 (dd, J = 20.0, 16.0 Hz, 1H), 1.28
(t, J = 7.0 Hz, 3H). 13C NMR (101 MHz, CDCl3): 155.2, 151.0 (d, J = 4.2 Hz), 137.0 (d, J = 9.0 Hz), 133.4, 131.4, 131.3, 131.2 (d, J = 10.0 Hz), 130.4 (d, J = 9.7 Hz) 129.8, 129.6, 128.8, 126.7, 126.1, 123.4, 122.8, 121.7, 121.5, 65.0 (d, J = 4.4 Hz), 62.5 (d, J = 6.1 Hz), 29.7 (d, J = 113.1 Hz), 16.5 (d, J = 6.1 Hz). 31P NMR (162 MHz, CDCl3): 24.08. HRMS (ESI) calcd. for C22H21NO3P+ (M + H+) m/z 378.1254, found 378.1259.

rel-(4bR,15R)-15-Ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3p)

Colorless crystals, 106 mg, 28%. M.p. 164–165 °C. Rf = 0.50 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.64 (dt, J = 8.0, 1.4 Hz, 1H), 7.40–7.27 (m, 3H), 7.25–7.12 (m, 5H), 6.98 (td, J = 7.3, 1.6 Hz, 1H), 6.86 (td, J = 7.3, 1.6 Hz, 1H), 6.43 (dt, J = 7.6, 1.1 Hz, 1H), 6.16 (d, J = 22.4 Hz, 1H), 3.73 (ddq, J = 10.2, 9.2, 7.0 Hz, 1H), 3.48 (ddq, J = 10.2, 9.2, 7.0 Hz, 1H), 3.24 (dd, J = 21.1, 16.0 Hz, 1H), 3.12 (dd, J = 19.2, 16.0 Hz, 1H), 0.86 (t, J = 7.0 Hz, 3H). 13C NMR (101 MHz, CDCl3): 155.2, 150.5 (d, J = 3.8 Hz), 134.7 (d, J = 8.3 Hz), 131.6, 131.0, 130.9 (d, J = 12.1 Hz), 130.8 (d, J = 8.1 Hz), 129.4, 128.4, 128.5 (d, J = 2.2 Hz), 127.8 (d, J = 1.7 Hz), 127.3 (d, J = 1.7 Hz), 126.6, 126.4, 123.0, 122.7, 121.0, 120.7, 64.9 (d, J = 3.4 Hz), 62.1 (d, J = 7.2 Hz), 30.4 (d, J = 119.4 Hz), 16.1 (d, J = 5.7 Hz). 31P NMR (162 MHz, CDCl3): 24.12. HRMS (ESI) calcd. for C22H21NO3P+ (M + H+) m/z 378.1254, found 378.1263.

rel-(4bR,15S)-3-Chloro-15-ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3q)

Colorless crystals, 55 mg, 13%. M.p. 210–211 °C. Rf = 0.15 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.42 (dt, J = 8.0, 1.6 Hz, 1H), 7.36–7.22 (m, 5H), 7.18 (td, J = 8.2, 1.6 Hz, 1H), 7.03 (td, J = 7.6, 1.6 Hz, 1H), 6.87 (dd, J = 8.2, 5.7, 2.9 Hz, 1H), 6.40 (d, J = 7.7 Hz, 1H), 6.44 (dt, J = 7.7, 1.2 Hz, 1H), 1.60 (d, J = 20.5 Hz, 1H), 4.15–3.93 (m, 2H), 3.34–3.01 (m, 2H), 1.28 (t, J = 7.0 Hz, 3H). 13C NMR (101 MHz, CDCl3): 155.2, 150.9 (d, J = 4.5 Hz), 137.0 (d, J = 9.3 Hz), 131.3 (d, J = 1.2 Hz), 131.2 (d, J = 10.1 Hz), 130.4, 130.3, 129.8, 129.6, 129.1, 128.7 (d, J = 2.6 Hz), 126.8, 126.1 (d, J = 1.9 Hz), 126.4, 122.9, 121.7, 121.5, 65.0 (d, J = 4.4 Hz), 62.5 (d, J = 6.1 Hz), 29.7 (d, J = 113.3 Hz), 16.5 (d, J = 6.1 Hz). 31P NMR (162 MHz, CDCl3): 24.15. HRMS (ESI) calcd. for C22H21ClNO3P+ (M + H+) m/z 412.0864, found 412.0865.

rel-(4bR,15R)-3-Chloro-15-ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3q)

Colorless crystals, 93 mg, 22%. M.p. 203–204 °C. Rf = 0.27 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.61 (dt, J = 8.0, 1.5 Hz, 1H), 7.37 (dt, J = 8.1, 1.7 Hz, 1H), 7.30–7.27 (m, 2H), 7.25–7.20 (m, 3H), 7.18–7.12 (m, 1H), 6.99 (td, J = 8.0, 1.7 Hz, 1H), 6.89 (dt, J = 7.7, 1.2 Hz, 1H), 6.44 (dt, J = 7.7, 1.2 Hz, 1H), 6.09 (d, J = 22.4 Hz, 1H), 3.74 (ddq, J = 10.2, 8.7, 7.0 Hz, 1H), 3.49 (ddq, J = 10.2, 8.7, 7.0 Hz, 1H), 3.20 (dd, J = 20.0, 16.0 Hz, 1H), 3.08 (dd, J = 20.0, 16.0 Hz, 1H), 0.86 (t, J = 7.0 Hz, 3H). 13C NMR (101 MHz, CDCl3): 155.2, 150.6 (d, J = 3.6 Hz), 136.5 (d, J = 7.9 Hz), 133.2 (d, J = 1.7 Hz), 132.1 (d, J = 12.2 Hz), 131.2, 130.2, 129.7, 129.4 (d, J = 8.2 Hz), 128.8, 128.5 (d, J = 2.2 Hz), 127.9, 126.7, 126.5, 123.1, 122.8, 121.0, 120.8, 64.5 (d, J = 3.5
Hz), 62.3 (d, J = 7.2 Hz), 30.0 (d, J = 119.6 Hz), 16.1 (d, J = 5.8 Hz). $^{31}$P NMR (162 MHz, CDCl$_3$): 23.33. HRMS (ESI) calcd. for C$_{22}$H$_{30}$ClNO$_3$P$^+$ (M + H$^+$) m/z 412.0864, found 412.0864.


Colorless crystals, 56 mg, 12%. M.p. 119–120 °C. R$_f$ = 0.18 (PE/EtOAc = 1/1, v/v). $^1$H NMR (400 MHz, CDCl$_3$): 7.57 (dt, J = 8.2, 1.6 Hz, 1H), 7.46 (d, J = 2.0 Hz, 2H), 7.33–7.27 (m, 3H), 7.25–7.15 (m, 2H), 7.02 (td, J = 7.6, 1.5 Hz, 1H), 6.88 (ddd, J = 8.3, 6.1, 2.5 Hz, 1H), 6.40 (d, J = 7.7 Hz, 1H), 6.05 (d, J = 20.6 Hz, 1H), 4.13–3.96 (m, 2H), 3.14 (dd, J = 20.0, 16.0 Hz, 1H), 3.08 (dd, J = 20.0, 16.0 Hz, 1H), 1.28 (t, J = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$): 155.2, 151.0 (d, J = 4.4 Hz), 137.3 (d, J = 9.1 Hz), 132.0, 131.6 (d, J = 2.2 Hz), 131.5 (d, J = 10.0 Hz), 131.3 (d, J = 1.1 Hz), 130.9 (d, J = 9.7 Hz), 129.8, 129.6, 126.12, 126.10, 123.4, 122.8, 121.7, 121.5, 121.3 (d, J = 2.5 Hz), 64.9 (d, J = 4.3 Hz), 62.5 (d, J = 6.0 Hz), 29.8 (d, J = 113.2 Hz), 16.5 (d, J = 6.1 Hz). $^{31}$P NMR (162 MHz, CDCl$_3$): 23.92. HRMS (ESI) calcd. for C$_{22}$H$_{30}$BrNO$_3$P$^+$ (M + H$^+$) m/z 456.0359, found 456.0356.


Colorless crystals, 108 mg, 24%. M.p. 110–111 °C. R$_f$ = 0.36 (PE/EtOAc = 1/1, v/v). $^1$H NMR (400 MHz, CDCl$_3$): 7.61 (d, J = 8.1 Hz, 1H), 7.51 (dt, J = 8.3, 1.8 Hz, 2H), 7.37 (d, J = 2.1 Hz, 1H), 7.33–7.26 (m, 1H), 7.25–7.19 (m, 2H), 7.18–7.12 (m, 1H), 7.04–6.95 (m, 1H), 6.89 (td, J = 7.4, 1.6 Hz, 1H), 6.44 (d, J = 7.7 Hz, 1H), 6.09 (d, J = 22.5 Hz, 1H), 3.83–3.64 (m, 1H), 3.58–3.40 (m, 1H), 3.20 (ddd, J = 21.2, 16.1 Hz, 1H), 3.04 (ddd, J = 21.2, 16.1 Hz, 1H), 0.86 (t, J = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$): 155.2, 150.6 (d, J = 3.1 Hz), 136.8 (d, J = 8.0 Hz), 132.4 (d, J = 12.2 Hz), 131.8, 131.4 (d, J = 2.2 Hz), 131.2, 130.2, 130.0 (d, J = 8.0 Hz), 129.7, 127.9, 126.7, 126.5, 123.1, 122.8, 121.1 (d, J = 2.1 Hz), 121.0, 120.8, 64.4 (d, J = 3.5 Hz), 62.3 (d, J = 7.2 Hz), 30.1 (d, J = 119.7 Hz), 16.1 (d, J = 5.6 Hz). $^{31}$P NMR (162 MHz, CDCl$_3$): 23.18. HRMS (ESI) calcd. for C$_{22}$H$_{30}$BrNO$_3$P$^+$ (M + H$^+$) m/z 456.0359, found 456.0357.

rel-(4bR,15S)-15-Ethoxy-3-methyl-4b,16-dihydrodibenz[o,f]benzo[4,5][1,2]azaphosphinino [1,6-d][1,4]oxazepine 15-oxide (cis-3r).

Colorless crystals, 59 mg, 15%. M.p. 151–152 °C. R$_f$ = 0.21 (PE/EtOAc = 1/1, v/v). $^1$H NMR (400 MHz, CDCl$_3$): 7.30 (dt, J = 8.0, 1.3 Hz, 1H), 7.27–7.18 (m, 5H), 7.12 (td, J = 7.8, 1.6 Hz, 1H), 7.08 (s, 1H), 6.98 (ddd, J = 8.7, 7.4, 1.6 Hz, 1H), 6.83 (ddd, J = 7.8, 5.7, 2.8 Hz, 1H), 6.41–6.28 (m, 1H), 6.09 (d, J = 20.4 Hz, 1H), 3.99 (m, 2H), 3.09 (dt, J = 20.0, 15.6 Hz, 1H), 2.37 (s, 3H), 1.24 (t, J = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$): 155.3, 150.4 (d, J = 4.7 Hz), 137.4, 134.8 (d, J = 9.6 Hz), 131.6, 130.8, 129.8 (d, J = 10.1 Hz), 129.7, 129.4 (d, J = 2.4 Hz), 128.5 (d, J = 9.8 Hz), 126.2, 125.8 (d, J = 2.3 Hz), 123.1, 122.8, 121.6, 121.3, 65.2 (d, J = 4.0 Hz), 62.5 (d, J = 6.2 Hz), 29.7 (d, J = 113.1 Hz), 21.2, 16.5 (d, J = 6.0 Hz). $^{31}$P NMR (162 MHz, CDCl$_3$): 25.23. HRMS (ESI) calcd. for C$_{22}$H$_{30}$NO$_3$P$^+$ (M + H$^+$) m/z 392.1410, found 392.1413.

S13
rel-(4bR,15R)-15-Ethoxy-3-methyl-4b,16-dihydrodibenzo[bf]benzo[4,5][1,2]azaphosphinino [1,6-d][1,4]oxazepine 15-oxide (trans-3s).

Colorless crystals, 52 mg, 13%. M.p. 156–157 °C. Rf = 0.37 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.66 (dt, J = 8.0, 1.4 Hz, 1H), 7.31–7.28 (m, 1H), 7.27–7.19 (m, 4H), 7.18–7.13 (m, 1H), 7.01 (ddd, J = 15.2, 7.9, 1.6 Hz, 2H), 6.89 (td, J = 7.4, 1.6 Hz, 1H), 6.48 (dt, J = 7.7, 1.1 Hz, 1H), 6.13 (d, J = 22.2 Hz, 1H), 3.75 (ddq, J = 10.2, 9.2, 7.1 Hz, 1H), 3.49 (ddd, J = 10.1, 8.7, 7.0 Hz, 1H), 3.37–3.29 (m, 2H), 2.37 (s, 3H), 0.88 (t, J = 7.0 Hz, 3H). 31C NMR (101 MHz, CDCl3): 155.2, 150.4, 137.1, 134.4 (d, J = 8.3 Hz), 131.6 (d, J = 4.1 Hz), 130.7 (d, J = 12.1 Hz), 129.4 (d, J = 2.2 Hz), 129.2 (d, J = 2.2 Hz), 127.7 (d, J = 1.4 Hz), 127.5, 126.7, 126.3, 122.9, 122.7, 121.0, 120.6, 64.9 (d, J = 3.1 Hz), 62.0 (d, J = 7.0 Hz), 29.9 (d, J = 119.5 Hz), 21.1, 16.1 (d, J = 5.8 Hz). 31P NMR (162 MHz, CDCl3): 24.54. HRMS (ESI) calcd. for C23H23NO3P+ (M + H+) m/z 392.1410, found 392.1411.

2-Chloro-15-ethoxy-4b,16-dihydrodibenzo[bf]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (3t) and 4-chloro-15-ethoxy-4b,16-dihydrodibenzo[bf]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (3t’).

The reaction of dibenzoc[bf][1,4]oxazepine (2a) and ethyl 3-chlorobenzylphosphonochloridate (1f) generated two different regioisomers 3t and 3t’, of which each had trans- and cis-diastereomers. Their ratio was determined as 38:11:37:14 for trans-3t: cis-3t: trans-3t’: cis-3t from the reaction mixture by 31P NMR analysis. Pure cis-3t was not obtained due to its less amount and close polarity with trans-3t’. Only a mixture of cis-3t and trans-3t’ was obtained in a ratio of 1.00:0.79. The structures of trans-3t, cis-3t, trans-3t’, and cis-3t’ were determined on the basis of their 1H and 31P NMR spectral data on nOe experiments, especially the chemical shifts and coupling constants of their NCH group in 1H NMR spectra. For both trans-3t’ and cis-3t’, their NCH appeared at relatively lower field that those of trans-3t and cis-3t possible because close electronegative chlorine atom and steric hindrance exist. The steric hindrance changes the conformation of the bicyclic ring system, leading to NCH to locate in less shielding region.


Colorless crystals, 42 mg, 10%. M.p. 166–167 °C. Rf = 0.45 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.62 (dd, J = 8.0, 1.4 Hz, 1H), 7.35 (d, J = 2.0 Hz, 1H), 7.31–7.27 (m, 2H), 7.22 (dt, J = 8.1, 1.7 Hz, 2H), 7.15 (td, J = 7.9, 2.1 Hz, 2H), 6.99 (td, J = 7.6, 1.6 Hz, 1H), 6.88 (td, J = 7.4, 1.5 Hz, 1H), 6.43 (d, J = 7.7 Hz, 1H), 6.13 (d, J = 22.3 Hz, 1H), 3.74 (tq, J = 9.7, 7.0 Hz, 1H), 3.55–3.39 (m, 1H), 3.32–3.01 (m, 2H), 0.86 (d, J = 7.1 Hz, 3H). 13C NMR (101 MHz, CDCl3): 155.2, 150.6 (d, δ = 3.7 Hz), 134.5 (d, δ = 1.5 Hz), 133.3 (d, δ = 8.2 Hz), 132.8 (d, δ = 7.9 Hz), 131.3, 130.8 (d, δ = 12.5 Hz), 130.5, 129.8 (d, δ = 2.1 Hz), 129.6, 127.8, 127.4 (d, δ = 1.3 Hz), 126.6, 126.5, 123.1, 122.8, 121.0, 120.8, 64.4 (d, J = 3.5 Hz), 62.3 (d, J = 7.1 Hz), 30.3 (d, δ = 119.9 Hz), 16.1 (d, δ = 5.8 Hz). 31P NMR (162 MHz, CDCl3): 22.91. HRMS (ESI) calcd. for C22H23ClNO3P+ (M + H+) m/z 412.0864; found 412.0873. HRMS (ESI) calcd. for C22H23ClNO3P+ (M + H+) m/z 412.0864, found 412.0873.
rel-(4bR,15R)-4-Chloro-15-ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino [1,6-d][1,4]oxazepine (cis-3t)

Colorless crystals, 49 mg, 12%. M.p. 181–182 °C. Rf = 0.08 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3) 7.42 (dq, J = 8.1, 1.1 Hz, 1H), 7.40–7.34 (m, 1H), 7.34–7.26 (m, 2H), 7.25 (d, J = 1.5 Hz, 2H), 7.25–7.14 (m, 2H), 7.06–6.97 (m, 1H), 6.89–6.77 (m, 1H), 6.57 (d, J = 22.1 Hz, 1H), 6.35 (dq, J = 7.8, 1.0 Hz, 1H), 4.15–3.90 (m, 2H), 3.26–3.03 (m, 2H), 1.27 (t, J = 7.0 Hz, 3H).

13C NMR (101 MHz, CDCl3): 155.3, 151.6 (d, J = 4.0 Hz), 134.3 (d, J = 9.7 Hz), 133.9 (d, J = 8.2 Hz), 133.5 (d, J = 3.0 Hz), 131.4, 129.9, 129.7, 128.6, 128.4, 128.0, 127.1, 126.5 (d, J = 1.9 Hz), 125.7, 123.3, 122.7, 121.8, 121.6, 62.6 (d, J = 6.0 Hz), 62.2 (d, J = 3.9 Hz), 30.3 (d, J = 112.5 Hz), 16.5 (d, J = 6.0 Hz). 31P NMR (162 MHz, CDCl3): 24.30. HRMS (ESI) calcd. for C22H20ClN2OsP (M + H+) m/z 412.0864, found 412.0865.

rel-(4bR,15R)-4-Chloro-15-ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino [1,6-d][1,4]oxazepine (trans-3t)

Colorless crystals, 26 mg, 6%. M.p. 178–179 °C. Rf = 0.16 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3) 7.60 (dt, J = 7.9, 1.4 Hz, 1H), 7.39 (dq J = 8.1, 1.1 Hz, 1H), 7.33 (td, J = 7.7, 1.7 Hz, 1H), 7.30–7.22 (m, 3H), 7.19 (td, J = 7.7, 1.7 Hz, 1H), 7.01 (td, J = 7.7, 1.7 Hz, 1H), 6.87 (td, J = 7.4, 1.7 Hz, 1H), 6.87 (td, J = 7.4, 1.7 Hz, 1H), 6.56 (d, J = 24.1 Hz, 1H), 6.40 (dt, J = 7.7, 1.1 Hz, 1H), 3.77 (t, J = 9.7, 7.0 Hz, 1H), 3.53 (ddq, J = 10.1, 8.8, 7.0 Hz, 1H), 3.30–2.97 (m, 2H), 0.87 (t, J = 7.0 Hz, 3H). 13C NMR (101 MHz, CDCl3): 155.2, 151.2 (d, J = 3.5 Hz), 133.4 (d, J = 2.3 Hz), 133.4, 133.3 (d, J = 10.5 Hz), 131.3, 129.6 (d, J = 17.1 Hz), 129.4 (d, J = 11.7 Hz), 128.6, 128.4 (d, J = 1.6 Hz), 128.2 (d, J = 1.5 Hz), 127.0, 125.9, 123.0, 122.6, 121.0, 120.9, 62.3 (d, J = 7.2 Hz), 62.1 (d, J = 2.8 Hz), 30.5 (d, J = 119.3 Hz), 16.1 (d, J = 5.6 Hz). 31P NMR (162 MHz, CDCl3): 23.78. HRMS (ESI) calcd. for C22H20ClN2OsP (M + H+) m/z 412.0864, found 412.0865.

rel-(4bR,15R,16S)-15-Ethoxy-16-phenyl-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino [1,6-d][1,4]oxazepine (trans,cis-3u)

Although the reaction of ethyl diphenymethylphosphonochloridate (Ig) and dibenzo[b,f][1,4]oxazepine (2a) generated four pairs of possible diastereomeric products due to existence of 3 chiral centers in the products, only two pairs of diastereomeric products [rel-(4bR,15R,16S)-3u (trans,cis-3u) and rel-(4bR,15S,16S)-3u (cis,trans-3u)] predominantly formed in a ratio of 2:1 on the basis of the formation mechanism (phenyl always located on the equatorial position in the transition state TS1 in the proposed mechanism in Scheme 3).2c After silica gel column chromatography, only major diastereomer rel-(4bR,15R,16S)-3u (trans,cis-3u) was obtained in pure form.

Colorless crystals, 68 mg, 15%. M.p. 164–165 °C. Rf = 0.50 (PE/EtOAc = 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.40–7.34 (m, 4H), 7.34–7.27 (m, 4H), 7.25–7.23 (m, 1H), 7.23–7.17 (m, 2H), 7.15–7.09 (m, 2H), 7.07 (td, J = 8.0, 4.0 Hz, 1H), 6.93 (td, J = 7.5, 1.5 Hz, 1H), 6.88–6.82 (m, 1H), 6.59 (dd, J = 7.7, 1.5 Hz, 1H), 6.50 (d, J = 19.2 Hz, 1H), 4.41 (d, J = 19.2 Hz, 1H), 3.61 (m, 1H), 2.95 (m, 1H), 0.75 (t, J = 7.0 Hz, 3H). 13C NMR (101 MHz, CDCl3): 155.6, 150.0 (d, J = 3.9 Hz), 135.7
(d, $J = 7.3$ Hz), 133.1, 132.7 (d, $J = 8.2$ Hz), 131.8, 130.7, 130.6, 130.5, 129.3, 128.8 (d, $J = 1.7$ Hz), 128.60, 128.56, 127.6 (d, $J = 2.8$ Hz), 127.4, 127.1, 127.0, 125.7, 122.6, 122.6, 120.7 (d, $J = 14.6$ Hz), 64.2 (d, $J = 2.6$ Hz), 61.8 (d, $J = 7.3$ Hz), 46.4 (d, $J = 121.9$ Hz), 16.0 (d, $J = 6.1$ Hz). 31P NMR (162 MHz, CDCl3): 21.65. HRMS (ESI) calcd. for C28H25NO3P+ (M + H+) m/z 454.1567, found 454.1565.


![Diagram of the molecule](image)

This diastereomeric product could not be obtained as pure form (with some impurities, especially in upfield in its 1H NMR spectrum). Just showing its existence here.

Colorless crystals, 54 mg, 12%. $R_f = 0.10$ (PE/EtOAc= 1/1, v/v). 1H NMR (400 MHz, CDCl3): 7.49–7.26 (m, 8H), 7.26–7.11 (m, 4H), 7.14–6.95 (m, 3H), 6.92–6.81 (m, 1H), 6.40 (d, $J = 7.7$ Hz, 1H), 6.11 (d, $J = 21.8$ Hz, 1H), 4.45 (d, $J = 24.8$ Hz, 1H), 3.81 (m, 1H), 3.63 (m, 1H), 2.95 (m, 1H), 1.13 (t, $J = 7.1$ Hz, 3H). 31P NMR (162 MHz, CDCl3): 21.80. HRMS (ESI) calcd. for C28H25NO3P+ (M + H+) m/z 454.1567, found 454.1565

1.4. Large-scaled synthesis of δ-phosphonolactam 3a

Ethyl hydrogen 4-trifloromethylbenzylphosphonic acid (4.576 g, 16 mmol) and thionyl chloride (8 mL) were added in a predried 100 mL round-bottom flask under nitrogen atmosphere. The mixture was refluxed at 80°C in an oil bath for 12 h. After concentrated, the residue was repeated azeotrope with alcohol-free dry chloroform to give yellowish oily product ethyl benzylphosphonochloridate 1a.

The prepared ethyl 4-trifloromethylbenzylphosphonochloridate 1a was dissolved in toluene (16 mL). To the solution was added dibenzo[b,f][1,4]oxazepine (2a) (780 mg, 4 mmol). The resulting solution was stirred and cooled to -78°C under nitrogen atmosphere and was added dropwise a solution of 0.5 mol/L KHMDS in toluene (32 mL, 16 mmol). The mixture was kept stirring at the same temperature for 10 min. and then was heated to 80°C in an oil bath and stirred at 80°C for 24 h. After cooled to room temperature and quenched with saturated aqueous ammonium chloride solution (20 mL), the solution was extracted with dichloromethane (80 mL×3). The combined organic phase was dried over sodium sulfate and concentrated under rotovap. The residue was purified on silica gel column chromatography with a mixture of petroleum ether (PE) and ethyl acetate (EA) (PE:EA 2:1 to 1:2, v/v) as eluent to give diastereomeric δ-phosphonolactams trans-3a (1.012 g, 69%) and cis-3a (376 mg, 23%).

2. References


3 Copies of $^1$H, $^{13}$C, $^{19}$F, and $^{31}$P NMR spectra

3.1 Copies of NMR spectra of δ-phosphonolactams 3

rel-(4bR,15S)-15-Ethoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]aza-phosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3a)

$^1$H NMR Spectrum of product cis-3a

$^{31}$P NMR Spectrum of product cis-3a
$^{19}$F NMR Spectrum of product $cis$-$3a$

$^{13}$C NMR Spectrum of product $cis$-$3a$
rel-(4bR,15R)-15-Ethoxy-3-(trifluoromethyl)-4b,16-dihydrobienzo[b,f]benzo[4,5][1,2]aza-phosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3a)

$^{1}H$ NMR Spectrum of product *trans*-3a

$^{31}P$ NMR Spectrum of product *trans*-3a
$^{19}$F NMR Spectrum of product $trans$-$3a$

$^{13}$C NMR Spectrum of product $trans$-$3a$
rel-(4bR,15S)-15-Ethoxy-7-methyl-3-(trifluoromethyl)-4b,16-dihydropyreno[6,7]-
[1,2]azaphosphinino[6,7][1,4]oxazepine 15-oxide (cis-3b)

$^{1}$H NMR Spectrum of product cis-3b

$^{31}$P NMR Spectrum of product cis-3b
$^{19}$F NMR Spectrum of product $cis$-$3b$

$^{13}$C NMR Spectrum of product $cis$-$3b$
rel-(4bR,15R)-15-Ethoxy-7-methyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5] [1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3b)

$^{1}$H NMR Spectrum of product trans-3b

$^{31}$P NMR Spectrum of product trans-3b
$^{19}$F NMR Spectrum of product trans-3b

$^{13}$C NMR Spectrum of product trans-3b
rel-(4bR,15S)-7-Chloro-15-ethoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3c)

$^{1}$H NMR Spectrum of product cis-3c

$^{31}$P NMR Spectrum of product cis-3c
$^{19}$F NMR Spectrum of product cis-3c

$^{13}$C NMR Spectrum of product cis-3c
rel-(4bR,15R)-7-Chloro-15-ethoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3c)

$^1$H NMR Spectrum of product trans-3c

$^{31}$P NMR Spectrum of product trans-3c
$^{19}$F NMR Spectrum of product trans-3c
rel-(4bR,15R)-15-Ethoxy-3,6-di(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3d)

\[
\text{1H NMR Spectrum of product trans-3d}
\]

\[
\text{31P NMR Spectrum of product trans-3d}
\]
$^{19}$F NMR Spectrum of product trans-$3d$

$^{13}$C NMR Spectrum of product trans-$3d$
rel-(4bR,15S)-15-Ethoxy-13-methyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3e)

^1H NMR Spectrum of product cis-3e

^31P NMR Spectrum of product cis-3e
$^{19}$F NMR Spectrum of product cis-3e
rel-(4bR,15R)-15-Ethoxy-13-methyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3e)

\[\text{1H NMR Spectrum of product } \text{trans-3e} \]

\[\text{31P NMR Spectrum of product } \text{trans-3e} \]
$^{19}$F NMR Spectrum of product $trans$-3e

$^{13}$C NMR Spectrum of product $trans$-3e
rel-(4bR,15S)-15-Ethoxy-12-methyl-3-(trifluoromethyl)-4b,16-dihydropyrido[3,4-c][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3f)

\[ \text{cis-3f} \]

**\(^{1}\text{H NMR Spectrum of product cis-3f}\)**

**\(^{31}\text{P NMR Spectrum of product cis-3f}\)**
$^{19}$F NMR Spectrum of product cis-3f

$^{13}$C NMR Spectrum of product cis-3f
rel-(4bR,15R)-15-Ethoxy-12-methyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5] [1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3f)

$\text{H NMR Spectrum of product \textit{trans-3f}}$

$\text{P NMR Spectrum of product \textit{trans-3f}}$
$^{19}$F NMR Spectrum of product $trans$-$3f$

$^{13}$C NMR Spectrum of product $trans$-$3f$
rel-(4bR,15S)-15-Ethoxy-12-methoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3g)

$^{1}$H NMR Spectrum of product cis-3g

$^{31}$P NMR Spectrum of product cis-3g
NMR Spectrum of product cis-3g

$^{13}$C NMR Spectrum of product cis-3g
rel-(4R,15R)-15-Ethoxy-12-methoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3g)

$^{1}$H NMR Spectrum of product trans-3g

$^{31}$P NMR Spectrum of product trans-3g
$^{19}$F NMR Spectrum of product trans-3g

$^{13}$C NMR Spectrum of product trans-3g
rel-(4bR,15S)-12-Chloro-15-ethoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3h)

$^1$H NMR Spectrum of product cis-3h

$^{31}$P NMR Spectrum of product cis-3h
$^{19}$F NMR Spectrum of product cis-3h

$^{13}$C NMR Spectrum of product cis-3h
rel-(4bR,15R)-12-Chloro-15-ethoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3h)

\[ \text{Product trans-3h} \]

\( ^1H \text{ NMR Spectrum of product trans-3h} \)

\( ^3P \text{ NMR Spectrum of product trans-3h} \)
$^{19}$F NMR Spectrum of product trans-3h

$^{13}$C NMR Spectrum of product trans-3h
rel-(4bR,15S)-12-Bromo-15-ethoxy-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3i)

$^{1}H$ NMR Spectrum of product cis-3i

$^{31}P$ NMR Spectrum of product cis-3i
$^{19}$F NMR Spectrum of product cis-3i

$^{13}$C NMR Spectrum of product cis-3i
rel-(4bR,15R)-12-Bromo-15-ethoxy-3-(trifluoromethyl)-4b,16-dihydropbenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3i)

$^{1}$H NMR Spectrum of product trans-3i

$^{31}$P NMR Spectrum of product trans-3i
$^{19}$F NMR Spectrum of product \textit{trans}-3i

$^{13}$C NMR Spectrum of product \textit{trans}-3i
rel-(4bR,15S)-11-Chloro-15-ethoxy-3-(trifluoromethyl)-4b,16-dihydropbenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3k)

1H NMR Spectrum of product cis-3k

31P NMR Spectrum of product cis-3k
NMR Spectrum of product cis-3k

$^{19}\text{F}$

$^{13}\text{C}$ NMR Spectrum of product cis-3k
rel-(4bR,15R)-11-Chloro-15-ethoxy-3-(trifluoromethyl)-4b,16-dihydridibenzo[b,f]benzo[4,5][1,2]azaphosphino[1,6-d][1,4]oxazepine 15-oxide (trans-3k)

\[ \text{trans-3k} \]

$^{1}H$ NMR Spectrum of product \textit{trans-3k}

$^{31}P$ NMR Spectrum of product \textit{trans-3k}
$^{19}$F NMR Spectrum of product *trans*-3k

$^{13}$C NMR Spectrum of product *trans*-3k
rel-(4bR,15S)-7-Chloro-15-ethoxy-11-methyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5] [1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3l)

$^1$H NMR Spectrum of product cis-3l

$^{31}$P NMR Spectrum of product cis-3l
$^{19}$F NMR Spectrum of product *cis*-3I

$^{13}$C NMR Spectrum of product *cis*-3I
rel-(4bR,15R)-7-Chloro-15-ethoxy-11-methyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3l)

$^{1}$H NMR Spectrum of product trans-3l

$^{31}$P NMR Spectrum of product trans-3l
$^{19}$F NMR Spectrum of product $trans$-$3l$

$^{13}$C NMR Spectrum of product $trans$-$3l$
rel-(4bR,15S)-15-Ethoxy-7,11-dimethyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo
[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3m)

\[ \text{\^{1}H NMR Spectrum of product cis-3m} \]

\[ \text{\textsuperscript{31}P NMR Spectrum of product cis-3m} \]
19F NMR Spectrum of product cis-3m

13C NMR Spectrum of product cis-3m
rel-(4bR,15R)-15-Ethoxy-7,11-dimethyl-3-(trifluoromethyl)-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3m)

\[ \text{trans-3m} \]

\[ \text{1H NMR Spectrum of product trans-3m} \]

\[ \text{31P NMR Spectrum of product trans-3m} \]
$^{19}$F NMR Spectrum of product $trans\cdot 3m$

$^{13}$C NMR Spectrum of product $trans\cdot 3m$
$rel-(4bR,15S)-15$-Ethoxy-$4b,16$-dihydrodibenzo[$b,f$]benzo[$4,5$][1,2]azaphosphinino[1,6-$d$][1,4]oxazepine 15-oxide ($cis$-$3p$)

$^1$H NMR Spectrum of product $cis$-$3p$

$^{13}$C NMR Spectrum of product $cis$-$3p$
$^3$P NMR Spectrum of product cis-3p

rel-(4bR,15R)-15-Ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3p)

$^1$H NMR Spectrum of product trans-3p
$^{13}$C NMR Spectrum of product trans-3p

$^{31}$P NMR Spectrum of product trans-3p
rel-(4bR,15S)-3-Chloro-15-ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3q)

$\text{H NMR Spectrum of product } \text{cis-3q}$

$\text{C NMR Spectrum of product } \text{cis-3q}$
$^{31}$P NMR Spectrum of product cis-3q

rel-(4bR,15R)-3-Chloro-15-ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3q)

$^1$H NMR Spectrum of product trans-3q
$^{13}$C NMR Spectrum of product trans-3q

$^{31}$P NMR Spectrum of product trans-3q
rel-(4bR,15S)-3-Bromo-15-ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3r)

**1H NMR Spectrum of product cis-3r**

**13C NMR Spectrum of product cis-3r**
**31P NMR Spectrum of product cis-3r**

*rel-(4bR,15R)-3-Bromo-15-ethoxy-4b,16-dihydrodibenzo[bf]benzo[4,5][1,2]azaphosphinino [1,6-d][1,4]oxazepine 15-oxide (trans-3r)*

**1H NMR Spectrum of product trans-3r**
\textbf{13C NMR Spectrum of product trans-3r}

\textbf{31P NMR Spectrum of product trans-3r}
rel-(4bR,15S)-15-Ethoxy-3-methyl-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3s).

$^1$H NMR Spectrum of product trans-3s

$^{13}$C NMR Spectrum of product trans-3s
SPEX 

31P NMR Spectrum of product cis-3s

rel-(4bR,15R)-15-Ethoxy-3-methyl-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3s).

1H NMR Spectrum of product trans-3s
$^{13}$C NMR Spectrum of product trans-3s

$^{31}$P NMR Spectrum of product trans-3s
2-Chloro-15-ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (3t) and 4-chloro-15-ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (3t’).

$^{31}$P NMR Spectrum of the reaction mixture


$^1$H NMR Spectrum of product *trans*-3t
$^{13}$C NMR Spectrum of product trans-$3t$

$^{31}$P NMR Spectrum of product trans-$3t$
Mixture of rel-(4bR,15R)-2-chloro-15-ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphos-phinino[1,6-d][1,4]oxazepine 15-oxide (cis-3t) and rel-(4bR,15S)-4-chloro-15-ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphos-phinino[1,6-d][1,4]oxazepine 15-oxide (trans-3t'). (Note: Cannot be separated completely, only for verification of their existence)

1H NMR Spectrum of mixed products cis-3t and trans-3t' with inseparable impurities

13C NMR Spectrum of mixed products cis-3t and trans-3t' with inseparable impurities
$^{31}$P NMR Spectrum of mixed products cis-3t and trans-3't with inseparable impurities $rel$-(4bR,15S)-4-Chloro-15-ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis-3t').

$^{1}$H NMR Spectrum of product cis-3t'}
$^{13}$C NMR Spectrum of product cis-3't

$^{31}$P NMR Spectrum of product cis-3't
rel-(4bR,15R)-4-Chloro-15-ethoxy-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans-3t').

**1H NMR Spectrum of product trans-3t’**

**13C NMR Spectrum of product trans-3t’**
$^{31}$P NMR Spectrum of product trans-3t'

rel-(4bR,15R,16S)-15-ethoxy-16-phenyl-4b,16-dihydropodbenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (trans,cis-3u)

$^1$H NMR Spectrum of product trans,cis-3u
$^{13}$C NMR Spectrum of product trans,cis-3u

$^{31}$P NMR Spectrum of product trans,cis-3u
**rel-(4bR,15S,16S)-15-Ethoxy-16-phenyl-4b,16-dihydrodibenzo[b,f]benzo[4,5][1,2]azaphosphinino[1,6-d][1,4]oxazepine 15-oxide (cis,trans-3u)**

(***Note: Cannot be purified completely, only for verification of existence of cis,trans-3u***)

**1H NMR Spectrum of product cis,trans-3u**

**31P NMR Spectrum of product cis,trans-3u**
3.2 Copies of nOe NMR spectra

nOe spectrum of cis-3t

nOe spectrum of trans-3t
nOe spectrum of trans-3t

nOe spectrum of cis-3t'
nOe spectrum of trans-3t'
4. X-Ray Crystallographic Data of product 3a

Experimental

Single crystals of C_{23}H_{19}F_{3}NO_{3}P [3a] were recrystallized from a mixture of petroleum ether (60–90 °C fraction) and ethyl acetate. One crystal was mounted in inert oil and transferred to the cold gas stream of the diffractometer.

Crystal Structure Determination of 3a

Crystal Data. C_{23}H_{19}F_{3}NO_{3}P, M=445.36, monoclinic, a = 12.2468(5) Å, b = 10.0570(5) Å, c = 16.8219(9) Å, β = 102.021(4)°, V = 2026.46(17) Å³, T = 112.35(10), space group P2₁/n (no. 14), Z = 4, μ(Mo Kα) = 0.189, 8380 reflections measured, 3971 unique (R_{int} = 0.0292) which were used in all calculations. The final wR(F²) was 0.0981 (all data).

Figure S1. X-Ray Structure of 3a (50% probability)
Table S1: Crystal Data and Structure Refinement for 3a

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<td>μ / mm^{-1}</td>
<td>0.189</td>
</tr>
<tr>
<td>F(000)</td>
<td>920</td>
</tr>
<tr>
<td>Crystal size / mm³</td>
<td>0.39 × 0.34 × 0.33</td>
</tr>
<tr>
<td>2θ range for data collection</td>
<td>6.14 to 52°</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-15 ≤ h ≤ 14, -7 ≤ k ≤ 12, -14 ≤ l ≤ 20</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>8380</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>3971[R(int) = 0.0292 (inf-0.9Å)]</td>
</tr>
<tr>
<td>Data/restraints/parameters</td>
<td>3971/51/309</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.028</td>
</tr>
<tr>
<td>Final R indexes [I&gt;2σ (I) i.e. F_o&gt;4σ (F_o)]</td>
<td>R₁ = 0.0427, wR₂ = 0.0912</td>
</tr>
<tr>
<td>Final R indexes [all data]</td>
<td>R₁ = 0.0538, wR₂ = 0.0981</td>
</tr>
<tr>
<td>Largest diff. peak/hole / e Å^{-3}</td>
<td>0.451/-0.390</td>
</tr>
<tr>
<td>Flack Parameters</td>
<td>N</td>
</tr>
<tr>
<td>Completeness</td>
<td>0.9977</td>
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