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ELECTRONIC SUPPLEMENTARY INFORMATION

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B E L O N G I N G TO T H E P A P E R

Enantioselectivity in visible light-induced, singlet oxygen [2+4] cycloaddition reactions (type II photooxygenations) of 2-pyridones

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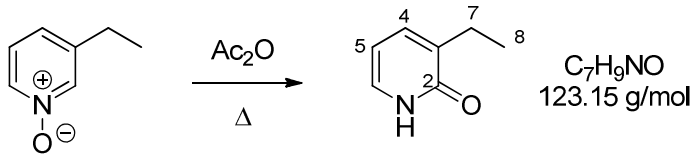
1. General Procedures

All reactions involving moisture-sensitive chemicals were carried out in flame-dried glassware with magnetic stirring under argon. TLC was performed on silica coated glass plates (silica gel 60 F_{254}) with detection by UV (254 nm) or ceric ammonium molybdate [CAM] (0.8 g $Ce(SO_4)_2\,4 \times H_2O$, 25 g $(NH_4)_6Mo_7O_{24} \times 4\,H_2O$ in 20 mL H_2SO_4 and 180 mL water) with subsequent heating. Flash chromatography was performed on silica gel 60 (Merck, 230-400 mesh) with the indicated eluent. All solvents for chromatography were distilled prior to use. HPLC analyses were performed using a chiral stationary phase [ChiralPak AD-H (250 × 4.6 mm), ChiralCell OD (250 × 4.6 mm), Chiralpak AS-H (250 × 4.6 mm, 5 µm), ChiralCell OJ-H (250 × 4.6 mm), Daicel Chemical Industries] employing *n*-hexane/*i*-propanol as eluents and UV-detection at 20 °C. Semi-preparative HPLC separation was performed using a chiral stationary phase [Chiralpak AS-H (250 × 20 mm, 5 µm), Daicel Chemical Industries] employing *n*-hexane/*i*-propanol (70/30) as eluent (flow rate: 19 mL/min) and UV-detection.

IR spectra were recorded on a JASCO IR-4100 (ATR), MS/HRMS measurements were performed on a Finnigan MAT 8200 (EI), a Finnigan MAT 95S (HR-EI), a Finnigan LCQ classic (ESI) and a Thermo Finnigan LTQ FT (HRMS-ESI). ^{1}H- and ^{13}C-NMR spectra were recorded at 303 K either on a Bruker AV-250, a Bruker AV-360 or a Bruker AV-500 spectrometer. The chemical shifts are reported relative to the solvent used ($CHCl_3$, DMSO, MeOH).[1] The multiplicities of the ^{13}C-NMR signals were determined by DEPT experiments. Optical rotations were measured using a Perkin-Elmer 241 MC Polarimeter. Elemental analyses were carried out on a Elementar Vario EL in the chemistry department at the Technische Universität München. UV-Vis spectra were recorded on a Perkin-Elmer Lambda 35 UV-Vis-spectrometer. Melting points were measured on a Koffler Thermopan and are uncorrected.

2. Synthesis of pyridones 9, 13 and 15

3-Ethylpyridine-2(1*H*)-one (**9**)



9

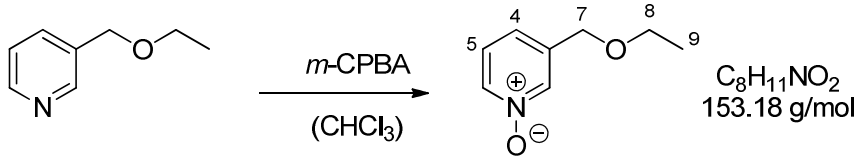
3.00 g (24.2 mmol) 3-Ethylpyridine-1-oxide[2] was heated at reflux in acetic anhydride (30 mL) for 4 h. The solvent was removed *in vacuo* and the residue was purified by flash chromatography on silica gel (eluent: EtOAc/MeOH = 1/0 → 4/1) to afford 319 mg (2.59 mmol, 11%) **9** as a white solid. Analytical

[1] V. Kotlyar and A. Nudelmann, *J. Org. Chem.*, 1997, **62**, 7512-7515.
[2] D. H. Bremner, K. R. Sturrock, G. Wishart, S. R. Mitchell, S. M. Nicoll and G. Jones, *Synth. Commun.*, 1997, **27**, 1535-1542.

data for **9**: R_f = 0.16 (EtOAc) [UV]; ^{1}H-NMR (360 MHz, $CDCl_3$): δ (ppm) = 1.20 (t, ^3J = 7.5 Hz, 3 H, CH_3), 2.57 (q, ^3J = 7.5 Hz, 2 H, CH_2), 6.23 (*virt.* t, $^3J \approx {}^3J \approx$ 6.6 Hz, 1 H, H-5), 7.29 (d, ^3J = 6.6 Hz, 2 H, H-4, H-6), 13.29 (s, 1 H, H-1); ^{13}C-NMR (91 MHz, $CDCl_3$): δ (ppm) = 12.6 (q, C-8), 23.1 (t, C-7), 106.7 (d, C-5), 131.8 (d, C-4), 134.7 (s, C-3), 137.0 (d, C-6), 165.2 (s, C-2); GC-MS (EI, 70 eV): *m/z* (%) = 123 (100) [M^+], 108 (88), 104 (22), 95 (17), 80 (42), 53 (23).

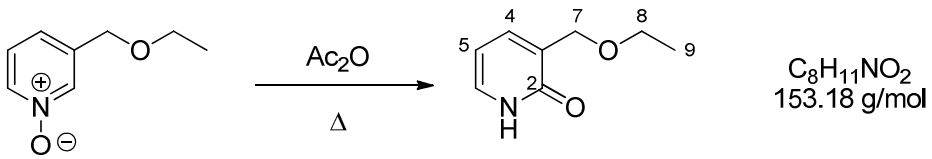
The spectroscopic data are in accordance with the literature.[3]

3-(Ethoxymethyl)pyridine-1-oxide



4.17 g (30.4 mmol, 1.0 eq.) 3-Ethyloxymethylpyridine[4] and 8.25 g (70%, 33.4 mmol, 1.1 eq.) *m*-CPBA in 30 mL chloroform were stirred for 1 d at ambient temperature. The solvent was removed *in vacuo* and the residue was purified by flash chromatography on silica gel (eluent: EtOAc/MeOH = 1/0 → 4/1) to afford 4.45 g (29.1 mmol, 96%) 3-[(ethyloxy)methyl]pyridine-1-oxide as a yellow oil. Analytical data: R_f = 0.25 (EtOAc/MeOH = 9/1) [UV]; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3389 (br), 1605 (m, C=N), 1484 (m), 1440 (s, N=C), 1295 (m, C-O, N-O), 1266 (s, C-O), 1155 (s), 1105 (s), 1013 (m), 800 (m), 757 (m); ^{1}H-NMR (360 MHz, $CDCl_3$): δ (ppm) = 1.24 (t, ^3J = 7.0 Hz, 3 H, H-9), 3.56 (q, ^3J = 7.0 Hz, 2 H, H-8), 4.46 (s, 2 H, H-7), 7.22-7.24 (m, 2 H, H-4, H-5), 8.10-8.13 (m, 1 H, H-6), 8.21-8.25 (m, 1 H, H-2); ^{13}C-NMR (90 MHz, $CDCl_3$): δ (ppm) = 15.0 (q, C-9), 66.5 (t, C-7/8), 68.8 (t, C-7/8), 124.7 (d, C-4), 125.6 (d, C-5), 138.0 (s, C-3), 138.0 (d, C-6), 138.4 (d, C-2); MS (EI, 70 eV) *m/z* (%) = 153 (45) [M^+], 137 (22) [(M–O)$^+$], 109 (100) [(M–C_2H_4O)$^+$], 92 (100) [(M–$C_2H_5O_2$)$^+$], 80 (38), 65 (33), 44 (48); HRMS (EI): calcd. for $C_8H_{11}NO_2$ [M^+]: 153.07898, found: 153.07892.

3-(Ethoxymethyl)pyridine-2(1*H*)-one (**13**)



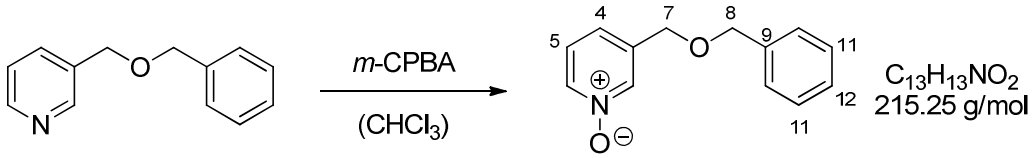
13

4.44 g (29.0 mmol) 3-[(Ethyloxy)methyl]pyridine-1-oxide was heated at reflux in 50 mL acetic anhydride for 4 h. After cooling to ambient temperature, the solvent was removed *in vacuo* and the residue was purified by flash chromatography on silica gel (eluent: EtOAc/MeOH = 1:0 → 4/1) to afford 520 mg (3.39 mmol, 12%) **13** as a colourless solid. Analytical data for **13**: R_f = 0.19 (EtOAc) [UV, CAM]; m.p.:

[3] S. Yamaguchi, E. Hamade, H. Yokoyama, Y. Hirai and S. Shiotani, *J. Heterocyclic Chem.,* 2002, **39**, 335-339.

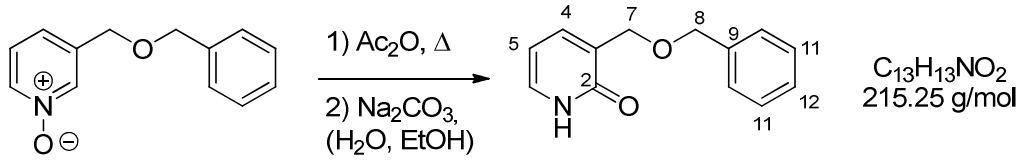
78 °C; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2857 (m), 2800 (m), 1643 (s, C=O), 1614 (s), 1567 (s), 1483 (m), 1327 (m), 1227 (m, C-O), 1113 (s), 1089 (s), 769 (s); ^{1}H-NMR (360 MHz, $CDCl_3$): δ (ppm) = 1.27 (t, ^3J = 6.8 Hz, 3 H, H-9), 3.63 (q, ^3J = 6.8 Hz, 2 H, H-8), 4.47 (s, 2 H, H-7), 6.32 (*virt.* t, $^3J \approx {}^3J \approx$ 6.5 Hz, 1 H, H-5), 7.34 (dd, ^3J = 6.5 Hz, ^4J =1.8 Hz, 1 H, H-6), 7.57-7.60 (m, 1 H, H-4), 13.27 (s, 1 H, H-1); ^{13}C-NMR (91 MHz, $CDCl_3$): δ (ppm) = 15.2 (q, C-9), 66.4 (t, C-8), 67.1 (t, C-7), 106.8 (d, C-5), 129.6 (s, C-3), 132.9 (d, C-6), 137.7 (d, C-4), 163.9 (s, C-2); MS (EI, 70 eV) *m/z* (%) = 153 (30) [M^+], 139 (1), 124 (60), 109 (100), 96 (10), 80 (30), 53 (24), 43 (15); HRMS (EI): calcd. for $C_8H_{11}NO_2$ [M^+]: 153.0789, found: 153.0789.

3-[(Benzyloxy)methyl]pyridine-1-oxide



1.42 g (7.14 mmol, 1.0 eq.) 3-(Benzyloxymethyl)-pyridine[5] and 1.36 g (70%, 7.86 mmol, 1.1 eq.) *m*-CPBA in 25 mL chloroform were stirred overnight at ambient temperature. The solvent was removed *in vacuo* and the residue was purified by flash chromatography on silica gel (eluent: EtOAc/MeOH = 4/1) to afford 1.45 g (6.74 mmol, 94%) 3-[(benzyloxy)methyl]pyridine-1-oxide as a yellow-brownish oil. Analytical data: R_f = 0.20 (EtOAc/MeOH = 9/1) [UV, CAM]; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2861 (w), 1707 (w), 1605 (w), 1495 (m), 1437 (s), 1364 (m), 1270 (br, C-O, N-O), 1153 (s), 1073 (br), 1014 (s), 738 (br); ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 4.48 (s, 2 H, H-7), 4.57 (s, 2 H, H-8), 7.20-7.23 (m, 2 H, H-4, H-5), 7.28-7.37 (m, 5 H, H-10, H-11, H-12), 8.12 (m, 1 H, H-6), 8.24 (s, 1 H, H-2); ^{13}C-NMR (90 MHz, $CDCl_3$): δ (ppm) = 68.1 (t, C-7), 72.8 (t, C-8), 124.8 (d, C-4), 125.6 (d, C-5), 127.7 (d, C-11), 128.0 (d, C-12), 128.5 (d, C-10), 137.0 (s, C-9), 138.0 (C-Py), 138.0 (C-Py), 138.1 (C-Py); MS (EI, 70 eV) *m/z* (%) = 215 (10) [M^+], 198 (1), 156 (5), 139 (5), 109 (100), 91 (43), 65 (17); HRMS (EI): calcd. for $C_{13}H_{13}NO_2$ [M^+]: 215.0946, found: 215.0946.

3-[(Benzyloxy)methyl]pyridine-2(1*H*)-one (**15**)



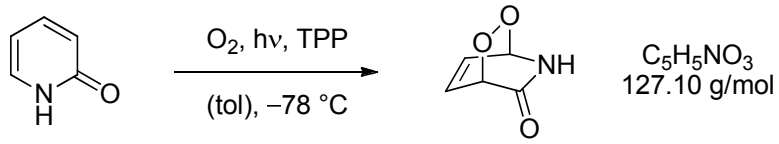
15

[4] L. Ford , J. R. Harjani , F. Atefi , M. T. Garcia , R. D. Singer and P. J. Scammells, *Green Chem.,* 2010, **12**, 1783-1789.
[5] E. Abele, R. Abele, A. Gaukhman and E. Lukevics, *Chem. Heterocyclic Comp., (New York, NY, United States)* 1998, **34**, 40-43.

1.43 g (6.64 mmol) 3-[(Benzyloxy)methyl]pyridine-1-oxide was heated at reflux in 50 mL acetic anhydride for 3 h. After cooling to ambient temperature, the solvent was removed *in vacuo* and the residue was purified by flash chromatography on silica gel (eluent: EtOAc/MeOH = 4/1) to afford a mixture of product **15** and *N*-acetylated product. The mixture was stirred overnight at ambient temperature with 581 mg (5.48 mmol) Na_2CO_3 in 10 mL water and 10 mL ethanol. The solvent was again removed and the residue was purified by flash chromatography on silica gel (eluent: EtOAc/MeOH = 4/1) to afford 476 mg (2.21 mmol, 33%) of **15** as colourless crystals. Analytical data for **15**: R_f = 0.30 (EtOAc) [UV, CAM]; m.p.: 106 °C; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2789 (br), 1650 (br, C=O), 1621 (s), 1567 (s), 1477 (m), 1115 (s), 1079 (s), 890 (s), 773 (s), 752 (s), 699 (s); ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 4.55 (s, 2 H, H-7), 4.67 (s, 2 H, H-8), 6.32 (*virt.* t, $^3J \approx {}^3J \approx$ 6.5 Hz, 1 H, H-5), 7.29 (*virt.* t, $^3J \approx {}^3J \approx$ 7.2 Hz, 1 H, H-12), 7.34-7.40 (m, 5 H, H-10, H-11, H-6), 7.64 (d, ^3J = 6.9 Hz, 1 H, H-4), 12.97 (s, 1 H, NH); ^{13}C-NMR (90 MHz, $CDCl_3$): δ (ppm) = 66.9 (t, C-7), 72.9 (t, C-8), 106.8 (d, C-5), 127.6 (d, C-12), 127.7 (d, C-10), 128.4 (d, C-11), 129.4 (s, C-3), 133.0 (d, C-6), 137.8 (d, C-4), 138.1 (s, C-9), 163.9 (s, C-2); MS (EI, 70 eV) *m/z* (%) = 215 (2) [M^+], 196 (5), 124 (28), 109 (100), 91 (54), 80 (15), 65 (10), 53 (10), 39 (8); HRMS (EI): calcd. for $C_{13}H_{13}NO_2$ [M^+]: 215.0946, found: 215.0946.

3. Synthesis of endoperoxides 4 and 5

2,3-Dioxa-5-azabicyclo[2.2.2]oct-7-en-6-one (*rac*-**4**)

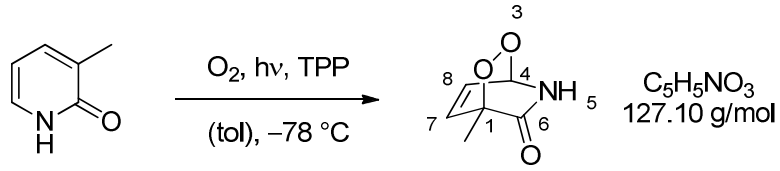


2 *rac*-**4**

In a dry flask pre-degassed with argon, a 136 mM solution of **2** (200 mg, 2.1 mmol) in dry toluene (15.5 mL) was prepared by heating and stirring the suspension at 60 °C. Tetraphenylporphyrin was added (1.12 mg, 0.1 mol%) and the solution was saturated with oxygen. The solution was then put inside the cooling dewar at –78 °C, and after having purged the tubes of the peristaltic pump with oxygen, the irradiation of the solution was started and carried on for 6 h. Oxygen was bubbled throughout the whole reaction and dry ice was added (approximately every 20 min) in the dewar. After 2 h the same amount of tetraphenylporphyrin was added to the solution with a syringe as a solution in dry toluene. After irradiation is completed the solution contained a thin precipitate, the solvent was removed at r.t. under reduced pressure using a liquid-N_2 rotary evaporator. The endoperoxide **4** was obtained with a 96% conversion and was stored in the freezer. The purification was accomplished by quick column chromatography on silica gel using EtOAc as the eluent and **4** was obtained in 90% yield. Analytical data for *rac*-**4**: R_f = 0.46 (EtOAc); ^{1}H-NMR (250 MHz, $CDCl_3$): δ (ppm) = 4.61 (d, ^3J = 6.0 Hz, 1 H), 5.60

(dt, ^3J = 5.3 Hz, ^4J = 2.1 Hz, 1 H), 6.47 (ddd, ^3J =7.9 Hz, ^3J = 6.0 Hz, ^4J = 2.0 Hz, 1 H), 6.6 Hz (ddd, ^3J = 7.2 Hz, ^3J = 5.2 Hz, ^4J = 1.8 Hz, 1 H), 7.9 (br s, 1 H, NH).[6]

1-Methyl-2,3-dioxa-5-azabicyclo[2.2.2]oct-7-en-6-one (*rac*-**5**)

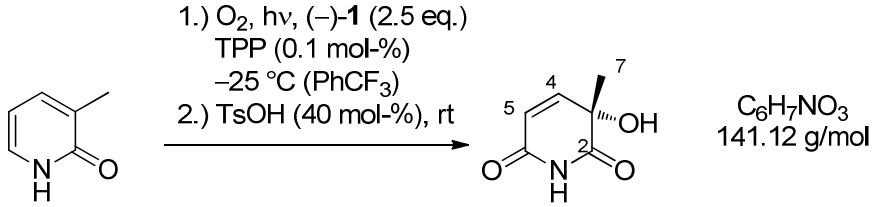


3 *rac*-**5**

Endoperoxide *rac*-**5** was obtained by irradiation of pyridone **3** (100 mg, 916 µmol, 1.0 eq.) with 0.56 mg (0.92 µmol, 0.1 mol%) tetraphenylporphyrin in 6.5 mL toluene for 45 minutes under an oxygen stream at –75 °C. The precipitated *rac*-**5** was filtered off and was washed with 10 mL Et_2O. 126 mg (893 µmol, 97%) of *rac*-**5** was afforded as a white-yellowish solid. Analytical data for *rac*-**5**: R_f = 0.67 (EtOAc) [CAM, $KMnO_4$]; m.p.: 109 °C (decomp.) (Et_2O); IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3229 (vs), 3126 (m), 1719 (vs), 1692 (vs), 1437 (m), 1264 (w), 1066 (s), 1292 (w), 856 (m), 795 (w), 660 (w); ^{1}H-NMR (360 MHz, DMSO-d6): δ (ppm) = 1.41 (s, 3 H, CH_3), 5.97 (*virt.* td, $^3J \approx {}^3J \approx$ 5.3 Hz, ^4J = 1.8 Hz, 1 H, H-4), 6.52 (dd, ^3J = 7.8 Hz, ^4J = 1.8 Hz, 1 H, H-7), 6.90 (dd, ^3J = 7.8 Hz, ^3J = 5.3 Hz, 1 H, H-8), 9.29 (s, 1 H, NH); ^{1}H-NMR (250 MHz, $CDCl_3$): δ (ppm) = 1.62 (s, 3 H, CH_3), 5.74 (*virt.* td, $^3J \approx {}^3J \approx$ 5.4 Hz, ^4J = 1.9 Hz, 1 H, H-4), 6.47 (dd, ^3J = 7.9 Hz, ^4J = 1.9 Hz, 1 H, H-7), 6.84 (dd, ^3J = 7.9 Hz, ^3J = 5.4 Hz, 1 H, H-8), 6.89 (s, 1 H, NH); ^{13}C-NMR (91 MHz, $CDCl_3$): δ (ppm) = 14.3 (q, CH_3), 80.2 (d, C-4), 81.8 (s, C-1), 133.0 (d, C-7), 134.1 (d, C-8), 171.8 (s, C-6); MS (EI, 70 eV): *m/z* (%) = 142 (8) [$(M+H)^+$], 126 (12) [$(M–CH_3)^+$], 114 (10), 109 (12) [$(M–O_2)^+$], 98 (15) [$(M–CONH)^+$], 83 (78) [$(M–C_2H_4NO)^+$], 71 (32), 55 (22); HRMS (EI): calcd. for $C_6H_7NO_3$ [$(M–CH_3)^+$]: 141.0426, found: 141.0428.[7]

4. Photooxygenations

(*S*)-3-Hydroxy-3-methylpyridine-2,6(1*H*,3*H*)-dione (**6**) [Represenative procedure]



3 **6**

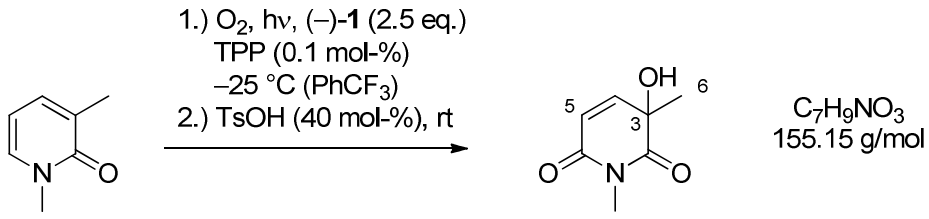
To a solution of 25.0 mg (200 µmol, 1.0 eq.) pyridone **4** and 202 mg (573 µmol, 2.5 eq.) (–)-template (**1**) in 2 mL trifluorotoluene was added 100 µL (2.28 mM in $PhCF_3$, 0.14 mg, 0.23 µmol, 0.1 mol%)

[6] C Cornaggia, *Laurea* thesis, University of Pavia, **2007**.

tetraphenylporphyrin solution. Under a continuous oxygen stream the solution was cooled to –25 °C. After equilibration at –25 °C for 15 minutes, the solution was irradiated for 20 minutes with two 400 W sodium vapour lamps (*Philips* Son-T-Agro) at –25 °C. After the first irradiation 17.4 mg (90.0 mmol, 40 mol%) *p*-toluenesulfonic acid monohydrate was added and the reaction was warmed to room temperature. After stirring for 8-13 h at room temperature, the reaction mixture was cooled, and subjected to two further irradiation cycles as described above. After three cycles, the solvent was removed *in vacuo* and the residue was purified by flash chromatography on silica gel (eluent: CH_2Cl_2/pentane/methanol = 29/10/1→ 9/0/1) to afford 29.0 mg **6** (200 µmol, 99%, 90% *ee*) as a colourless solid. Analytical data for **6**: R_f = 0.62 (EtOAc) [CAM]; HPLC (AS-H, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 70/30, 1 mL/min): t_R = 9.1 min, 12.4 min; $[\alpha]_D^{20}$ = –23.0 (c = 0.5 in MeOH) [90% *ee*]; m.p.: 91 °C; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3448 (m, OH), 1686 (vs, C=O), 1633 (s), 1381 (w), 1279 (m, C-O), 1192 (w), 1144 (m), 1116 (m), 844 (m), 777 (m), 680 (w); ^{1}H-NMR (250 MHz, $CDCl_3$): δ (ppm) = 1.61 (s, 3 H, H-7), 3.44 (s, 1 H, OH), 6.11 (dd, ^3J = 10.2 Hz, ^4J = 2.0 Hz, 1 H, H-5), 6.87 (d, ^3J = 10.2 Hz, 1 H, H-4), 8.47 (s, 1 H, H-1); ^{13}C-NMR (63 MHz, $CDCl_3$): δ (ppm) = 29.1 (q, C-7), 70.0 (s, C-3), 120.2 (d, C-5), 148.8 (d, C-4), 164.3 (s, C-6), 176.5 (s, C-2); MS (EI, 70 eV): *m/z* (%) = 126 (10) [$(M–CH_3)^+$], 98 (100), 70 (20), 55 (46), 43 (35); HRMS (EI): calcd. for $C_7H_9NO_3$ [$(M–CH_3)^+$]: 126.0191, found: 126.0192.

The spectroscopic data are in accordance with the literature.[8]

3-Hydroxy-1,3-dimethylpyridine-2,6(1*H*,3*H*)-dione (**8**)



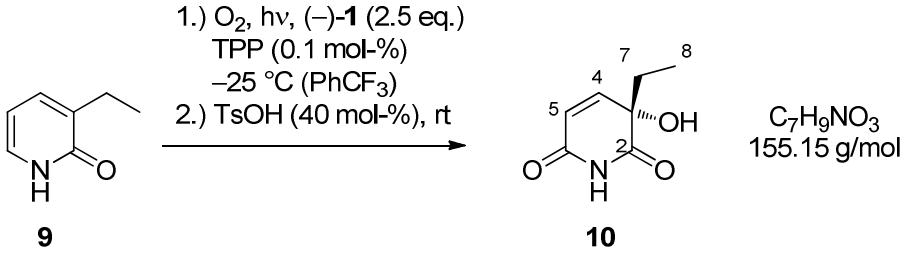
7 **8**

Following the representative procedure, pyridone **7**[9] (28.2 mg, 229 µmol, 1.0 eq.) was reacted with 203 mg (576 µmol, 2.5 eq.) (–)-template (**1**) in 2 mL trifluorotoluene and 125 µL (1.80 mM in $PhCF_3$, 0.14 mg, 0.22 µmol, 0.1 mol%) tetraphenylporphyrin solution. After the first irradiation interval, 16.0 mg (90.0 µmol, 40 mol%) *p*-toluenesulfonic acid monohydrate was added and after purification by flash chromatography on silica gel (eluent: CH_2Cl_2/pentane/methanol = 29/15/1) 34.0 mg (219 µmol, 96%, 0% *ee*) **8** was obtained as a colourless solid. Analytical data for **8**: R_f = 0.68 (EtOAc) [CAM]; HPLC (AD-H, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 90/10, 1 mL/min): t_R = 9.6 min, 11.6 min; ^{1}H-NMR (250 MHz,

[7] M. Cakmak, Diploma thesis, TU Munich, **2007**.
[8] E. Sato, Y. Ikeda and Y. Kanaoka, *Chem. Pharm. Bull.,* 1987, **35**, 507-513.

$CDCl_3$): δ (ppm) = 1.55 (s, 3 H, H-7), 3.23 (s, 3 H, NCH_3), 3.48 (s, 1 H, OH), 6.14 (d, ^3J = 10.1 Hz, 1 H, H-5), 6.82 (d, ^3J = 10.1 Hz, 1 H, H-4); ^{13}C-NMR (63 MHz, $CDCl_3$): δ (ppm) = 26.4 (q, NCH_3), 29.9 (q, C-7), 70.0 (s, C-3), 120.6 (d, C-5), 146.4 (d, C-4), 164.0 (s, C-6), 176.9 (s, C-2); GC-MS (EI, 70 eV, t_R = 6.81 min [STD]): *m/z* (%) = 165 (1) [$(M+H)^+$], 140 (8) [$(M–CH_3)^+$], 112 (22), 98 (100), 70 (23), 55 (52). The spectroscopic data are in accordance with the literature.[8]

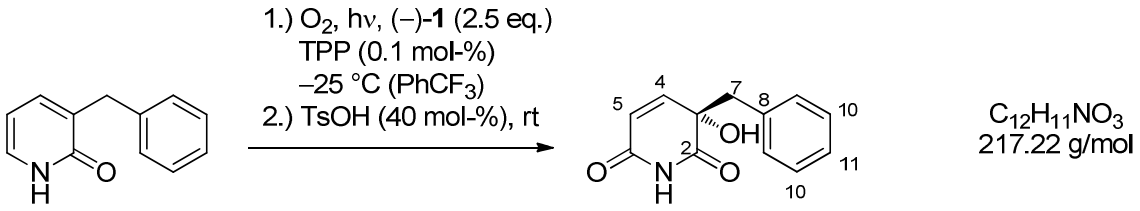
(*S*)-3-Ethyl-3-hydroxypyridine-2,6(1*H*,3*H*)-dione (**10**)



Following the representative procedure, pyridone **9**[3] (28.0 mg, 227 µmol, 1.0 eq.) was reacted with 201 mg (570 µmol, 2.5 eq.) (–)-template (**1**) in 2 mL trifluorotoluene and 125 µL (1.80 mM in $PhCF_3$, 0.14 mg, 0.22 µmol, 0.1 mol%) tetraphenylporphyrin solution. After the first irradiation interval 16.0 mg (90.0 µmol, 40 mol%) *p*-toluenesulfonic acid monohydrate was added and after purification by flash chromatography on silica gel (eluent: CH_2Cl_2/pentane/methanol = 29/15/1) 35.0 mg (226 µmol, 99%, 86% *ee*) **10** was obtained as a colourless solid. Analytical data for **10**: R_f = 0.68 (EtOAc) [CAM]; HPLC (AS-H, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 70/30, 1 mL/min): t_R = 9.5 min, 12.0 min; $[\alpha]_D^{20}$ = –98.5 (c = 0.34 in CH_2Cl_2) [86% *ee*]; m.p.: 65 °C; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3360 (br, NH), 1712 (w, C=O), 1685 (vs, CONHCO), 1631 (s), 1436 (w), 1305 (w), 1271 (m), 1248 (m, C-O), 1183 (w), 1134 (m), 1118 (m), 837 (m); ^{1}H-NMR (360 MHz, $CDCl_3$): δ (ppm) = 0.91 (t, ^3J = 7.6 Hz, 3 H, H-8), 1.77-2.04 (m, 2 H, H-7), 3.73 (s, 1 H, OH), 6.18 (dd, ^3J = 10.1 Hz, ^4J = 2.2 Hz, 1 H, H-5), 6.80 (d, ^3J = 10.1 Hz, 1 H, H-4), 8.89 (s, 1 H, H-1); ^{13}C-NMR (91 MHz, $CDCl_3$): δ (ppm) = 7.5 (q, C-8), 35.6 (t, C-7), 73.5 (s, C-3), 121.4 (d, C-5), 147.7 (d, C-4), 164.3 (s, C-6), 176.0 (s, C-1); MS (EI, 70 eV): *m/z* (%) = 155 (30) [M^+], 126 (98) [$(M–C_2H_5)^+$], 112 (100) [$(M–CONH)^+$], 99 (60), 82 (38), 55 (63); HRMS (EI): calcd. for $C_7H_9NO_3$ [M^+]: 155.0582, found: 155.0579.

(*S*)-3-Benzyl-3-hydroxypyridine-2,6(1*H*,3*H*)-dione (**12**)

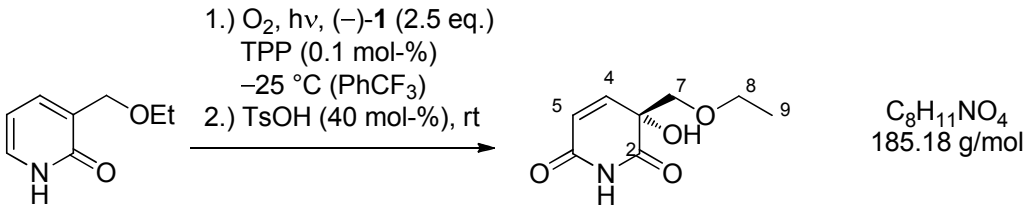
[9] H. L. Bradlow and C. A. Vanderwerf, *J. Org. Chem.,* 1951, **16**, 73-83.



11 **12**

Following the representative procedure, pyridone **11**[10] (42.0 mg, 227 µmol, 1.0 eq.) was reacted with 203 mg (576 µmol, 2.5 eq.) (–)-template (**1**) in 6 mL trifluorotoluene and 125 µL (2.00 mM in $PhCF_3$, 0.18 mg, 0.29 µmol, 0.1 mol%) tetraphenylporphyrin solution. After the first irradiation interval, 16.0 mg (90.0 mmol, 40 mol%) *p*-toluenesulfonic acid monohydrate was added and after purification by flash chromatography on silica gel (eluent: EtOAc/pentane = 3/7 → 1/0, followed by a second chromatography with CH_2Cl_2/pentane/methanol = 29/10/1 → 9/0/1) 36.0 mg (166 µmol, 73%, 69% *ee*) **12** was obtained as a colourless solid. Analytical data for **12**: R_f = 0.73 (EtOAc) [CAM]; HPLC (AD-H, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 90/10, 1 mL/min): t_R = 24.7 min, 34.6 min; $[\alpha]_D^{20}$ = –173.0 (c = 0.06 in CH_2Cl_2) [69% *ee*]; m.p.: 125-138 °C; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3434 (m, NH), 3092 (m), 1719 (m, C=O), 1681 (vs, CONHCO), 1632 (s), 1387 (w), 1258 (s, C-O), 1153 (m), 1113 (m), 863 (w), 700 (w); ^{1}H-NMR (360 MHz, $CDCl_3$): δ (ppm) = 3.08 (d, ^2J = 13.2 Hz, 1 H, H-7), 3.17 (d, ^2J = 13.2 Hz, 1 H, H-7), 3.64 (s, 1 H, OH), 6.09 (dd, ^3J = 10.3 Hz, ^4J = 2.2 Hz, 1 H, H-5), 6.75 (d, ^3J = 10.3 Hz, 1 H, H-4), 7.09-7.13 (m, 2 H, H-9), 7.26-7.29 (m, 3 H, H-10, H-11), 8.37 (s, 1 H, H-1); ^{13}C-NMR (90 MHz, $CDCl_3$): δ (ppm) = 48.8 (t, C-7), 73.7 (s, C-3), 121.4 (d, C-5), 127.8 (d, C-11), 128.4 (d, C-10), 130.3 (d, C-9), 132.5 (s, C-8), 147.0 (d, C-4), 163.8 (s, C-6), 175.4 (s, C-2); MS (EI, 70 eV): *m/z* (%) = 214 (2) [M^+], 198 (1), 171 (1), 157 (1), 145 (1), 91 (100), 65 (10), 39 (3); HRMS (EI): calcd. for $C_{12}H_{11}NO_3$ [M^+]: 217.0739, found: 217.0740.

(*R*)-3-(Ethoxymethyl)-3-hydroxypyridine-2,6(1*H*,3*H*)-dione (**14**)



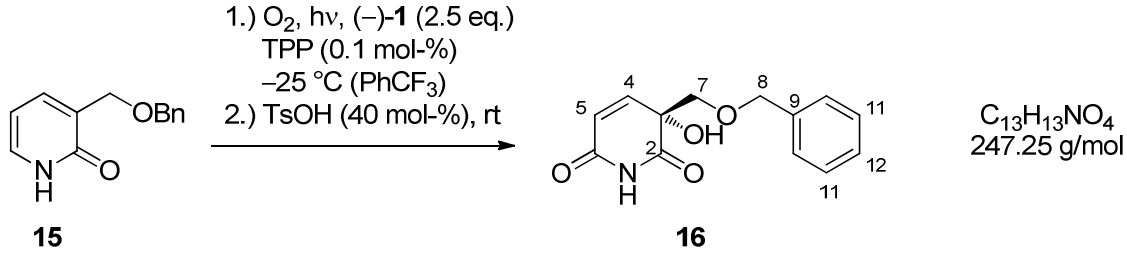
13 **14**

Following the representative procedure, pyridone **13** (25.0 mg, 163 µmol, 1.0 eq.) was reacted with 144 mg (408 µmol, 2.5 eq.) (–)-template (**1**) in 5 mL trifluorotoluene and 100 µL (3.3 mM in $PhCF_3$, 0.20 mg, 0.33 µmol, 0.1 mol%) tetraphenylporphyrin solution. After the first irradiation interval, 11.2 mg (65.0 µmol, 40 mol%) *p*-toluenesulfonic acid monohydrate was added and after purification by flash

[10] L. I. Kruse, C. Kaiser, W. E. DeWolf, J. A. Finkelstein, J. S. Frazee, E. L. Hilbert, S. T. Ross, K. E. Flaim and J. L. Sawyer, *J. Med. Chem.,* 1990, **33**, 781-789.

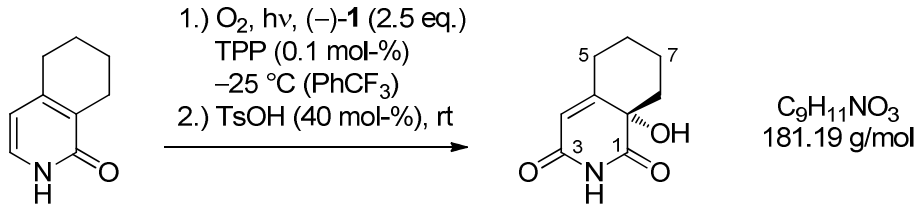
chromatography on silica gel (eluent: CH_2Cl_2/pentane/methanol = 29/10/1) 9.0 mg (49.0 µmol, 30%, 79% *ee*) **14** was obtained as colourless crystals. Analytical data for **14**: R_f = 0.74 (EtOAc) [CAM]; HPLC (OD, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 90/10, 1 mL/min): t_R = 21.4 min, 23.4 min; $[\alpha]_D^{20}$ = –138.3 (c = 4.1 in CH_2Cl_2) [79% *ee*]; m.p.: 105 °C; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3458 (m, NH), 3414 (m), 1687 (br, C=O), 1633 (s, CONHCO), 1378 (m), 1264 (s), 1184 (w), 1119 (s), 1100 (m), 849 (m), 685 (w); ^{1}H-NMR (360 MHz, $CDCl_3$): δ (ppm) = 1.12 (t, ^3J = 7.2 Hz, 3 H, H-9), 3.49 (q, ^3J = 7.2 Hz, 2 H, H-8), 3.52 (d, ^2J = 9.2 Hz, 1 H, H-7), 3.63 (d, ^2J = 9.2 Hz, 1 H, H-7), 6.22 (dd, ^3J = 10.1 Hz, ^4J = 1.8 Hz, 1 H, H-5), 6.78 (d, ^3J = 10.1 Hz, 1 H, H-4), 8.41 (s, 1 H, NH); ^{13}C-NMR (90 MHz, $CDCl_3$): δ (ppm) = 14.8 (q, C-9), 67.7 (t, C-8), 72.7 (s, C-3), 76.0 (t, C-7), 123.0 (d, C-5), 145.2 (d, C-4), 164.1 (s, C-6), 174.5 (s, C-2); MS (EI, 70 eV) *m/z* (%) = 185 (1) [M^+], 168 (3) [$(M–OH)^+$], 127 (20), 91 (17), 82 (33), 61 (25), 59 (100), 45 (28), 43 (89); HRMS (EI): calcd. for $C_8H_{10}NO_3$ [$(M–OH)^+$]: 168.0655, found: 168.0655.

(*R*)-3-[(Benzyloxy)methyl]-3-hydroxypyridine-2,6(1*H*,3*H*)-dione (**16**)



Following the representative procedure, pyridone **15** (25.0 mg, 116 µmol, 1.0 eq.) was reacted with 102 mg (290 µmol, 2.5 eq.) (–)-template (**1**) in 5 mL trifluorotoluene and 100 µL (1.16 mM in $PhCF_3$, 71.0 µg, 0.12 µmol, 0.1 mol%) tetraphenylporphyrin solution. After the first irradiation interval, 8.0 mg (64.0 µmol, 40 mol%) *p*-toluenesulfonic acid monohydrate was added and after purification by flash chromatography on silica gel (eluent: EtOAc/pentane = 7/3 → 1/1 → 1/0) 11.0 mg (45.0 µmol, 38%, 85% *ee*) **16** was obtained as a yellow-brownish solid. Analytical data for **16**: R_f = 0.77 (EtOAc) [CAM]; HPLC (OD-H, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 80/20, 1 mL/min): t_R = 12.2 min, 14.8 min; $[\alpha]_D^{20}$ = –120.0 (c = 5.3 in CH_2Cl_2) [85% *ee*]; m.p.: 82 °C; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3380 (w, NH), 1693 (br, C=O), 1637 (s, CONHCO), 1366 (m), 1289 (m, C-O), 1183 (m), 1128 (m), 1081 (m), 849 (m), 745 (m), 695 (m); ^{1}H-NMR (360 MHz, $CDCl_3$): δ (ppm) = 3.46 (d, ^2J = 8.8 Hz, 1 H, H-7), 3.60 (d, ^2J = 8.8 Hz, 1 H, H-7), 4.43 (s, 2 H, H-8), 6.15 (dd, ^3J = 10.1 Hz, ^4J = 1.8 Hz, 1 H, H-5), 6.69 (d, ^3J = 10.1 Hz, 1 H, H-4), 7.12-7.30 (m, 5 H, H-10, H-11, H-12), 8.54 (s, 1 H, NH); ^{13}C-NMR (90 MHz, $CDCl_3$): δ (ppm) = 72.5 (s, C-3), 73.7 (t, C-8), 75.2 (t, C-7), 123.1 (d, C-5), 127.5 (d, 2 C, C-10), 128.0 (d, C-12), 128.5 (d, 2 C, C-11), 136.8 (s, C-9), 145.2 (d, C-4), 164.1 (s, C-6), 174.5 (s, C-2); MS (EI, 70 eV) *m/z* (%) = 247 (1) [M^+], 217 (5) [$(M–CH_2O)^+$], 181 (8), 152 (8), 139 (9), 125 (55), 110 (77), 92 (55), 91 (100), 89 (17); HRMS (EI): calcd. for $C_{12}H_{11}NO_3$ [$(M–CH_2O)^+$]: 217.0733, found: 217.0730.

(*S*)-8a-Hydroxy-6,7,8,8a-tetrahydroisoquinoline-1,3(2*H*,5*H*)-dione (**18**)



17 **18**

Following the representative procedure, tetrahydroisoquinolone[11] **17** (25.0 mg, 168 µmol, 1.0 eq.) was reacted with 148 mg (419 µmol, 2.5 eq.) (–)-template (**1**) in 5 mL trifluorotoluene and 100 µL (1.68 mM in $PhCF_3$, 0.10 mg, 0.17 µmol, 0.1 mol%) tetraphenylporphyrin solution. After the first irradiation interval, 12.0 mg (67.0 µmol, 40 mol%) *p*-toluenesulfonic acid monohydrate was added and after purification by flash chromatography on silica gel (eluent: EtOAc/pentane = 3/7 → 1/0, followed by a second chromatography with CH_2Cl_2/pentane/methanol = 29/15/1) 14.0 mg (77.0 µmol, 46%, 71% *ee*) **18** was obtained as a colourless solid. Analytical data for **18**: R_f = 0.74 (EtOAc) [CAM]; HPLC (OJ-H, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 70/30, 1 mL/min): t_R = 10.3 min, 15.8 min; $[\alpha]_D^{20}$ = –82.2 (c = 0.45 in CH_2Cl_2) [68% *ee*]; m.p.: 137 °C; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3460 (w, NH), 2938 (w, C_{al}), 1694 (s, C=O), 1640 (m, CONHCO), 1428 (w), 1389 (w), 1292 (m), 1263 (m, C-O), 1106 (w), 999 (w), 848 (w); ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 1.45 (*virt.* qt, $^2J \approx {}^3J \approx {}^3J \approx$ 13.2 Hz, $^3J \approx {}^3J \approx$ 3.9 Hz, 1 H, C-6*H*H), 1.60 (*virt.* td, $^2J \approx {}^3J \approx$ 13.5 Hz, ^3J = 4.4 Hz, 1 H, C-8*H*H), 1.68-1.72 (m, 1 H, C-7*H*H), 2.02-2.09 (m, 2 H, C-6*H*H, C-7H*H*), 2.21-2.25 (m, 1 H, C-8H*H*), 2.34-2.37 (m, 1 H, C-5*H*H), 2.74 (*virt.* tdd, $^2J \approx {}^3J \approx$ 13.1 Hz, ^3J = 5.0 Hz, ^4J = 1.4 Hz, 1 H, C-5H*H*), 3.70 (s, 1 H, OH), 5.92 (d, ^4J = 1.4 Hz, 1 H, H-4), 8.96 (s, 1 H, NH); ^{13}C-NMR (90 MHz, $CDCl_3$): δ (ppm) = 20.3 (t, C-7), 29.2 (t, C-6), 31.4 (t, C-5), 40.2 (t, C-8), 70.8 (s, C-8a), 114.8 (d, C-4), 163.0 (s, C-4a), 164.2 (s, C-3), 177.0 (s, C-1); MS (EI, 70 eV): *m/z* (%) = 181 (50) [M^+], 138 (75) [$(M–CONH)^+$], 125 (30), 115 (23), 109 (20), 67 (32), 53 (26), 39 (100); HRMS (EI): calcd. for $C_9H_{11}NO_3$ [M^+]: 181.0739, found: 181.0737.

[11] E. Ochiai and Y. Kawazoe, *Pharm. Soc. Japan,* 1957, **5**, 606-610.

5. Single Crystal X-Ray Structure Determination of Compound 6

General:

The data were collected on an X-ray single crystal diffractometer equipped with a CCD detector (APEX II, κ–CCD), a rotating anode (Bruker AXS, FR591) with CuK_α radiation (λ = 1.54180 Å), and a graphite monochromator by using the SMART software package. [1] The measurement was performed on a single crystal coated with perfluorinated ether. The crystal was fixed on the top of a glass fiber and transferred to the diffractometer and was frozen under a stream of cold nitrogen. A matrix scan using three short runs was used to determine the initial lattice parameters. Reflections were merged and corrected for Lorenz and polarization effects, scan speed, and background using SAINT. [2] Absorption corrections, including odd and even ordered spherical harmonics were performed using SADABS. [2] Space group assignments were based upon systematic absences, *E* statistics, and successful refinement of the structures. Structures were solved by direct methods with the aid of successive difference Fourier maps, and were refined against all data using WinGX [7] based on SIR-92. [3] Hydrogen atoms could be located in the difference Fourier maps and were allowed to refine freely. If not mentioned otherwise, non-hydrogen atoms were refined with anisotropic displacement parameters. Full-matrix least-squares refinements were carried out by minimizing $\Sigma w(F_o^2-F_c^2)^2$ with SHELXL-97 [5] weighting scheme. Neutral atom scattering factors for all atoms and anomalous dispersion corrections for the non-hydrogen atoms were taken from *International Tables for Crystallography*. [4] Images of the crystal structures were generated by PLATON [6].

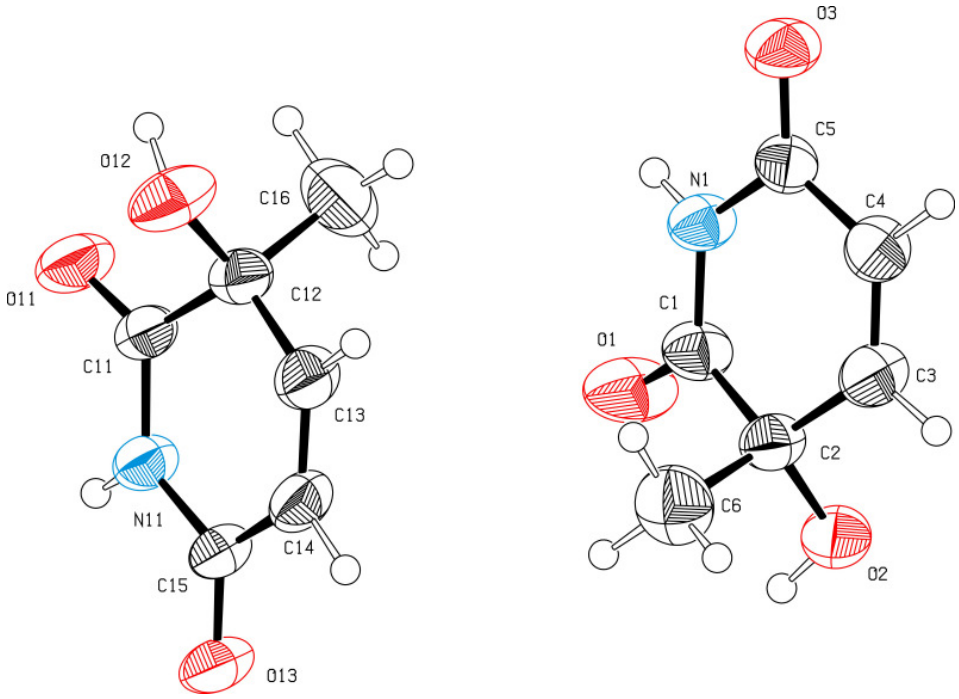


Figure F2 – Ortep drawing of compound **6** with 50% ellipsoids. [6] The asymmetric unit contains two crystallographical independent molecules **A** (right) and **B** (left).

Operator:	*** Herdtweck ***
Molecular Formula:	C_6 H_7 N O_3
Crystal Color / Shape	Colorless plate
Crystal Size	Approximate size of crystal fragment used for data collection: 0.08 × 0.36 × 0.56 mm
Molecular Weight:	141.13 a.m.u.
F_{000}:	592
Systematic Absences:	h00: h≠2n; 0k0: k≠2n, 00l: l≠2n
Space Group:	Orthorhombic $P\,2_12_12_1$ (I.T.-No.: 19)
Cell Constants:	Least-squares refinement of 9954 reflections with the programs "APEX suite" and "SAINT" [1,2]; theta range 4.83° < θ < 64.98°; Cu(K$\bar{\alpha}$); λ = 154.180 pm a = 751.39(3) pm b = 1117.98(5) pm c = 1598.07(7) pm V = 1342.44(10)· 10^6 pm^3; Z = 8; D_{calc} = 1.396 g cm^{-3}; Mos. = 0.77
Diffractometer:	Kappa APEX II (Area Diffraction System; BRUKER AXS); sealed tube; graphite monochromator; 40 kV; 30 mA; λ = 154.180 pm; Cu(K$\bar{\alpha}$)
Temperature:	(20±1) °C; (293±1) K
Measurement Range:	4.83° < θ < 64.98°; h: -8/8, k: -11/12, l: -18/18
Measurement Time:	2 × 15 s per film
Measurement Mode:	measured: 19 runs; 4977 films / scaled: 18 runs; 4617 films φ– and ω–movement; Increment: $\Delta\varphi/\Delta\omega$ = 1.00°; dx = 35.0 mm
LP - Correction:	Yes [2]
Intensity Correction	No/Yes; during scaling [2]
Absorption Correction:	Multi-scan; during scaling; μ = 0.971 mm^{-1} [2] Correction Factors: T_{min} = 0.6561 T_{max} = 0.7526
Reflection Data:	22880 reflections were integrated and scaled 134 reflections systematic absent and rejected 22746 reflections to be merged

2226	independent reflections
0.028	R_{int}: (basis F_o^2)
2226	independent reflections (all) were used in refinements
2116	independent reflections with $I_o > 2\sigma(I_o)$
97.8 %	completeness of the data set
238	parameter full-matrix refinement
9.4	reflections per parameter

Solution: Direct Methods [3]; Difference Fourier syntheses

Refinement Parameters: In the asymmetric unit:

20	Non-hydrogen atoms with anisotropic displacement parameters
14	Hydrogen atoms with isotropic displacement parameters

Hydrogen Atoms: All hydrogen atom positions were found in the difference map calculated from the model containing all non-hydrogen atoms. The hydrogen positions were refined with individual isotropic displacement parameters.

Atomic Form Factors: For neutral atoms and anomalous dispersion [4]

Extinction Correction: F_c (korr) = kF_c[1+ 0.001 · ε· F_c^2· λ^3/sin(2Θ)]$^{-1/4}$ SHELXL-97 [5]
ε refined to ε = 0.0007(2)

Weighting Scheme: $w^{-1} = \sigma^2(F_o^2)+(a*P)^2+b*P$
with a: 0.0426; b: 0.1805; P: [Maximum(0 or F_o^2)+2*F_c^2]/3

Shift/Err: Less than 0.001 in the last cycle of refinement:

Resid. Electron Density: +0.12 e_0^-/Å^3; -0.10 e_0^-/Å^3

R1: $\Sigma(||F_o|-|F_c||)/\Sigma|F_o|$

[$F_o > 4\sigma(F_o)$; N=2116]:	= 0.0272
[all reflctns; N=2226]:	= 0.0288

wR2: $[\Sigma w(F_o^2-F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$

[$F_o > 4\sigma(F_o)$; N=2116]:	= 0.0778
[all reflctns; N=2226]:	= 0.0792

Goodness of fit: $[\Sigma w(F_o^2-F_c^2)^2/(NO-NV)]^{1/2}$ = 1.042

Flack's Parameter : x = 0.02(21)

Remarks: Refinement expression $\Sigma w(F_o^2-F_c^2)^2$

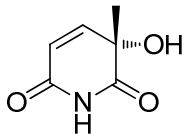
The correct enantiomere is proved by Flack's Parameter.

References:

[1] APEX suite of crystallographic software. APEX 2 Version 2008.4. Bruker AXS Inc., Madison, Wisconsin, USA (2008).
[2] SAINT, Version 7.56a and SADABS Version 2008/1. Bruker AXS Inc., Madison, Wisconsin, USA (2008).
[3] Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, Moliterni A. G. G.; A.; Burla, M. C.; Polidori, G.; Camalli, M.; Spagna, R. "**SIR97**", A New Tool for Crystal Structure Determination and Refinement; *J. Appl. Crystallogr.* **1999**, *32*, 115-119.
[4] International Tables for Crystallography, Vol. C, Tables 6.1.1.4 (pp. 500-502), 4.2.6.8 (pp. 219-222), and 4.2.4.2 (pp. 193-199), Wilson, A. J. C., Ed., Kluwer Academic Publishers, Dordrecht, The Netherlands, 1992.
[5] Sheldrick, G. M. "**SHELXL-97**", University of Göttingen, Göttingen, Germany, (1998).
[6] Spek, A. L. "**PLATON**", A Multipurpose Crystallographic Tool, Utrecht University, Utrecht, The Netherlands, (2010).
[7] L. J. Farrugia, "**WinGX** (Version 1.70.01 January 2005) ", *J. Appl. Cryst.* **1999**, *32*, 837-838.

6. HPLC traces of chiral alcohols

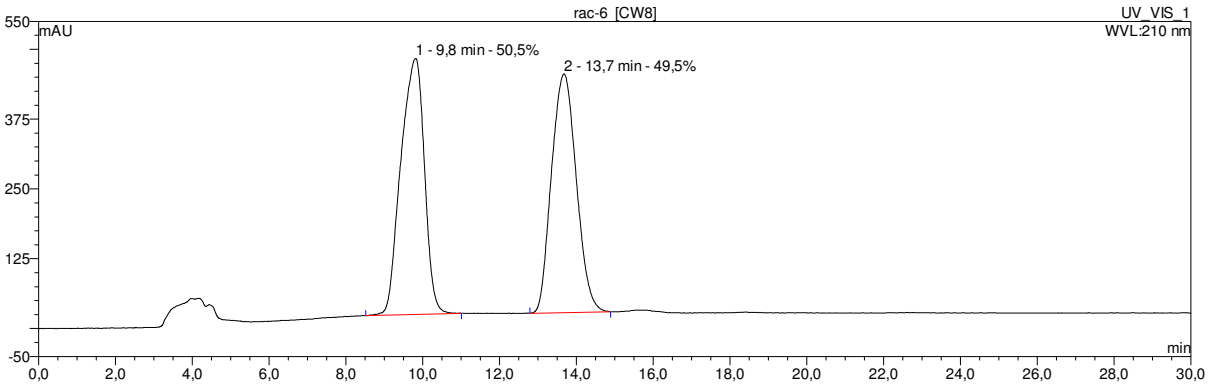
HPLC traces of chiral alcohol **6**



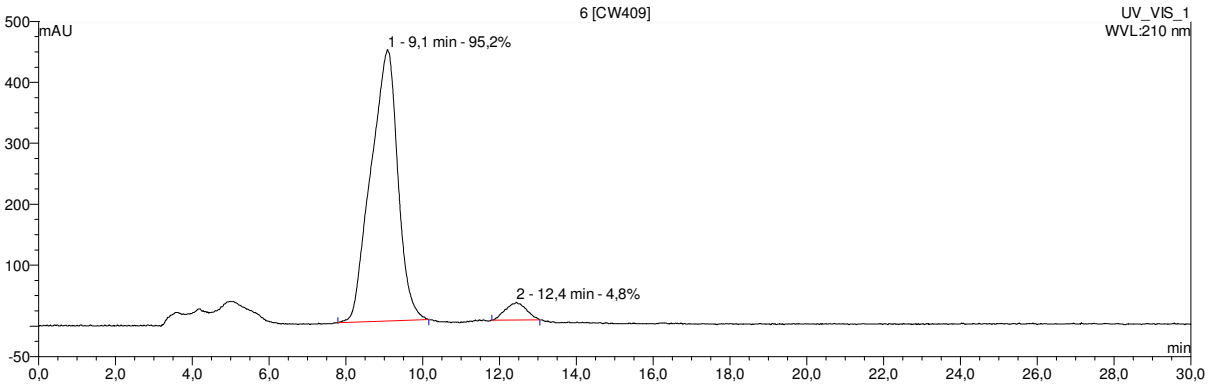
6

HPLC (AS-H, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 70/30, 1 mL/min).

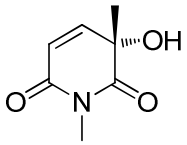
Racemate



Enantioenriched (Table 1, entry 4)



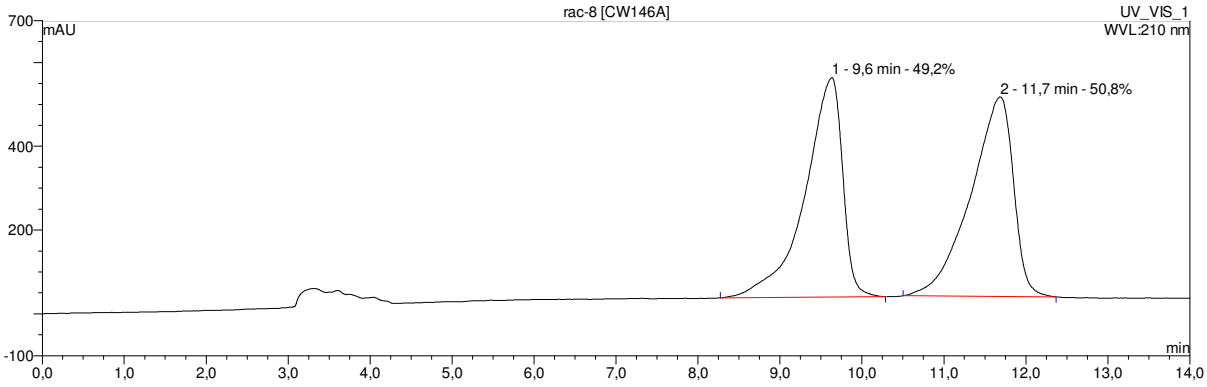
HPLC traces of chiral alcohol **8**



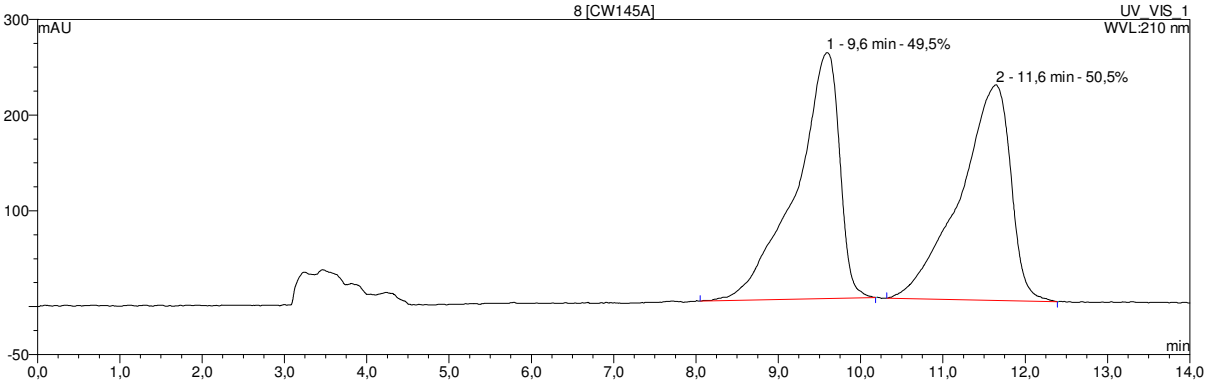
8

HPLC (AD-H, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 90/10, 1 mL/min).

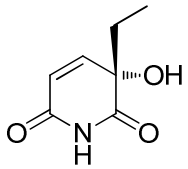
Racemate



Reaction performed in the presence of template **1** (Table 1, entry 5)



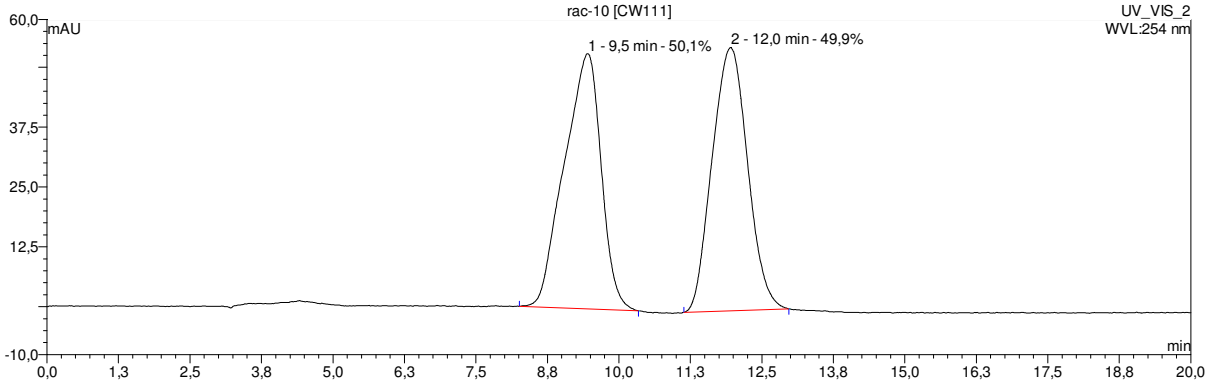
HPLC traces of chiral alcohol **10**



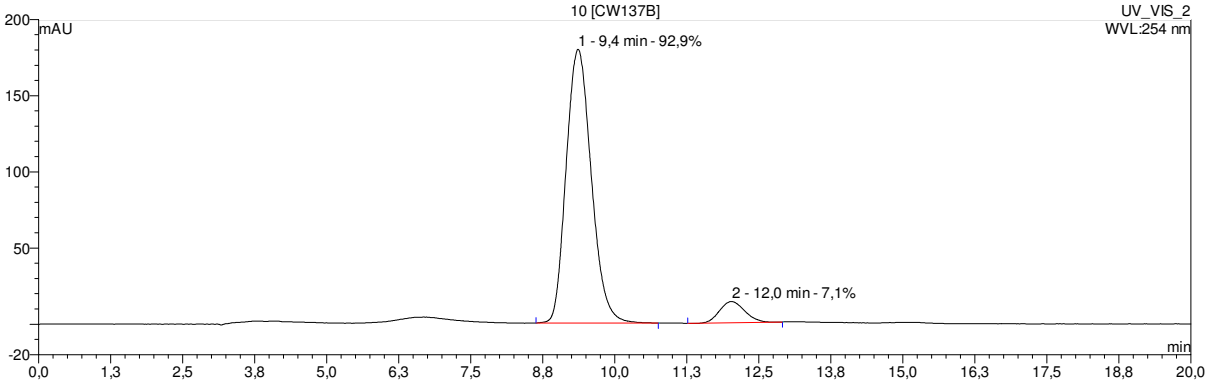
10

HPLC (AS-H, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 70/30, 1 mL/min).

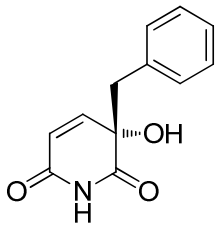
Racemate



Enantioenriched (Table 2, entry 1)



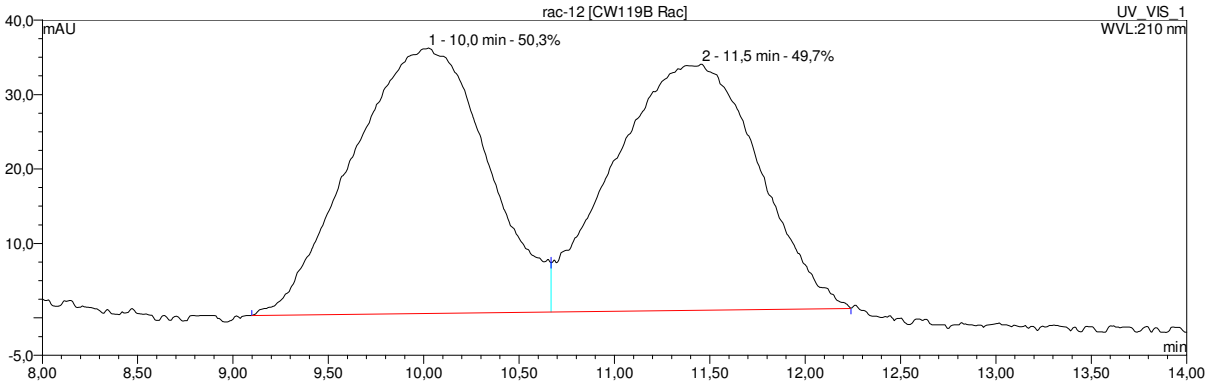
HPLC traces of chiral alcohol **12**



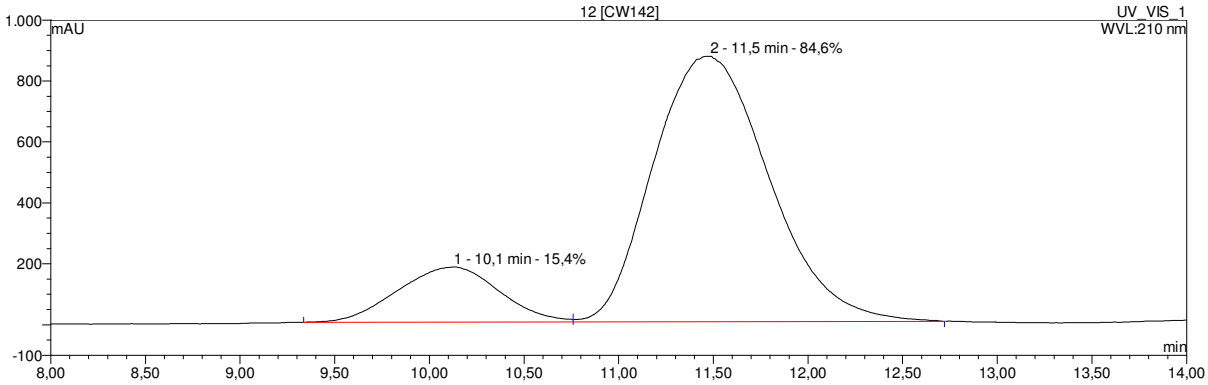
12

HPLC (AS-H, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 70/30, 1 mL/min).

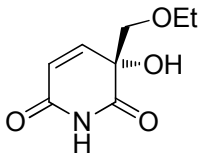
Racemate



Enantioenriched (Table 2, entry 2)



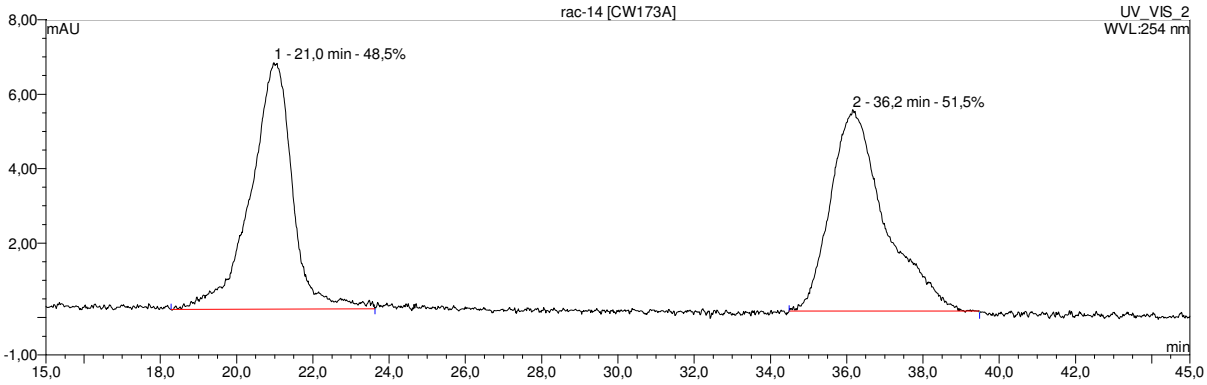
HPLC traces of chiral alcohol **14**



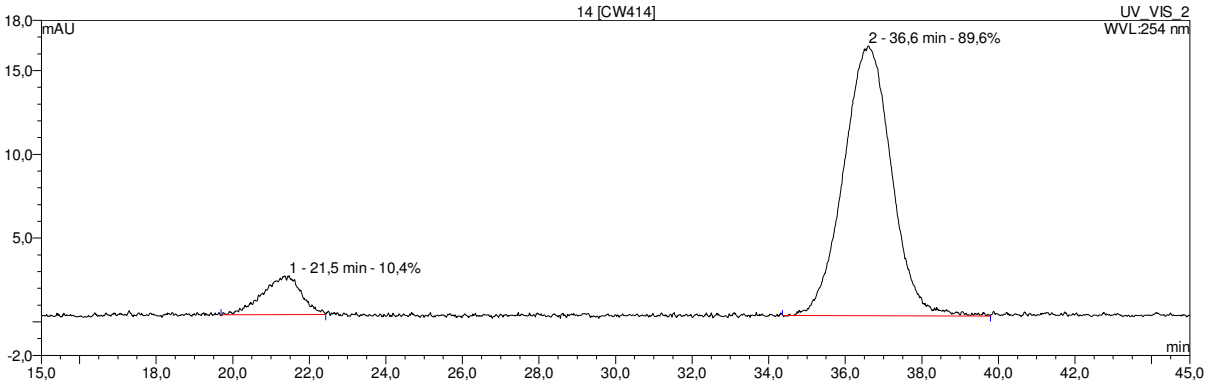
14

HPLC (AD-H, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 90/10, 1 mL/min).

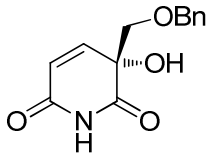
Racemate



Enantioenriched (Table 2, entry 3)



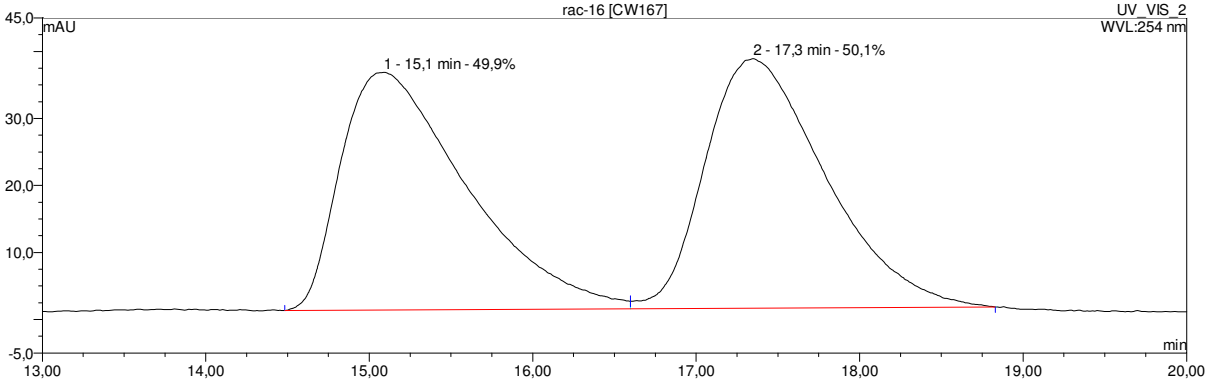
HPLC traces of chiral alcohol **16**



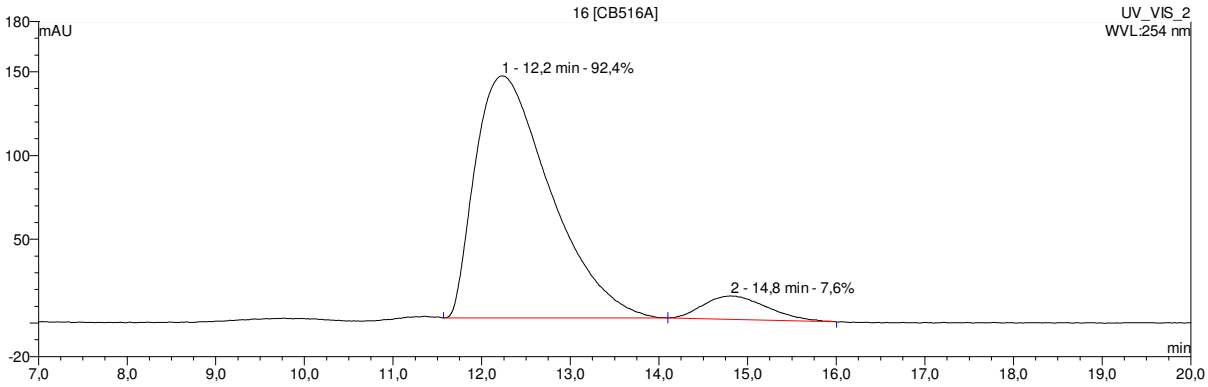
16

HPLC (OD-H, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 80/20, 1 mL/min).

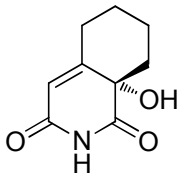
Racemate



Enantioenriched (Table 2, entry 4)



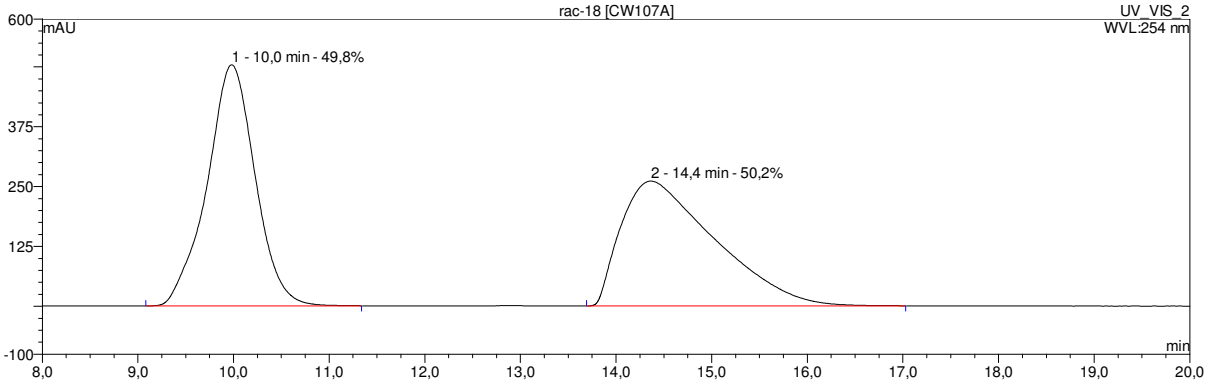
HPLC traces of chiral alcohol **18**



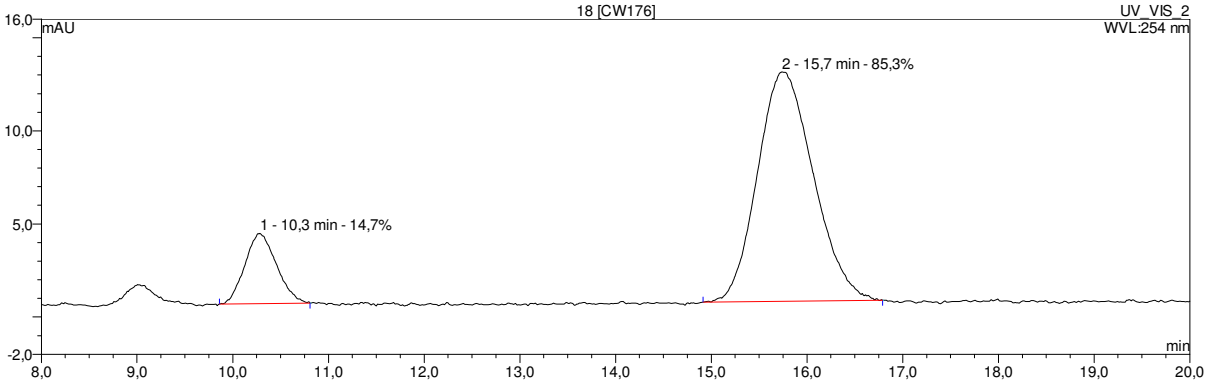
18

HPLC (OJ-H, 250 × 4.6 mm, *n*-Hex/*i*-PrOH = 70/30, 1 mL/min).

Racemate

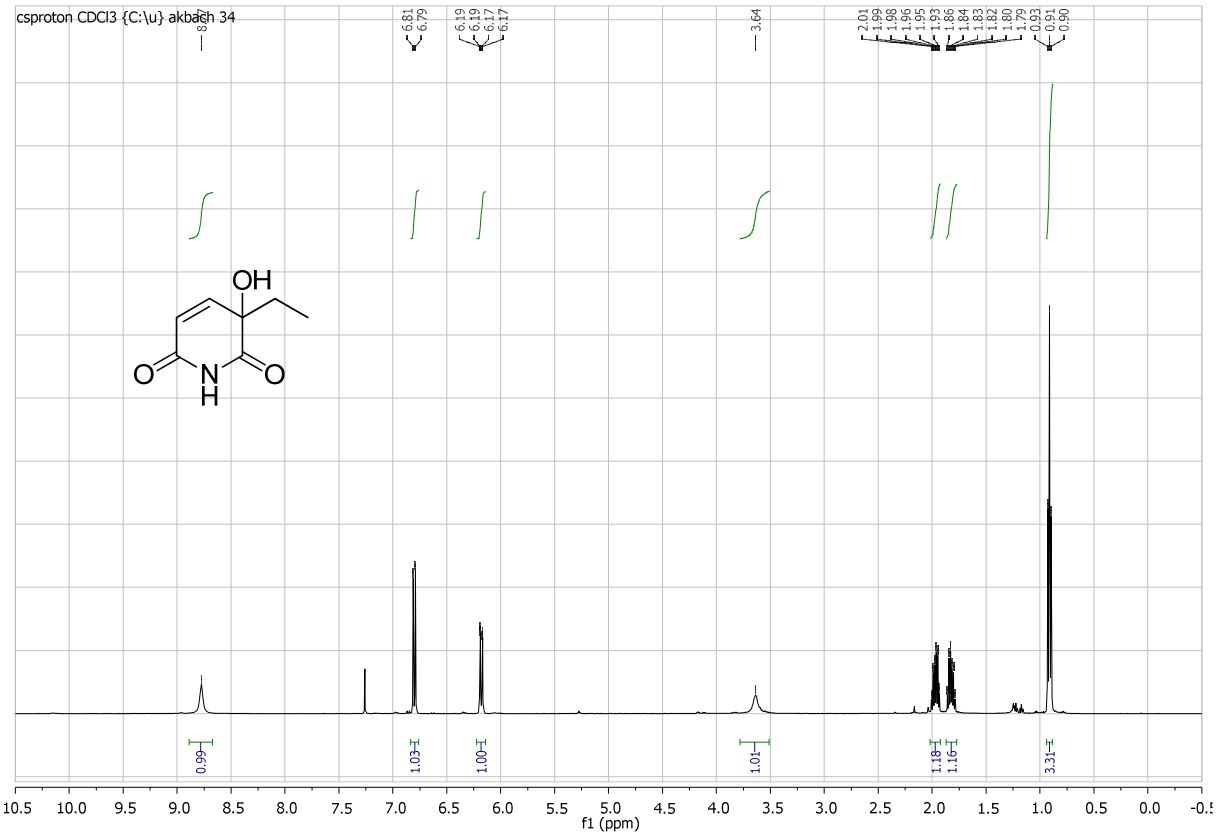


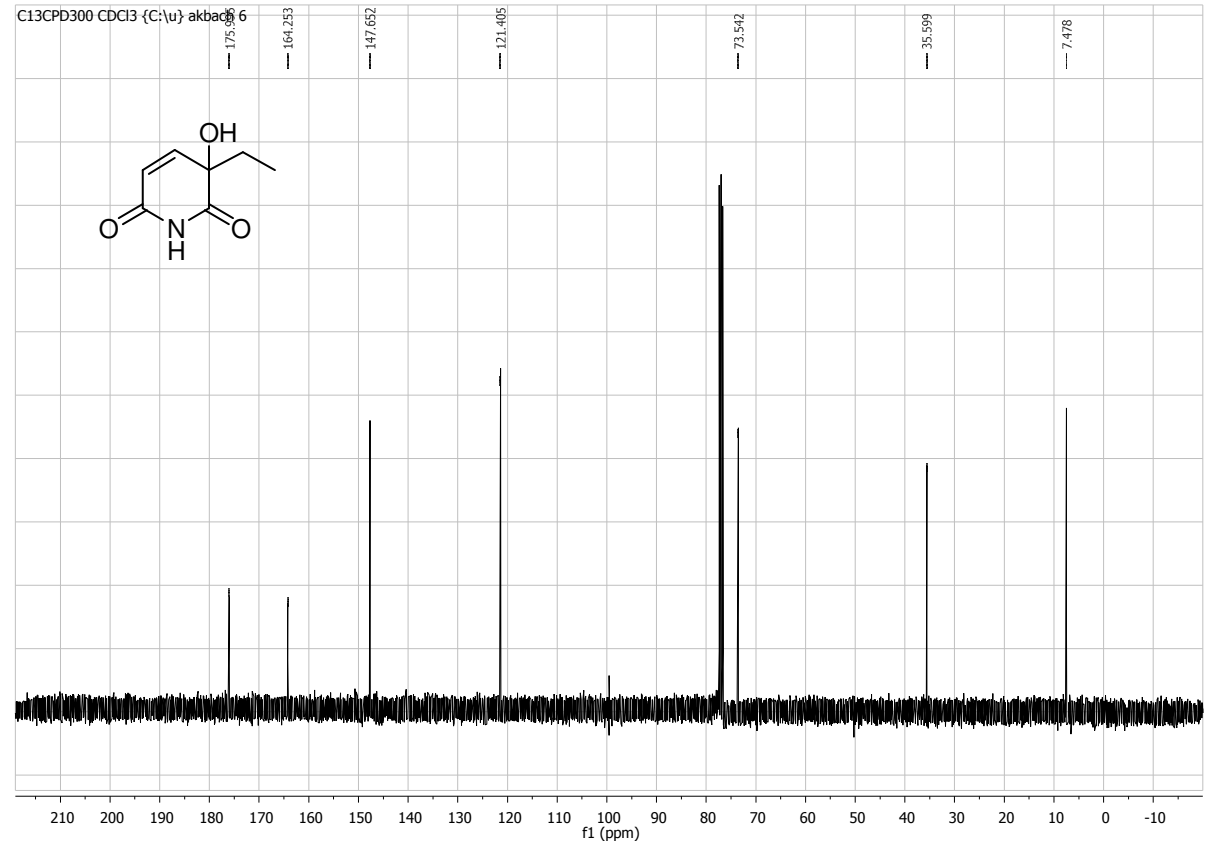
Enantioenriched (Table 5, entry 2)



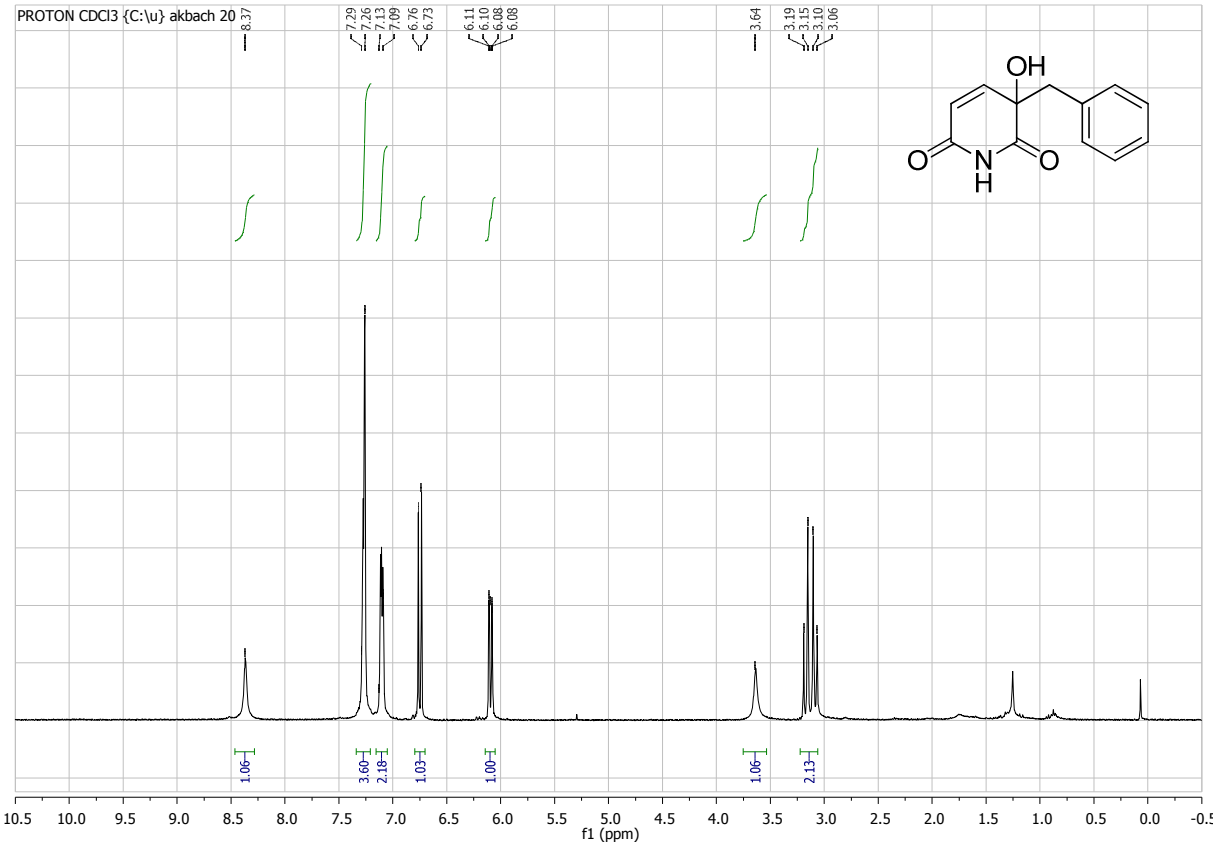
7. NMR spectra of new compounds

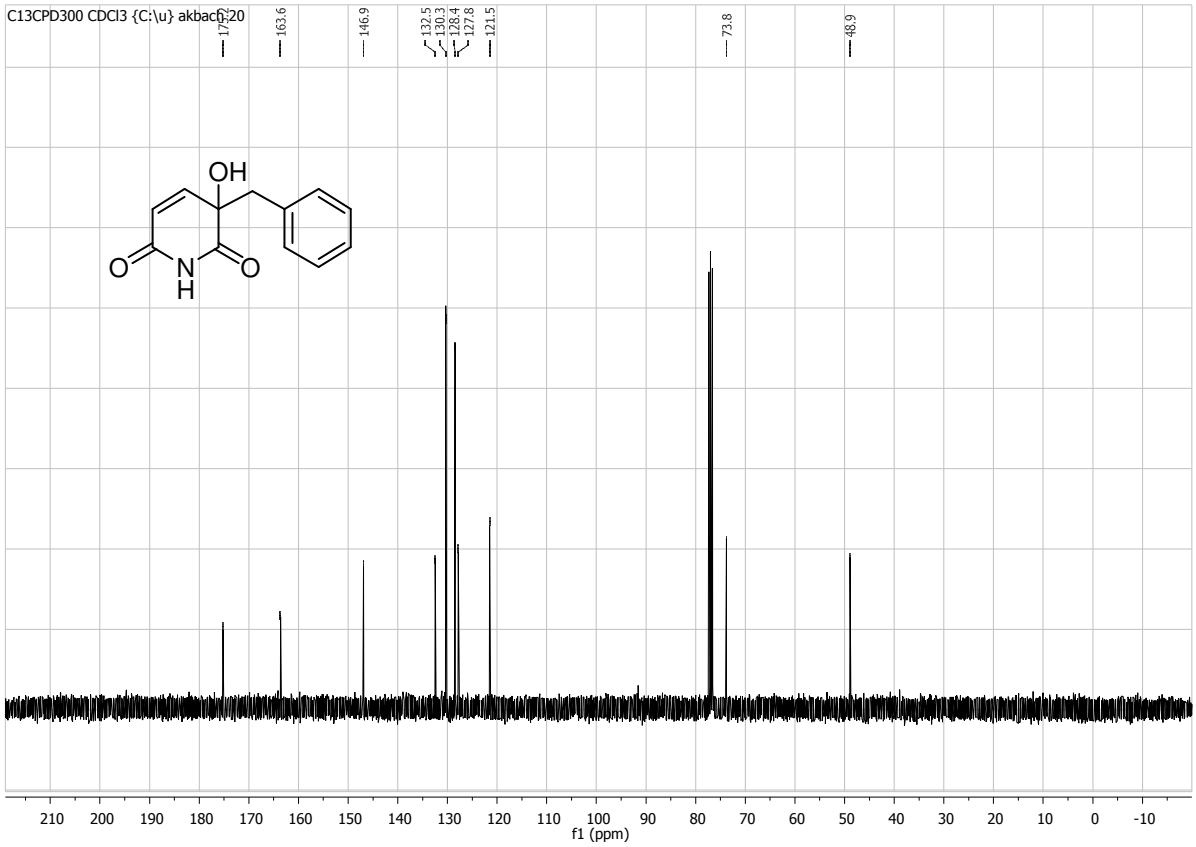
3-Ethyl-3-hydroxypyridine-2,6(1*H*,3*H*)-dione (*rac*-**10**)



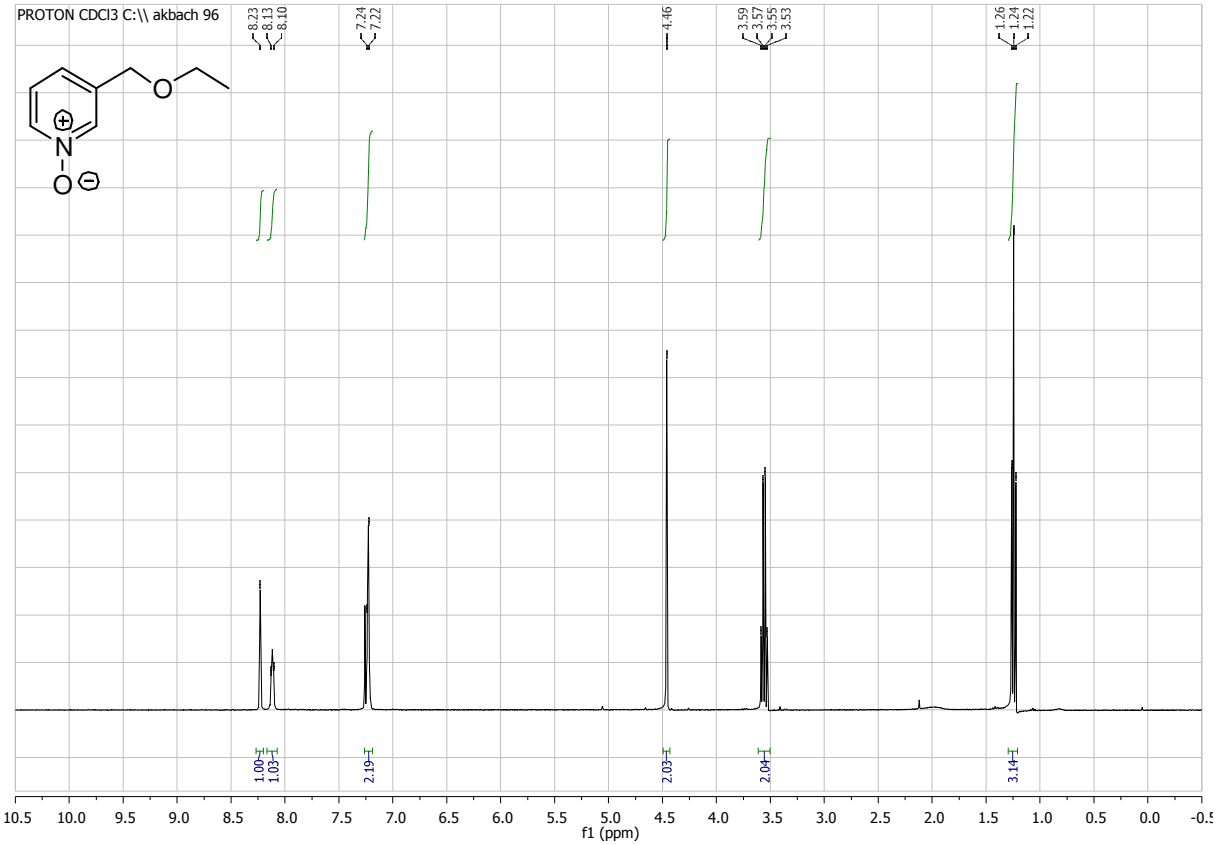


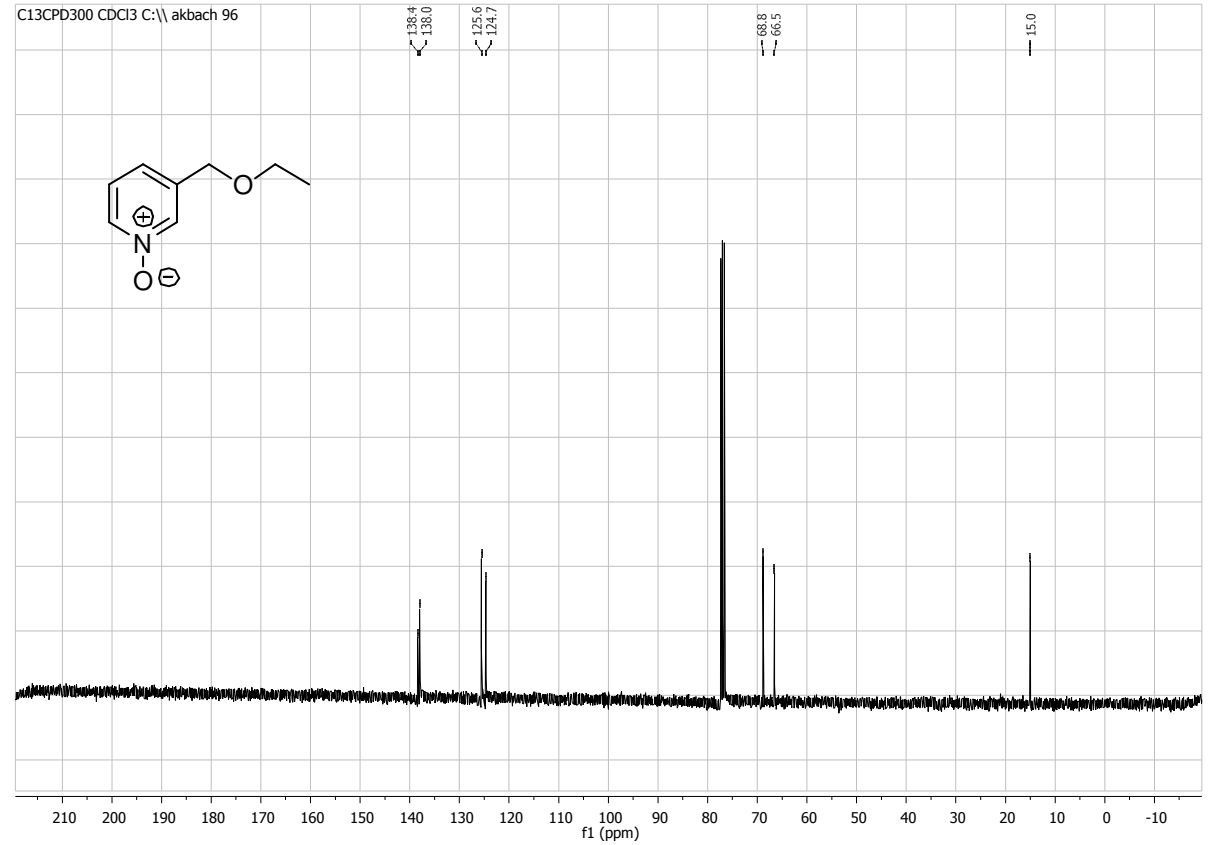
3-Benzyl-3-hydroxypyridine-2,6(1*H*,3*H*)-dione (*rac*-**12**)



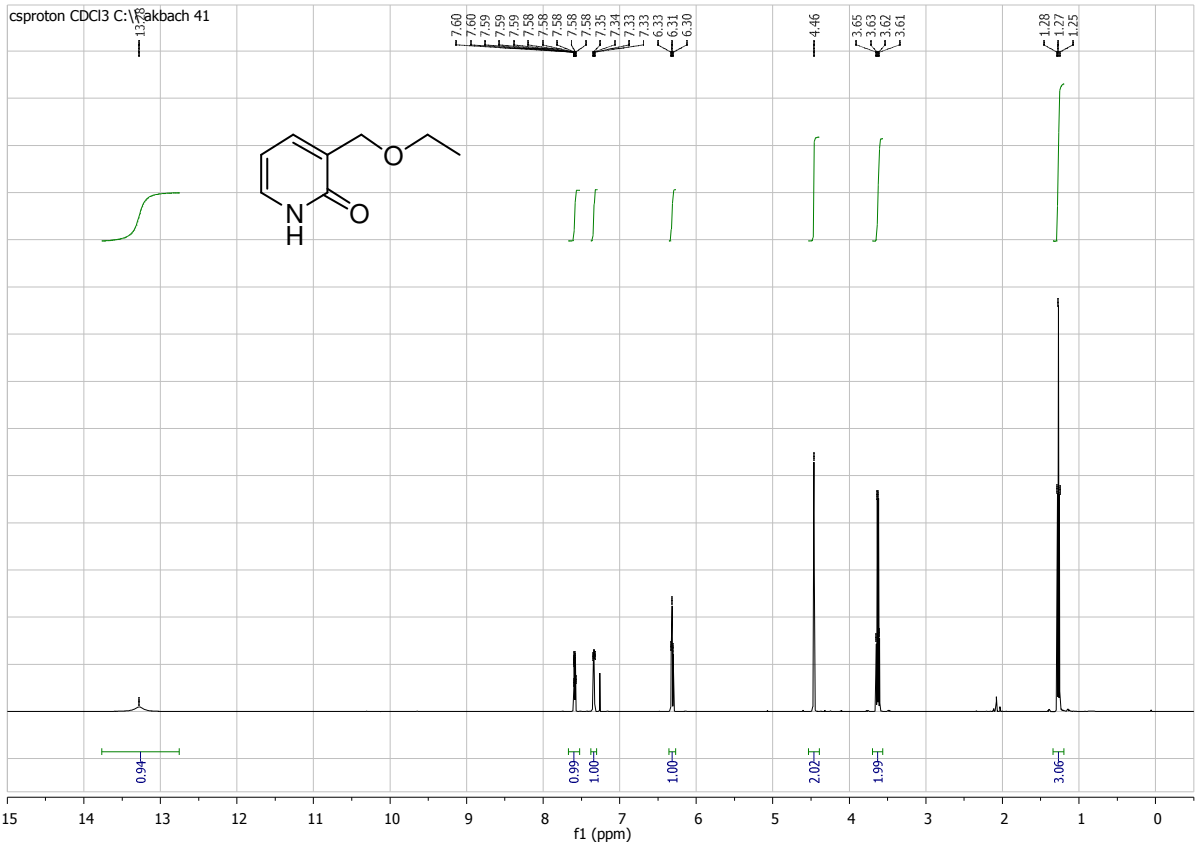


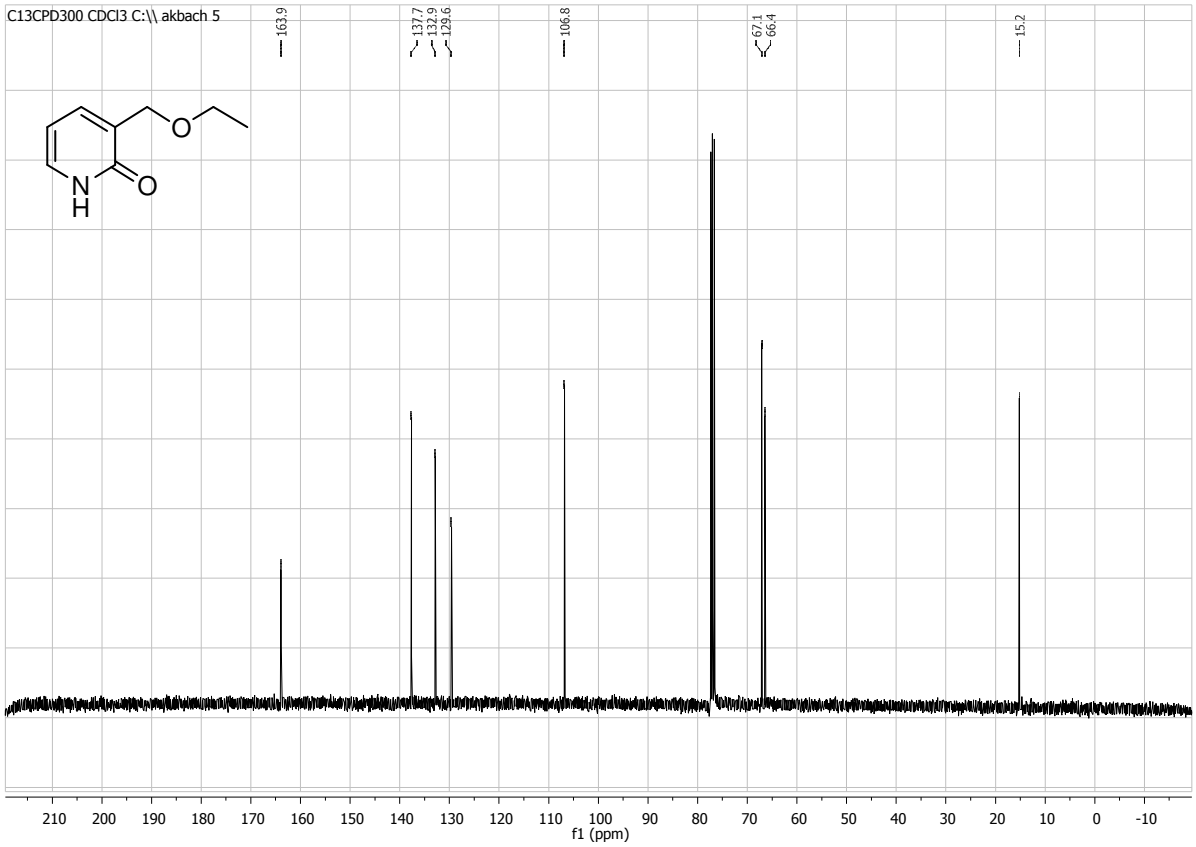
3-(Ethoxymethyl)pyridine 1-oxide



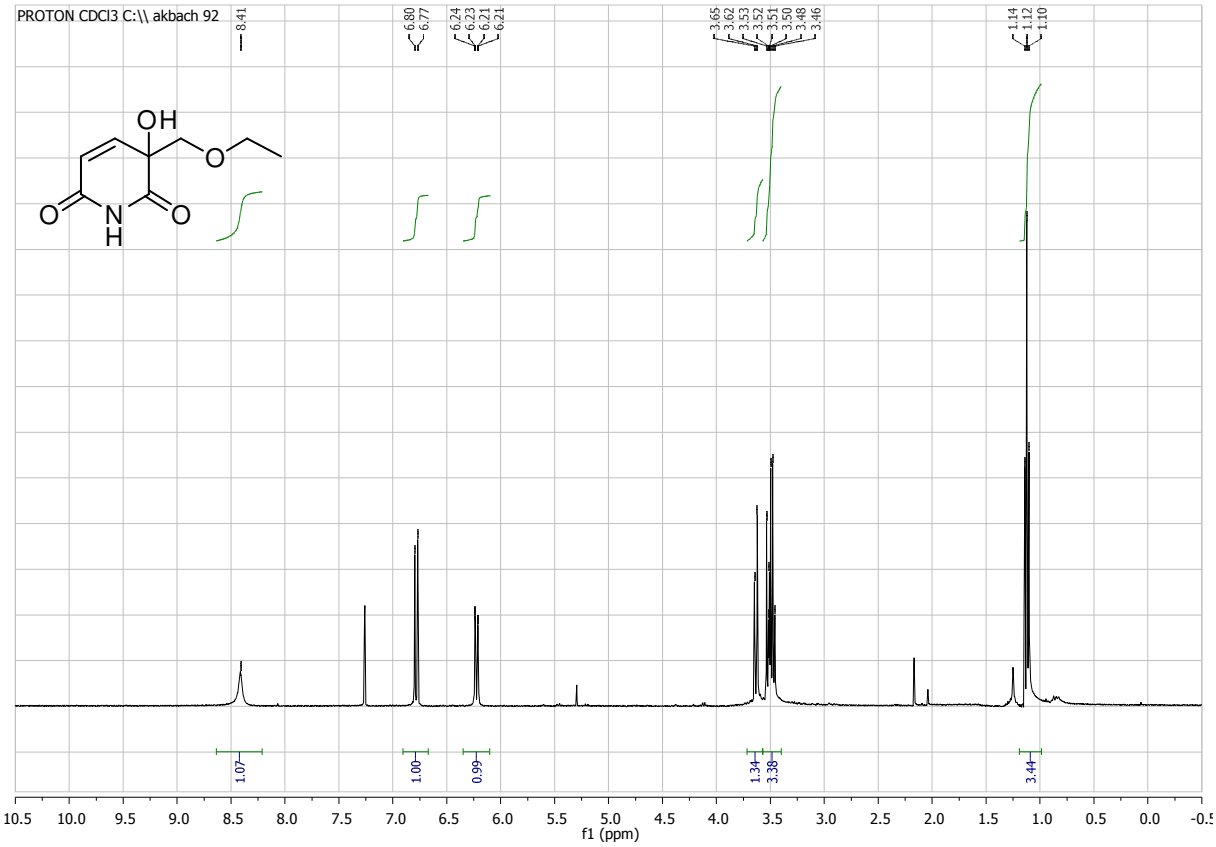


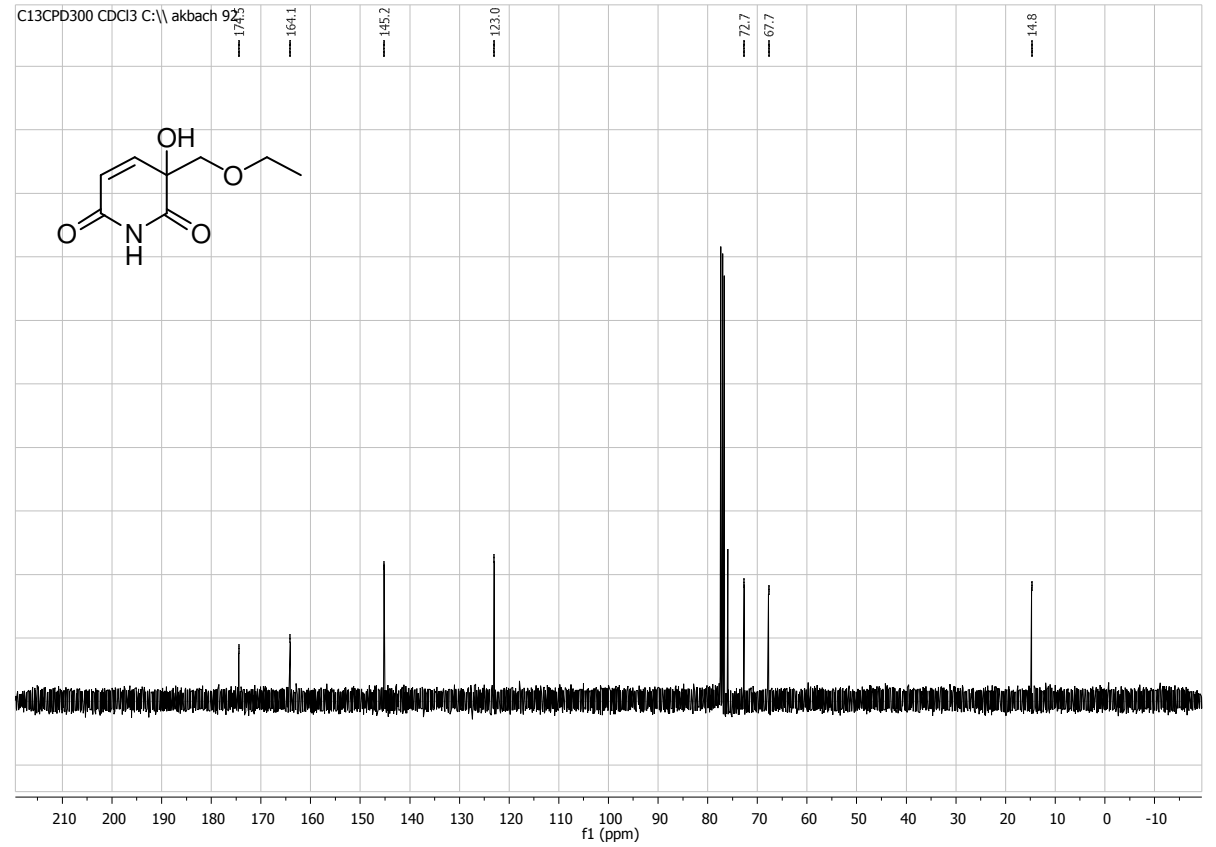
3-(Ethoxymethyl)pyridine-2(1*H*)-one (**13**)



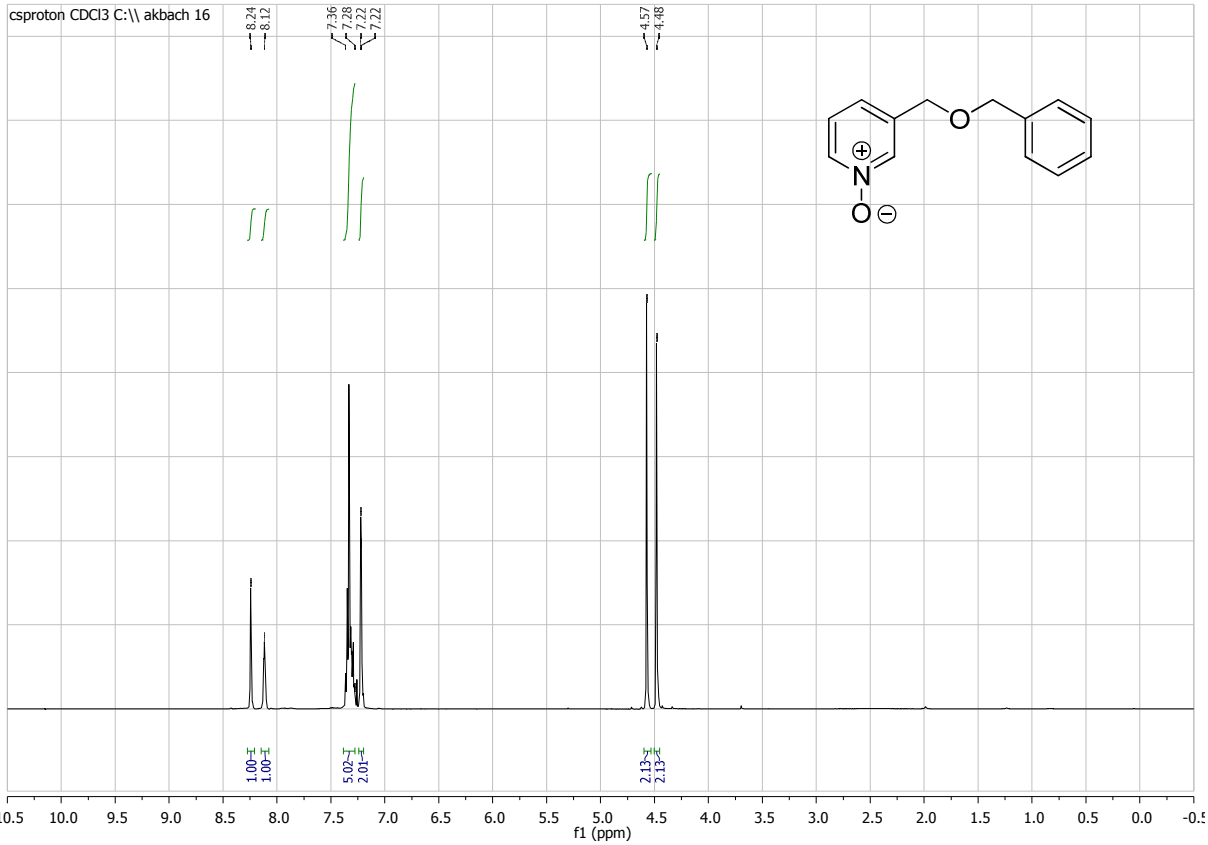


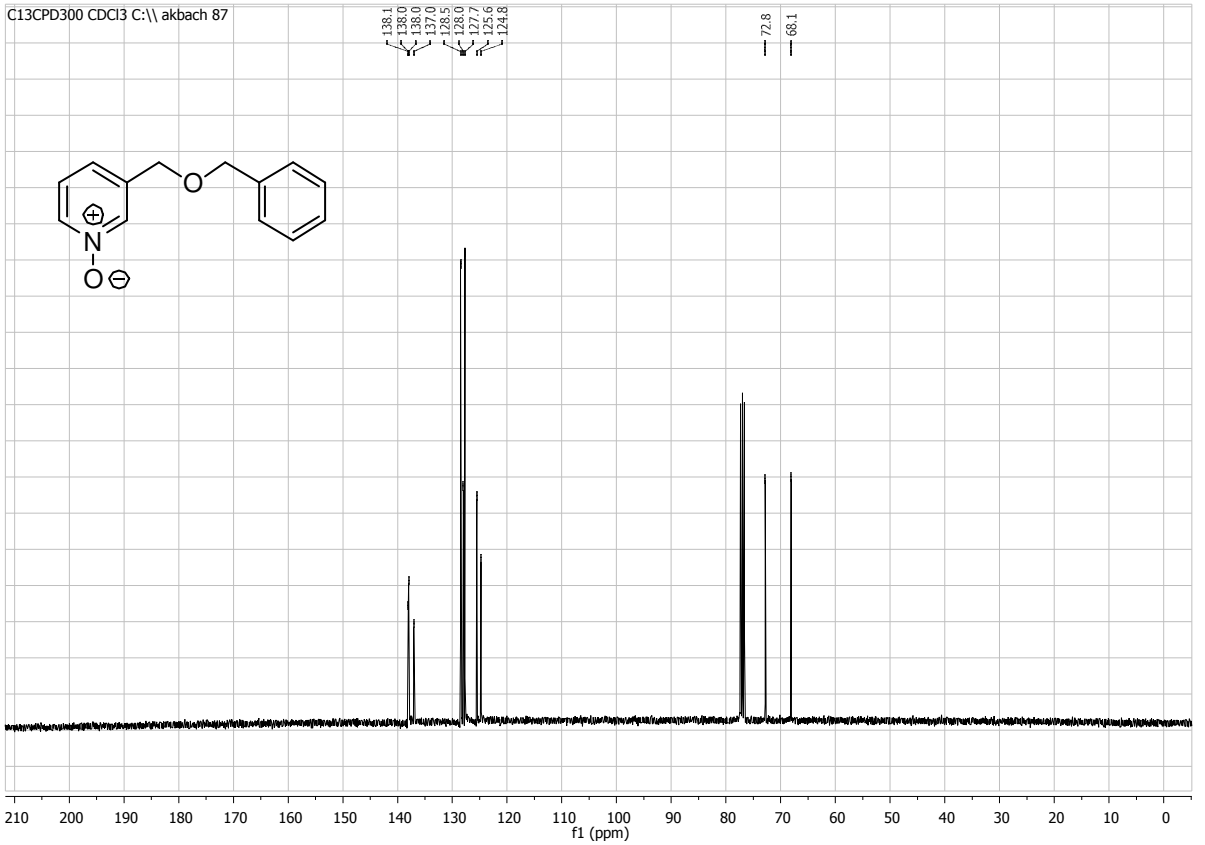
3-(Ethoxymethyl)-3-hydroxypyridine-2,6(1*H*,3*H*)-dione (*rac*-**14**)



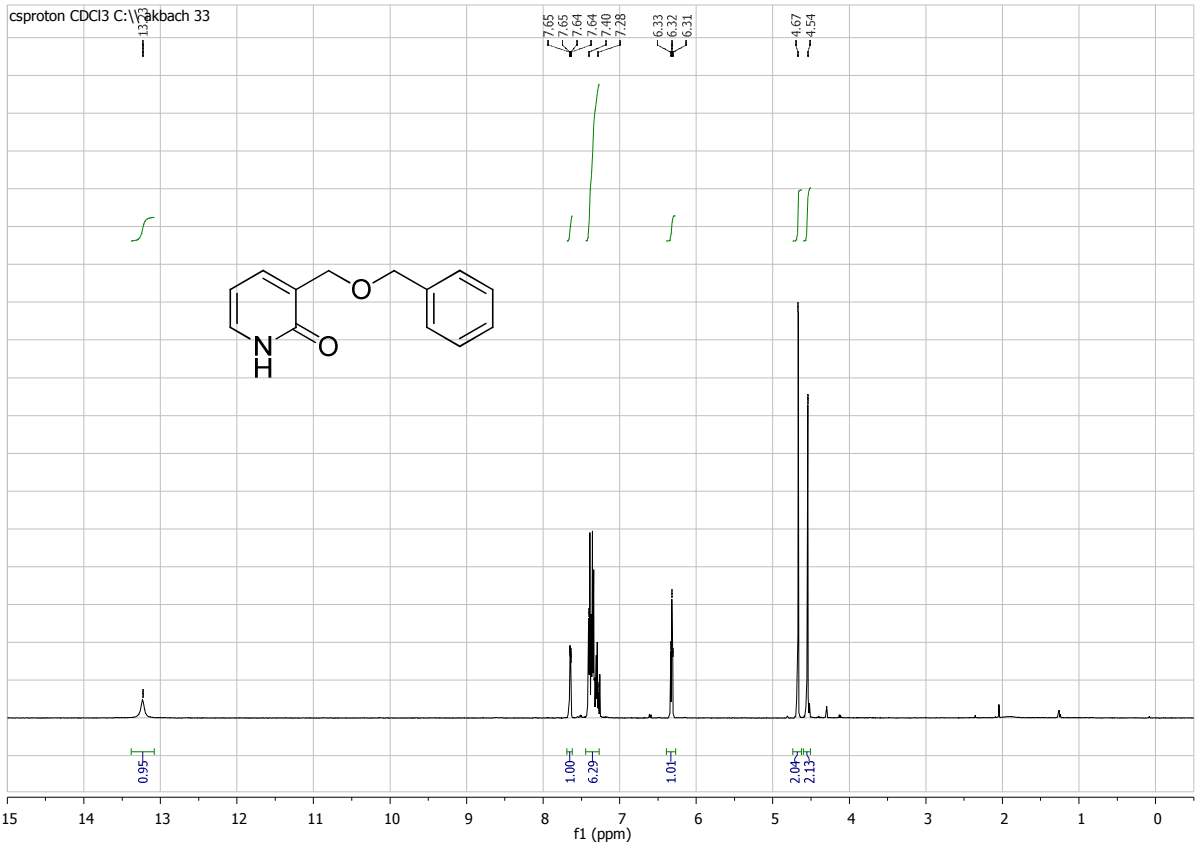


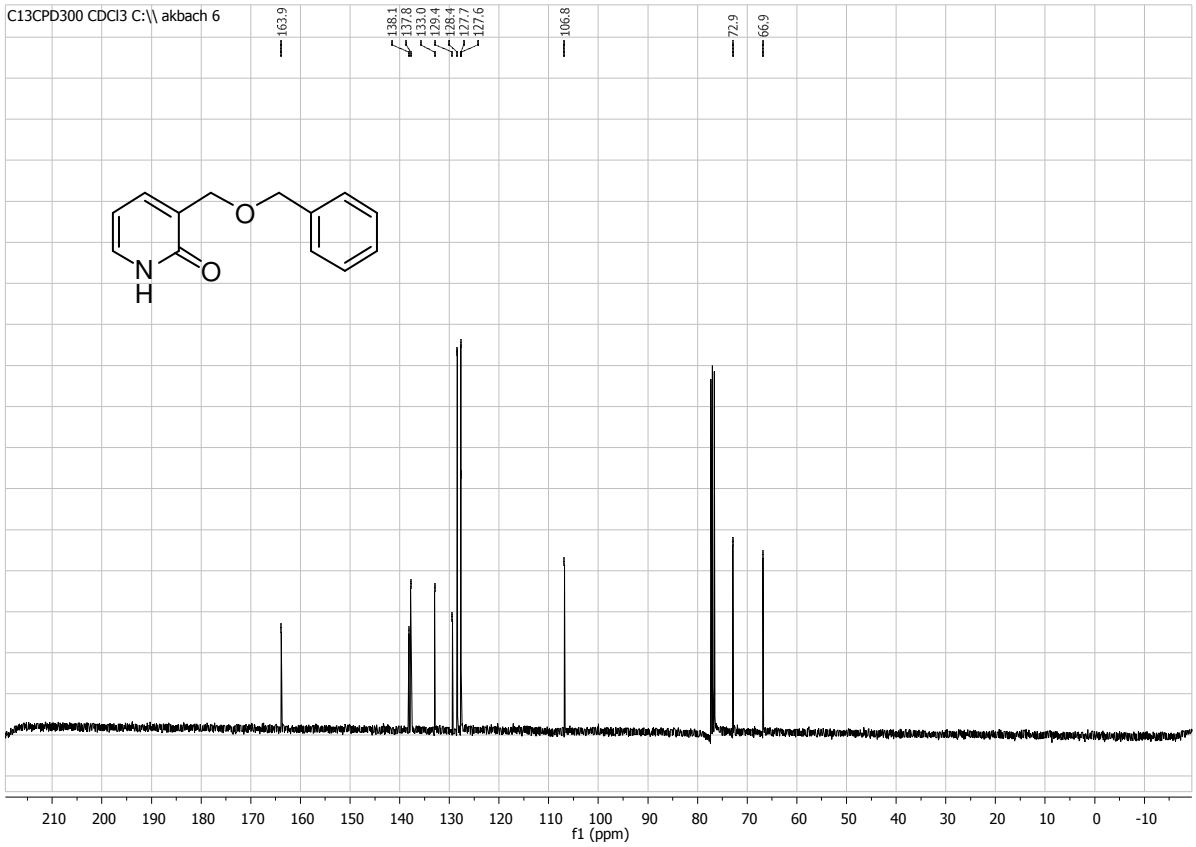
3-((Benzyloxy)methyl)pyridine 1-oxide



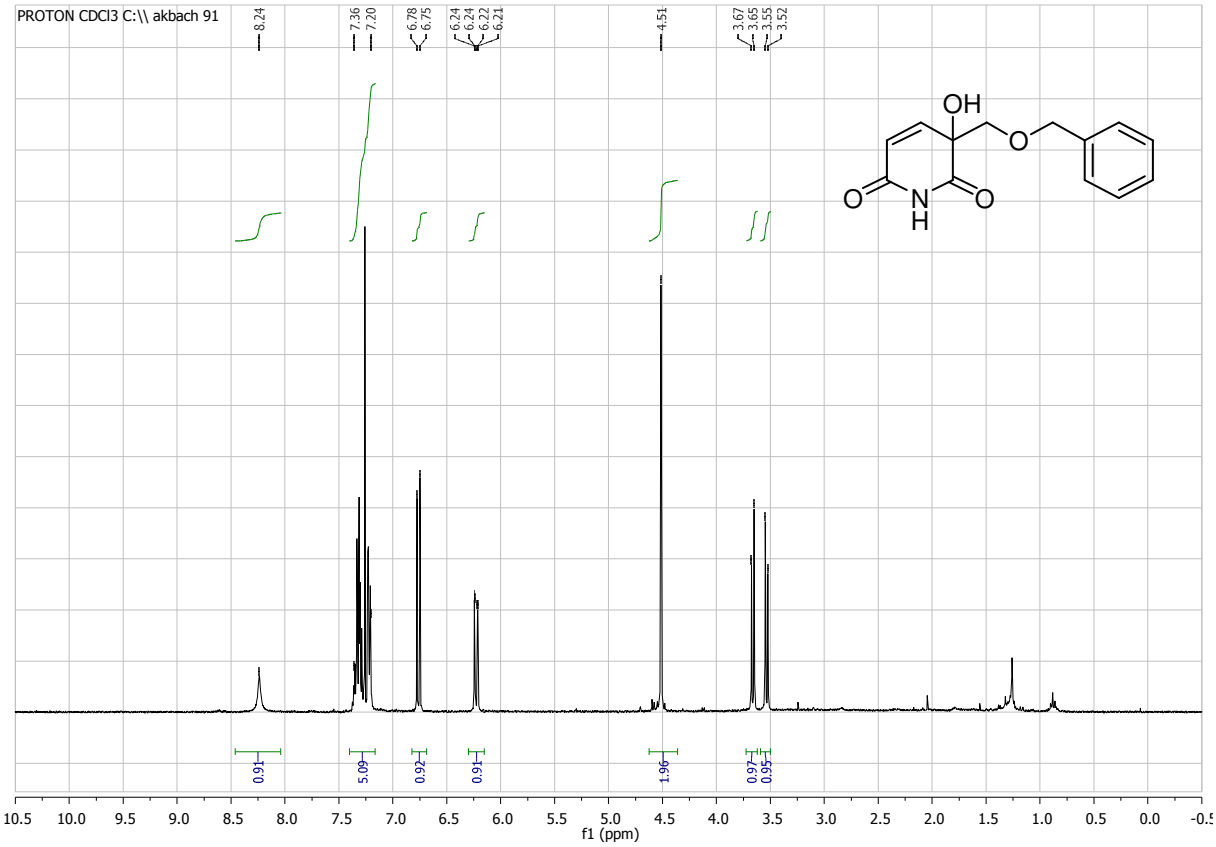


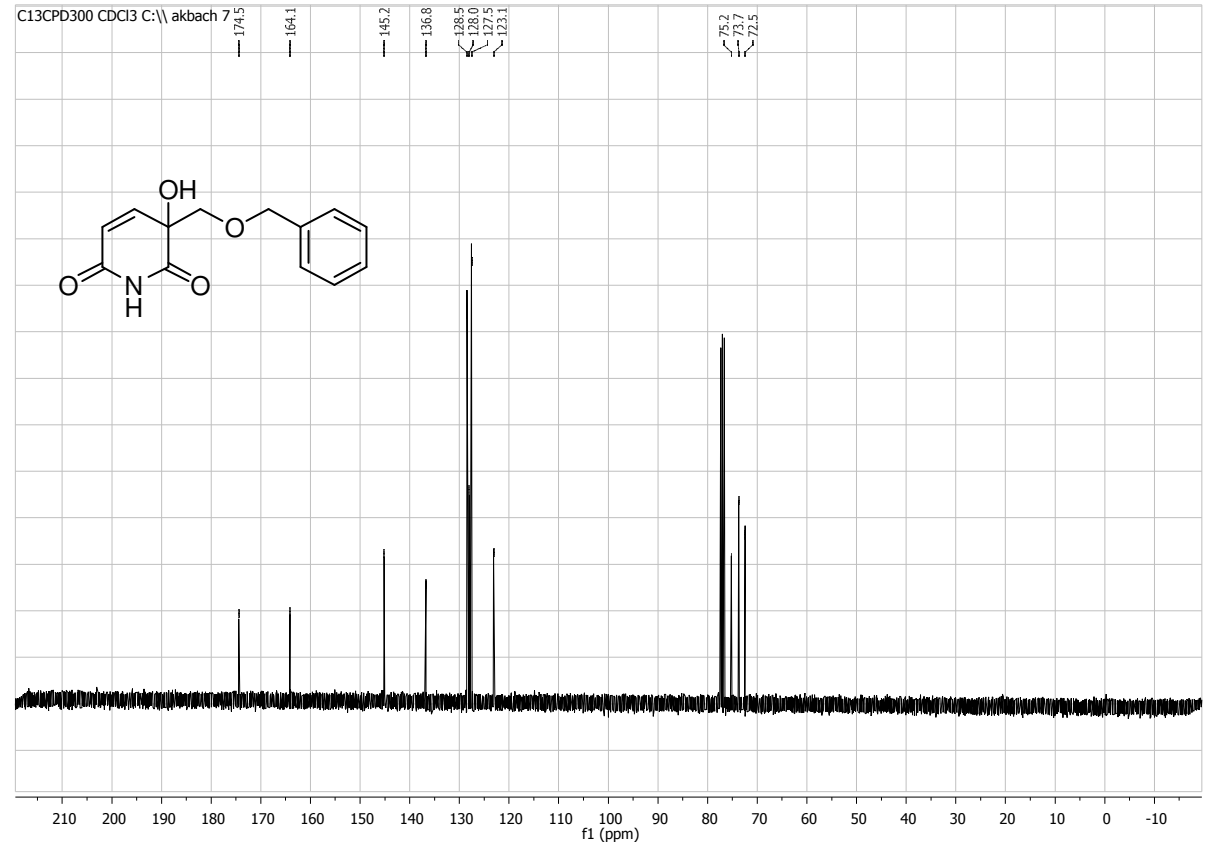
3-((Benzyloxy)methyl)pyridine-2(1*H*)-one (**15**)





3-((Benzyloxy)methyl)-3-hydroxypyridine-2,6(1*H*,3*H*)-dione (*rac*-**16**)





8a-Hydroxy-6,7,8,8a-tetrahydroisoquinoline-1,3(2*H*,5*H*)-dione (*rac*-**18**)