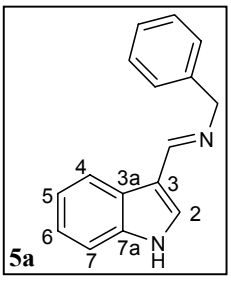
Electronic Supplementary Material for PCCP

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 (CH_2Cl_2) was distilled from calcium hydride. Acetonitrile was distilled over CaH_2 and stored over 3Å molecular sieves. Yields refer to chromatographically and spectroscopically (^{1}H 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.

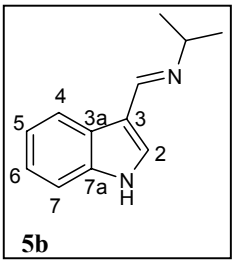
GENERAL PROCEDURE FOR THE IMINE-FORMATION:

To a stirred solution of indole-3-carbaldehyde (1 equiv.) in CH_2Cl_2 was added the respective amine (1 equiv.) and $MgSO_4$ (0.5 equiv.). The reaction mixture was refluxed. After filtration of the $MgSO_4$ 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 :
P. Kumar, C. Nath, K.P. Bhargava, K. Shanker, *Indian Journal of Chem.*, **1982**, *21B*, 1128.
A. Alemany, E. Fernandez Alvarez, J.M. Martinez-Lopez, *Bull. Soc. Chim. France,* **1975**, *5*-6, 1223.
Y. Shimoji, T. Hashimoto, Y. Furukawa, H. Yanagisawa, *Heterocycles*, **1993**, *36*, 123.



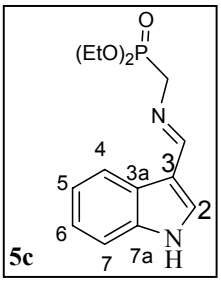
5a

^{1}H-NMR (270 MHz, $CDCl_3$, ppm): δ = 4.84 (2H, s, NC$\underline{H}_2$(Ph)), 7.14-7.47 (10H, m, $C_2\underline{H}$, $C_4\underline{H}$, $C_5\underline{H}$, $C_6\underline{H}$, $C_7\underline{H}$, 5x C$\underline{H}$(Ph)), 8.35 (1H, ~d, C$\underline{H}$=N), 8.55 (1H, s, N$\underline{H}$); **^{13}C-NMR (68 MHz, $CDCl_3$, ppm):** δ = 65.23 (N$\underline{C}H_2$(Ph)), 111.78 ($\underline{C}_7$H), 114.99 ($\underline{C}_3$), 121.49 ($\underline{C}_4$H), 123.31 ($\underline{C}_5$H), 125.60 ($\underline{C}_{3a}$), 127.02 ($\underline{C}_6$H), 128.02 (2x $\underline{C}$H(Ph)), 128.19 ($\underline{C}$H(Ph)), 128.65 (2x $\underline{C}$H(Ph)), 129.56 ($\underline{C}_{quat}$(Ph)), 136.97 ($\underline{C}_2$H), 140.33 ($\underline{C}_{7a}$), 157.12 ($\underline{C}$H=N); **IR (KBr, cm^{-1}):** 3413 (ν_{NH}); **MS (70eV):** m/z = 237 (MH^+); **Mp.:** 141.1 °C.



5b

^{1}H-NMR (300 MHz, $CDCl_3$, ppm): δ = 1.29 (6H, d, J = 6.3 Hz, 2x C$\underline{H}_3$(iPr)), 3.50 (1H, sept, J = 6.3 Hz, C$\underline{H}$(iPr)), 7.18-7.25 (2H, m, $C_5\underline{H}$, $C_6\underline{H}$), 7.37 (1H, ~d, J = 8.5 Hz, $C_4\underline{H}$ or $C_7\underline{H}$), 7.51 (1H, s, $C_2\underline{H}$), 8.30 (1H, d, J = 6.3 Hz, $C_4\underline{H}$ or $C_7\underline{H}$), 8.54 (1H, s, (Ind)C$\underline{H}$=N), N$\underline{H}$ not visible; **^{13}C-NMR (75,6 MHz, $CDCl_3$, ppm):** 24.58 (2x $\underline{C}H_3$(iPr)), 61.90 ($\underline{C}$H(iPr)), 111.41 ($\underline{C}_4$H or $\underline{C}_7$H), 114.95 ($\underline{C}_3$), 120.98 ($\underline{C}_4$H or $\underline{C}_7$H or $\underline{C}_5$H or $\underline{C}_6$H), 121.06 ($\underline{C}_4$H or $\underline{C}_7$H or $\underline{C}_5$H or $\underline{C}_6$H), 122.98 ($\underline{C}_5$H or $\underline{C}_6$H), 125.90 ($\underline{C}_{3a}$), 127.58 ($\underline{C}_2$H), 136.60 ($\underline{C}_{7a}$), 152.48 ((Ind)$\underline{C}$H=N); **IR (KBr, cm^{-1}):** 1629 ($\nu_{C=N}$), 1531, 1455, 1391, 1238; **MS (ESI): m/z =** 187 (M^++1); **Mp.:** 137.2 °C.

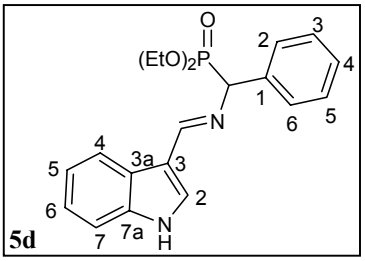


5c

^{1}H-NMR (270 MHz, $CDCl_3$, ppm): δ = 1.41 (6H, t, J = 7.1 Hz, P(O)OCH$_2$C<u>H</u>$_3$), 4.07 (2H, d, J_{HP} = 17.2 Hz, NC<u>H</u>$_2$P), 4.28 (4H, m, P(O)OC<u>H</u>$_2$CH$_3$), 7.07 (1H, s, C$_2$<u>H</u>), 7.20 (2H, m, C$_5$<u>H</u>, C$_6$<u>H</u>), 7.42 (1H, dd, J_{HP} = 6.8 Hz J = 1.5 Hz, C$_7$<u>H</u>), 8.09 (1H, d, J = 4.6 Hz, C$_4$<u>H</u>), 8.27 (1H, d, J = 7.6 Hz, CH=N), 10.00 (1H, s, N<u>H</u>);**^{13}C-NMR (68 MHz, $CDCl_3$, ppm):** δ = 16.56 (2C, J_{CP} = 6.1 Hz, P(O)OCH$_2$<u>C</u>H$_3$), 58.26 (J_{CP} = 153.8 Hz, N<u>C</u>H$_2$P), 62.86 (2C, J_{CP} = 7.3 Hz, P(O)O<u>C</u>H$_2$CH$_3$), 111.82 (<u>C</u>$_7$H), 114.50 (d, J_{CP} = 2.4 Hz <u>C</u>$_3$), 121.04 (<u>C</u>$_4$H), 121.69 (<u>C</u>$_5$H), 122.86 (<u>C</u>$_6$H), 125.19 (<u>C</u>$_{3a}$), 131.39 (<u>C</u>$_2$H), 137.18 (<u>C</u>$_{7a}$), 160.95 (J_{CP} = 17.1 Hz, <u>C</u>H=N); **^{31}P-NMR (109 MHz, $CDCl_3$, ppm):** δ = 24.38; **IR (KBr, cm^{-1}):** 3170 (ν_{NH}), 1629 ($\nu_{C=N}$); **MS (70eV):** m/z = 294 (MH^+); **Mp.:** 114.0 °C.

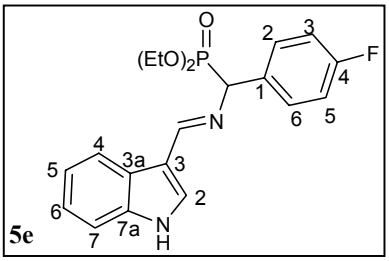
Preparation of 5d-5g.

To a stirred solution of indole-3-carbaldehyde (0.58 g, 1 equiv.) in acetonitrile (20 mL) was added diëthyl amino(phenyl)methylphosphonate (0.98 g, 1 equiv.) and 0.24 g (0.5 equiv.) $MgSO_4$. The reaction mixture was refluxed for 4 days. After filtration of the $MgSO_4$ and evaporation of the solvent, diëthyl (phenyl){[(E)-1H-indole-3-ylmethylideen]amino} methylphosphonate was obtained with a yield of 98 %. Crystallisation in ethanol afforded yellow crystals with 82% yield.



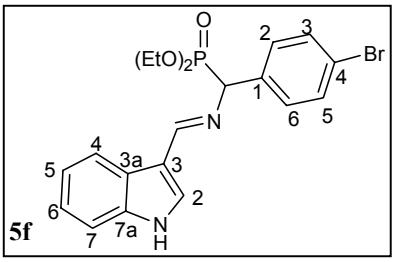
5d

^{1}H-NMR (270 MHz, $CDCl_3$, ppm): δ = 1.19 (3H, t, J = 6.4 Hz, P(O)OCH$_2$C<u>H</u>$_3$), 1.24 (3H, t, J = 6.9 Hz, P(O)OCH$_2$C<u>H</u>$_3$), 4.09 (4H, m, P(O)OC<u>H</u>$_2$CH$_3$), 4.83 (1H, d, J_{HP} = 17.8 Hz, NC<u>H</u>P), 7.09 (1H, s, C$_2$<u>H</u>), 7.17-7.33 (6H, m, C$_5$<u>H</u>, C$_6$<u>H</u>, C$_7$<u>H</u>, C$_3$<u>H</u>(Ph), C$_4$<u>H</u>(Ph), C$_5$<u>H</u>(Ph)), 7.68 (2H, d, J = 6.9 Hz, C$_2$<u>H</u>(Ph), C$_6$<u>H</u>(Ph)), 8.27 (1H, d, J = 4.3 Hz, C<u>H</u>=N), 8.47 (1H, d, J = 7.3 Hz, C$_4$<u>H</u>), 10.70 (1H, s, N<u>H</u>); **^{13}C-NMR (68 MHz, $CDCl_3$, ppm):** δ = 16.37 (2C, J_{CP} = 4.9 Hz, P(O)OCH$_2$<u>C</u>H$_3$), 63.34 (J_{CP} = 7.3 Hz, P(O)O<u>C</u>H$_2$CH$_3$), 63.52 (J_{CP} = 7.3 Hz, P(O)O<u>C</u>H$_2$CH$_3$), 74.28 (J_{CP} = 152.6 Hz, N<u>C</u>HP), 111.97 (<u>C</u>$_7$H), 114.63 (<u>C</u>$_3$), 121.11 (<u>C</u>$_5$H), 121.96 (<u>C</u>$_4$H), 122.87 (<u>C</u>$_6$H), 125.28 (<u>C</u>$_{3a}$), 127.53 (J_{CP} = 2.5 Hz, <u>C</u>H(Ph)), 128.24 (2C, J_{CP} = 4.9 Hz, <u>C</u>H(Ph)), 128.44 (2C, J_{CP} = 4.9 Hz, <u>C</u>H(Ph)), 131.68 (<u>C</u>$_2$H), 137.25 (d, J_{CP} = 7.3 Hz, <u>C</u>$_{quat}$(Ph)), 137.36 (<u>C</u>$_{7a}$), 159.45 (J_{CP} = 15.8 Hz, <u>C</u>H=N); **^{31}P-NMR (109 MHz, $CDCl_3$, ppm):** δ = 21.59; **IR (KBr, cm^{-1}):** 3206 (ν_{NH}), 1629 ($\nu_{C=N}$); **MS (70eV):** m/z = 371 (MH^+); **Mp.:** 130.1 °C.



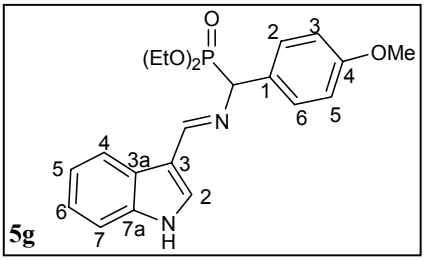
5e

^{1}H-NMR (270 MHz, $CDCl_3$, ppm): δ = 1.27 (3H, t, J = 6.9 Hz, P(O)OCH$_2$C<u>H</u>$_3$), 1.31 (3H, t, J = 7.1 Hz, P(O)OCH$_2$C<u>H</u>$_3$), 4.15 (4H, m, P(O)OC<u>H</u>$_2$CH$_3$), 4.81 (1H, d, J_{HP} = 17.5 Hz, NC<u>H</u>P), 7.06 (3H, m, C$_2$<u>H</u>, 2x C<u>H</u>(Ph)), 7.24 (2H, m, C$_5$<u>H</u>, C$_6$<u>H</u>), 7.42 (1H, dd, J = 6.4 Hz, J = 2.8 Hz, C$_7$<u>H</u>), 7.64 (2H, m, 2x C<u>H</u>(Ph)), 8.26 (1H, d, J_{HP}= 4.6 Hz, C<u>H</u>=N), 8.43 (1H, dd, J = 6.1 Hz, J = 2.8 Hz, C$_4$<u>H</u>), 10.17 (1H, s, N<u>H</u>);**^{13}C-NMR (68 MHz, $CDCl_3$, ppm):** δ = 16.48 (2C, J_{CP} = 6.1 Hz, P(O)OCH$_2$<u>C</u>H$_3$), 63.09 (J_{CP} = 7.4 Hz, P(O)O<u>C</u>H$_2$CH$_3$), 64.01 (J_{CP} = 7.3 Hz, P(O)O<u>C</u>H$_2$CH$_3$), 73.70 (J_{CP} = 152.6 Hz, N<u>C</u>HP), 111.88 (<u>C</u>$_7$H), 114.63 (J_{CP} = 2.5 Hz, <u>C</u>$_3$), 115.11 (2C, d, J_{CF} = 21.4 Hz, <u>C</u>H(Ph)), 121.20 (<u>C</u>$_5$H), 121.90 (<u>C</u>$_4$H), 122.98 (<u>C</u>$_6$H), 125.28 (<u>C</u>$_{3a}$), 129.88 (2C, t, J_{CF} = 6.7 Hz, <u>C</u>H(Ph)), 131.53 (<u>C</u>$_2$H), 133.14 (dd, J = 7.3 Hz, J = 3.7 Hz, <u>C</u>$_{quat}$(Ph)), 137.25 (<u>C</u>$_{7a}$), 159.37 (J_{CP} = 15.9 Hz, <u>C</u>H=N), 162.22 (dd, J_{CF} = 245.4 Hz, J_{CP} = 3.7 Hz, <u>C</u>F), **^{31}P-NMR (109 MHz, $CDCl_3$, ppm):** δ = 20.43; **IR (KBr, cm^{-1}):** 3178 (ν_{NH}), 1629 ($\nu_{C=N}$); **MS (70eV):** m/z = 388 (MH^+); **Mp.:** 125.8 °C.



5f

^{1}H-NMR (270 MHz, $CDCl_3$, ppm): δ = 1.28 (3H, t, J = 7.1 Hz, P(O)OCH$_2$C<u>H</u>$_3$), 1.32 (3H, t, J = 7.1 Hz, P(O)OCH$_2$C<u>H</u>$_3$), 4.16 (4H, m, P(O)OC<u>H</u>$_2$CH$_3$), 4.77 (1H, d, J_{HP} = 18.1 Hz, NC<u>H</u>P), 7.03 (1H, s, C$_2$<u>H</u>), 7.25 (2H, m, C$_5$<u>H</u>, C$_6$<u>H</u>), 7.49 (5H, m, C$_7$<u>H</u>, 4x C<u>H</u>(Ph)), 8.23 (1H, d, J = 4.6 Hz, C<u>H</u>=N), 8.43 (1H, m, C$_4$<u>H</u>), 10.10 (1H, s, N<u>H</u>);**^{13}C-NMR (68 MHz, $CDCl_3$, ppm):** δ = 16.48 (2C, t, J_{CP} = 6.1 Hz, P(O)OCH$_2$<u>C</u>H$_3$), 63.12 (J_{CP} = 8.6 Hz, P(O)O<u>C</u>H$_2$CH$_3$), 64.08 (J_{CP} = 7.4 Hz, P(O)O<u>C</u>H$_2$CH$_3$), 73.84 (J_{CP} = 153.8 Hz, N<u>C</u>HP), 111.88 (<u>C</u>$_7$H), 114.61 (J_{CP} = 2.4 Hz, <u>C</u>$_3$), 121.24 (<u>C</u>$_5$H), 121.40 (d, J_{CP} = 4.9 Hz, CBr), 121.92 (<u>C</u>$_4$H), 123.02 (<u>C</u>$_6$H), 125.25 (<u>C</u>$_{3a}$), 130.00 (2C, J_{CP} = 4.9 Hz, <u>C</u>H(Ph)), 131.33 (2C, J_{CP} = 3.7 Hz, <u>C</u>H(Ph)), 131.61 (<u>C</u>$_2$H), 136.54 (d, J = 8.5 Hz, <u>C</u>$_{quat}$(Ph)), 137.25 (<u>C</u>$_{7a}$), 159.53 (J_{CP} = 15.9 Hz, <u>C</u>H=N); **^{31}P-NMR (109 MHz, $CDCl_3$, ppm):** δ = 20.43; **IR (KBr, cm^{-1}):** 3435 (ν_{NH}), 1626 ($\nu_{C=N}$); **MS (70eV):** m/z = 451/449 (MH^+); **Mp.:** 171.1 °C.



5g

^{1}H-NMR (270 MHz, $CDCl_3$, ppm): δ = 1.29 (3H, t, J = 6.8 Hz, P(O)OCH$_2$C<u>H</u>$_3$), 1.33 (3H, t, J = 6.5 Hz, P(O)OCH$_2$C<u>H</u>$_3$), 3.80 (3H, s, OC<u>H</u>$_3$), 4.19 (4H, m, P(O)OC<u>H</u>$_2$CH$_3$), 4.81 (1H, d, J_{HP} = 17.1 Hz, NC<u>H</u>P), 6.92 (2H, d, J = 8.3 Hz, C<u>H</u>(Ph)), 7.02 (1H, s, C$_2$<u>H</u>), 7.24 (2H, m, C$_5$<u>H</u>, C$_6$<u>H</u>), 7.43 (1H, C$_7$<u>H</u>), 7.61 (2H, m, C<u>H</u>(Ph)), 8.23 (1H, t, J = 4.4 Hz, C<u>H</u>=N), 8.45 (1H, m, C$_4$<u>H</u>), 10.52 (1H, s, N<u>H</u>);**^{13}C-NMR (68 MHz, $CDCl_3$, ppm):** δ = 16.64 (2C, P(O)OCH$_2$<u>C</u>H$_3$), 55.36 (OC<u>H</u>$_3$) 63.31 (J_{CP} = 6.3 Hz, P(O)O<u>C</u>H$_2$CH$_3$), 63.95 (J_{CP} = 5.8 Hz, P(O)O<u>C</u>H$_2$CH$_3$), 73.81 (J_{CP} = 154.0 Hz, N<u>C</u>HP), 112.00 (<u>C</u>$_7$H), 113.86 (2C, <u>C</u>H(Ph)), 114.81 (<u>C</u>$_3$), 121.23 (<u>C</u>$_5$H), 122.06 (<u>C</u>$_4$H), 123.02 (<u>C</u>$_6$H), 125.44 (<u>C</u>$_{3a}$), 129.36 (<u>C</u>$_{7a}$), 159.13 (<u>C</u>OMe), 159.23 (J_{CP} = 16.2 Hz, <u>C</u>H=N); **^{31}P-NMR (109 MHz, $CDCl_3$, ppm):** δ = 21.90; **IR (KBr, cm^{-1}):** 3178 (ν_{NH}), 1629 ($\nu_{P=O}$); **MS (70eV):** m/z = 401.1 (MH^+); **Mp.:** 141.1 °C.

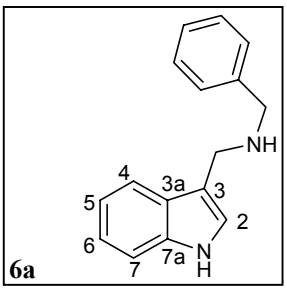
Summary

Compound	*Reaction Time (hours)*	*Yield (%)*
5a	20	95
5b	18	88
5c	7	66

Compound	*Reaction Time(days)*	*Yield (%)*
5d	4	82
5e	3	84
5f	5	56
5g	1	88

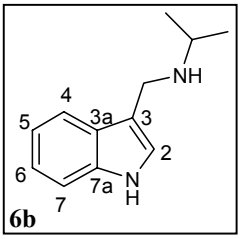
GENERAL PROCEDURE FOR THE AMINE-FORMATION:

The imine **5** from the previous section was dissolved in absolute ethanol and 1 equiv. $NaBH_4$ 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 $MgSO_4$ and evaporation of the solvent, the amine was obtained in good yields.



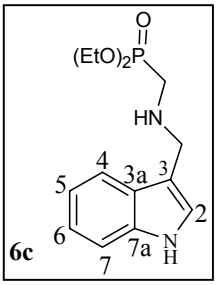
6a

^{1}H-NMR (270 MHz, $CDCl_3$, ppm): δ = 1.80 (1H, bs, NH), 3.87 (2H, s, (NCH_2(Ph)), 4.00 (2H, s, (Ind)CH_2N), 7.05 (1H, s, C_2H), 7.11-7.32 (8H, m, C_4H, C_5H, C_6H, 5x CH(Ph)), 7.63 (1H, d, J = 7.4 Hz, C_7H), 8.34 (1H, bs, NH(ind)); **^{13}C-NMR (68 MHz, $CDCl_3$, ppm):** δ = 44.34 (NCH_2(Ph)), 53.65 ((Ind)CH_2N), 111.63 (C_7H), 114.39 (C_3), 118.92 (C_4H), 119.57 (C_5H), 122.13 (C_6H), 123.21 (C_2H), 127.26 (C_{3a}), 128.44 (CH(Ph)), 128.53 (2C, 2x CH(Ph)), 28.72 (2C, 2x CH(Ph)), 136.61 (C_{7a}), 140.41 (C_{quat}(Ph)); **IR (KBr, cm^{-1}):** 3413 (ν_{NH}); **MS (70eV):** m/z = 237 (MH^+); **Mp.:** 152.7 °C.



6b

^{1}H-NMR (300 MHz, $CDCl_3$, ppm): 1.14 (6H, d, J = 6,3 Hz, 2x CH_3(iPr)), 1.86 (1H, bs, NH), 2.97 (1H, sept, J = 6.3 Hz, CH(iPr)), 3.98 (2H, s, (Ind)CH_2N), 6.97 (1H, s, C_2H), 7.11 (1H, dxd, $J_1 = J_2$ =7.4 Hz, C_5H or C_6H), 7.16 Hz (1H, ~t, $J_1 = J_2$ = 7.4 Hz, C_5H or C_6H), 7.26 (1H, d, J = 8.5 Hz, C_4H or C_7H), 7.62 (1H, d, J = 7.4 Hz, C_4H or C_7H), 8.98 (1H, bs, NH(Ind)); **^{13}C-NMR (75.6 MHz, CDCl3, ppm):** 22.83 (2x CH_3(iPr)), 42.31 ((Ind)CH_2N), 48.48 (CH(iPr)), 111.37 (C_4H or C_7H), 114.40 (C_3), 118.42 (C_4H or C_7H), 119.29 (C_5H or C_6H), 121.86 (C_5H or C_6H), 122.70 (C_2H), 126.96 (C_{3a} or C_{7a}), 136.36 (C_{3a} or C_{7a}); **IR (NaCl, cm-1):** 3412 (ν_{NH}), 1456, 1340; **MS (ESI):** m/z = 190 (M++1), 131 (Ind-CH_2^++1).

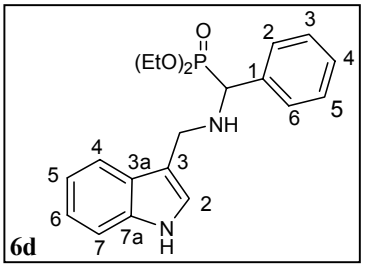


6c

^{1}H-NMR (270 MHz, $CDCl_3$, ppm): δ = 1.29 (6H, t, J = 6.9 Hz, P(O)OCH_2CH_3), 2.22 (1H, s, NH), 3.03 (2H, d, J_{HP} = 15.5 Hz, NCH_2P), 4.12 (6H, m, P(O)OCH_2CH_3, (Ind)CH_2N), 7.07 (1H, d, J = 2.0 Hz, C_2H), 7.14 (2H, m, C_5H, C_6H), 7.36 (1H, d, 7.9 Hz, C_7H), 7.66 (1H, d, J = 7.9 Hz, C_4H), 8.97 (1H, s, NH(Ind)); **^{13}C-NMR (68 MHz, $CDCl_3$, ppm):** δ = 16.44 (2C, J_{CP} = 4.9 Hz, P(O)OCH_2CH_3), 43.86 (J_{CP} = 153.8 Hz, NCH_2P), 45.81 (J_{CP} = 15.9 Hz, (Ind)CH_2N), 62.22 (2C, J_{CP} = 6.1 Hz, P(O)OCH_2CH_3), 111.41 (C_7H), 112.95 (C_3), 118.72 (C_4H), 119.33 (C_5H), 121.92 (C_6H), 123.50 (C_2H), 126.97 (C_{3a}), 136.53 (C_{7a}), **^{31}P-NMR (109 MHz, $CDCl_3$, ppm):** δ = 26.85; **IR (NaCl, cm^{-1}):** 1225 ($\nu_{P=O}$), 3245 (ν_{NH}) ; **MS (70eV):** m/z = 246 (MH^+).

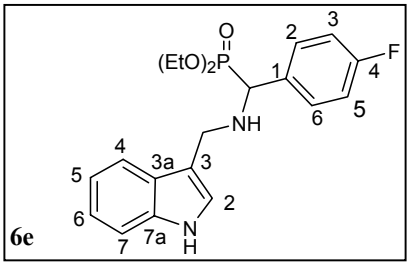
Preparation of 6d-6g.

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.) $NaBH_4$. 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 CH_2Cl_2 (30 ml).The organic phase was washed three times with 30 ml 0.2 M NaOH and dried over anhydrous $MgSO_4$. 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%).



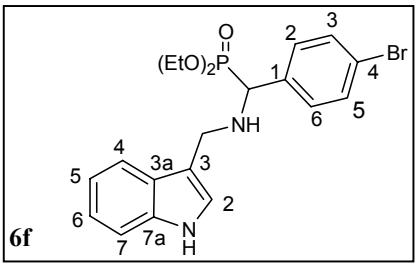
6d

^{1}H-NMR (300 MHz, $CDCl_3$, ppm): δ = 1.12 (3H, t, J = 7.0 Hz, P(O)OCH$_2$C$\underline{H}_3$), 1.24 (3H, t, J = 7.0 Hz, P(O)OCH$_2$C$\underline{H}_3$), 2.37 (1H, s, N$\underline{H}$), 3.76 (1H, d, J_{AB} = 13.2 Hz, (Ind)C$\underline{H}_2$N), 3.98 (4H, m, P(O)OC$\underline{H}_2$CH$_3$), 4.04 (1H, d, J_{AB} = 13.2 Hz, (Ind)C$\underline{H}_2$N), 4.21 (1H, d, J_{HP} = 19.8 Hz, NC$\underline{H}$P), 6.93 (1H, d, J = 2.2 Hz, C$_2\underline{H}$), 7.10 (1H, dxdxd, J_1 = J_2 = 7.4 Hz, J_3 = 1.0 Hz, C$_5\underline{H}$), 7.17 (1H, dxdxd, J_1 = J_2 = 7.5 Hz, J_3 = 1.2 Hz, C$_6\underline{H}$), 7.38 (4H, m, C$_7\underline{H}$, 3x C$\underline{H}$(Ph)), 7.52 (2H, m, 2x C$\underline{H}$(Ph)), 7.62 (1H, d, 7.7 Hz, C$_4\underline{H}$), 9.29 (1H, s, N$\underline{H}$(Ind)); **^{13}C-NMR (75.4 MHz, $CDCl_3$, ppm):** δ = 16.34 (J_{CP} = 5.2 Hz, P(O)OCH$_2\underline{C}$H$_3$), 16.51 (J_{CP} = 5.2 Hz, P(O)OCH$_2\underline{C}$H$_3$), 42.75 (J_{CP} = 18.5 Hz, (Ind)$\underline{C}$H$_2$N), 59.73 (J_{CP} = 153.4 Hz, N$\underline{C}$HP), 62.98 (J_{CP} = 6.3 Hz, P(O)O$\underline{C}$H$_2$CH$_3$), 63.20 (J_{CP} = 6.9 Hz, P(O)O$\underline{C}$H$_2$CH$_3$), 111.61 ($\underline{C}_7$H), 113.16 ($\underline{C}_3$), 119.00 ($\underline{C}_4$H), 119.21 ($\underline{C}_5$H), 121.86 ($\underline{C}_6$H), 123.65 ($\underline{C}_2$H), 127.16 ($\underline{C}_{3a}$), 128.08 ($\underline{C}_4$H(Ph)), 128.64 ($\underline{C}_3$H(Ph), $\underline{C}_5$H(Ph)), 128.93 (2C, J_{CP} = 5.2 Hz, $\underline{C}_2$H(Ph), $\underline{C}_6$H(Ph)), 135.94 ($\underline{C}_{7a}$), 136.79 ($\underline{C}_1$(Ph)); **^{31}P-NMR (121.4 MHz, $CDCl_3$, ppm):** δ = 24.66; **IR (NaCl, cm^{-1}):** 3409 (ν_{NH}), 3249 (ν_{NH}), 1230 ($\nu_{P=O}$); **MS (70eV):** m/z = 373 (MH^+).



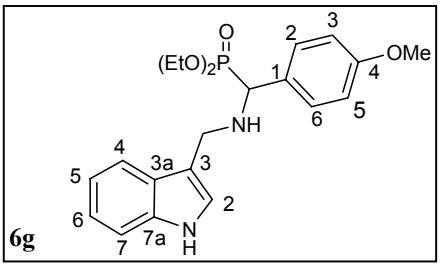
6e

^{1}H-NMR (270 MHz, $CDCl_3$, ppm): δ = 1.13 (3H, t, J = 7.0 Hz, P(O)OCH$_2$C$\underline{H}_3$), 1.23 (3H, t, J = 7.0 Hz, P(O)OCH$_2$C$\underline{H}_3$), 2.25 (1H, s, N$\underline{H}$), 3.72 (1H, d, J_{AB} = 13.2 Hz, (Ind)C$\underline{H}_2$N), 4.01 (4H, m, P(O)OC$\underline{H}_2$CH$_3$), 4.04 (1H, d, J_{AB} = 13.2 Hz, (Ind)C$\underline{H}_2$N), 4.15 (1H, d, J_{HP} = 19.3 Hz, NC$\underline{H}$P), 6.93 (1H, d, J = 2.2 Hz, C$_2\underline{H}$), 7.07 (3H, m, 2x C$\underline{H}$(Ph), C$_5\underline{H}$), 7.17 (1H, dxd, J_1 = J_2 = 7.0 Hz, C$_6\underline{H}$), 7.33 (1H, d, J = 8,3 Hz, C$_7\underline{H}$), 7.45 (2H, m, C$\underline{H}$(Ph)), 7.58 (1H, d, J = 7.7 Hz, C$_4\underline{H}$), 8.96 (1H, s, N$\underline{H}$(Ind)); **^{13}C-NMR (75.4 MHz, $CDCl_3$, ppm):** δ = 16.44 (2C, t, J_{CP} = 7.8 Hz, P(O)OCH$_2\underline{C}$H$_3$), 42.64 (J_{CP} = 17.9 Hz, (Ind)$\underline{C}$H$_2$N), 58.97 (J_{CP} = 154.0 Hz, N$\underline{C}$HP), 62.96 (J_{CP} = 6.3 Hz, P(O)O$\underline{C}$H$_2$CH$_3$), 63.14 (J_{CP} = 6.3 Hz, P(O)O$\underline{C}$H$_2$CH$_3$), 111.50 ($\underline{C}_7$H), 113.24 ($\underline{C}_3$), 115.50 (2C, d, J_{CF} = 20.8 Hz, $\underline{C}$H(Ph)), 130.45 (2x $\underline{C}$H(Ph)), 131.64 ($\underline{C}_{7a}$), 136.69 ($\underline{C}_q$(Ph)), 162.56 (d, J_{CP} = 246.3 Hz, $\underline{C}$F); **^{31}P-NMR (109 MHz, $CDCl_3$, ppm):** δ = 24.27; **IR (KBr, cm^{-1}):** 1225 ($\nu_{P=O}$), 3256 (ν_{NH}); **MS (70eV):** m/z = 391 (MH^+), **Rf** (ethylacetate) = 0.20.



6f

^{1}H-NMR (270 MHz, $CDCl_3$, ppm): δ = 1.14 (3H, t, J = 7.2 Hz, P(O)OCH$_2$C$\underline{H}_3$), 1.22 (3H, t, J = 7.2 Hz, P(O)OCH$_2$C$\underline{H}_3$), 2.15 (1H, s, N$\underline{H}$), 3.71 (1H, d, J_{AB} = 13.2 Hz, (Ind)C$\underline{H}_2$N), 3.94 (4H, m, P(O)OC$\underline{H}_2$CH$_3$), 3.99 (1H, d, J_{AB} = 13.2 Hz, (Ind)C$\underline{H}_2$N), 4.11 (1H, d, J_{HP} = 19.8 Hz, NC$\underline{H}$P), 6.93 (1H, d, J = 1.9 Hz, C$_2\underline{H}$), 7.09 (1H, dxd, J_1 = J_2 = 7.4 Hz, C$_5\underline{H}$), 7.18 (1H, dxd, J_1 = J_2 = 7.4 Hz, C$_6\underline{H}$), 7.40 (5H, m, C$_7\underline{H}$ 4x C$\underline{H}$(Ph)), 7.58 (1H, d, J = 7.7 Hz, C$_4\underline{H}$), 8.67 (1H, s, N$\underline{H}$(Ind));**^{13}C-NMR (68 MHz, $CDCl_3$, ppm):** δ = 16.42 (2C, t, J_{CP} = 7.5 Hz, P(O)OCH$_2\underline{C}$H$_3$), 42.67 (J_{CP} = 17.9 Hz, (Ind)$\underline{C}$H$_2$N), 59.13 (J_{CP} = 152.9 Hz, N$\underline{C}$HP), 63.00 (J_{CP} = 6.9 Hz, P(O)O$\underline{C}$H$_2$CH$_3$), 63.18 (J_{CP} = 6.3 Hz, P(O)O$\underline{C}$H$_2$CH$_3$), 111.44 ($\underline{C}_7$H), 113.31 ($\underline{C}_3$), 119.04 ($\underline{C}_4$H), 119.47 ($\underline{C}_5$H), 121.91 ($\underline{C}$Br), 122.14 ($\underline{C}_6$H), 123.33 ($\underline{C}_2$H), 127.07 ($\underline{C}_{3a}$H), 130.55 (d, J_{CP} = 5.2 Hz, 2x $\underline{C}$H(Ph)),131.68 (2x $\underline{C}$H(Ph)), 135.11 ($\underline{C}_{7a}$), 136.62 ($\underline{C}_q$(Ph)); **^{31}P-NMR (109 MHz, $CDCl_3$, ppm):** δ = 23.74; **IR (KBr, cm^{-1}):** 1234 ($\nu_{P=O}$), 3256 (ν_{NH}); **MS (70eV):** m/z = 453 (MH^+), **Rf** (ethylacetate/petrolether 9/1) = 0.20.



6g

^{1}H-NMR (270 MHz, $CDCl_3$, ppm): δ = 1.22 (3H, t, J = 7.2 Hz, P(O)OCH$_2$C<u>H</u>$_3$), 1.26 (3H, t, J = 7.2 Hz, P(O)OCH$_2$C<u>H</u>$_3$), 2.31 (1H, s, N<u>H</u>), 3.72 (1H, d, J_{AB} = 13.2 Hz, (Ind)C<u>H</u>$_2$N), 3.82 (3H, s, OC<u>H</u>$_3$), 4.00 (1H, d, J_{AB} = 13.5 Hz, (Ind)C<u>H</u>$_2$N), 4.02 (4H, m, P(O)OC<u>H</u>$_2$CH$_3$), 4.10 (1H, d, J_{HP} = 19.3 Hz, NC<u>H</u>P), 6.92 (2H, d, J = 8.5 Hz, C<u>H</u>(Ph)), 6.97 (1H, d, J = 2.2 Hz, C$_2$<u>H</u>), 7.08 (1H, dxdxd, $J_1 = J_2$ = 7.4 Hz, J_3 = 1.1 Hz, C$_5$<u>H</u>), 7.18 (1H, dxdxd, $J_1 = J_2$ = 7.5 Hz, J_3 = 1.2 Hz C$_6$<u>H</u>), 7.34 (1H, d, J = 8.0 Hz, C$_7$<u>H</u>), 7.39 (2H, dd, J_{HP} = 8.8 Hz, J = 2.2 Hz, 2x C<u>H</u>(Ph)), 7.59 (1H, d, J = 8.0 Hz, C$_4$<u>H</u>), 8.80 (1H, s, N<u>H</u>(Ind)); **^{13}C-NMR (68 MHz, $CDCl_3$, ppm):** δ = 16.38 (d, J_{CP} = 5.8 Hz, P(O)OCH$_2$<u>C</u>H$_3$), 16.51 (d, J_{CP} = 5.8 Hz, P(O)OCH$_2$<u>C</u>H$_3$), 42.52 (J_{CP} = 18.5 Hz, (Ind)<u>C</u>H$_2$N), 55.36 (O<u>C</u>H$_3$), 58.99 (J_{CP} = 154.6 Hz, N<u>C</u>HP), 62.83 (J_{CP} = 6.9 Hz, P(O)O<u>C</u>H$_2$CH$_3$), 63.02 (J_{CP} = 6.3 Hz, P(O)O<u>C</u>H$_2$CH$_3$), 111.41 (<u>C</u>$_7$H), 113.61 (<u>C</u>$_3$), 114.00 (2x <u>C</u>H(Ph)), 119.08 (<u>C</u>$_4$H), 119.31 (<u>C</u>$_5$H), 121.98 (<u>C</u>$_6$H), 123.34 (<u>C</u>$_2$H), 127.15 (<u>C</u>$_{3a}$), 127.73 (<u>C</u>$_q$(Ph)), 129.97 (2C, J_{CP} = 5.8 Hz, 2x <u>C</u>H(Ph)), 136.64 (<u>C</u>$_{7a}$), 159.40 (<u>C</u>(Ph)OMe); **^{31}P-NMR (109 MHz, $CDCl_3$, ppm):** δ = 24.91; **IR (NaCl, cm^{-1}):** 1248 ($\nu_{P=O}$), 3247 (ν_{NH}); **MS (70eV):** m/z = 403 (MH^+), **Rf** (ethyl acetate/petrolether 7/3) = 0.27.

Summary

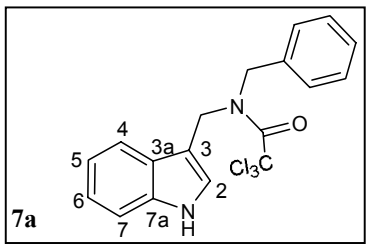
Compound	*Yield (%)*
6a	91
6b	91
6c	80

Compound	*Yield (%)*
6d	42
6e	44
6f	52
6g	61

GENERAL PROCEDURE FOR THE ACYLATION:

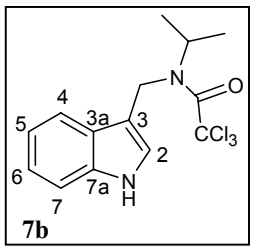
To a stirred solution of the respective amine **6** and 2 equiv. of pyridine, 2 equiv. trichloroacetyl chloride was added dropwise at 0°C and under nitrogen atmosphere. The reaction mixture was carefully protected from the light and stirred for 24 to 48 h at room temperature under a nitrogen atmosphere. The reaction mixture was poured in 1M NaOH and extracted three times with CH_2Cl_2. The combined organic fractions were dried over $MgSO_4$. The crude mixture was further purified through filtration over a small (5 cm) silica column using petroleumether/ 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 existance of 2 rotamers. The mixture consist of 66 % rotamer 'A' and 33 % rotamer 'B'.



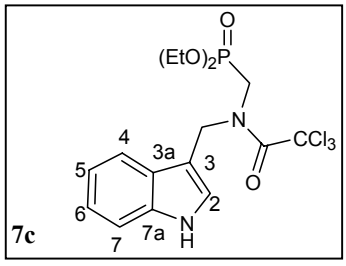
7a

^{1}H-NMR (300 MHz, $CDCl_3$, ppm): δ = 4.62 (2H, s, NC$\underline{H}_2$(Ph), rot B), 4.77 (2H, s, (Ind)C$\underline{H}_2$N, rot A), 4.87 (2H, s, NC$\underline{H}_2$(Ph), rot A), 5.08 (2H, s, (Ind)C$\underline{H}_2$N, rot B), 7.07 (1H, s, $C_2\underline{H}$, rot A), 7.10 (1H, s, $C_2\underline{H}$, rot B), 7.13-7.50 (8H (rot A), 8H (rot B), m, $C_5\underline{H}$, $C_6\underline{H}$, $C_4\underline{H}$ or $C_7\underline{H}$, 5x C$\underline{H}$(Ph), rot A, rot B), 7.60 (2H, ~d, J = 14.31 Hz, $C_4\underline{H}$ or $C_7\underline{H}$, rot A, rot B), 8.36 (1H, bs, N$\underline{H}$, rot A), 8.48 (1H, bs, N$\underline{H}$, rot B);
^{13}C-NMR (75.4 MHz, $CDCl_3$, ppm): δ = 42.21 ((Ind)$\underline{C}H_2$N, rot A), 45.46 ((Ind)$\underline{C}H_2$N, rot B), 50.04 (N$\underline{C}H_2$(Ph)), rot B), 51.57 (N$\underline{C}H_2$(Ph)), rot A), 93.68 ($\underline{C}Cl_3$, rot A, rot B), 110.05 ($\underline{C}_3$, rot B), 110.06 ($\underline{C}_3$, rot A), 111.57 ($\underline{C}_4$H or $\underline{C}_7$H, rot A), 111.58 ($\underline{C}_4$H or $\underline{C}_7$H, rot B), 119.09 ($\underline{C}_4$H or $\underline{C}_7$H, rot B), 119.10 ($\underline{C}_4$H or $\underline{C}_7$H, rot A), 120.22 ($\underline{C}_5$H or $\underline{C}_6$H, rot A, rot B), 122.59 ($\underline{C}_5$H or $\underline{C}_6$H, rot A, rot B), 123.57 ($\underline{C}_2$H, rot B), 125.10 ($\underline{C}_2$H, rot A), 127.03 ($\underline{C}_{3a}$), 127.27 (2C, 2x $\underline{C}$H(Ph)), 127.98 (2C, 2x $\underline{C}$H(Ph)), 129.04 ($\underline{C}$H(Ph)), 135.51 ($\underline{C}_{quat}$(Ph), rot A, rot B), 136.31 ($\underline{C}_{7a}$, rot A), 136.32 ($\underline{C}_{7a}$, rot B), 161.32 ($\underline{C}$=O, rot A, rot B); **IR (KBr, cm^{-1}):** 3350(ν_{NH}), 1655 ($\nu_{NC=O}$), 1496, 1457, 1432; **MS (ESI):** m/z = 130 (Ind-CH_2^+); **Mp.:** 116.7 °C.



7b

^{1}H-NMR (300 MHz, $CDCl_3$, ppm): 1.31 (6H, d, J = 6.6 Hz, 2x C$\underline{H}_3$(iPr)), 4.72 (2H, s, (Ind)C$\underline{H}_2$N), 4.80-5.00 (1H, m, C$\underline{H}$(iPr)), 7.13-7.23 (3H, m, $C_2\underline{H}$, $C_5\underline{H}$, $C_6\underline{H}$), 7.37 (1H, d, J = 7.7 Hz, $C_4\underline{H}$ or $C_7\underline{H}$), 7.64 (1H, d, J = 8.3 Hz, $C_4\underline{H}$ or $C_7\underline{H}$), 8.09 (1H, bs, N$\underline{H}$(Ind)); **^{13}C-NMR (75.6 MHz, CDCl3, ppm):** 20.46 (2x $\underline{C}H_3$(iPr)), 38.70 ((Ind)$\underline{C}H_2$N), 50.83 ($\underline{C}$H(iPr)), 93.99 ($\underline{C}Cl_3$), 111.38 ($\underline{C}_4$H or $\underline{C}_7$H), 112.56 ($\underline{C}_3$), 118.28 ($\underline{C}_4$H or $\underline{C}_7$H), 119.56, 121.99, 123.21 ($\underline{C}_2$H, $\underline{C}_5$H, $\underline{C}_6$H), 126.18 ($\underline{C}_{3a}$ or $\underline{C}_{7a}$), 135.76 ($\underline{C}_{3a}$ or $\underline{C}_{7a}$), 160.47 ($\underline{C}$=O); **IR (KBr, cm-1):** 3394 (ν_{NH}), 1663 ($\nu_{NC=O}$); **MS (ESI):** m/z = 131 (Ind-CH_2^++1); **Mp.:** 141.8 °C.

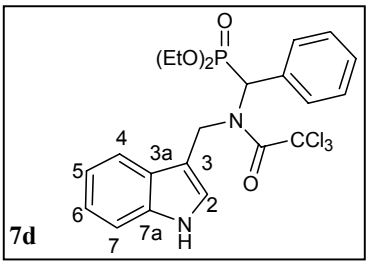


7c

^{1}H-NMR (270 MHz, $CDCl_3$, ppm): δ = 1.26 (3H, t, J = 7.1 Hz, P(O)OCH$_2$C$\underline{H}_3$), 1.32 (3H, t, J = 6.9 Hz, P(O)OCH$_2$C$\underline{H}_3$), 3.86 (2H, d, J_{HP} = 11.2 Hz, NC$\underline{H}_2$P), 4.15 (4H, m, P(O)OC$\underline{H}_2$CH$_3$), 5.35 (2H, s, (Ind)C$\underline{H}_2$N), 7.12 (1H, dxd, $J_1 = J_2$ = 7.3 Hz, $C_6\underline{H}$), 7.22 (2H, m, $C_2\underline{H}$, $C_5\underline{H}$), 7.41 (1H, d, J = 7.9 Hz, $C_7\underline{H}$), 7.64 (1H, d, J = 7.9 Hz, $C_4\underline{H}$), 9.06 (1H, s, N$\underline{H}$(Ind));
^{13}C-NMR (68 MHz, $CDCl_3$, ppm): δ = 16.43 (2C, J_{CP} = 6.1 Hz, P(O)OCH$_2\underline{C}$H$_3$), 41.68 (J_{CP} = 155.0 Hz, N$\underline{C}$H$_2$P), 46.90 ((Ind)$\underline{C}H_2$N), 62.65 (2C, J_{CP} = 6.1 Hz, P(O)O$\underline{C}$H$_2$CH$_3$), 93.10 ($\underline{C}Cl_3$), 108.86 ($\underline{C}_3$), 111.68 ($\underline{C}_7$H), 118.87 ($\underline{C}_4$H), 120.11 ($\underline{C}_6$H), 122.55 ($\underline{C}_5$H), 124.62 ($\underline{C}_2$H), 126.47 ($\underline{C}_{3a}$), 136.53 ($\underline{C}_{7a}$), 160.61 ($\underline{C}$=O); **^{31}P-NMR (109 MHz, $CDCl_3$, ppm):** δ = 22.00; **IR (NaCl, cm^{-1}):** 1225 ($\nu_{P=O}$), 3247 (ν_{NH}), 1676 ($\nu_{NC=O}$), ; **MS (70eV):** m/z = 130.1 (Ind-CH_2^+).

Preparation of 7d.

To a stirred solution of 0.6 g diëthyl (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 Et_2O was added to the reaction mixture and stirred for 10 minutes at 0°C. The salts were filtered over celite and washed with Et_2O. The organic layer was washed three times with water (50 ml), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford (63 %) as a bright yellow oil. The residue has a purity > 95 %. Because of the photo lability it is important to protect the reaction mixture as much as possible from the light.



7d

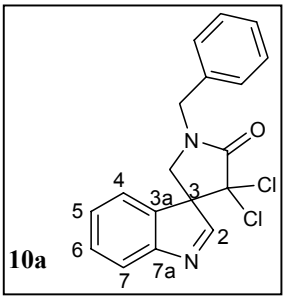
^{1}H-NMR (300 MHz, $CDCl_3$, ppm): 1.08 (3H, t, J = 7.0 Hz, P(O)OCH$_2$C<u>H</u>$_3$), 1.20 (3H, t, J = 7.2 Hz, P(O)OCH$_2$C<u>H</u>$_3$), 3.74-3.90 (2H, m, P(O)OC<u>H</u>$_2$CH$_3$), 4.27 (2H, q, J = 7.2 Hz, P(O)OC<u>H</u>$_2$CH$_3$), 4.72 (1H, d, J_{AB} = 16.5 Hz, (Ind)C<u>H</u>$_2$N), 4.89 (1H, d, $J_{H\text{-}P}$ = 25.6 Hz, NC<u>H</u>P), 5.58 (1H, dxd, J_{AB} = 16.5 Hz, J_2 = 5.6 Hz, (Ind)C<u>H</u>$_2$N), 7.10 (1H, dxd, $J_1 = J_2$ = 7.2 Hz, C$_5$<u>H</u> or C$_6$<u>H</u>), 7.20 (1H, dxd, $J_1 = J_2$ = 7.2 Hz, C$_5$<u>H</u> or C$_6$<u>H</u>), 7.25-7.39 (5H, m, 5x C<u>H</u>(Ph)), 7.45 (2H, ~ t, C$_4$<u>H</u>, C$_7$<u>H</u>), 7.59 (1H, s, C$_2$<u>H</u>), 9.62 (1H, bs, N<u>H</u>(ind)); **^{13}C-NMR (75.4 MHz, $CDCl_3$, ppm):** δ = 16.23 (J_{CP} = 6.9 Hz, P(O)OCH$_2$<u>C</u>H$_3$), 16.48 (J_{CP} = 5.8 Hz, P(O)OCH$_2$<u>C</u>H$_3$), 47.68 ((Ind)<u>C</u>H$_2$N), 61.77 (J_{CP} = 7.1 Hz, P(O)O<u>C</u>H$_2$CH$_3$),), 62.18 (J_{CP}= 159.2 Hz, N<u>C</u>HP), 64.52 (J_{CP} = 7.1 Hz, P(O)O<u>C</u>H$_2$CH$_3$), 93.04 (<u>C</u>Cl$_3$), 108.79 (<u>C</u>$_3$), 111.95 (<u>C</u>$_4$H or <u>C</u>$_7$H), 118.02 (<u>C</u>$_4$H or <u>C</u>$_7$H), 119.70 (<u>C</u>$_5$H or <u>C</u>$_6$H), 122.25 (<u>C</u>$_5$H or <u>C</u>$_6$H), 124.55 (<u>C</u>$_2$H), 126.58 (<u>C</u>$_{3a}$), 128.29 (<u>C</u>H(Ph)), 128.55 (<u>C</u>H(Ph)), 128.63 (<u>C</u>H(Ph)), 128.68 (2C, 2x <u>C</u>H(Ph)), 133.54 (<u>C</u>$_{quat}$(Ph)), 136.52 (<u>C</u>$_{7a}$), 161.53 (<u>C</u>=O); **^{31}P-NMR (121.4 MHz, $CDCl_3$, ppm):** δ = 20.76; **IR (NaCl, cm^{-1}):** 3224(ν_{NH}), 2930, 1684($\nu_{NC=O}$), 1246 ($\nu_{P=O}$), 1029 ($\nu_{P\text{-}O}$); **MS (ESI):** m/z = 130 (Ind-CH_2^+).

Summary

Compound	*Reaction Time (hours)*	*Yield (%)*
7a	48	74-94
7b	24	33
7c	48	45
7d	6	63

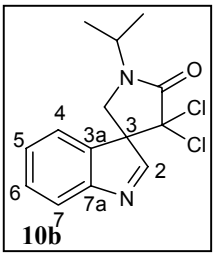
GENERAL PROCEDURE FOR THE HALOGEN TRANSFER RADICAL CYCLIZATION:

A mixture of the trichloroacetyl amino-derivative **7** (1 equiv.) and TMEDA (0.8 equiv.) was dissolved in CH_2Cl_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 amorf (more pure) precipitate.



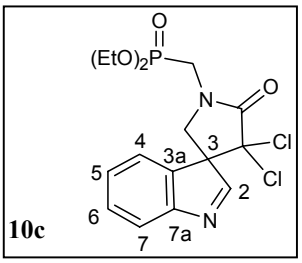
10a

^{1}H-NMR (300 MHz, $CDCl_3$, ppm): δ = 3.45 (1H, d, J_{AB} = 10.5 Hz, (Ind)C$\underline{H}_2$N), 3.49 (1H, d, J_{AB} = 10.5 Hz, (Ind)C$\underline{H}_2$N), 4.59 (1H, d, J_{AB} = 14.6 Hz, NC$\underline{H}_2$(Ph)), 4.71 (1H, d, J_{AB} = 14.6 Hz, NC$\underline{H}_2$(Ph)), 7.10-7.46 (8H, m, $C_5\underline{H}$, $C_6\underline{H}$, $C_4\underline{H}$ or $C_7\underline{H}$, 5x C$\underline{H}$ Ph)), 7.62 (1H, dxd, J_1 = 8.1 Hz, J_2 = 1.1 Hz, $C_4\underline{H}$ or $C_7\underline{H}$), 7.98 (1H, s, $C_2\underline{H}$); **^{13}C-NMR (75.4 MHz, $CDCl_3$, ppm):** δ = 48.09 ((Ind)$\underline{C}H_2$N), 48.38 (N$\underline{C}H_2$(Ph)), 67.77 ($\underline{C}_3$), 84.14 ($\underline{C}Cl_2$), 122.15 ($\underline{C}_4$H or $\underline{C}_7$H), {124.35, 127.31, 128.75, 130.61 ($\underline{C}_5$H, $\underline{C}_6$H, $\underline{C}$H(Ph), $\underline{C}_4$H or $\underline{C}_7$H)}, 128.61 (2C, 2x $\underline{C}$H(Ph)), 129.33 (2C, 2x $\underline{C}$H(Ph)), 133.76 ($\underline{C}_{3a}$), 134.22 ($\underline{C}_{quat,}$(Ph)), 155.76 ($\underline{C}_{7a}$), 165.68 ($\underline{C}$=O), 169.01 ($\underline{C}_2$H); **IR (NaCl, cm^{-1}):** 3339($\nu_{N=C(Ind)}$), 1725 ($\nu_{NC=O}$), 1478, 1457, 1428; **MS (ESI):** m/z = 345/47/49 ($M+1^+$).



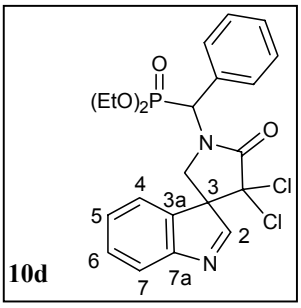
10b

^{1}H-NMR (300 MHz, $CDCl_3$, ppm): 1.25 (3H, d, J =4.4 Hz, C$\underline{H}_3$(iPr)), 1.27 (3H, d, J = 4.4 Hz, C$\underline{H}_3$(iPr)), 3.52 (1H, d, J_{AB} = 9.9 Hz, (Ind)C$\underline{H}_2$N)), 3.62 (1H, d, J_{AB} = 10.2 Hz, (Ind)C$\underline{H}_2$N)), 4.53 (1H, sept, J = 6.7 Hz, C$\underline{H}$(iPr)), 7.33 (1H, dxdxd, J_1 = J_2 = 7.4 Hz, J_3 = 0.8 Hz, $C_5\underline{H}$ or $C_6\underline{H}$), 7.50 (1H, dxdxd, J_1 = J_2= 7.4 Hz, J_3 = 1.2 Hz, $C_5\underline{H}$ or $C_6\underline{H}$), 7.53 (1H, d, J = 7.4 Hz, $C_4\underline{H}$ or $C_7\underline{H}$), 7.70 (1H, d, J = 7.7 Hz, $C_4\underline{H}$ or $C_7\underline{H}$), 8.12 (1H, s, $C_2\underline{H}$); **^{13}C-NMR (75.6 MHz, $CDCl_3$, ppm):** 19.34 ($\underline{C}H_3$(iPr)), 19.41 ($\underline{C}H_3$(iPr)), 44.06 ((Ind)$\underline{C}H_2$N), 44.93 ($\underline{C}$H(iPr)), 67.68 ($\underline{C}_3$), 84.49 ($\underline{C}Cl_2$), 122.18 ($\underline{C}_4$H or $\underline{C}_7$H), 123.96 ($\underline{C}_4$H or $\underline{C}_7$H), 127.24 ($\underline{C}_5$H or $\underline{C}_6$H), 130.47 ($\underline{C}_5$H or $\underline{C}_6$H), 134.30 ($\underline{C}_{3a}$), 155.77 ($\underline{C}_{7a}$), 164.85 ($\underline{C}$=O), 169.06 ($\underline{C}_2$H); **IR (NaCl, cm^{-1}):** 3342 ($\nu_{N=C(Ind)}$), 1724 ($\nu_{NC=O}$); **MS (ESI): m/z =** 297/299/301 (M^++1).



10c

^{1}H-NMR (300 MHz, $CDCl_3$, ppm): 1.31 (3H, t, J = 6.9 Hz, P(O)OCH$_2$C$\underline{H}_3$), 1.34 (3H, t, J = 7.0 Hz, P(O)OCH$_2$C$\underline{H}_3$), 3.81 (2H, s, (Ind)C$\underline{H}_2$N), 3.83 (1H, dd, J_{HP} = 15.8 Hz, J = 11.1 Hz, NC$\underline{H}_2$P), 3.94 (1H, dd, J_{HP} = 15.8 Hz, J = 11.7 Hz, NC$\underline{H}_2$P), 4.17 (4H, m, P(O)OC$\underline{H}_2$CH$_3$), 7.32 (1H, dxd, J_1 =J_2 = 7.6 Hz, $C_6\underline{H}$), 7.48 (1H, dxdxd, J_1 = J_2 = 7.7 Hz, J_3 = 1.1 Hz, $C_5\underline{H}$), 7.58 (1H, d, J = 7.4 Hz, $C_7\underline{H}$), 7.68 (1H, d, J = 7.4 Hz, $C_4\underline{H}$), 8.12 (1H, s, $C_2\underline{H}$); **^{13}C-NMR (68 MHz, $CDCl_3$, ppm):** δ = 16.41 (J_{CP} = 3.5 Hz, P(O)OCH$_2\underline{C}$H$_3$), 16.48 (J_{CP} = 3.5 Hz, P(O)OCH$_2\underline{C}$H$_3$), 39.58 (J_{CP} = 155.8 Hz, N$\underline{C}$H$_2$P), 49.55 ((Ind)$\underline{C}H_2$N), 63.06 (J_{CP} = 1.7 Hz, P(O)O$\underline{C}$H$_2$CH$_3$), 63.15 (J_{CP} = 1.7 Hz, P(O)O$\underline{C}$H$_2$CH$_3$), 68.01 ($\underline{C}_3$), 83.36 ($\underline{C}Cl_2$), 122.13 ($\underline{C}_4$H), 124.48 ($\underline{C}_7$H), 127.23 ($\underline{C}_6$H), 130.64 ($\underline{C}_5$H), 133.42 ($\underline{C}_{3a}$), 155.89 ($\underline{C}_{7a}$), 165.47 ($\underline{C}$=O), 168.85 ($\underline{C}_2$H); **^{31}P-NMR (109 MHz, $CDCl_3$, ppm):** δ = 19.81; **IR (NaCl, cm^{-1}):** 1243 ($\nu_{P=O}$),1735 ($\nu_{NC=O}$), 3247 (ν_{NH}); **MS (70eV):** m/z = 409.



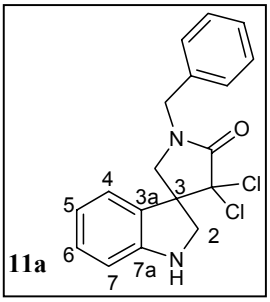
10d

^{1}H-NMR (300 MHz, $CDCl_3$, ppm): 1.13-1.43 (6H, m, P(O)OCH$_2$C<u>H</u>$_3$), 3.49 (1H, ~t, (Ind)C<u>H</u>$_2$N), 3.96-4.31 (5H, m, (Ind)C<u>H</u>$_2$N, P(O)OC<u>H</u>$_2$CH$_3$), 5.79 (1H, d, J_{HP} = 20.4 Hz, NC<u>H</u>P, *m*), 5.80 (1H, d, J_{H-P} = 20.9 Hz, NC<u>H</u>P, *M*), 7.11-7.72 (9H, C$_4$<u>H</u>, C$_5$<u>H</u>, C$_6$<u>H</u>, C$_7$<u>H</u>, 5x C<u>H</u>(Ph)), 8.16 (1H, s, C$_2$<u>H</u>, *M*), 8.48 (1H, ~dxd, C$_2$<u>H</u>, *m*); **^{13}C-NMR (75.4 MHz, $CDCl_3$, ppm):** 16.18 (J_{CP} = 5.8 Hz, P(O)OCH$_2$<u>C</u>H$_3$), 16.49 (J_{CP} = 6.9 Hz, P(O)OCH$_2$<u>C</u>H$_3$), 46.55 ((Ind)<u>C</u>H$_2$N, *m*), 46.90 ((Ind)<u>C</u>H$_2$N, *M*), 53.29 (J_{CP}= 158.1 Hz, N<u>C</u>HP), 62.98 (J_{CP} = 6.9 Hz, P(O)O<u>C</u>H$_2$CH$_3$, *M*), 63.07 (J_{CP} = 6.9 Hz, P(O)O<u>C</u>H$_2$CH$_3$, *m*), 63.91 (J_{CP} = 6.9 Hz, P(O)O<u>C</u>H$_2$CH$_3$, *M*), 64.01 (J_{CP} = 6.9 Hz, P(O)O<u>C</u>H$_2$CH$_3$, *m*), 67.94 (<u>C</u>$_3$), 83.53 (<u>C</u>Cl$_2$), {121.99, 124.02, 126.96, 130.39 (<u>C</u>$_4$H, <u>C</u>$_5$H, <u>C</u>$_6$H and <u>C</u>$_7$H)}, 129.43 (2C, 2x <u>C</u>H(Ph)), 129.78 (2C, 2x <u>C</u>H(Ph)), 129.89 (<u>C</u>H(Ph)), 133.28 (<u>C</u>$_{3a}$ or <u>C</u>$_{quat}$(Ph)), 136.93 (<u>C</u>$_{3a}$ or <u>C</u>$_{quat}$(Ph)), 155.80 (<u>C</u>$_{7a}$), 165.35 (<u>C</u>=O), 168.48 (<u>C</u>$_2$H, *m*), 168.79 (<u>C</u>$_2$H, *M*); **^{31}P-NMR (121.4 MHz, $CDCl_3$, ppm):** δ = 18.73 (*M*), 18.40 (*m*); **IR (NaCl, cm^{-1}):** 3280(ν_{NH}), 2983, 1731 ($\nu_{NC=O}$), 1251 ($\nu_{P=O}$), 1029 (ν_{P-O}) ; **MS (ESI):** m/z = 480/83/85 (M+1$^+$), 371.

Compound	*Yield (%)*	*Purity (%)*
10a	96	84
10b	79	90
10c	59	85
10d	83	75

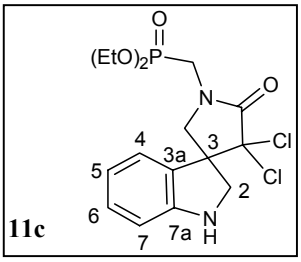
<u>GENERAL PROCEDURE FOR THE REDUCTION OF THE SPIRO-IMINE:</u>

To a mixture of the previous spiro-imine **10** and 1.1 equiv. of glacial acetic acid in methanol was added 1 equiv. of $NaCNBH_3$. 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 $MgSO_4$ the compound was obtained with moderate purity.



11a

^{1}H-NMR (300 MHz, $CDCl_3$, ppm): δ = 3.42 (1H, d, J_{AB} = 9.8 Hz, C$_2$<u>H</u>$_2$), 3.50 (1H, d, J_{AB} = 9.8 Hz, C$_2$<u>H</u>$_2$), 3.51 (1H, d, J_{AB} = 10.5 Hz, (Ind)C<u>H</u>$_2$N), 3.80 (1H, bs, N<u>H</u>), 4.09 (1H, d, J_{AB} = 10.5 Hz, (Ind)C<u>H</u>$_2$N), 4.39 (1H, d, J_{AB} = 14.4 Hz, NC<u>H</u>$_2$(Ph)), 4.81 (1H, d, J_{AB} = 14.4 Hz, NC<u>H</u>$_2$(Ph)), 6.64-6.69 (2H, m, C$_4$<u>H</u>, C$_6$<u>H</u>), 6.91 (1H, dxd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, C$_7$<u>H</u>), 7.12 (1H, dxdxd, J_1 = J_2 = 7.6 Hz, J_3 = 1.1Hz, C$_5$<u>H</u>), 7.24-7.34 (5H, m, 5x C<u>H</u>(Ph)); **^{13}C-NMR (75.4 MHz, $CDCl_3$, ppm):** δ = 48.23 (N<u>C</u>H$_2$(Ph)), 53.51 ((Ind)<u>C</u>H$_2$N), 56.07 (<u>C</u>$_2$H$_2$), 59.62 (<u>C</u>$_3$), 88.99 (<u>C</u>Cl$_2$), 110.83 (<u>C</u>$_4$H), 119.02 (<u>C</u>$_6$H), 123.80 (<u>C</u>$_7$H), 128.29 (<u>C</u>$_{3a}$), 128.44 (<u>C</u>H(Ph)), 128.58 (2C, 2x <u>C</u>H(Ph)), 129.13 (2C, 2x <u>C</u>H(Ph)), 130.02 (<u>C</u>$_5$H), 134.58 (<u>C</u>$_{quat,}$(Ph)), 151.39 (<u>C</u>$_{7a}$), 166.57 (<u>C</u>=O); **IR (NaCl, cm^{-1}):** 3348(ν_{NH}), 1720 ($\nu_{NC=O}$), 1487, 145, 1428; **MS (ESI):** m/z = 347/49/51 (M+1$^+$).



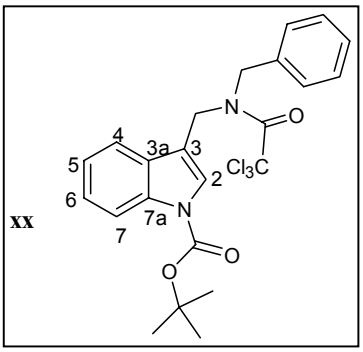
11c

^{1}H-NMR (270 MHz, $CDCl_3$, ppm): 1.21 (3H, t, J = 7.0 Hz, P(O)$OCH_2C\underline{H}_3$), 1.33 (3H, t, J = 7.2 Hz, P(O)$OCH_2C\underline{H}_3$), 3.58 (1H, d, J = 10.7 Hz, (Ind)$C\underline{H}_2N$), 3.68 (1H, dd, J_{HP} = 15.5 Hz, J = 10.9 Hz, $NC\underline{H}_2P$), 3.69 (1H, d, J = 10.0 Hz, $C_2\underline{H}_2$), 3.82 (1H, d, J = 10.2 Hz, $C_2\underline{H}_2$), 3.91 (1H, dd, J_{HP} = 16.0 Hz, J = 12.1 Hz, $NC\underline{H}_2P$), 4.07 (1H,dt, J = 10.7 Hz, (Ind)$C\underline{H}_2N$), 4.11 (4H, m, P(O)$OCH_2C\underline{H}_3$), 6.68 (2H, m, $C_4\underline{H}$, $C_6\underline{H}$), 6.98 (1H, dxd, J = 8.0 Hz, J = 1.1 Hz, $C_7\underline{H}$), 7.12 (1H, dxdxd, $J_1 = J_2$ = 7.7 Hz, J_3 = 1.1 Hz, $C_5\underline{H}$); **^{13}C-NMR (68 MHz, $CDCl_3$, ppm):** δ = 16.34 (J_{CP} = 5.8 Hz, P(O)$OCH_2\underline{C}H_3$), 16.53 (J_{CP} = 5.8 Hz, P(O)$OCH_2\underline{C}H_3$), 39.60 (J_{CP} = 156.3 Hz, $N\underline{C}H_2P$), 53.36 ((Ind)$\underline{C}H_2N$), 57.56 ($\underline{C}_2H_2$), 59.82 ($\underline{C}_3$), 62.78 (J_{CP} = 6.3 Hz, P(O)$O\underline{C}H_2CH_3$), 63.10 (J_{CP} = 5.8 Hz, P(O)$O\underline{C}H_2CH_3$), 87.90 ($\underline{C}Cl_2$), 110.74 ($\underline{C}_4H$), 119.05 ($\underline{C}_6H$), 123.99 ($\underline{C}_7H$), 128.14 ($\underline{C}_{3a}$), 130.03 ($\underline{C}_5H$), 151.26 ($\underline{C}_{7a}$), 166.38($\underline{C}$=O); **^{31}P-NMR (109 MHz, $CDCl_3$, ppm):** δ = 20.13; **IR (NaCl, cm^{-1}):** 1730 ($\nu_{NC=O}$), 3326 (ν_{NH}); **MS (70eV):** m/z = 411.

Compound	*Yield (%)*	*Purity (%)*
11a	88	67
11c	63	90

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.) Boc_2O 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 CH_2Cl_2. The organic layer was washed 2 times with 1M NaOH. After drying over $MgSO_4$ 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 %).



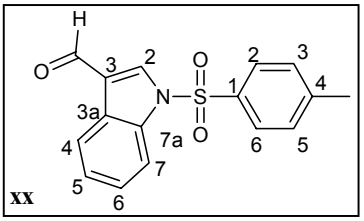
xx

The spectrum shows the existance of 2 rotamers.

^{1}H-NMR (300 MHz, $CDCl_3$, ppm): δ = 1.67 (9H, bs, $C(C\underline{H}_3)_3$), 4.72 (2H, bs, (Ind)$C\underline{H}_2N$), 4.94 (2H,~ d, $NC\underline{H}_2$(Ph)), 7.21-7.52 (9H, m, $C_2\underline{H}$, $C_4\underline{H}$ or $C_7\underline{H}$, $C_5\underline{H}$, $C_6\underline{H}$, 5x $C\underline{H}$(Ph)), 8.13 (1H, d, J = 6.9 Hz, ($C_4\underline{H}$ or $C_7\underline{H}$); **^{13}C-NMR (75.4 MHz, $CDCl_3$, ppm):** δ = 28.08 (3C, $C(\underline{C}H_3)_3$), 41.58 ((Ind)$\underline{C}H_2N$), 51.56 ($N\underline{C}H_2$(Ph)), 83.73 ($\underline{C}CH_3$), 93.26 ($\underline{C}Cl_3$), 114.61 ($\underline{C}_3$), 115.22 ($\underline{C}_4H$ or $\underline{C}_7H$), 119.29 ($\underline{C}_4H$ or $\underline{C}_7H$), {122.85, 124.76, 125.42, 127.06, 127.87, 128.85, 134.99, 135.46 ($\underline{C}_2H$, $\underline{C}_5H$, $\underline{C}_6H$, $\underline{C}_{3a}$, $\underline{C}_{7a}$, 2x $\underline{C}H$(Ph), 2x $\underline{C}H$(Ph), $\underline{C}H$(Ph))}, 149.28 ($\underline{C}$=O(O)), 160.85 ($\underline{C}$=O(CCl_3)) The signal of $\underline{C}_{quat}$(Ph) coincide with an other peak; **IR (KBr, cm^{-1}):** 3445, 1733 ($\nu_{C=O(O)}$), 1674 ($\nu_{C=O(CCl3)}$), 1475, 1456, 1413, 1088; **MS (70eV):** m/z =100, 130 (Ind-CH_2^+), 230 (Boc-Ind-CH_2^+), 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 werd 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.

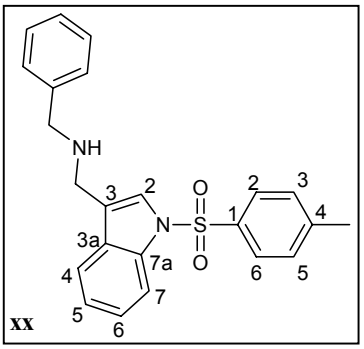


xx

^{1}H-NMR (300 MHz, $CDCl_3$, ppm): 2.38 (3H, s, C$\underline{H}_3$), 7.26-7.48 (4H, m, $C_3\underline{H}$(Ts), $C_5\underline{H}$(Ts), $C_5\underline{H}$, $C_6\underline{H}$), 7.84-7.87 (2H, m, $C_2\underline{H}$(Ts), $C_6\underline{H}$(Ts)), 7.93-7.97 (1H, m, $C_4\underline{H}$ or $C_7\underline{H}$), 8.23 (1H, s, $C_2\underline{H}$), 8.24-8.27 (1H, m, $C_4\underline{H}$ or $C_7\underline{H}$), 10.10 (1H, s, (C=O)$\underline{H}$); **^{13}C-NMR (75.4 MHz, $CDCl_3$, ppm):** δ = 21.77 ($\underline{C}H_3$), 113.34 ($\underline{C}_4$H or $\underline{C}_7$H), 122.44 ($\underline{C}_3$ or $\underline{C}_{3a}$ or $\underline{C}_{7a}$), 122.69 ($\underline{C}_4$H or $\underline{C}_7$H), 125.15 ($\underline{C}_5$H or $\underline{C}_6$H), 126.41 ($\underline{C}_5$H or $\underline{C}_6$H), 127.33 (2C, $\underline{C}_2$H(Ts), $\underline{C}_6$H(Ts)), 130.43 (2C, $\underline{C}_3$H(Ts), $\underline{C}_5$H(Ts)), 134.41 ($\underline{C}_3$ or $\underline{C}_{3a}$ or $\underline{C}_{7a}$), 135.32 ($\underline{C}_3$ or $\underline{C}_{3a}$ or $\underline{C}_{7a}$), 136.35($\underline{C}_2$H), 146.28 ($\underline{C}_{quat}$(Ts)), 185.49 ((C=O)H), the signal $\underline{C}_{quat}$(Ts) coincide with an other peak; **IR (KBr, cm^{-1}):** 1666 ($\nu_{C=O(H)}$), 1539, 1447, 1377, 1175 (ν_{SO2}); **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.

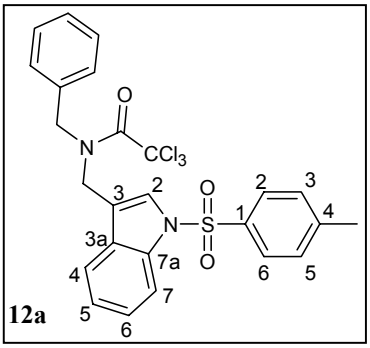
The imine obtained according the general procedure was immediately reduced according the general procudere for reduction. Crystallisation in ethanol/0.2 M NaOH afforded yellow crystals in 36 % yield.



xx

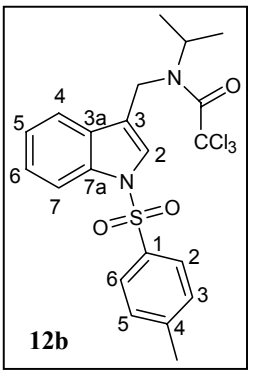
^{1}H-NMR (300 MHz, $CDCl_3$, ppm): 1.65 (1H, bs, N$\underline{H}$), 2.27 (3H, s, C$\underline{H}_3$), 3.79 (2H, s, NC$\underline{H}_2$(Ph)), 3.87 (2H, s, (Ind)C$\underline{H}_2$N), 7.14 (2H, d, J = 8.0 Hz, $C_3\underline{H}$(Ts), $C_5\underline{H}$(Ts)), 7.18-7.32 (7H, m, $C_5\underline{H}$, $C_6\underline{H}$, 5x C$\underline{H}$(Ph)), 7.49 (1H, s, $C_2\underline{H}$), 7.53 (1H, d, J = 7.7 Hz, $C_4\underline{H}$ or $C_7\underline{H}$), 7.73 (2H, d, J = 7.6 Hz, $C_2\underline{H}$(Ts), $C_6\underline{H}$(Ts)), 7.99 (1H, d, J = 8.3 Hz, $C_4\underline{H}$ or $C_7\underline{H}$);
^{13}C-NMR (75.4 MHz, $CDCl_3$, ppm): δ = 21.66 ($\underline{C}H_3$), 43.95 ((Ind)$\underline{C}H_2$N), 53.49 (N$\underline{C}H_2$(Ph)), 113.88 ($\underline{C}_4$H or $\underline{C}_7$H), 119.99 ($\underline{C}_4$H or $\underline{C}_7$H), 121.74 ($\underline{C}_3$), 123.28 ($\underline{C}_5$H or $\underline{C}_6$H), 123.89 ($\underline{C}_2$H), 124.92 ($\underline{C}_5$H or $\underline{C}_6$H), 126.92 (2C, $\underline{C}_2$H(Ts), $\underline{C}_6$H(Ts)), 127.21 ($\underline{C}$H(Ph)), 128.34 (2C, 2x $\underline{C}$H(Ph)), 128.60 (2C, 2x $\underline{C}$H(Ph)), 129.96 (2C, $\underline{C}_3$H(Ts), $\underline{C}_5$H(Ts)), 130.46 ($\underline{C}_{3a}$ or $\underline{C}_{7a}$ or $\underline{C}_{quat}$(Ts)), 135.38 $\underline{C}_{3a}$ or $\underline{C}_{7a}$ or $\underline{C}_{quat}$(Ts)), 135.62 ($\underline{C}_{3a}$ or $\underline{C}_{7a}$ or $\underline{C}_{quat}$(Ts)), 140.17 ($\underline{C}_{quat}$(Ph)), 144.98 ($\underline{C}_{quat}$(Ts)); **IR (KBr, cm^{-1}):** 3433 (ν_{NH}), 1597, 1449, 1374, 1176 (ν_{SO2}); **MS (ESI):** m/z = 284 (Ts-Ind-CH_2^+); **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'.



12a

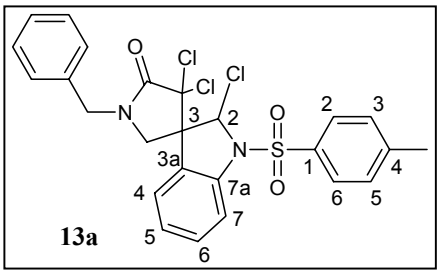
^{1}H-NMR (300 MHz, $CDCl_3$, ppm): δ = 2.34 (6H, s, C$\underline{H}_3$, rot A, rot B), 4.62 (2H, s, NC$\underline{H}_2$(Ph), rot B), 4.69 (2H, s, (Ind)C$\underline{H}_2$N, rot A), 4.83 (2H, s, NC$\underline{H}_2$(Ph), rot A), 4.95 (2H, s, (Ind)C$\underline{H}_2$N, rot B), 7.08-7.42 (22H, m, $C_2\underline{H}$, $C_4\underline{H}$ or $C_7\underline{H}$, $C_5\underline{H}$, $C_6\underline{H}$, 5x C$\underline{H}$(Ph), {$C_3\underline{H}$(Ts), $C_5\underline{H}$(Ts) or $C_2\underline{H}$(Ts), $C_6\underline{H}$(Ts)}, rot A, rot B), 7.74 (4H, d, J = 8.26 Hz, $C_2\underline{H}$(Ts), $C_6\underline{H}$(Ts) or $C_3\underline{H}$(Ts), $C_5\underline{H}$(Ts), rot A, rot B), 8.0 (2H, d, J = 8.0 Hz, $C_4\underline{H}$ or $C_7\underline{H}$, rot A, rot B);
^{13}C-NMR (75.4 MHz, $CDCl_3$, ppm): δ = 21.53 ($\underline{C}H_3$, rot A, rot B), 41.33 ((Ind)$\underline{C}H_2$N, rot A), 44.74 ((Ind)$\underline{C}H_2$N, rot B), 50.46 (N$\underline{C}H_2$(Ph)), rot B), 51.68 (N$\underline{C}H_2$(Ph)), rot A), 93.14 ($\underline{C}Cl_3$, rot A, rot B), 113.86 ($\underline{C}_4$H or $\underline{C}_7$H, rot A), 113.93 ($\underline{C}_4$H or $\underline{C}_7$H, rot B), 116.70 ($\underline{C}_3$, rot A, rot B), 119.40 ($\underline{C}_4$H or $\underline{C}_7$H, rot B), 119.78 ($\underline{C}_4$H or $\underline{C}_7$H, rot A), 123.54 ($\underline{C}_2$H), {125.17, 125.95, 127.08, 128.09, 128.97, 129.51 ($\underline{C}_5$H, $\underline{C}_6$H, 2x $\underline{C}$H(Ph), 2x $\underline{C}$H(Ph), $\underline{C}$H(Ph), $\underline{C}_{quat}$(Ph), rot A, rot B)}, 126.76 ($\underline{C}_2$H(Ts), $\underline{C}_6$H(Ts) or $\underline{C}_3$H(Ts), $\underline{C}_5$H(Ts), rot A, rot B), 129.89 ($\underline{C}_2$H(Ts), $\underline{C}_6$H(Ts) or $\underline{C}_3$H(Ts), $\underline{C}_5$H(Ts), rot A, rot B), {134.67, 134.96, 135.17 ($\underline{C}_{3a}$, $\underline{C}_{7a}$, $\underline{C}_{quat}$(Ts), rot A, rot B)}, 145.16 ($\underline{C}_{quat}$(Ts), rot A, rot B), 161.00 ($\underline{C}$=O, rot A, rot B); **IR (KBr, cm^{-1}):** 3413, 1678 ($\nu_{NC=O}$), 1448, 1374, 1176 (ν_{SO2}); **MS (ESI):** m/z = 284 (Ts-Ind-CH_2^+); **Mp.:** 132.7 °C.



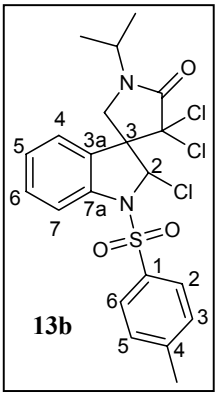
Reaction time: 24h, yield: 67 %.
^{1}H-NMR (300 MHz, $CDCl_3$, ppm): 1.28 (6H, d, J=6.6 Hz, 2x C$\underline{H}_3$(iPr)), 2.32 (3H, s, C$\underline{H}_3$(Ts)), 4.59 (2H, s, (Ind)C$\underline{H}_2$N), 4.94-4.95 (1H, m, C$\underline{H}$(iPr)), 7.18 (2H, d, J = 8.3 Hz, $C_3\underline{H}$(Ts), $C_5\underline{H}$(Ts)), 7.26 (1H, dxdxd, $J_1 = J_2 = 7.4$ Hz, $J_3 = 1.1$ Hz, $C_5\underline{H}$ or $C_6\underline{H}$), 7.32 (1H, dxd, $J_1 = J_2 = 7.4$ Hz, $C_5\underline{H}$ or $C_6\underline{H}$), 7.42 (1H, s, $C_2\underline{H}$), 7.51 (1H, d, J = 8.0 Hz, $C_4\underline{H}$ or $C_7\underline{H}$), 7.69 (2H, d, J = 8.3 Hz, $C_2\underline{H}$(Ts), $C_6\underline{H}$(Ts)), 7.98 (1H, d, J = 8.0 Hz, $C_4\underline{H}$ or $C_7\underline{H}$); **^{13}C-NMR (75.6 MHz, $CDCl_3$, ppm):** 20.37 (2x $\underline{C}H_3$(iPr)), 21.50 ($\underline{C}H_3$(Ts)), 38.34 ((Ind)$\underline{C}H_2$N), 50.92 ($\underline{C}$H(iPr)), 93.65 ($\underline{C}Cl_3$), 113.96 and 119.11 ($\underline{C}_4$H and $\underline{C}_7$H), 119.85 ($\underline{C}_3$), 123.38 ($\underline{C}_5$H or $\underline{C}_6$H), 124.08 ($\underline{C}_2$H), 124.92 ($\underline{C}_5$H or $\underline{C}_6$H), 126.71 (2C, $\underline{C}_2$H(Ts), $\underline{C}_6$H(Ts)), 129.52 ($\underline{C}_{3a}$ or $\underline{C}_{7a}$), 129.81 (2C, $\underline{C}_3$H(Ts), $\underline{C}_5$H(Ts)), 134.95 ($\underline{C}_1$(Ts)), 135.11 ($\underline{C}_{3a}$ or $\underline{C}_{7a}$), 144.91 ($\underline{C}_4$(Ts)), 160.25 ($\underline{C}$=O); **IR (KBr, cm^{-1}):** 3436, 1655 ($\nu_{NC=O}$), 1374, 1169 ($\nu_{S=O}$); **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 CH_2Cl_2 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 $MgSO_4$, filtration and evaporation of the solvent the spiro compound was obtained. Crystallisation in chloroform/diethylether afforded the compound in 64 % yield.



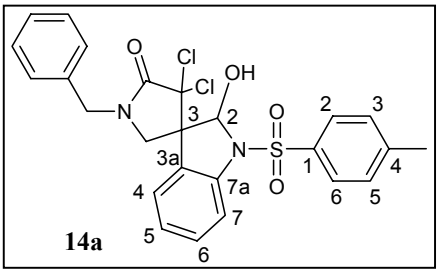
^{1}H-NMR (300 MHz, $CDCl_3$, ppm): δ = 2.39 (3H, s, C$\underline{H}_3$), 3.58 (1H, d, J_{AB} = 10.59 Hz, (Ind)C$\underline{H}_2$N), 3.86 (1H, d, J_{AB} = 10.59 Hz, (Ind)C$\underline{H}_2$N), 4.58 (1H, d, J_{AB} = 14.3 Hz, NC$\underline{H}_2$(Ph)), 4.70 (1H, d, J_{AB} = 14.3 Hz, NC$\underline{H}_2$(Ph)), 6.74 (1H, d, J = 7.7 Hz, $C_4\underline{H}$ or $C_7\underline{H}$), 6.92 (1H, dxd, $J_1 = J_2 = 7.7$ Hz, $C_5\underline{H}$ or $C_6\underline{H}$), 6.99 (1H, s, $C_2\underline{H}$Cl), 7.26-7.44 (8H, m, $C_5\underline{H}$ or $C_6\underline{H}$, 5x C$\underline{H}$(Ph), 2x C$\underline{H}$(Ts)), 7.49 (1H, d, J = 8.0 Hz, $C_4\underline{H}$ or $C_7\underline{H}$), 7.88 (2H, d, J = 8.0 Hz, 2x C$\underline{H}$(Ts)); **^{13}C-NMR (75.4 MHz, $CDCl_3$, ppm):** δ = 21.74 ($\underline{C}H_3$), 48.30 (N$\underline{C}H_2$(Ph)), 50.78 ((Ind)$\underline{C}H_2$N), 62.75 ($\underline{C}_3$), 80.95 ($\underline{C}_2$HCl), 86.62 ($\underline{C}Cl_2$), 114.55 ($\underline{C}_4$H or $\underline{C}_7$H), 123.24 ($\underline{C}_4$H or $\underline{C}_7$H), 124.87 ($\underline{C}_5$H or $\underline{C}_6$H), 127.88 (2C, 2x $\underline{C}$H(Ts)), 128.80 ($\underline{C}$H(Ph)), 128.90 (2C, 2x $\underline{C}$H(Ph)), 129.33 (2C, 2x $\underline{C}$H(Ph)), 129.48 ($\underline{C}_{3a}$ or $\underline{C}_{7a}$ or $\underline{C}_{quat}$(Ts)), 130.06 ($\underline{C}_5$H or $\underline{C}_6$H), 131.21 (2C, 2x $\underline{C}$H(Ts)), 134.11 ($\underline{C}_{quat}$(Ph)), 135.42 ($\underline{C}_{3a}$ or $\underline{C}_{7a}$ or $\underline{C}_{quat}$(Ts)), 139.54 ($\underline{C}_{3a}$ or $\underline{C}_{7a}$ or $\underline{C}_{quat}$(Ts)), 145.48 ($\underline{C}_{quat}$(Ts)), 164.86 ($\underline{C}$=O); **IR (KBr, cm^{-1}):** 3432, 1725 ($\nu_{NC=O}$), 1598, 1366, 1172 (ν_{SO2}); **MS (ESI):):** m/z = 517/19/21 (M+1$^+$); **Mp./decomposition temperature:** 207.2 °C.



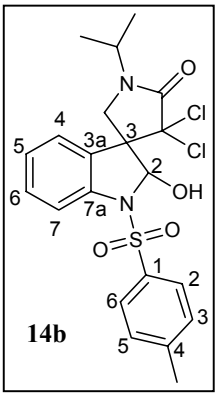
Crystallisation in methanol; yield: 64 % .**^{1}H-NMR (300 MHz, $CDCl_3$, ppm):** 1.26 (3H, d, J = 6.9 Hz, C<u>H</u>$_3$(iPr)), 135 (3H, d, J = 6.9 Hz, C<u>H</u>$_3$(iPr)), 2.39 (3H, s, C<u>H</u>$_3$(Ts)), 3.70 (1H, d, J_{AB} = 10.7 Hz, (Ind)C<u>H</u>$_2$N), 3.88 (1H, d, J_{AB} = 10.7 Hz, (Ind)C<u>H</u>$_2$N), 4,49 (1H, sept, J = 6.9 Hz, C<u>H</u>(iPr)), 7.03 (1H, s, C_2<u>H</u>Cl), 7.04-7.12 (2H, m, C_5<u>H</u> or C_6<u>H</u> and C_4<u>H</u> or C_7<u>H</u>), 7.30 (2H, d, J = 8.0 Hz, C_3<u>H</u>(Ts), C_5<u>H</u>(Ts)), 7.38 (1H, dxdxd, $J_1 = J_2$ = 6.9 Hz, J_3 = 1.9 Hz, C_5<u>H</u> or C_6<u>H</u>), 7.56 (1H, d, J = 8,3 Hz, C_4<u>H</u> or C_7<u>H</u>), 7.90 (2H, d, J = 8.3 Hz, C_2<u>H</u>(Ts), C_6<u>H</u>(Ts));
^{13}C-NMR (75,6 MHz, $CDCl_3$, ppm): 19.15 (<u>C</u>H$_3$(iPr)), 19.50 (<u>C</u>H$_3$(iPr)), 21.63 (<u>C</u>H$_3$(Ts)), 45.04 (<u>C</u>H(iPr)), 46.61 ((Ind)<u>C</u>H$_2$N), 62.37 (<u>C</u>$_3$), 81.16 (<u>C</u>$_2$HCl), 87.23 (<u>C</u>Cl$_2$), 114.59 (<u>C</u>$_4$H or <u>C</u>$_7$H), 123.32 and 124.85 (<u>C</u>$_4$H or <u>C</u>$_7$H and <u>C</u>$_5$H or <u>C</u>$_6$H), 127.81 (2C, <u>C</u>$_2$H(Ts), <u>C</u>$_6$H(Ts)), 129.47 (<u>C</u>$_{3a}$ or <u>C</u>$_{7a}$), 129.99 (2C, <u>C</u>$_3$H(Ts), <u>C</u>$_5$H(Ts)), 131.20 (<u>C</u>$_5$H or <u>C</u>$_6$H), 135.38, 139.66 and 145.40 (<u>C</u>$_{quat}$(Ts), <u>C</u>$_{3a}$ and <u>C</u>$_{7a}$), 164.30 (<u>C</u>=O); **IR (KBr, cm^{-1}):** 1725 ($\nu_{NC=O}$), 1366, 1169 ($\nu_{S=O}$); **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 CH_2Cl_2 together with 0.45 g silica. The mixture was stirred for 24 h at room temperature. The silica was filtrated over celite and the solvent was concentrated in vacuo. The compound was obtained in 80 % yield.



^{1}H-NMR (300 MHz, $CDCl_3$, ppm): δ = 2.36 (3H, s, C<u>H</u>$_3$), 3.35 (1H, d, J_{AB} = 10.73 Hz, (Ind)C<u>H</u>$_2$N), 3.50 (1H, d, J = 3.0 Hz, C_2HO<u>H</u>, D_2O exchangeable), 3.99 (1H, d, J_{AB} = 10.73 Hz, (Ind)C<u>H</u>$_2$N), 4.54 (1H, d, J_{AB} = 14.6 Hz, NC<u>H</u>$_2$(Ph)), 4.66 (1H, d, J_{AB} = 14.6 Hz, NC<u>H</u>$_2$(Ph)), 6.06 (1H, d, J = 3.0 Hz, C_2<u>H</u>OH), 6.81 (1H, dxd, J_1 = 7.7 Hz, J_2 = 0.8 Hz, C_4<u>H</u> or C_7<u>H</u>), 6.89 (1H, dxdxd, $J_1 = J_2$ = 7.7 Hz, J_3 = 0.8 Hz, C_5<u>H</u> or C_6<u>H</u>), 7.25-7.40 (8H, m, C_5<u>H</u> or C_6<u>H</u>, 5x C<u>H</u>(Ph), 2x C<u>H</u>(Ts)), 7.59 (1H, d, J = 8.0 Hz, C_4<u>H</u> or C_7<u>H</u>), 7.76 (2H, d, J = 8.2 Hz, 2x C<u>H</u>(Ts)); **^{13}C-NMR (75.4 MHz, $CDCl_3$, ppm):** δ = 21.66 (<u>C</u>H$_3$), 48.33 (N<u>C</u>H$_2$(Ph)), 49.29 ((Ind)<u>C</u>H$_2$N), 61.28 (<u>C</u>$_3$), 87.40 (<u>C</u>$_2$HOH), 87.54 (<u>C</u>Cl$_2$), 114.09 (<u>C</u>$_4$H or <u>C</u>$_7$H), 123.85 (<u>C</u>$_4$H or <u>C</u>$_7$H), 124.31 (<u>C</u>$_5$H or <u>C</u>$_6$H), 127.27 (2C, 2x <u>C</u>H(Ph) or 2x <u>C</u>H(Ts)), 128.55 (<u>C</u>H(Ph)), 128.81 (2C, 2x <u>C</u>H(Ph) or 2x <u>C</u>H(Ts)), 129.16 (2C, 2x <u>C</u>H(Ph) or 2x <u>C</u>H(Ts)), 129.28 (<u>C</u>$_{quat}$(Ts)), 130.06 (2C, 2x <u>C</u>H(Ph) or 2x <u>C</u>H(Ts)), 130.83 (<u>C</u>$_5$H or <u>C</u>$_6$H), {134.11, 135.42, 139.54 (<u>C</u>$_{3a}$, <u>C</u>$_{7a}$, <u>C</u>$_{quat}$(Ph))}, 145.10 (<u>C</u>$_{quat}$(Ts)), 165.16 (<u>C</u>=O); **IR (KBr, cm^{-1}):** 3436 (ν_{OH}), 1716 ($\nu_{NC=O}$), 1599, 1478, 1364, 1173 (ν_{SO2}); **MS (ESI):):** m/z = 517/19/21 (M+1$^+$); **Mp./decomposition temperature:** 205.7 °C.



yield: 61 %.
^{1}H-NMR (300 MHz, $CDCl_3$, ppm): 1.22 (3H, d, J = 6.6 Hz, C<u>H</u>$_3$(iPr)), 1.24 (3H, d, J = 6.6 Hz, C<u>H</u>$_3$(iPr)), 2.36 (3H, s, C<u>H</u>$_3$(Ts)), 3.44 (1H, d, J_{AB} = 10.7 Hz, (Ind)C<u>H</u>$_2$N), 3.63 (1H, d, J = 3.0 Hz, O<u>H</u>), 4.03 (1H, d, J_{AB} = 10.5 Hz, (Ind)C<u>H</u>$_2$N), 4.46 (1H, sept, J = 6.9 Hz, C<u>H</u>(iPr)), 6.07 (1H, d, J = 3.0 Hz, C_2<u>H</u>OH), 7.02 (1H, d, J = 8.0 Hz, C_4<u>H</u> or C_7<u>H</u>), 7.06 (1H, dxdxd, $J_1 = J_2$ = 8.0 Hz, J_3 = 1.7 Hz, C_5<u>H</u> or C_6<u>H</u>), 7.26 (2H, d, J = 8.3 Hz, C_3<u>H</u>(Ts), C_5<u>H</u>(Ts)), 7.36 (1H, dxd, $J_1 = J_2$ = 7.6 Hz, C_5<u>H</u> or C_6<u>H</u>), 7.64 (1H, d, J = 8.0 Hz, C_4<u>H</u> or C_7<u>H</u>), 7.78 (2H, d, J = 8.5 Hz, C_2<u>H</u>(Ts), C_6<u>H</u>(Ts)); **^{13}C-NMR (75,6 MHz, $CDCl_3$, ppm):** 19.22 (<u>C</u>H$_3$(iPr)), 19.31 (<u>C</u>H$_3$(iPr)), 21.57 (<u>C</u>H$_3$(Ts)), 44.77 (2C, (Ind)<u>C</u>H$_2$N, <u>C</u>H(iPr)), 60.92 (<u>C</u>$_3$), 87.38 (<u>C</u>$_2$HOH), 87.96 (<u>C</u>Cl$_2$), 114.10 (<u>C</u>$_4$H or <u>C</u>$_7$H), 123.95 (<u>C</u>$_4$H or <u>C</u>$_7$H), 124.27 (<u>C</u>$_5$H or <u>C</u>$_6$H), 127.18 (2C, <u>C</u>$_2$H(Ts), <u>C</u>$_6$H(Ts)), 129.24 (<u>C</u>$_{3a}$), 129.99 (2C, <u>C</u>$_3$H(Ts), <u>C</u>$_5$H(Ts)), 130.80 (<u>C</u>$_5$H or <u>C</u>$_6$H), 134.86 (<u>C</u>$_1$(Ts)), 140.24 (<u>C</u>$_{7a}$), 145.06 (<u>C</u>$_4$(Ts)), 164.44 (<u>C</u>=O); **IR (KBr, cm^{-1}):** 3401 (ν_{OH}), 1719 ($\nu_{NC=O}$), 1358, 1169 ($\nu_{S=O}$); **MS (ESI): m/z =** 469/471/473 (M$^+$+1); **Mp.:** 97.3 °C.