EXPERIMENTAL SECTION

General Techniques: All reactions were carried out with dry, freshly distilled solvents under anhydrous conditions, unless otherwise stated. Tetrahydrofuran (THF) was distilled from sodium–benzophenone, and methylene chloride (CH₂Cl₂) was distilled from calcium hydride. Acetonitrile was distilled over CaH₂ and stored over 3Å molecular sieves. Yields refer to chromatographically and spectroscopically (¹H NMR) homogeneous materials, unless otherwise stated.

All reactions were monitored by thin–layer chromatography (TLC) carried out on 0.25–mm E. Merck silica gel plates (60F–254) using UV–light (254 nm). Merck silica gel (230–400 mesh) was used for flash chromatography.

NMR spectra were recorded on JEOL JNM-EX270 (270 MHz) or JEOL Eclipse FT (300 MHz) instruments and calibrated using a solvent peak as an internal reference. The following abbreviations are used to indicate the multiplicities; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra were obtained using Agilent 1100 via Electron Spray Ionisation geometry. IR spectra were recorded on a Perkin Elmer Spectrum One spectrophotometer and only typical absorptions were cited.

GENERAL PROCEDURE FOR THE IMINE-FORMATION:

To a stirred solution of indole-3-carbaldehyde (1 equiv.) in CH₂Cl₂ was added the respective amine (1 equiv.) and MgSO₄ (0.5 equiv.). The reaction mixture was refluxed. After filtration of the MgSO₄ and evaporation of the solvent, the imine was obtained with good yield (92-95 %). If necessary, crystallisation in ethanol is possible.

Compounds 5a, 5b have been described before in:


¹H-NMR (270 MHz, CDCl₃, ppm): δ = 4.84 (2H, s, NCH₂(Ph)), 7.14-7.47 (10H, m, C₃H, C₄H, C₅H, C₆H, C₇H, 5x CH(Ph)), 8.35 (1H, ~d, CH=N), 8.55 (1H, s, NH);

¹C-NMR (68 MHz, CDCl₃, ppm): δ = 65.23 (NCH₃(Ph)), 111.78 (C₄H), 114.99 (C₅), 121.49 (C₆H), 123.31 (C₇H), 125.60 (C₈H), 127.02 (2x CH(Ph)), 128.19 (CH(Ph)), 128.65 (2x CH(Ph)), 129.56 (2x CH=CH), 136.97 (C₇H), 140.33 (C₆H), 157.12 (CH=N); IR (KBr, cm⁻¹): 3413 (νNH); MS (70eV): m/z = 237 (MH⁺); Mp.: 141.1 °C.

¹H-NMR (300 MHz, CDCl₃, ppm): δ = 1.29 (6H, d, J = 6.3 Hz, 2x CH₃(iPr)), 3.50 (1H, sept, J = 6.3 Hz, CH(iPr)), 7.18-7.25 (2H, m, C₃H, C₄H), 7.37 (1H, ~d, J = 8.5 Hz, C₅H or C₆H), 7.51 (1H, s, C₇H), 8.30 (1H, d, J = 6.3 Hz, C₈H or C₉H), 8.54 (1H, s, (Ind)CH=N), NH not visible; ¹C-NMR (75.6 MHz, CDCl₃, ppm): 24.58 (2x CH₃(iPr)), 61.90 (CH(iPr)), 111.41 (C₃H or C₄H), 114.95 (C₅), 120.98 (C₆H or C₇H or C₈H), 121.06 (C₉H or C₃H or C₅H or C₆H), 122.98 (C₄H or C₈H), 125.90 (C₉H), 127.58 (C₃H), 136.60 (C₄H), 152.48 ((Ind)CH=N); IR (KBr, cm⁻¹): 1629 (νC=N), 1531, 1455, 1391, 1238; MS (ESI): m/z = 187 (M⁺+1); Mp.: 137.2 °C.
1H-NMR (270 MHz, CDCl₃, ppm): δ = 1.41 (6H, t, J = 7.1 Hz, P(O)OCH₂CH₃), 4.07 (2H, d, JHP = 17.2 Hz, NCH₂P₃), 4.28 (4H, m, P(O)OCH₂CH₃), 7.07 (1H, s, C₂H), 7.20 (2H, m, C₅H, C₆H), 7.42 (1H, dd, JHP = 6.8 Hz J = 1.5 Hz, C₇H), 8.09 (1H, d, J = 4.6 Hz, C₄H), 8.27 (1H, d, J = 7.6 Hz, CH=N), 10.00 (1H, s, NH); 13C-NMR (68 MHz, CDCl₃, ppm): δ = 16.56 (2C, JCP = 6.1 Hz, P(O)OCH₂C₃H), 58.26 (JCP = 153.8 Hz, NC₃H₂P), 62.86 (2C, JCP = 7.3 Hz, P(O)OCH₂C₃H), 111.82 (C₇H), 114.50 (d, JCP = 2.4 Hz C₃), 121.04 (C₄H), 121.69 (C₅H), 122.86 (C₆H), 125.19 (C₃a), 131.39 (C₂H), 137.18 (C₇a), 160.95 (JCP = 17.1 Hz CH=N); 31P-NMR (109 MHz, CDCl₃, ppm): δ = 24.38; IR (KBr, cm⁻¹): 3170 (νNH), 1629 (νC=N); MS (70eV): m/z = 294 (MH⁺); Mp.: 114.0 °C.

Preparation of 5d-5g.

To a stirred solution of indole-3-carbaldehyde (0.58 g, 1 equiv.) in acetonitrile (20 mL) was added diethyl amino(phenyl)methylphosphonate (0.98 g, 1 equiv.) and 0.24 g (0.5 equiv.) MgSO₄. The reaction mixture was refluxed for 4 days. After filtration of the MgSO₄ and evaporation of the solvent, diethyl (phenyl){[(E)-1H-indole-3-ylmethyliden]amino} methylphosphonate was obtained with a yield of 98 %. Crystallisation in ethanol afforded yellow crystals with 82% yield.

1H-NMR (270 MHz, CDCl₃, ppm): δ = 1.19 (3H, t, J = 6.4 Hz, P(O)OCH₂CH₃), 1.24 (3H, t, J = 6.9 Hz, P(O)OCH₂CH₃), 4.09 (4H, m, P(O)OCH₂CH₃), 4.83 (1H, d, JHP = 17.8 Hz, NCH₂P₃), 7.09 (1H, s, C₂H), 7.17-7.33 (6H, m, C₅H, C₆H, C₇H, C₃H(Ph), C₄H(Ph), C₅H(Ph)), 7.68 (2H, d, J = 6.9 Hz, C₇H(Ph), C₇H(Ph)), 8.27 (1H, d, J = 4.3 Hz, CH=N), 8.47 (1H, d, J = 7.3 Hz, C₆H), 10.70 (1H, s, NH); 13C-NMR (68 MHz, CDCl₃, ppm): δ = 16.37 (2C, JCP = 6.1 Hz, P(O)OCH₂C₃H), 63.34 (JCP = 7.4 Hz, P(O)OC₃H₂), 74.28 (JCP = 152.6 Hz, NC₃H₂P), 111.97 (C₇H), 114.63 (C₃), 115.11 (2C, d, JCF = 21.4 Hz, C₇H(Ph)), 121.20 (C₄H), 121.90 (C₅H), 122.87 (C₆H), 125.28 (C₇a), 127.53 (JCP = 2.5 Hz, CH(Ph)), 128.24 (2C, JCP = 4.9 Hz, CH(Ph)), 128.44 (2C, JCP = 4.9 Hz, CH(Ph)), 131.68 (C₇H), 137.25 (d, JCP = 7.3 Hz, C₃H(Ph)), 137.36 (C₇a), 159.45 (JCP = 15.8 Hz, CH=N); 31P-NMR (109 MHz, CDCl₃, ppm): δ = 21.59; IR (KBr, cm⁻¹): 3206 (νNH), 1629 (νC=N); MS (70eV): m/z = 371 (MH⁺); Mp.: 130.1 °C.

1H-NMR (270 MHz, CDCl₃, ppm): δ = 1.27 (3H, t, J = 6.9 Hz, P(O)OCH₂CH₃), 1.31 (3H, t, J = 7.1 Hz, P(O)OCH₂CH₃), 4.15 (4H, m, P(O)OCH₂CH₃), 4.81 (1H, d, JHP = 17.5 Hz, NCH₂P₃), 7.06 (3H, m, C₅H, 2x CH(Ph)), 7.24 (2H, m, C₅H, C₆H), 7.42 (1H, d, J = 6.4 Hz, J = 2.8 Hz, C₇H), 7.64 (2H, m, 2x CH(Ph)), 8.26 (1H, d, J = 4.6 Hz, CH=N), 8.43 (1H, d, J = 6.1 Hz, J = 2.8 Hz, C₅H), 10.17 (1H, s, NH); 13C-NMR (68 MHz, CDCl₃, ppm): δ = 16.48 (2C, JCP = 6.1 Hz, P(O)OCH₂CH₃), 63.09 (JCP = 7.4 Hz, P(O)OCH₂CH₃), 64.01 (JCP = 7.3 Hz, P(O)OCH₂CH₃), 73.70 (JCP = 152.6 Hz, NC₃H₂P), 111.88 (C₇H), 114.63 (JCP = 2.5 Hz, C₃), 115.11 (2C, d, JCP = 21.4 Hz, CH(Ph)), 121.20 (C₄H), 121.90 (C₅H), 122.98 (C₆H), 125.28 (C₇a), 129.88 (2C, t, JCF = 6.7 Hz, CH(Ph)), 131.53 (C₇H), 133.14 (dd, J = 7.3 Hz, J = 3.7 Hz, C₃H(Ph)), 137.25 (C₇a), 159.37 (JCP = 15.9 Hz, CH=N), 162.22 (dd, JCP = 245.4 Hz, JCF = 3.7 Hz, CF); 31P-NMR (109 MHz, CDCl₃, ppm): δ = 20.43; IR (KBr, cm⁻¹): 3178 (νNH), 1629 (νC=N); MS (70eV): m/z = 388 (MH⁺); Mp.: 125.8 °C.

114.0 °C.
Summary

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GENERAL PROCEDURE FOR THE AMINE-FORMATION:

The imine 5 from the previous section was dissolved in absolute ethanol and 1 equiv. NaBH₄ was added. After stirring at room temperature 24 h, the mixture was quenched by the addition of 0.2 M NaOH and stirred for 10 minutes. Next, the mixture was poured in dichloromethane and washed three times with 0.2 M NaOH. After filtration of the MgSO₄ and evaporation of the solvent, the amine was obtained in good yields.

1H-NMR (270 MHz, CDCl₃, ppm): δ = 1.80 (1H, bs, NH), 3.87 (2H, s, (NCH₂)₂(Ph)), 7.05 (1H, s, C₂H), 7.11-7.32 (8H, m, C₄H, C₅H, C₆H, 5x C(CH₂)), 7.63 (1H, d, J = 7.4 Hz, C₇H), 8.34 (1H, bs, NH(Ind)); 13C-NMR (68 MHz, CDCl₃, ppm): δ = 44.34 (NC₃H₂(Ph)), 53.65 ((Ind)C₂H₂N), 111.63 (C₇H), 114.39 (C₃), 118.92 (C₄H), 119.57 (C₅H), 122.13 (C₆H), 123.21 (C₇H), 127.26 (C₃a), 128.44 (CH(Ph)), 128.53 (2C, 2x CH(Ph)), 28.72 (2C, 2x CH(Ph)), 136.61 (C₇a), 140.41 (C₉a(Ph)); IR (KBr, cm⁻¹): 3413 (νNH); MS (70eV): m/z = 237 (MH⁺); Mp.: 152.7 °C.

1H-NMR (270 MHz, CDCl₃, ppm): δ = 1.80 (1H, bs, NH), 3.87 (2H, s, (NCH₂)₂(Ph)), 7.05 (1H, s, C₂H), 7.11-7.32 (8H, m, C₄H, C₅H, C₆H, 5x C(CH₂)), 7.63 (1H, d, J = 7.4 Hz, C₇H), 8.34 (1H, bs, NH(Ind)); 13C-NMR (68 MHz, CDCl₃, ppm): δ = 44.34 (NC₃H₂(Ph)), 53.65 ((Ind)C₂H₂N), 111.63 (C₇H), 114.39 (C₃), 118.92 (C₄H), 119.57 (C₅H), 122.13 (C₆H), 123.21 (C₇H), 127.26 (C₃a), 128.44 (CH(Ph)), 128.53 (2C, 2x CH(Ph)), 28.72 (2C, 2x CH(Ph)), 136.61 (C₇a), 140.41 (C₉a(Ph)); IR (KBr, cm⁻¹): 3413 (νNH); MS (70eV): m/z = 237 (MH⁺); Mp.: 152.7 °C.

Preparation of 6d-6g.

To a stirred solution of diëthyl (phenyl){[(E)-1H-indole-3-ylmethylideen] amino} methylphosphonate 5d in ethanol (10 ml) was added at 0°C 0.12 g (3.3 equiv.) NaBH₄. After 5 days at room temperature the reaction mixture was quenched with 10 ml of 0.2 M NaOH. The reaction mixture was poured in CH₂Cl₂ (30 ml).The organic phase was washed three times with 30 ml 0.2 M NaOH and dried over anhydrous MgSO₄. After filtration and evaporation of the solvent the crude residue was further purified by flash chromatography (EtOAc/PE/triethylamine: 89/10/1, Rf= 0.20, yield= 42%).
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\[ \delta = 1.12 (3H, t, J = 7.0 \text{ Hz}, \text{P(O)OCH}_2\text{CH}_3), 1.24 (3H, t, J = 7.0 \text{ Hz}, \text{P(O)OCH}_2\text{CH}_3), 2.37 (1H, s, \text{NH}), 3.76 (1H, d, J = 12.3 \text{ Hz}, \text{Ind})\text{CH}_2\text{N}), 4.04 (1H, d, J = 12.3 \text{ Hz}, \text{Ind})\text{CH}_2\text{N}), 4.21 (1H, d, J = 2.2 \text{ Hz}, \text{C}_5\text{H}), 7.10 (1H, d, d, J = 7.4 \text{ Hz}, \text{C}_5\text{H}), 7.17 (1H, d, d, d, J = 7.4 \text{ Hz}, \text{C}_5\text{H}), 7.38 (4H, m, \text{C}_7\text{H}), 7.52 (2H, m, 2x \text{CH}(\text{Ph})), 7.62 (1H, d, J = 7.7 \text{ Hz}, \text{C}_6\text{H}), 9.29 (1H, s, \text{NH}(\text{Ind})); \]

\[ \delta = 24.66; \text{IR (KBr, cm}^{-1}) : 3256 (\nu \text{NH}), 1225 (\nu \text{P=O}); \text{MS (70eV)} : m/z = 391 (\text{MH}^+), \text{Rf (ethylacetate/petrolether 9/1)} = 0.20. \]

1H-NMR (300 MHz, CDCl₃, ppm): δ = 1.14 (3H, t, J = 7.2 Hz, \text{P(O)OCH}_2\text{CH}_3), 1.22 (3H, t, J = 7.2 Hz, \text{P(O)OCH}_2\text{CH}_3), 2.15 (1H, s, \text{NH}), 3.71 (1H, d, J = 13.2 Hz, \text{Ind})\text{CH}_2\text{N}), 3.94 (4H, m, \text{P(O)OCH}_2\text{CH}_3), 3.95 (1H, d, J = 13.2 Hz, \text{Ind})\text{CH}_2\text{N}), 4.11 (1H, d, J = 19.8 Hz, \text{NCH}), 6.93 (1H, d, J = 1.9 Hz, \text{C}_7\text{H}), 7.09 (1H, d, d, J = 7.4 Hz, \text{C}_5\text{H}), 7.18 (1H, d, d, J = 7.4 Hz, \text{C}_6\text{H}), 7.40 (5H, m, \text{C}_7\text{H}), 7.58 (1H, d, J = 7.7 Hz, \text{C}_6\text{H}), 8.67 (1H, s, \text{NH}(\text{Ind})); 13C-NMR (68 MHz, CDCl₃, ppm): δ = 16.42 (2C, t, J = 7.5 Hz, \text{P(O)OCH}_2\text{CH}_3), 42.67 (J_Cp = 17.9 Hz, \text{Ind})\text{CH}_2\text{N}), 59.13 (J_Cp = 152.9 Hz, \text{NCH}), 63.00 (J_Cp = 6.3 Hz, \text{P(O)OCH}_2\text{CH}_3), 61.44 (J_Cp = 6.3 Hz, \text{P(O)OCH}_2\text{CH}_3), 119.04 (J_Cp = 6.3 Hz, \text{P(O)OCH}_2\text{CH}_3), 119.47 (J_Cp = 6.3 Hz, \text{P(O)OCH}_2\text{CH}_3), 121.91 (J_Cp = 6.3 Hz, \text{P(O)OCH}_2\text{CH}_3), 122.14 (J_Cp = 6.3 Hz, \text{P(O)OCH}_2\text{CH}_3), 123.33 (J_Cp = 6.3 Hz, \text{P(O)OCH}_2\text{CH}_3), 127.07 (J_Cp = 6.3 Hz, \text{P(O)OCH}_2\text{CH}_3), 130.55 (J_Cp = 5.2 Hz, \text{P(O)OCH}_2\text{CH}_3), 131.68 (2x \text{CH}(\text{Ph})), 135.11 (J_Cp = 6.3 Hz, \text{P(O)OCH}_2\text{CH}_3), 135.62 (J_Cp = 6.3 Hz, \text{P(O)OCH}_2\text{CH}_3); 31P-NMR (109 MHz, CDCl₃, ppm): δ = 23.74; \text{IR (KBr, cm}^{-1}) : 1225 (\nu \text{P=O}), 3256 (\nu \text{NH}); \text{MS (70eV)} : m/z = 453 (\text{MH}^+), \text{Rf (ethylacetate/petrolether 9/1)} = 0.20. \]
**1H-NMR (270 MHz, CDCl<sub>3</sub>, ppm):** δ = 1.22 (3H, t, J = 7.2 Hz, P(O)OCH<sub>2</sub>CH<sub>3</sub>), 1.26 (3H, t, J = 7.2 Hz, P(O)OCH<sub>2</sub>CH<sub>3</sub>), 2.31 (1H, s, NH<sub>2</sub>), 3.72 (1H, d, J<sub>AB</sub> = 13.2 Hz, (Ind)CH<sub>2</sub>N), 3.82 (3H, s, OCH<sub>3</sub>), 4.00 (1H, d, J<sub>AB</sub> = 13.5 Hz, (Ind)CH<sub>2</sub>N), 4.02 (4H, m, P(O)OCH<sub>2</sub>CH<sub>3</sub>), 4.10 (1H, d, J<sub>HP</sub> = 19.3 Hz, NCH(P)), 6.92 (2H, d, J = 8.5 Hz, CH(Ph)), 6.97 (1H, d, J = 2.2 Hz, C<sub>6</sub>H), 7.08 (1H, d, J = 7.4 Hz, J<sub>1</sub> = J<sub>2</sub> = 1 Hz, C<sub>5</sub>H), 7.18 (1H, d, J<sub>1</sub> = J<sub>2</sub> = 7.5 Hz, J = 1.2 Hz, C<sub>7</sub>H), 7.34 (1H, d, J = 8.0 Hz, C<sub>2</sub>H), 7.39 (2H, dd, J<sub>HP</sub> = 8.8 Hz, J = 2.2 Hz, 2x CH(Ph)), 7.59 (1H, d, J = 8.0 Hz, C<sub>3</sub>H), 8.80 (1H, s, NH(Ind));

**13C-NMR (68 MHz, CDCl<sub>3</sub>, ppm):** δ = 16.38 (d, J<sub>CP</sub> = 5.8 Hz, P(O)OCH<sub>2</sub>CH<sub>3</sub>), 16.51 (d, J<sub>CP</sub> = 5.8 Hz, P(O)OCH<sub>2</sub>CH<sub>3</sub>), 42.52 (J<sub>CP</sub> = 18.5 Hz, (Ind)CH<sub>2</sub>N), 55.36 (OCH<sub>3</sub>), 58.99 (J<sub>CP</sub> = 154.6 Hz, NCH(P)), 62.83 (J<sub>CP</sub> = 6.9 Hz, P(O)OCH<sub>2</sub>CH<sub>3</sub>), 63.02 (J<sub>CP</sub> = 6.3 Hz, P(O)OCH<sub>2</sub>CH<sub>3</sub>), 111.41 (C<sub>7</sub>H), 113.61 (C<sub>5</sub>H), 114.00 (2x CH(Ph)), 119.08 (C<sub>3</sub>H), 119.31 (C<sub>6</sub>H), 121.98 (C<sub>2</sub>H), 123.34 (C<sub>3</sub>H), 127.15 (C<sub>3a</sub>), 127.73 (C<sub>q</sub>(Ph)), 129.97 (2C, J<sub>CP</sub> = 5.8 Hz, 2x CH(Ph)), 136.64 (C<sub>7a</sub>), 159.40 (C(Ph)OMe);

**31P-NMR (109 MHz, CDCl<sub>3</sub>, ppm):** δ = 24.91; IR (NaCl, cm<sup>-1</sup>): 1248 (ν<sub>P=O</sub>), 3247 (ν<sub>NH</sub>);

**MS (70eV):** m/z = 403 (MH<sup>+</sup>), Rf (ethyl acetate/petroleum ether 7/3) = 0.27.

### Summary

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GENERAL PROCEDURE FOR THE ACYLATION:

To a stirred solution of the respective amine 6 and 2 equiv. of pyridine, 2 equiv. trichloroacetyl chloride was added dropwise at 0°C and under nitrogen atmosphere. The reaction mixture was carefully protected from the light and stirred for 24 to 48 h at room temperature under a nitrogen atmosphere. The reaction mixture was poured in 1M NaOH and extracted three times with CH₂Cl₂. The combined organic fractions were dried over MgSO₄. The crude mixture was further purified through filtration over a small (5 cm) silica column using petroleum ether/ethyl acetate.

Because of the photo lability of the compound, it is important to protect the compound as much as possible from the light.

The spectrum shows the existence of 2 rotamers. The mixture consist of 66 % rotamer ‘A’ and 33 % rotamer ‘B’.

1H-NMR (300 MHz, CDCl₃, ppm): δ = 4.62 (2H, s, NCH₂(Ph), rot B), 4.77 (2H, s, (Ind)CH₂N, rot A), 4.87 (2H, s, NCH₂(Ph), rot A), 5.08 (2H, s, (Ind)CH₂N, rot B), 7.07 (1H, s, C₆H, rot A), 7.10 (1H, s, C₆H, rot B), 7.13-7.50 (8H (rot A), 8H (rot B), m, C₆H, C₅H or C₄H, 5x CH(Ph), rot A, rot B), 7.60 (2H, ~d, J = 14.31 Hz, C₄H or C₇H, rot A, rot B), 8.36 (1H, bs, NH, rot A), 8.48 (1H, bs, NH, rot B);

13C-NMR (75.4 MHz, CDCl₃, ppm): δ = 42.21 ((Ind)C₆H₂N, rot A), 45.46 ((Ind)C₆H₂N, rot B), 50.04 (NC₃H₂(Ph)), rot B), 51.57 (NC₃H₂(Ph)), rot A), 93.68 (CCl₃, rot A, rot B), 110.05 (C₃, rot B), 106.06 (C₃, rot A), 111.57 (C₆H or C₇H, rot A), 111.58 (C₆H or C₇H, rot B), 119.09 (C₆H or C₇H, rot B), 120.22 (C₆H or C₇H, rot A, rot B), 122.59 (C₆H or C₇H, rot A, rot B), 123.57 (C₅H, rot B), 125.10 (C₄H, rot A), 127.03 (C₅₇H, 127.27 (2C, 2x CH(Ph)), 127.98 (2C, 2x CH(Ph)), 135.51 (C₅₆H, rot B), 136.31 (C₇₇H, rot A), 136.32 (C₇₇H, rot B), 161.32 (C=O, rot A, rot B); IR (KBr, cm⁻¹): 3350 (νNH), 1655 (νNC=O), 1496, 1457, 1432; MS (ESI): m/z = 130 (Ind-CH₂⁺);

Mp.: 116.7 °C.

1H-NMR (300 MHz, CDCl₃, ppm): δ = 1.31 (6H, d, J = 6.6 Hz, 2x CH₃(iPr)), 4.72 (2H, s, (Ind)CH₂N), 4.80-5.00 (1H, m, CH(iPr)), 7.13-7.23 (3H, m, C₂H, C₅H, C₆H), 7.37 (1H, d, J = 7.7 Hz, C₇H or C₄H), 7.64 (1H, d, J = 8.3 Hz, C₆H or C₇H), 8.09 (1H, bs, NH(Ind)); 13C-NMR (75.4 MHz, CDCl₃, ppm): 20.46 (2x C₃H₃(iPr)), 38.70 ((Ind)C₆H₂N), 50.83 ((CH(iPr)), 93.99 (C₈C), 111.38 (C₆H or C₇H), 112.56 (C₇₇C), 118.28 (C₄H or C₇H), 119.56, 121.99, 123.21 (C₂H, C₅H, C₆H), 126.18 (C₃₇C or C₅₇C), 135.76 (C₃₇C or C₇₇C), 160.47 (C=O); IR (KBr, cm⁻¹): 3394 (νNH), 1663 (νNC=O), MS (ESI): m/z = 131 (Ind-CH₂⁺ +1); Mp.: 141.8 °C.

1H-NMR (270 MHz, CDCl₃, ppm): δ = 1.26 (3H, t, J = 7.1 Hz, P(O)OCH₂CH₃), 1.32 (3H, t, J = 6.9 Hz, P(O)OCH₂CH₃), 3.86 (2H, d, J₈P = 11.2 Hz, NCH₂P), 4.15 (4H, m, P(O)OCH₂CH₃), 5.35 (2H, s, (Ind)CH₂N), 7.12 (1H, dxd, J₁ = J₂ = 7.3 Hz, C₅H), 7.22 (2H, s, C₆H, C₇H), 7.41 (1H, d, J = 7.9 Hz, C₅H), 7.64 (1H, d, J = 7.9 Hz, C₆H), 9.06 (1H, s, NH(Ind)); 31P-NMR (109 MHz, CDCl₃, ppm): δ = 22.00; IR (NaCl, cm⁻¹): 1225 (νP=O), 3247 (νNH), 1676 (νC=O); MS (70eV): m/z = 130.1 (Ind-CH₂⁺).
Preparation of 7d.

To a stirred solution of 0.6 g diethyl (phenyl)[(1H-indole-3-ylmethyl)amino]methylphosphonate 6d and pyridine (0.28 g, 2 equiv.) in 10 ml THF, was added trichloroacetyl chloride (0.64 g, 2 equiv.) dropwise at 0°C and under a nitrogen atmosphere. The reaction mixture was carefully protected from the light and stirred for exactly 6 hours at room temperature under a nitrogen atmosphere. An excess of Et₂O was added to the reaction mixture and stirred for 10 minutes at 0°C. The salts were filtered over celite and washed with Et₂O. The organic layer was washed three times with water (50 ml), dried over MgSO₄, filtered, and concentrated under reduced pressure to afford (63 %) as a bright yellow oil. The residue has a purity > 95 %. Because of the photolability it is important to protect the reaction mixture as much as possible from the light.

\[ \text{1H-NMR (300 MHz, CDCl₃, ppm):} \]
\[ \delta = 1.08 (3H, t, J = 7.0 Hz, P(O)OCH₂CH₃), 1.20 (3H, t, J = 7.2 Hz, P(O)OCH₂CH₃), 3.74-3.90 (2H, m, P(O)OCH₂CH₃), 4.27 (2H, q, J = 7.2 Hz, P(O)OCH₂CH₃), 4.72 (1H, d, JAB = 16.5 Hz, (Ind)CH₂N), 4.89 (1H, d, JH-P = 25.6 Hz, NCHP), 5.58 (1H, dxd, JAB = 16.5 Hz, J₂ = 5.6 Hz, (Ind)CH₂N), 7.10 (1H, dxd, J₁ = J₂ = 7.2 Hz, C₅H or C₆H), 7.20 (1H, dxd, J₁ = J₂ = 7.2 Hz, C₅H or C₆H), 7.25-7.39 (5H, m, 5x CH(Ph)), 7.45 (2H, ~ t, C₅H, C₆H), 7.59 (1H, s, C₂H), 9.62 (1H, bs, NH(ind)); \]

\[ \text{13C-NMR (75.4 MHz, CDCl₃, ppm):} \]
\[ \text{δ = 16.23 (JCP = 6.9 Hz, P(O)OCH₂CH₃), 16.48 (JCP = 5.8 Hz, P(O)OCH₂CH₃), 47.68 ((Ind)CH₂N), 61.77 (JCP = 7.1 Hz, P(O)OCH₂CH₃), 62.18 (JCP = 159.2 Hz, NCHP), 64.52 (JCP = 7.1 Hz, P(O)OCH₂CH₃), 93.04 (CCl₃), 108.79 (C₅), 111.95 (C₆H or C₅H), 118.02 (C₆H or C₅H), 119.70 (C₆H or C₅H), 122.25 (C₆H or C₅H), 126.58 (C₆H), 128.29 (CH(Ph)), 128.55 (CH(Ph)), 128.63 (CH(Ph)), 128.68 (2C, 2x CH(Ph)), 133.54 (C₅H₄(Ph)), 136.52 (C₅a), 161.53 (C=O); \]

\[ \text{31P-NMR (121.4 MHz, CDCl₃, ppm):} \]
\[ \text{δ = 20.76; IR (NaCl, cm⁻¹):} \]
\[ \text{3224(νNH), 2930, 1684(νNC-O), 1246 (νP=O), 1029 (νP-O); MS (ESI):} m/z = 130 (Ind-CH₂⁺). \]

Summary

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<td>7d</td>
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GENERAL PROCEDURE FOR THE HALOGEN TRANSFER RADICAL CYCLIZATION:

A mixture of the trichloroacetyl amino-derivative 7 (1 equiv.) and TMEDA (0.8 equiv.) was dissolved in CH$_2$Cl$_2$ and flushed with argon for 15 minutes. Cu(I)Cl (0.4 equiv.) was added and the reaction mixture was stirred for 24 hours at room temperature under argon atmosphere and finally quenched with water and stirred for 10 minutes. The organic phase was washed with water until the blue colour of the wash water disappeared. After drying over MgSO$_4$, filtration and evaporation of the solvent, the spiro compound was obtained. By adding chloroform/diethylether or ethanol it was sometimes possible to obtain the compound as an amorph (more pure) precipitate.

$^1$H-NMR (300 MHz, CDCl$_3$, ppm): $\delta = 3.45$ (1H, d, $J_{AB} = 10.5$ Hz, (Ind)CH$_2$N), 3.49 (1H, d, $J_{AB} = 10.5$ Hz, (Ind)CH$_2$N), 4.59 (1H, d, $J_{AB} = 14.6$ Hz, NCH$_3$(Ph)), 4.71 (1H, d, $J_{AB} = 14.6$ Hz, NCH$_3$(Ph)), 7.10-7.46 (8H, m, C$_5$H, C$_6$H, C$_4$H or C$_7$H, 5x CH$_2$Ph)), 7.62 (1H, dxd, $J_1 = 8.1$ Hz, $J_2 = 1.1$ Hz, C$_6$H or C$_5$H)), 7.98 (1H, s, C$_5$H$_2$N); $^13$C-NMR (75.4 MHz, CDCl$_3$, ppm): $\delta = 48.09$ ((Ind)C$_2$H$_2$N), 48.38 (NCH$_2$(Ph)), 67.77 (C$_3$), 84.14 (C$_{Cl2}$), 122.15 (C$_5$H or C$_7$H), {124.35, 127.31, 128.75, 130.61 (C$_5$H, C$_6$H, C$_{Ph}$, C$_5$H or C$_7$H)), 128.61 (2C, 2x CH$_2$(Ph)), 129.33 (2C, 2x CH$_2$(Ph)), 133.76 (C$_3$a), 134.22 (C$_{quat}$(Ph)), 133.76 (C$_3$a), 155.76 (C$_7$a), 165.68 (C$_2$=O), 169.01 (C$_2$H); IR (NaCl, cm$^{-1}$): 3339(ν$\text{N=C(Ind)}$), 1725 (ν$\text{NC=O}$), 1478, 1457, 1428; MS (ESI): m/z = 345/47/49 (M$^+$+1).

$^1$H-NMR (300 MHz, CDCl$_3$, ppm): 1.25 (3H, d, $J = 4.4$ Hz, CH$_3$(iPr)), 1.27 (3H, d, $J = 4.4$ Hz, CH$_3$(iPr)), 3.52 (1H, d, $J_{AB} = 9.9$ Hz, (Ind)CH$_2$N)), 3.62 (1H, d, $J_{AB} = 10.2$ Hz, (Ind)CH$_2$N)), 4.53 (1H, sept, $J = 6.7$ Hz, CH$_2$(iPr)), 7.32  (1H, dxd, $J_1 = J_2 = 7.6$ Hz, $J_3 = 0.8$ Hz, C$_5$H or C$_6$H), 7.50 (1H, dxdxd, $J_1 = J_2 = 7.4$ Hz, $J_3 = 1.2$ Hz, C$_5$H or C$_6$H), 7.53 (1H, d, $J = 7.4$ Hz, C$_6$H or C$_5$H), 7.70 (1H, d, $J = 7.7$ Hz, C$_6$H or C$_5$H), 8.12 (1H, s, C$_7$H); $^13$C-NMR (75.6 MHz, CDCl$_3$, ppm): 19.34 (C$_3$H$_3$(iPr)), 19.41 (C$_3$H$_3$(iPr)), 44.06  ((Ind)C$_2$H$_2$N), 44.93 (CH$_3$(iPr)), 67.68 (C$_3$), 84.49 (C$_{Cl2}$), 122.18 (C$_5$H or C$_7$H), 123.96 (C$_5$H or C$_7$H), 127.24 (C$_6$H or C$_7$H), 130.47 (C$_5$H or C$_6$H), 134.30 (C$_3$a), 155.76 (C$_3$a), 164.85 (C$_2$=O), 169.06 (C$_2$H); IR (NaCl, cm$^{-1}$): 3342 (ν$\text{N=C(Ind)}$), 1724 (ν$\text{NC=O}$); MS (ESI): m/z = 297/299/301 (M$^+$+1).

$^1$H-NMR (300 MHz, CDCl$_3$, ppm): 1.31 (3H, t, $J = 6.9$ Hz, P(O)OCH$_2$CH$_3$), 1.34 (3H, t, $J = 6.9$ Hz, P(O)OCH$_2$CH$_3$), 3.81 (2H, s, (Ind)CH$_2$N), 3.83 (1H, dd, $J_{HP} = 15.8$ Hz, $J = 11.1$ Hz, NCH$_3$P), 3.94 (1H, dd, $J_{HP} = 11.7$ Hz, $J = 11.1$ Hz, NCH$_3$P), 4.17 (4H, m, P(O)OCH$_2$CH$_3$), 7.32 (1H, dxd, $J_1 = J_2 = 7.6$ Hz, C$_7$H), 7.48 (1H, dxdxd, $J_1 = J_2 = 7.7$ Hz, $J_3 = 1.1$ Hz, C$_6$H), 7.58 (1H, d, $J = 7.4$ Hz, C$_6$H), 7.68 (1H, d, $J = 7.4$ Hz, C$_6$H), 8.12 (1H, s, C$_7$H); $^{31}$P-NMR (109 MHz, CDCl$_3$, ppm): $\delta = 19.81$; IR (NaCl, cm$^{-1}$): 1243 (v$_{P=O}$), 1735 (v$_{NC=O}$), 3247 (v$_{NH}$); MS (70eV): m/z = 409.
**1H-NMR (300 MHz, CDCl₃, ppm):** 1.13-1.43 (6H, m, P(O)OCH₂CH₃), 3.49 (1H, ~t, (Ind)CH₂N), 3.96-4.31 (5H, m, (Ind)CH₂N, P(O)OCH₂CH₃), 5.79 (1H, d, JₜP = 20.4 Hz, NCH₃, M), 5.80 (1H, d, JₜH-P = 20.9 Hz, NCH₃, M), 7.11-7.72 (9H, C₄H, C₅H, C₆H, C₇H, 5x CH(Ph)), 8.16 (1H, s, C₇H, M), 8.48 (1H, ~dxd, C₂H, M);

**13C-NMR (75.4 MHz, CDCl₃, ppm):** 16.18 (J CP = 5.8 Hz, P(O)OCH₂C₃H₃), 16.49 (J CP = 6.9 Hz, P(O)OCH₂C₃H₃), 46.55 ((Ind)C₆H₂N, m), 46.90 ((Ind)C₆H₂N, M), 53.29 (J CP= 158.1 Hz, NC₇H₂), 62.98 (J CP = 6.9 Hz, P(O)OC₂H₂CH₃, M), 63.07 (J CP = 6.9 Hz, P(O)OC₂H₂CH₃, m), 63.91 (J CP = 6.9 Hz, P(O)OC₂H₂CH₃, M), 64.01 (J CP = 6.9 Hz, P(O)OC₂H₂CH₃, m), 67.94 (C₃), 83.53 (CCl₃), {121.99, 124.02, 126.96, 130.39 (C₄H, C₅H, C₆H and C₇H)}, 129.43 (2C, 2x CH(Ph)), 129.78 (2C, 2x CH(Ph)), 129.89 (CH(Ph)), 133.28 (C₃a or C₆quat(Ph)), 136.93 (C₃a or C₆quat(Ph)), 155.80 (C₇a), 165.35 (C=O), 168.48 (C₅H, m), 168.79 (C₅H, M);

**31P-NMR (121.4 MHz, CDCl₃, ppm):** δ = 18.73 (M), 18.40 (m);

**IR (NaCl, cm⁻¹):** 3280 (ν NH), 2983, 1731 (ν NC=O), 1251 (ν P=O), 1029 (ν P-O);

**MS (ESI):** m/z = 480/83/85 (M+1+), 371.

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<th>Purity (%)</th>
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**GENERAL PROCEDURE FOR THE REDUCTION OF THE SPIRO-IMINE:**

To a mixture of the previous spiro-imine 10 and 1.1 equiv. of glacial acetic acid in methanol was added 1 equiv. of NaCNBH₃. The reaction mixture was stirred for 24 h at room temperature, poured in 0.2 M NaOH and extracted three times with dichloromethane. After drying over MgSO₄ the compound was obtained with moderate purity.

**1H-NMR (300 MHz, CDCl₃, ppm):** δ = 3.42 (1H, d, J AB = 9.8 Hz, C₇H₂), 3.50 (1H, d, J AB = 9.8 Hz, C₇H₂), 3.51 (1H, d, J AB = 10.5 Hz, (Ind)CH₃N), 3.80 (1H, bs, NH), 4.09 (1H, d, J AB = 10.5 Hz, (Ind)CH₂N), 4.39 (1H, d, J AB = 14.4 Hz, NCH₃(Ph)), 4.81 (1H, d, J AB = 14.4 Hz, NCH₃(Ph)), 6.46-6.69 (2H, m, C₅H, C₆H), 6.91 (1H, dxd, J₁ = 1.2 Hz, J₂ = 1.2 Hz, C₇H), 7.12 (1H, dxd, J₁ = J₂ = 7.6 Hz, J₃ = 1.1Hz, C₇H), 7.24-7.34 (5H, m, 5x CH(Ph));

**13C-NMR (75.4 MHz, CDCl₃, ppm):** δ = 48.23 (NCH₂(Ph)), 53.51 ((Ind)CH₂N), 56.07 (C₆H₂), 59.62 (C₅H), 88.99 (CCl₃), 110.83 (C₅H), 119.02 (C₇H), 123.80 (C₇H), 128.29 (C₃a), 128.44 (CH(Ph)), 128.58 (2C, 2x CH(Ph)), 129.13 (2C, 2x CH(Ph)), 130.02 (C₇H), 134.58 (C₆quat(Ph)), 136.93 (C₆quat(Ph)), 151.39 (C₃a), 166.57 (C=O);

**IR (NaCl, cm⁻¹):** 3348(ν NH), 1720 (ν NC=O), 1487, 145, 1428; **MS (ESI):** m/z = 480/83/85 (M+1+).
**1H-NMR (270 MHz, CDCl₃, ppm):** 1.21 (3H, t, J = 7.0 Hz, P(O)OCH₂CH₃), 1.33 (3H, t, J = 7.2 Hz, P(O)OCH₂CH₃), 3.58 (1H, d, J = 10.7 Hz, (Ind)CH₂N), 3.68 (1H, dd, Jₕp = 15.5 Hz, J = 10.9 Hz, NCH₂P), 3.69 (1H, d, J = 10.0 Hz, C₂H₂), 3.82 (1H, d, J = 10.2 Hz, C₂H₂), 3.91 (1H, dt, J = 10.7 Hz, (Ind)CH₂N), 4.07 (1H, dt, J = 10.7 Hz, (Ind)CH₂N), 4.11 (4H, m, P(O)OCH₂CH₃), 6.68 (2H, m, C₄H₄, C₆H₆), 6.98 (1H, dxd, J = 8.0 Hz, J = 1.1 Hz, C₇H), 7.12 (1H, dxdxd, J₁ = J₂ = 7.7 Hz, J₃ = 1.1 Hz, C₅H);

**13C-NMR (68 MHz, CDCl₃, ppm):** δ = 16.34 (JCP = 5.8 Hz, P(O)OCH₂C₃H₃), 16.53 (JCP = 5.8 Hz, P(O)OCH₂C₃H₃), 39.60 (JCP = 156.3 Hz, NC₂H₂P), 53.36 ((Ind)C₅H₂N), 57.56 (C₂H₂), 59.82 (C₃), 62.78 (JCP = 6.3 Hz, P(O)OCH₂CH₃), 63.10 (JCP = 5.8 Hz, P(O)OCH₂CH₃), 87.90 (CCl₂), 110.74 (C₄H), 119.05 (C₆H), 123.99 (C₇H), 128.14 (C₃a), 130.03 (C₅H), 151.26 (C₇a), 166.38 (C=O);

**31P-NMR (109 MHz, CDCl₃, ppm):** δ = 20.13;

**IR (NaCl, cm⁻¹):** 1730 (ν₁)=O), 3326 (ν₁=NH);

**MS (70eV):** m/z = 411.

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**Procedure for the synthesis of the Boc-derivate**

2 g (5.25 mmol) of 7a was dissolved together with 2.75 g (12.59 mmol, 2.4 equiv.) Boc₂O and 0.06 g (0.53 mmol, 0.1 equiv.) DMAP in acetonitrile. The reaction was stirred for 24 h at room temperature. The solvent was then concentrated in vacuo and the mixture was again dissolved in CH₂Cl₂. The organic layer was washed 2 times with 1M NaOH. After drying over MgSO₄ and evaporating the solvent, the crude mixture was further purified through filtration over a small silica column (5 cm) with ethylacetate/petroleum ether (3/7) as solvent. The compound was obtained as a yellow powder (95 %).

The spectrum shows the existence of 2 rotamers.

**1H-NMR (300 MHz, CDCl₃, ppm):** δ = 1.67 (9H, bs, C(CH₃)₃), 4.72 (2H, bs, (Ind)CH₂N), 4.94 (2H, ~ d, NCH₃(Ph)), 7.21-7.52 (9H, m, C₃H or C₇H, C₄H or C₅H, C₆H, 5x CH(Ph)), 8.13 (1H, d, J = 6.9 Hz, C₃H or C₇H);

**13C-NMR (75.4 MHz, CDCl₃, ppm):** δ = 28.08 (3C, C(CH₃)₃), 41.58 ((Ind)CH₂N), 4.94 (2H, ~ d, NCH₃(Ph)), 7.21-7.52 (9H, m, C₃H or C₇H, C₄H or C₅H, C₆H, 5x CH(Ph)), 8.13 (1H, d, J = 6.9 Hz, C₃H or C₇H);

**IR (KBr, cm⁻¹):** 3445, 1733 (ν₁=O(O)), 1674 (ν₁=O(CCl₃)), 1475, 1456, 1413, 1088; MS (70eV): m/z =100, 130 (Ind-CH₂⁺), 230 (Boc-Ind-CH₂⁺), 306; **Mp.:** 116.7 °C.

**Procedure for the synthesis of 1-[(4-methylphenyl)sulfonyl]-1H-indole-3-carbaldehyde**

To a solution of 10 g (68.87 mmol) indole-3-carbaldehyde in THF was added at 0°C 1.81 g (75.76 mmol, 1.1 equiv) NaH. The reaction mixture was stirred for 1 h at room temperature. Next 13.13 g (68.87 mmol, 1 equiv.) tosylchloride was added and the mixture was stirred for 24 h at room temperature. The mixture was quenched with an excess of water. Carefully stirring for 5 minutes afforded rose crystals. These crystals were filtrated and washed three times with 0.2M cold NaOH. After drying at high vacuum the compound was obtained with a yield of 68 %. If necessary recrystallisation is possible in THF/water.
Electronic Supplementary Material for PCCP
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1H-NMR (300 MHz, CDCl₃, ppm): 2.38 (3H, s, CH₃), 7.26-7.48 (4H, m, C₆H(Ts), C₅H(Ts), C₅H, C₆H), 7.84-7.87 (2H, m, C₆H(Ts), C₅H(Ts)), 7.93-7.97 (1H, m, C₆H or C₅H), 8.23 (1H, s, C₂H), 8.24-8.27 (1H, m, C₆H or C₅H), 10.10 (1H, s, (C=O)H); 13C-NMR (75.4 MHz, CDCl₃, ppm): δ = 21.77 (CH₃), 113.34 (C₆H or C₅H), 122.44 (C₅ or C₆), 122.69 (C₅ or C₆), 124.15 (C₅ or C₆), 124.46 (C₆ or C₅), 127.33 (2C, C₆H(Ts), C₅H(Ts)), 130.43 (2C, C₅H(Ts), C₆H(Ts)), 134.44 (C₅ or C₆), 135.52 (C₆), 136.32 (C₅ or C₆), 138.01 (C₆), 140.19 (C₄ or C₅), 143.85 (C₆), 154.27 (C₅ or C₆), 161.00 (C=O, rot A, rot B); IR (KBr, cm⁻¹): 1666 (νC=O(H)), 1539, 1447, 1377, 1175 (νSO₂); MS (ESI): m/z = 300(M+1⁻); Mp.: 107.2 °C.

Procedure for the synthesis of N-benzyl-[1-[(4-methylfenyl)sulfonyl]-1H-indole-3yl]metanamine via reductive amination.

The imine obtained according the general procedure was immediately reduced according the general procudere for reduction. Crystallisation in ethanol/0.2 M NaOH afforded yellow crystals in 36 % yield.

1H-NMR (300 MHz, CDCl₃, ppm): 1.65 (1H, bs, NH), 2.27 (3H, s, CH₃), 3.79 (2H, s, NCH₂(Ph)), 3.87 (2H, s, (Ind)CH₂N), 7.14 (2H, d, J = 8.0 Hz, C₆H(Ts), C₅H(Ts)), 7.38-7.32 (7H, m, C₆H, C₅H, 5x CH(Ph)), 7.49 (1H, s, C₂H), 7.53 (1H, d, J = 7.7 Hz, C₆H or C₅H), 7.73 (2H, d, J = 7.6 Hz, C₅H(Ts), C₆H(Ts)), 7.99 (1H, d, J = 8.3 Hz, C₆H or C₅H); 13C-NMR (75.4 MHz, CDCl₃, ppm): δ = 21.66 (CH₃), 43.95 ((Ind)CH₂N), 53.49 (NCH₂(Ph)), 113.81 (C₆H or C₅H), 119.99 (C₆H or C₅H), 121.74 (C₅), 123.28 (C₆H or C₅H), 123.89 (C₆H), 124.92 (C₆H or C₅H), 126.92 (2C, C₆H(Ts), C₅H(Ts)), 127.21 (CH(Ph)), 128.34 (2C, 2x CH(Ph)), 128.60 (2C, 2x CH(Ph)), 129.96 (2C, C₆H(Ts), C₅H(Ts)), 130.46 (C₅ or C₆), 134.17 (C₆ or C₅), 135.38 (C₆ or C₅), 135.62 (C₅ or C₆), 144.98 (C₅ or C₆), 149.98 (C₅ or C₆), 1597, 1449, 1374, 1176 (νSO₂); MS (ESI): m/z = 284(Ts-Ind-CH₂); Mp.: 93.7 °C.

The acylation was performed according the previous general procedure. Reaction time 24 h, yield: 64%. The spectrum shows the existance of 2 rotamers. The mixture consist of 66 % rotamer ‘A’ and 33 % rotamer ‘B’.

1H-NMR (300 MHz, CDCl₃, ppm): δ = 2.34 (6H, s, CH₃, rot A, rot B), 4.62 (2H, s, NCH₂(Ph), rot B), 4.69 (2H, s, (Ind)CH₂N, rot A), 4.83 (2H, s, NCH₂(Ph), rot A), 4.95 (2H, s, (Ind)CH₂N, rot B), 7.08-7.42 (22H, m, C₆H, C₅H or C₅H, C₆H, C₆H, 5x CH(Ph), {C₆H(Ts), C₅H(Ts) or C₅H(Ts), C₆H(Ts)}) or rot A, rot B), 7.74 (4H, d, J = 8.26 Hz, C₆H(Ts), C₅H(Ts) or C₅H(Ts), C₆H(Ts)), rot A, rot B), 8.0 (2H, d, J = 8.0 Hz, C₆H or C₅H, rot A, rot B); 13C-NMR (75.4 MHz, CDCl₃, ppm): δ = 21.53 (CH₃, rot A, rot B), 41.33 ((Ind)CH₂N, rot A), 44.74 ((Ind)CH₂N, rot B), 50.46 (NCH₂(Ph), rot A), 51.68 (NCH₂(Ph), rot A), 93.14 (C₆H, rot A, rot B), 113.86 (C₆H or C₅H, rot A), 113.93 (C₆H or C₅H, rot B), 116.70 (C₅), 119.40 (C₆H or C₅H, rot B), 119.78 (C₆H or C₅H, rot A), 123.54 (C₅H), {125.17, 125.95, 127.08, 128.09, 128.97, 129.51 (C₆H, C₅H, 2x CH(Ph), 2x CH(Ph), CH(Ph), C₅H(Ts), C₅H(Ts)) or rot A, rot B), 126.76 (C₆H(Ts), C₅H(Ts) or C₅H(Ts), C₆H(Ts), rot A, rot B), 129.89 (C₆H(Ts), C₅H(Ts) or C₅H(Ts), C₆H(Ts), rot A, rot B), 134.67, 134.96, 135.17 (C₅ or C₆, C₆ or C₅, C₅ or C₆, rot A, rot B), 145.16 (C₅ or C₆, rot A, rot B), 161.00 (C=O, rot A, rot B); IR (KBr, cm⁻¹): 3413, 1678 (νN=C=O), 1448, 1374, 1176 (νSO₂); MS (ESI): m/z = 284(Ts-Ind-CH₂); Mp.: 132.7 °C.
Reaction time: 24h, yield: 67 %.

1H-NMR (300 MHz, CDCl3, ppm): 1.28 (6H, d, J=6.6 Hz, 2x CH3(iPr)), 2.32 (3H, s, CH3(Ts)); 4.59 (2H, s, (Ind)CH2N), 4.94-4.95 (1H, m, CH(iPr)); 7.18 (2H, d, J = 8.3 Hz, C3H(Ts), C5H(Ts)), 7.26 (1H, dxdxd, J1 = J2 = 7.4 Hz, J3 = 1.1 Hz, C5H or C6H), 7.32 (1H, dxd, J1 = J2 = 7.4 Hz, C5H or C6H)), 7.42 (1H, s, C2H), 7.51 (1H, d, J = 8.0 Hz, C4H or C7H), 7.69 (2H, d, J = 8.3 Hz, Cl3H(Ts), C6H(Ts)), 7.98 (1H, d, J = 8.0 Hz, C7H or C4H); 13C-NMR (75.6 MHz, CDCl3, ppm): 20.37 (2xCH3(iPr)), 21.50 (CH3(Ts)), 38.34 ((Ind)CH2N), 50.92 (CH(iPr)), 93.65 (Cl3), 113.96 and 119.11 (C4H and C7H), 119.85 (C3), 123.38 (C5H or C6H), 124.08 (C2H), 124.92 (C5H or C6H), 126.71 (2C, C3H(Ts), C5H(Ts)), 129.52 (C3a or C7a), 129.81 (2C, C4H(Ts), C5H(Ts)), 134.95 (C3(Ts)), 135.11 (C3a or C7a), 144.91 (C4(Ts)), 145.48 (C7(Ts)); IR (KBr, cm−1): 3436, 1655 (νNC=O), 1374, 1169 (νS=O); MS (ESI): m/z = 469/471/473 ([M–Cl+OH]+1); Mp.: 158.7 °C.

Procedure for the preparation of 13a

A mixture of 0.35 g (0.66 mmol, 1 equiv.) 12a and 61.2 mg (0.53mmol, 0.8 equiv.) TMEDA was dissolved in refluxing CH2Cl2 and was flushed with argon for 15 minutes. 26.1 mg (0.26 mmol, 0.4 equiv.) Cu(I)Cl was added to the reaction mixture. The reaction mixture was refluxed for 6 h under argon atmosphere and finally quenched with water and stirred for 10 minutes. The organic phase was washed three times with water until the blue colour of the wash water disappeared. After drying over MgSO4, filtration and evaporation of the solvent the spiro compound was obtained. Crystallisation in chloroform/diethylether afforded the compound in 64 % yield.

1H-NMR (300 MHz, CDCl3, ppm): δ = 2.39 (3H, s, CH3), 3.58 (1H, d, JAB = 10.59 Hz, (Ind)CH2N), 3.86 (1H, d, JAB = 10.59 Hz, (Ind)CH2N), 4.58 (1H, d, JAB = 14.3 Hz, NCH2(Ph)), 4.70 (1H, d, JAB = 14.3 Hz, NCH2(Ph)), 6.74 (1H, d, J = 7.7 Hz, C4H or C7H), 6.92 (1H, dd, J1 = J2 = 7.7 Hz, C5H or C6H), 6.99 (1H, s, C2HCl), 7.26-7.44 (8H, m, C5H or C6H, 5x CH(Ph), 2x CH(Ts)), 7.49 (1H, d, J = 8.0 Hz, C4H or C7H), 7.88 (2H, d, J = 8.0 Hz, 2x CH(Ts)); 13C-NMR (75.4 MHz, CDCl3, ppm): δ = 21.74 (CH3), 48.30 (NCH2(Ph)), 50.78 ((Ind)CH2N), 62.75 (C3), 80.95 (C1HCl), 86.62 (C2H), 114.55 (C4H or C7H), 123.24 (C5H or C6H), 124.87 (C3H or C5H), 127.88 (C2H or C7H), 128.80 (CH(Ph)), 128.90 (C4H or C7H), 129.33 (C5H or C6H), 129.48 (C3a or C7a or C5a or C7a), 130.06 (C4H or C7H), 131.21 (C5H or C6H), 134.11 (C4a(Ts)), 135.42 (C3a or C7a or C5a or C7a or C5a(Ts)), 144.41 (C4(Ts)), 145.48 (C7(Ts)), 164.86 (C=O); IR (KBr, cm−1): 3432, 1725 (νNC=O), 1598, 1366, 1172 (νSO2); MS (ESI): m/z = 469/471/473 ([M–Cl+OH]+1); Mp./decomposition temperature: 207.2 °C.
Crystallisation in methanol; yield: 64 %. 1H-NMR (300 MHz, CDCl3, ppm): 1.26 (3H, d, J = 6.9 Hz, CH3(iPr)), 135 (3H, d, J = 6.9 Hz, CH3(iPr)), 2.39 (3H, s, CH3(Ts)), 3.70 (1H, d, JAB = 10.7 Hz, (Ind)CH2N), 3.88 (1H, d, JAB = 10.7 Hz, (Ind)CH2N), 4.49 (1H, sept, J = 6.9 Hz, CH3(iPr)), 7.03 (1H, s, C3H), 7.04-7.12 (2H, m, C3H or C5H and C6H or C7H), 7.30 (2H, d, J = 8.0 Hz, C6H(Ts), C7H(Ts)), 7.38 (1H, dxdxd, J1 = J2 = 6.9 Hz, J1 = 1.9 Hz, C6H or C7H), 7.56 (1H, d, J = 8.3 Hz, C6H or C7H), 7.90 (2H, d, J = 8.3 Hz, C6H(Ts), C7H(Ts)); 13C-NMR (75.6 MHz, CDCl3, ppm): 19.15 (CH3(iPr)), 19.50 (CH3(iPr)), 21.63 (CH3(Ts)), 45.04 (CH3(iPr)), 46.61 ((Ind)CH2N), 62.37 (C3), 81.16 (C3HCl), 87.23 (C3Cl), 114.59 (C6H or C7H), 123.32 and 124.85 (C6H or C7H and C6H or C7H), 127.81 (2C, C6H(Ts), C7H(Ts)), 129.47 (C3a or C3b), 129.99 (2C, C6H(Ts), C7H(Ts)), 131.20 (C6H or C7H), 135.38, 139.66 and 145.40 (Cquat(Ts), C3b and C3a, 164.30 (C=O); IR (KBr, cm−1): 1725 (ν(C=O)), 1366, 1169 (νSO2); MS (ESI): m/z = 469/471/473 ([M−Cl+OH]+1); Mp./decomposition temperature: 164.2 °C.

**GENERAL PROCEDURE FOR THE SYNTHESIS OF THE HEMI-AMINAL**

0.3 g of 13 was dissolved in CH2Cl2 together with 0.45 g silica. The mixture was stirred for 24 h at room temperature. The silica was filtered over celite and the solvent was concentrated in vacuo. The compound was obtained in 80 % yield.

1H-NMR (300 MHz, CDCl3, ppm): δ = 2.36 (3H, s, CH3), 3.35 (1H, d, JAB = 10.73 Hz, (Ind)CH2N), 3.50 (1H, d, J = 3.0 Hz, C3H2OH, D2O exchangeable), 3.99 (1H, d, JAB = 10.73 Hz, (Ind)CH2N), 4.54 (1H, d, JAB = 14.6 Hz, NCH2(Ph)), 4.66 (1H, d, JAB = 14.6 Hz, NCH2(Ph)), 6.06 (1H, d, J = 3.0 Hz, C3H2OH), 6.81 (1H, dxdxd, J1 = J2 = 7.7 Hz, J1 = 0.8 Hz, C6H or C7H), 6.89 (1H, dxdxd, J1 = J2 = 7.7 Hz, J1 = 0.8 Hz, C6H or C7H), 7.25-7.40 (8H, m, C6H or C7H, 5x CH(Ph), 2x CH(Ts)), 7.59 (1H, d, J = 8.0 Hz, C6H or C7H), 7.76 (2H, d, J = 8.2 Hz, 2x CH(Ts)); 13C-NMR (75.4 MHz, CDCl3, ppm): δ = 21.66 (CH3), 48.33 (NCH2(Ph)), 49.29 ((Ind)CH2N), 61.28 (C3), 87.40 (C3H2OH), 87.54 (C3Cl), 114.09 (C6H or C7H), 123.85 (C6H or C7H), 124.31 (C6H or C7H), 127.27 (2C, 2x CH(Ph) or 2x CH(Ts), 128.55 (CH(Ph)), 128.81 (2C, 2x CH(Ph) or 2x CH(Ts)), 129.16 (2C, 2x CH(Ph) or 2x CH(Ts)), 129.28 (Cquat(Ts)), 130.06 (2C, 2x CH(Ph) or 2x CH(Ts)), 130.83 (C3H or C3H, 134.11, 134.32, 135.49 (C3a, C3b, Cquat(Ph)), 145.10 (Cquat(Ts)), 165.16 (C=O); IR (KBr, cm−1): 3436 (νOH), 1716 (ν(C=O)), 1599, 1478, 1364, 1173 (νSO2); MS (ESI): m/z = 517/19/21 (M+1); Mp./decomposition temperature: 205.7 °C.