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Nickel-coordinated chiral enols and Michael addition intermediate stabilized by the Ni–C bond

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Chemicals. Di-*tert*-butyl acetylenedicarboxylate, trifluroacetic anhydride, $CHCl_3$, Ac_2O, AcOH, acetone, CH_2Cl_2, Cs_2CO_3, and K_2CO_3 were purchased from Aldrich.

Instrumentation. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 300 or Bruker Avance III-400 NMR spectrometer (operating at 300/75 or 400/101 MHz, respectively, referring to the $^1H/^{13}C$ nucleus). Chemical shifts are reported in ppm relative to the residual solvent peak ($CDCl_3$: δ=7.26 ppm for ^1H-NMR, δ=77.2 for ^{13}C-NMR; D_2O: δ=4.79 ppm for ^1H-NMR). NMR data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet), coupling constant, integration, and nucleus. High-resolution mass spectra were recorded on an AB Sciex TripleTOF 5600+ instrument using the Electrospray ionization (ESI) ionization method (DuoSpray source).

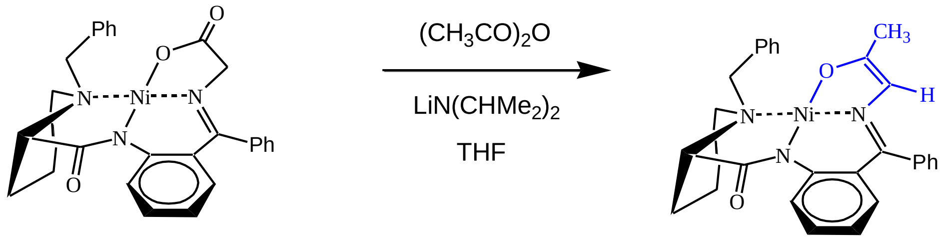
The crystal of compound **(*S*)-2** “**Ni^{II}-*(S)*-BPB-AAT**” (CCDC 1839383, $C_{28}H_{27}N_3NiO_{2.5}$, M=504.23) is monoclinic with a space group, $P2_1/c$, at T=100 K, a=9.5859(19) Å, b=16.393(3) Å, c=14.917(3) Å, β=95.45(3)°, V=2333.5(8) Å^3, Z=4, d_{calc}=1.435 g cm^{-3}, $F(000)$=1056, and μ=1.196 mm^{-1}. X-ray diffraction (XRD) data was collected on the ‘Belok’ beamline (λ=0.80246 Å) of the National Research Center ‘Kurchatov Institute’ (Moscow, Russian Federation) using a Rayonix SX165 Charge-coupled device (CCD) detector. A total of 360 images (19197 reflections, 5039 independent reflections, R_{int}=0.0469) were collected using an oscillation range of 1.0° (φ scan mode, $2\theta_{max}$=61.96°) and corrected for absorption using the *Scala* program (T_{min}=0.760, T_{max}=0.820) [S1]. The data was indexed, integrated, and scaled using the utility *iMOSFLM* in the CCP4 program [S2]. The structure was determined by direct methods and refined using the full-matrix least squares technique on F^2 with anisotropic displacement parameters for non-hydrogen atoms. The hydrogen atom of the OH-group was localized in the difference-Fourier map and included in the refinement with fixed positional and isotropic displacement parameters [$U_{iso}(H)=1.5U_{eq}(O)$]. The other hydrogen atoms were placed in calculated positions and refined within the riding model with fixed isotropic displacement parameters [$U_{iso}(H)=1.5U_{eq}(C)$ for the methyl groups and $1.2U_{eq}(C)$ for the other groups]. The final divergence factors were R_1=0.0470 for 4793 independent reflections with $I > 2\sigma(I)$ and wR_2=0.1146 for all independent reflections (S=1.087). The calculations were carried out using the SHELXTL program [S3].

[S1] P. R. Evans. *Acta Crystallogr. D*, 2005, **D62**, 72–82.

[S2] T. G. G. Battye, L. Kontogiannis, O. Johnson, H. R. Powell and A. G. W. Leslie. *Acta Crystallogr. D*, 2011, **D67**, 271–281.

[S3] G. M. Sheldrick. *Acta Crystallogr. D*, 2015, **C71**, 3–8.

General procedure for the synthesis of compound (*S*)-2 “Ni^{II}-*(S)*-BPB-AAT”



(*S*)-1

(*S*)-2

Scheme S1.

Butyllithium (2.5 *M* hexane solution, ca. 10 ml) was added to a solution of diisopropylamine (4.4 ml, 0.025 mol) in THF (50 ml) at -40°C under argon. The mixture was stirred at -40°C for 60 minutes. A solution of compolex **(*S*)-1** (5 g, 0.01 mol) in THF (150 ml) was added to the thus obtained LDA, and stirring was continued for 1 hour at -40°C. Acetic anhydride (1 ml, 0.01 mol) was then added. The mixture was warmed to room temperature, and stirring was continued for 2 hours (TLC monitoring, $CHCl_3$/acetone, 7:1). The mixture was neutralized with 5% acetic acid (aq) water and partly evaporated *in vacuo* to remove THF. Water (150 ml) was added to the residue, and the mixture was extracted several times with CH_2Cl_2 (150 ml in total). The product was purified by flash chromatography (SiO_2, chloroform/acetone, 7:1). Yield: 2.5 g (51%).

$C_{28}H_{27}N_3NiO_2$ (495.15): *Mass Spectrometry*: 496.1534: Anal. calc. for $C_{28}H_{27}N_3NiO_2{*}0.5H_2O$ (%): C 66,64; H 5.55; N 8.33. Found (%): C 66.31; H 5.44; N 8.09; Mp. 111–113°C. $[\alpha]_D^{20}$ = +338.67° (c 0.15, CH_3COCH_3). ^1H NMR: (600 MHz, CD_2Cl_2 *δ*, J/Hz) δ 1.65 (3H, s, CH_3); 2.02–2.07 (1H, m, β-Pro); 2.25–2.29 (1H, td, *J* = 10.8, 6.2 Hz, β-Pro), 2.39–2.46 (1H ddd, *J*=19.9, 13.3, 9.2 Hz, γ-Pro), 2.50–2.55 (1H, tdd, *J*=8.5, 5.0, 3.4 Hz, γ-Pro), 3.11–3.19 (1H, m, δ-Pro), 3.47–3.48 (1H, dd, *J*=10.6, 5.3 Hz, δ-Pro), 3.77–3.80 (1H, d, *J*=12.5 Hz, CH_2 Ph), 3.86–3.90 (1H, m, α-Pro), 4.46–4.48 (1H, d, *J*=12.5 Hz, CH_2 Ph), 5.33 (1H, s, =C-H), 6.68–6.70 (1H m, Ar), 6.76–6.78 (1H d, *J* = 8.2 Hz, Ar), 7.05–7.08 (1H, m, Ar), 7.17 (2H, s, w, Ar), 7.37–7.40 (1H, m, Ar), 7.46–7.47 (2H, t, *J*=7.6 Hz, Ar), 7.50–7.53 (1H, m, Ar), 7.55–7.57 (2H, t, w, *J*=6.9 Hz, Ar), 8.21–8.22 (2H, d, *J*=7.2 Hz, Ar), 8.40–8.42 (1H, d, *J*=8.6 Hz, Ar); ^{13}C (600 MHz, CD_2Cl_2): 17.70(CH_3); 23.36 (CH_2-Pro); 30.71 (CH_2-Pro); 56.69 (CH_2-Pro); 63.14 (CH_2-Ph); 69.92 (CH-Pro); 114.19 (=C-H); 124.04, 127.48, 128.27, 128.44, 128.62, 128.80, 131.37, 131.96 (CH-Ar); 120.53, 133.53, 136.27, 139.64 (C-Ar); 150.80 (C=N); 169.19 (C=O); 181.05 (O-$\underline{C}$-CH_3): IR (ART, cm^{-1}): $\tilde{\nu}$=2911, 1632, 1595, 1583, 1563, 1495, 1471, 1437, 1380, 1358, 1337, 1307, 1266, 1231, 1166, 1115, 1062, 1028, 979, 939, 796, 754, 702, 683, 616, 536, and 510.

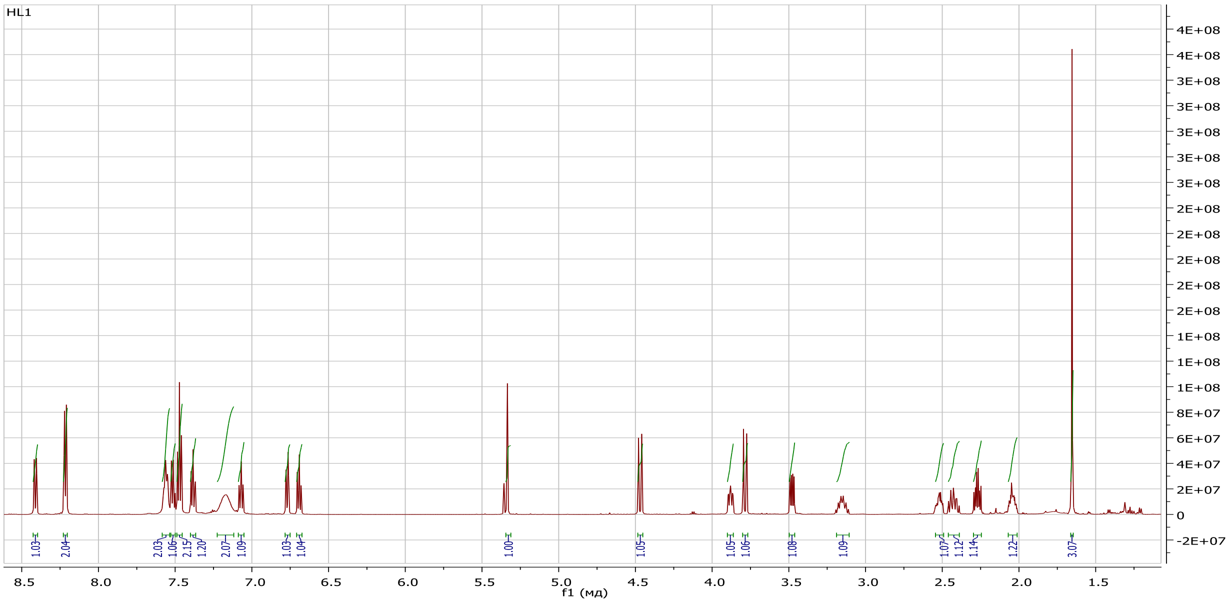


Figure S1. ^{1}H NMR (CD_2Cl_2) of (*S*)-**2**.

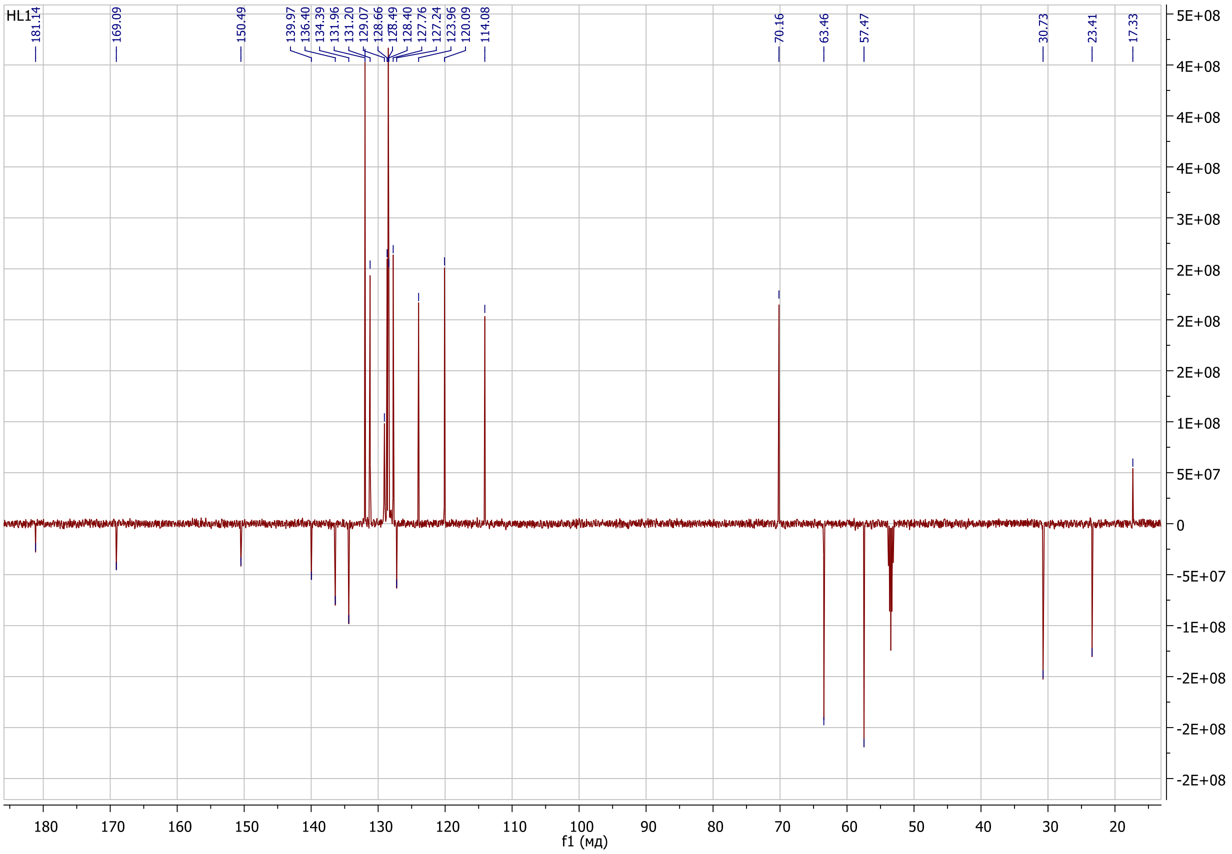


Figure S2. ^{13}C NMR (CD_2Cl_2) of (*S*)-**2**.

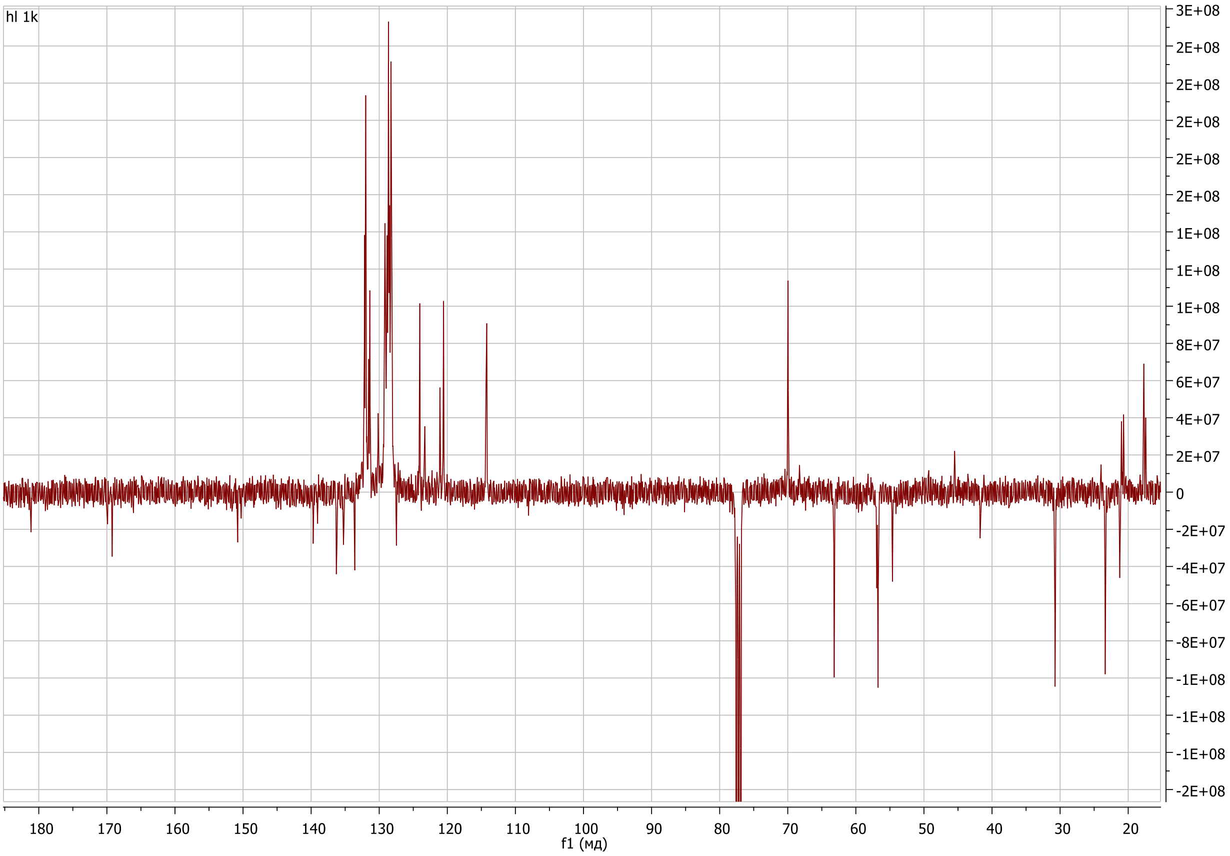


Figure S3. ^{13}C NMR ($CDCl_3$) of (*S*)-**2** after crystallization.

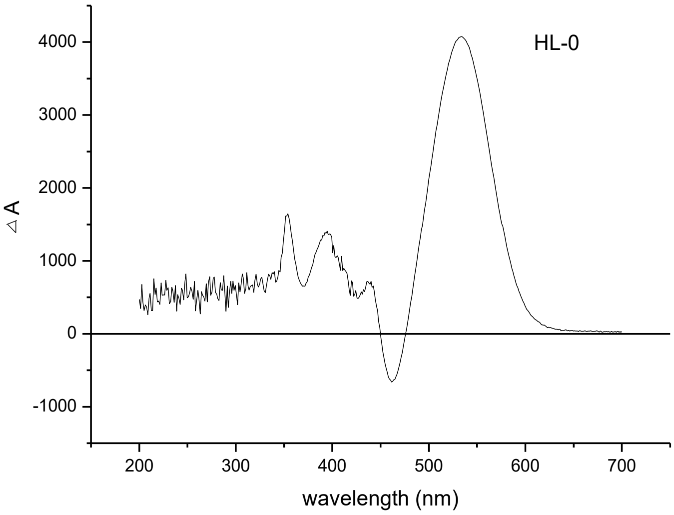


Figure S4. CD (c = 0.6 g dm^{-3}, Me_2CO) of (*S*)-**1**.

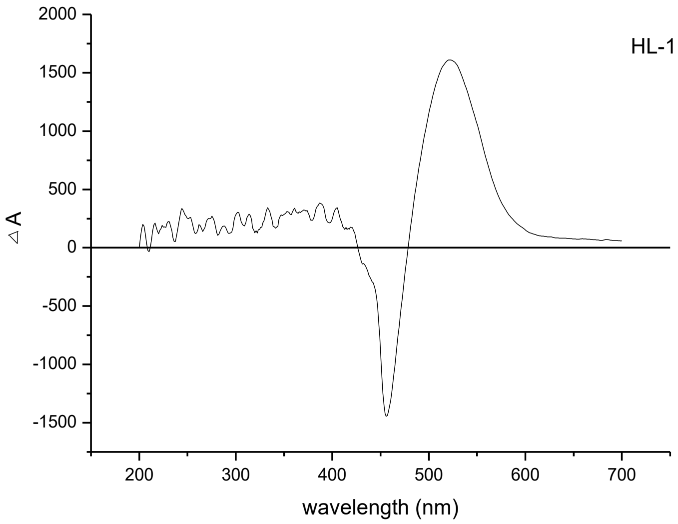
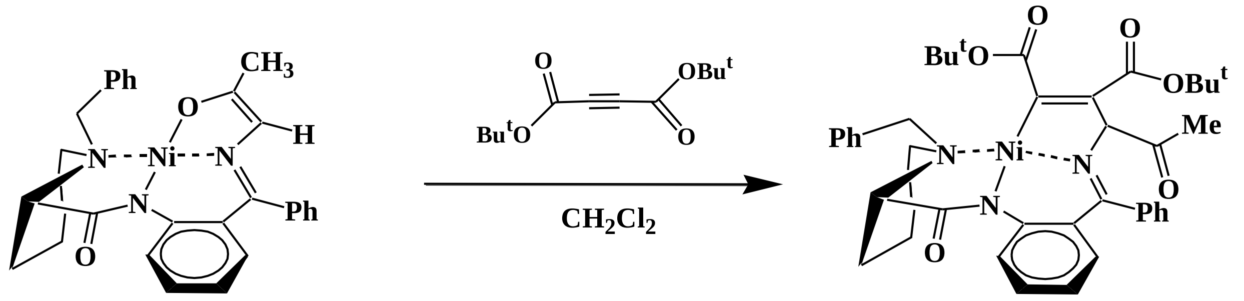


Figure S5. CD CD (c = 0.6 g dm^{-3}, Me$_2$CO) of (S)-**2**.

General procedure for the synthesis of 4



2

4

Di-*tert*-butyl acetylenedicarboxylate (0.273 g, 1.0 mmol) was added to a solution of complex (S)-**2** (0.25 g, 0.5 mmol) in CH_2Cl_2 (15 ml) at 25°C with stirring (TLC control, SiO_2, $CHCl_3$/acetone, 7:1). The product was purified by column chromatography (SEPHADEX LH-20, eluent toluene/ethanol, 3:1), yield: 0.27 g (75%).

$C_{40}H_{45}N_3NiO_7$ (721.27): ***Mass Spectrometry*:** 722.2752: **Anal. calc. for $C_{40}H_{45}N_3NiO_7$*H_2O** C-64.88, H-6.40, N-5.67: **Found** C-64.30, H-6.02, N-5.40. **Mp.** 132–134°C. **$[\alpha]_D^{20}$** = -1494° (c 0.15, CH_3COCH_3). **^{1}H NMR: (600 MHz, CD_2Cl_2 δ, J/Hz)**: δ 1.42 (9H, s, $(CH_3)_3$), 1.50–1.52 (1H, m, β-Pro endo), 1.53 (an admixture)1.58 (9H, s, $(CH_3)_3$), 1.80–1.88 (2H, m, β-Pro exo, γ-Pro endo), 1.98 (3H, s, CH_3), 2.08–2.13 (1H, m, γ-Pro exo), 3.15–3.19 (1H, ddd, *J*=12.7, 7.6, 5.3 Hz, δ-Pro exo), 3.81–3.83 (1H, dd, *J*=8.1, 4.2 Hz, α-Pro), 3.90–3.92 (1H, d, *J*=13.6 Hz, CH_2 Ph), 4.02–4.06 (1H, m, δ-Pro endo), 4.94–4.96 (1H, d, *J*=13.6 Hz, CH_2 Ph), 5.47 (1H, s, N-C-H), 6.74–6.77 (1H, ddd, *J*=8.2, 7.0, 1.1 Hz, Ar), 6.82–6.84 (1H dd, *J*=8.2, 1.6 Hz, Ar), 6.91–6.93 (1H, d, *J*=7.7 Hz, Ar), 7.25–7.27 (1H, dd, *J*=5.0, 1.6 Hz, Ar), 7.31–7.34 (1H, ddd, *J*=8.6, 7.0, 1.7 Hz, Ar), 7.43–7.49 (4H, m, Ar), 7.50–7.56 (2H, m, Ar), 7.98–7.99 (2H, d, *J*=6.9 Hz, Ar), 8.34–8.36 (1H, d, *J*=8.6 Hz, Ar). **^{13}C (600 MHz, CD_2Cl_2):** 23.50 (CH_2-Pro); 27.62, (CH_3); 27.77 ($(CH_3)_3$); 28.16 ($(CH_3)_3$); 28.2 (an admixture); 29.79 (CH_2-Pro); 57.86 (CH_2-Ph); 63.10 (CH_2-Pro); 71.74 (CH-Pro); 80.71 ($\underline{C}$-$(CH_3)_3$); 80.75 ($\underline{C}$-$(CH_3)_3$); 85.86 (=$\underline{C}$H-); 120.24, 124.77, 126.97; 127.15; 128.23; 128.42; 128.72, 129.13; 129.21; 131.15; 131.40; 133.01 (CH-Ar);126.45; 134.59; 135.30; 144.63 (C-Ar); 132,08 (Ni-$\underline{C}$-COO^{t}Bu); 158.94 (=$\underline{C}$-COO^{t}Bu);

170.64 (=COO); 171.08 (C=N); 175.88 (COO); 180.79 (C=O); 201.83 (O=C-CH_3): **IR (ART, cm^{-1}):** 3061, 2974, 2930, 1714, 1692, 1633, 1587, 1587, 1543, 1474, 1441, 1367, 1322, 1266, 1236, 1164, 1149, 1125, 1076, 1024, 914, 847, 749, and 705.

The crystal of **4** (CCDC 1847225, 2($C_{40}H_{45}N_3NiO_6$)•$(CH_3)_2O$, M=1503.04) is monoclinic with a space group $P2_1$/c, at T=100 K, a=10.358(2) Å, b=35.608(7) Å, c=10.973(2) Å, β=96.67(3)°, V=4019.8(14) Å^3,Z=2, d_{calc}=1.242 g cm^{-3}, F(000)=1592, and μ=0.733 mm^{-1}. X-ray diffraction (XRD) data was collected on the 'Belok' beamline (λ=0.80246 Å) of the National Research Center 'Kurchatov Institute' (Moscow, Russian Federation) using a Rayonix SX165 CCD detector. A total of 360 images (32334 reflections, 8807 independent reflections, R_{int}=0.0667) were collected using an oscillation range of 1.0° (φ scan mode, $2\theta_{max}$=61.94°) and corrected for absorption using the *Scala* program (T_{min}=0.820; T_{max}=0.850) [S1]. The data was indexed, integrated, and scaled using the utility *iMOSFLM* in the CCP4 program [S2]. The structure was determined by direct methods and refined by the full-matrix least squares technique on F^2 with anisotropic displacement parameters for non-hydrogen atoms. The crystal of **1** contained a solvate acetone molecule with the partial occupancy of position equal to ~0.5. The hydrogen atoms were placed in calculated positions and refined within the riding model with fixed isotropic displacement parameters [U_{iso}(H)=1.5U_{eq}(C) for the methyl groups and 1.2U_{eq}(C) for the other groups]. The final divergence factors were R_1=0.0849 for 6555 independent reflections with $I > 2\sigma(I)$ and wR_2=0.2172 for all independent reflections (S=1.067). The calculations were carried out using the SHELXTL program [S3].

[S1] P. R. Evans, *Acta Crystallogr.*, 2005, **D62**, 72.
[S2] T. G. G. Battye, L. Kontogiannis, O. Johnson, H. R. Powell and A. G. W. Leslie, *Acta Crystallogr.*, 2011, **D67**, 271.
[S3] G. M. Sheldrick, *Acta Crystallogr.*, 2015, **C71**, 3.

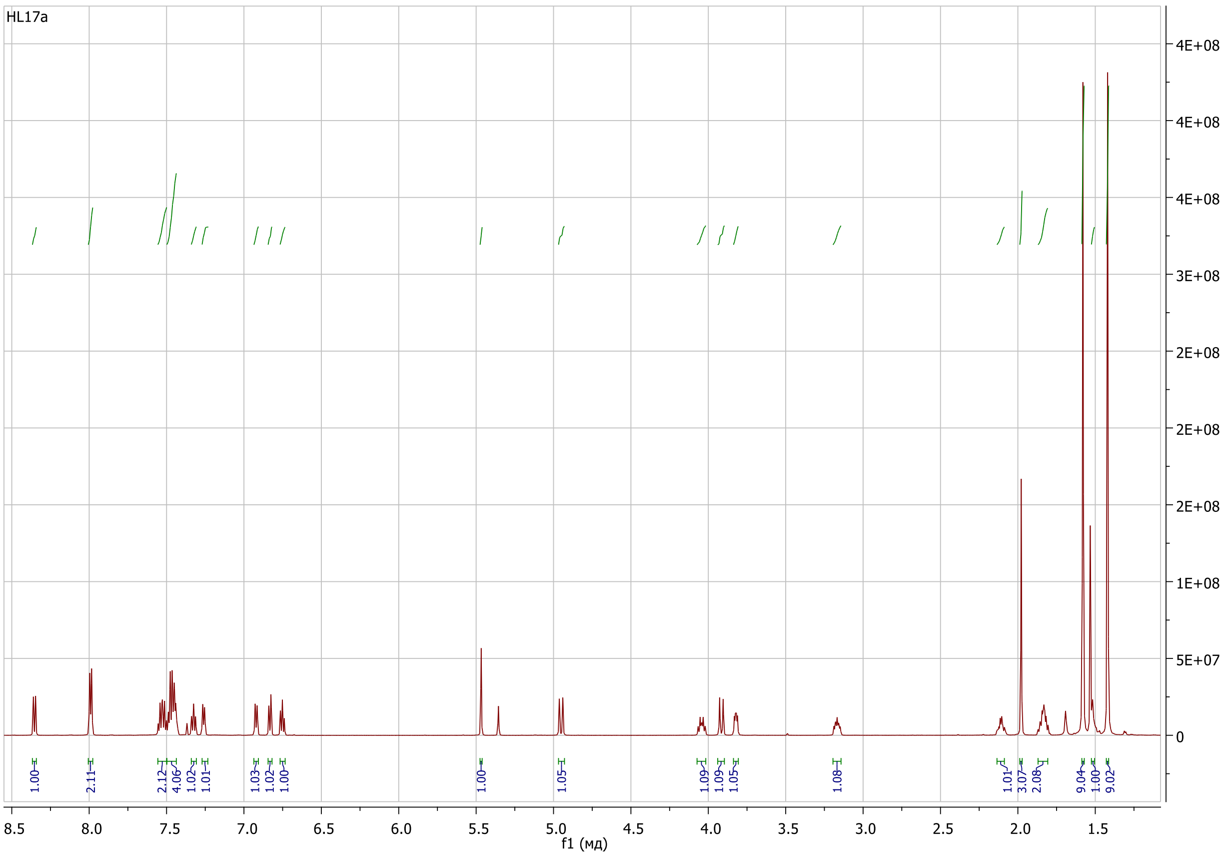


Figure S6. ^{1}H NMR (CD_2Cl_2) of complex **4**.

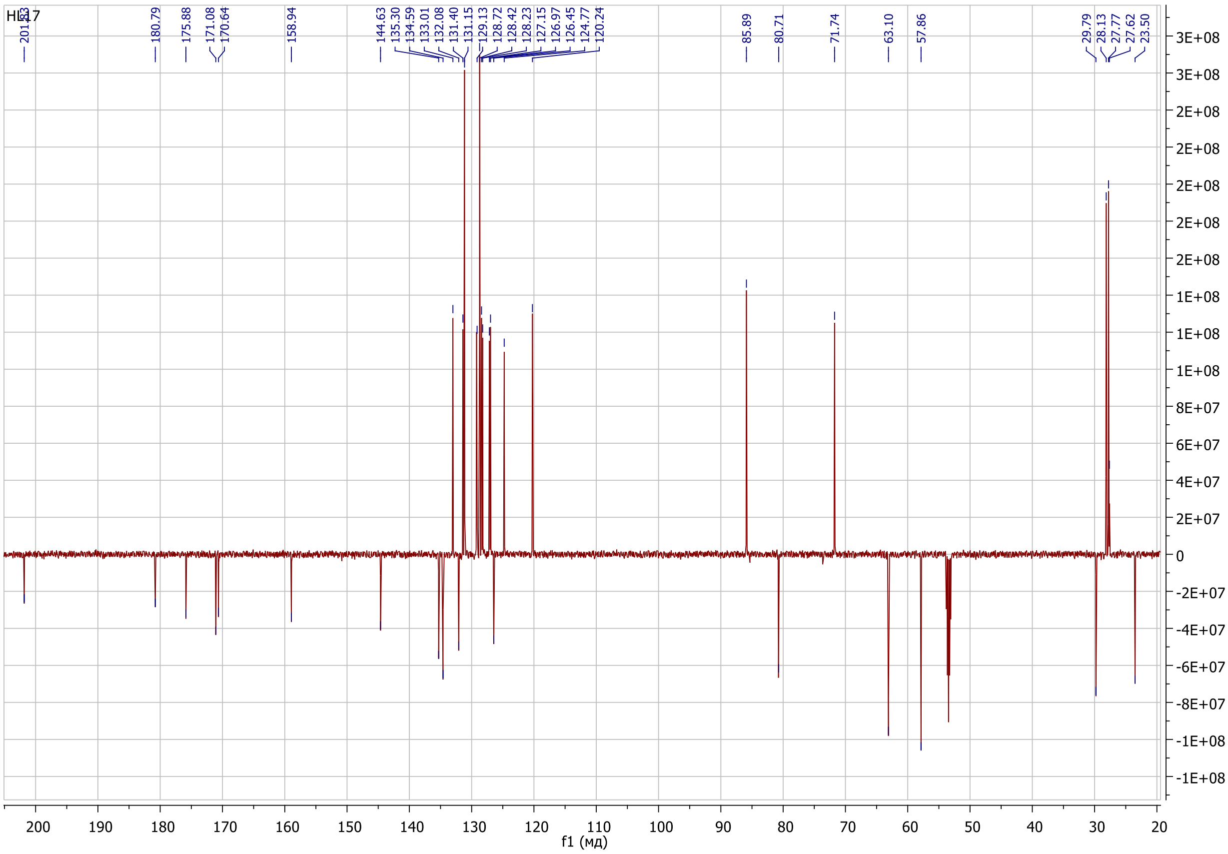


Figure S7. ^{13}C NMR (CD_2Cl_2) of complex **4**.

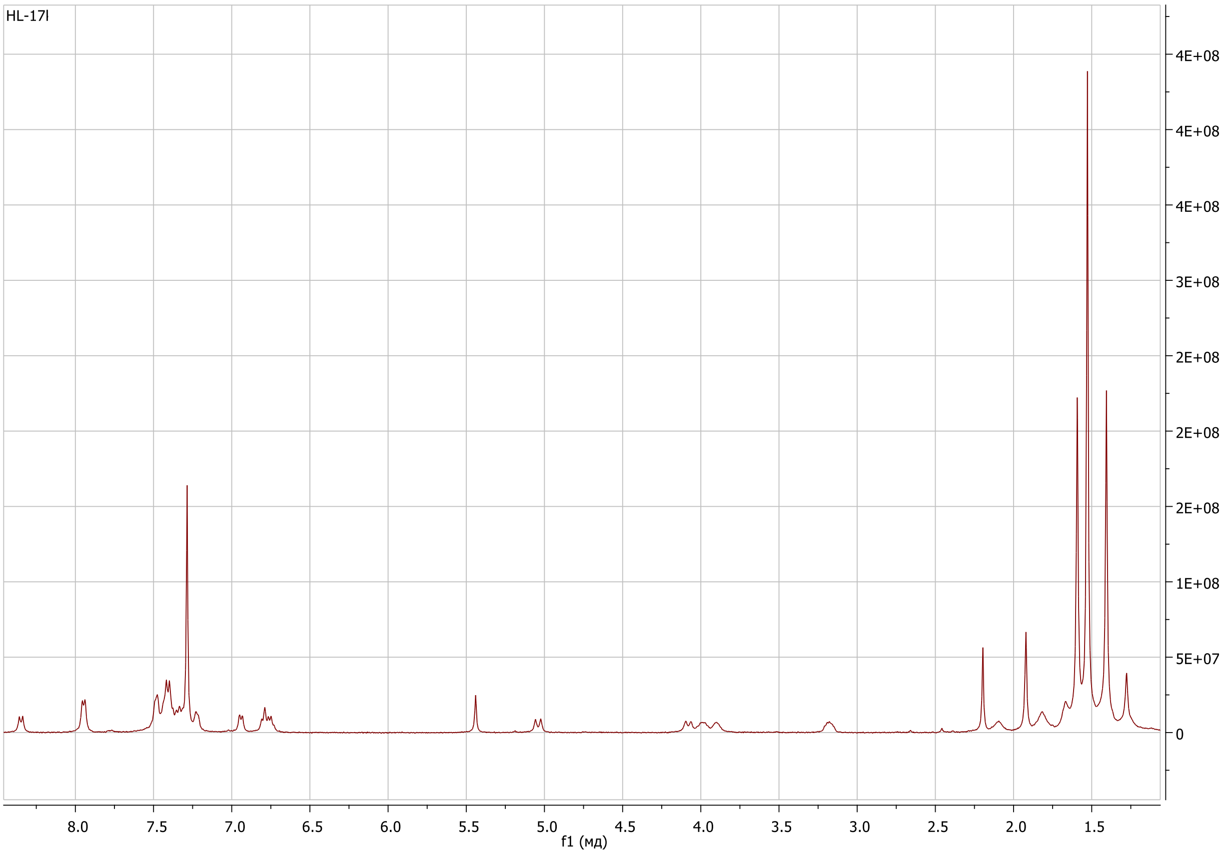


Figure S8. ^{1}H NMR ($CDCl_3$) of the racemic crystals of **4** dissolved in $CDCl_3$.

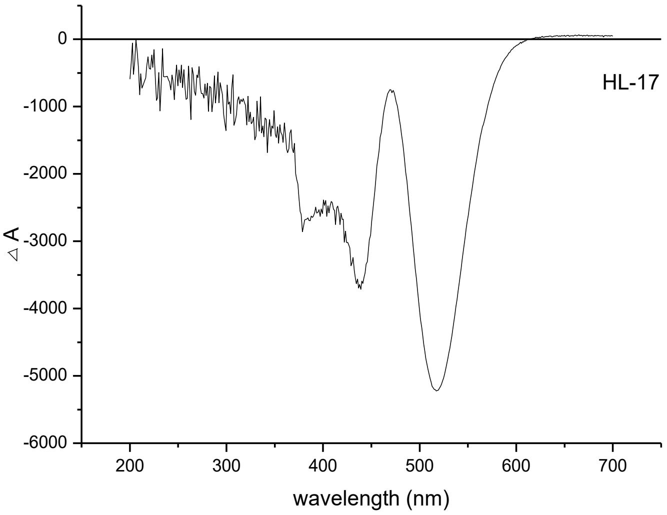
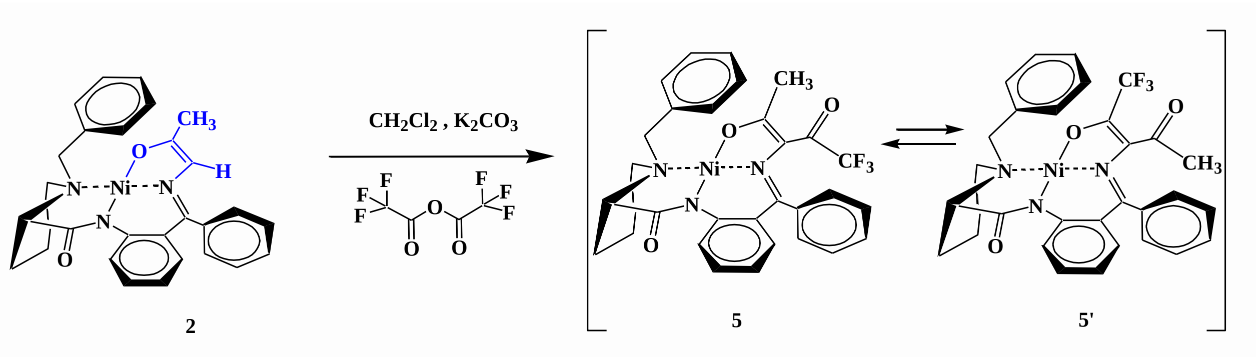


Figure S9. CD spectra of **4** (*c* = 0.6 g dm^{-3}, Me_2CO).

General procedure for the synthesis of complex 5



Scheme S3. Potassium carbonate (0.82 g, 0.3 mmol) and trifluroacetic anhydride (0.056 ml, 0.4 mmol) were added to a solution of complex **(*S*)-2** (0.1 g, 0.2 mmol) in CH_2Cl_2 (10 ml) at 25°C with stirring. The product was purified by flash chromatography (SiO_2, eluent chloroform/acetone, 7:1), yield: 56.3 mg (48%).

$C_{30}H_{32}N_3F_3NiO_4$ (591,13): ***Mass Spectrometry***` 592.1370: **Anal. calc. for $C_{40}H_{45}N_3NiO_7$*CH_3COCH_3** C-60.95, H-4.96, N-6.46, F-8.76: Found C-61.42, H-5.18, N-6.51, F-8.95. **Mp.** 87°C. **IR (ART, cm^{-1}):** 2924, 2856, 1645, 1595, 1566, 1523, 1488, 1466, 1387, 1437, 1387, 1367, 1339, 1257, 1215, 1192, 1134, 1089, 1065, 1014, 977, 924, 903, 750, 702, 558.

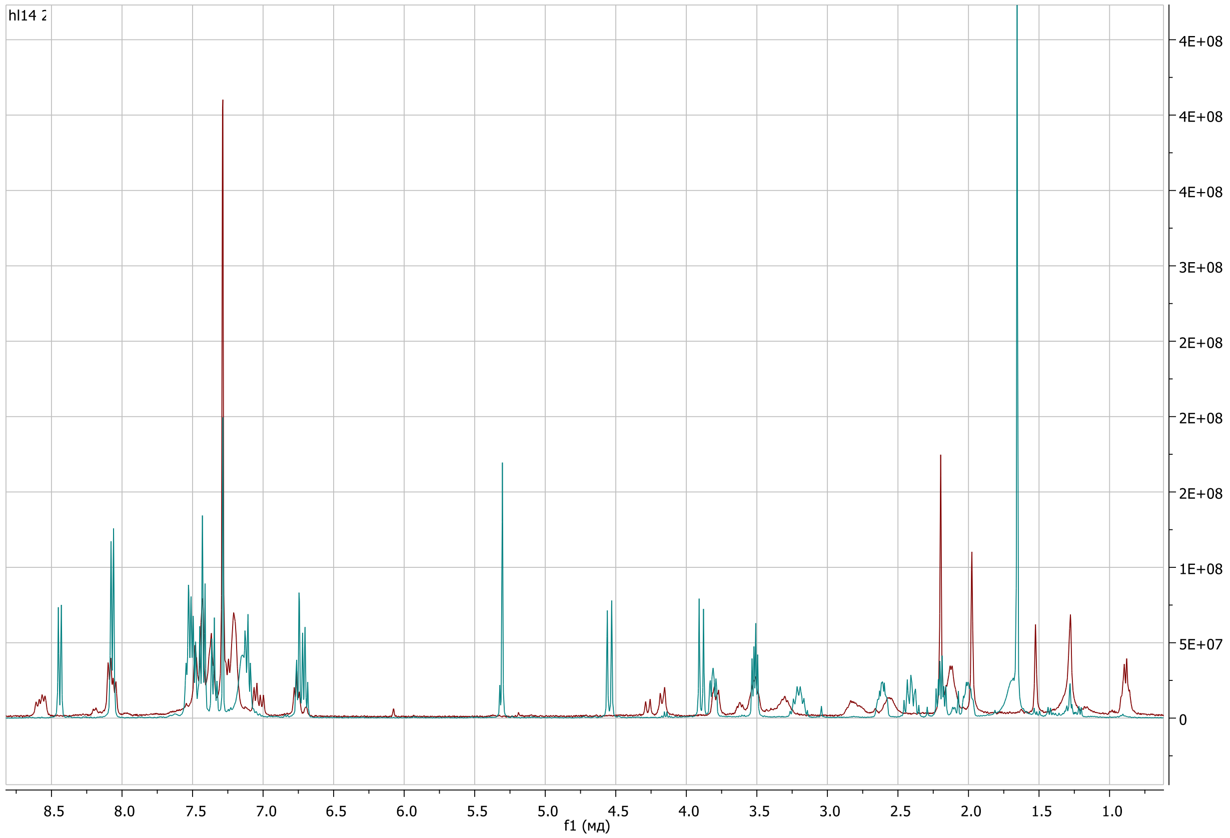


Figure S10. Interposition of ^{1}H NMR spectra ($CDCl_3$) of complex **5** (red) and that of **2** (blue).

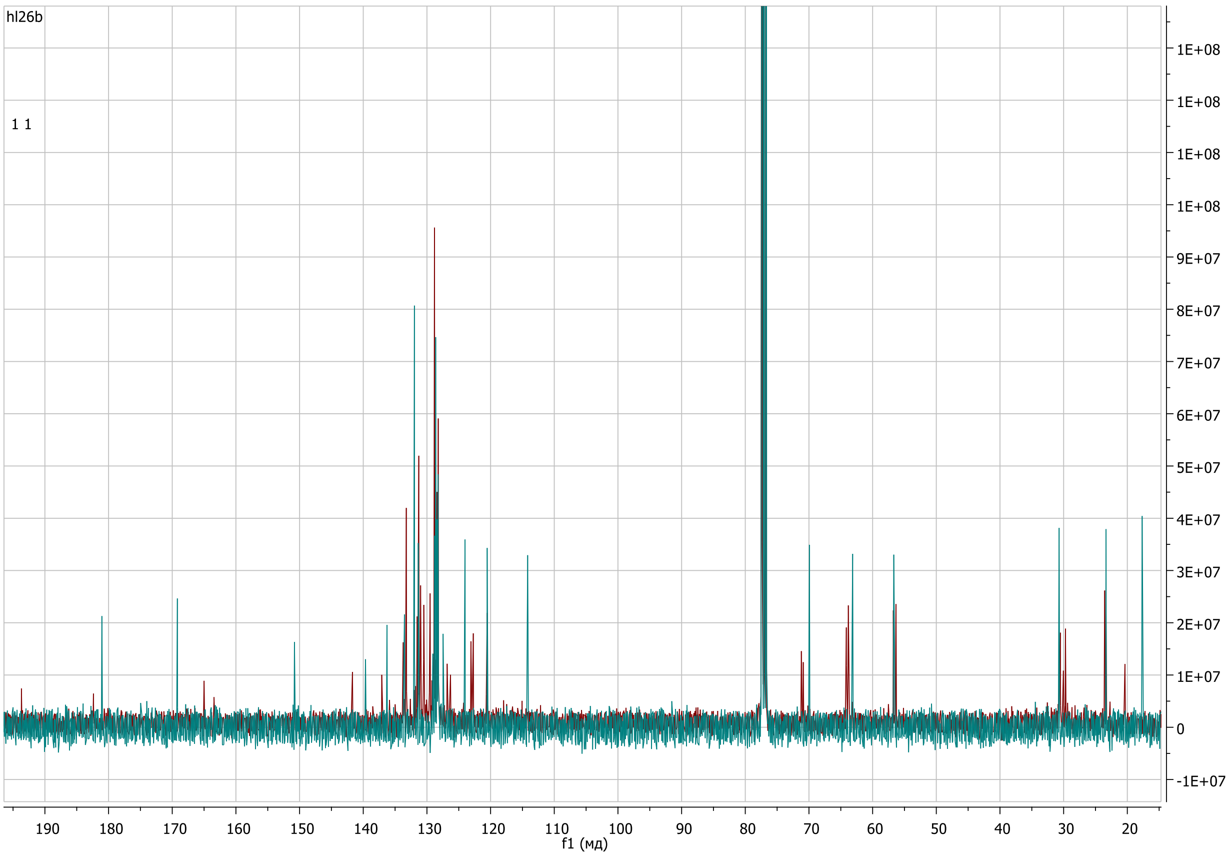


Figure S11. Interposition of ^{13}C NMR spectra ($CDCl_3$) of complex **5** (red) and that of **2** (blue).

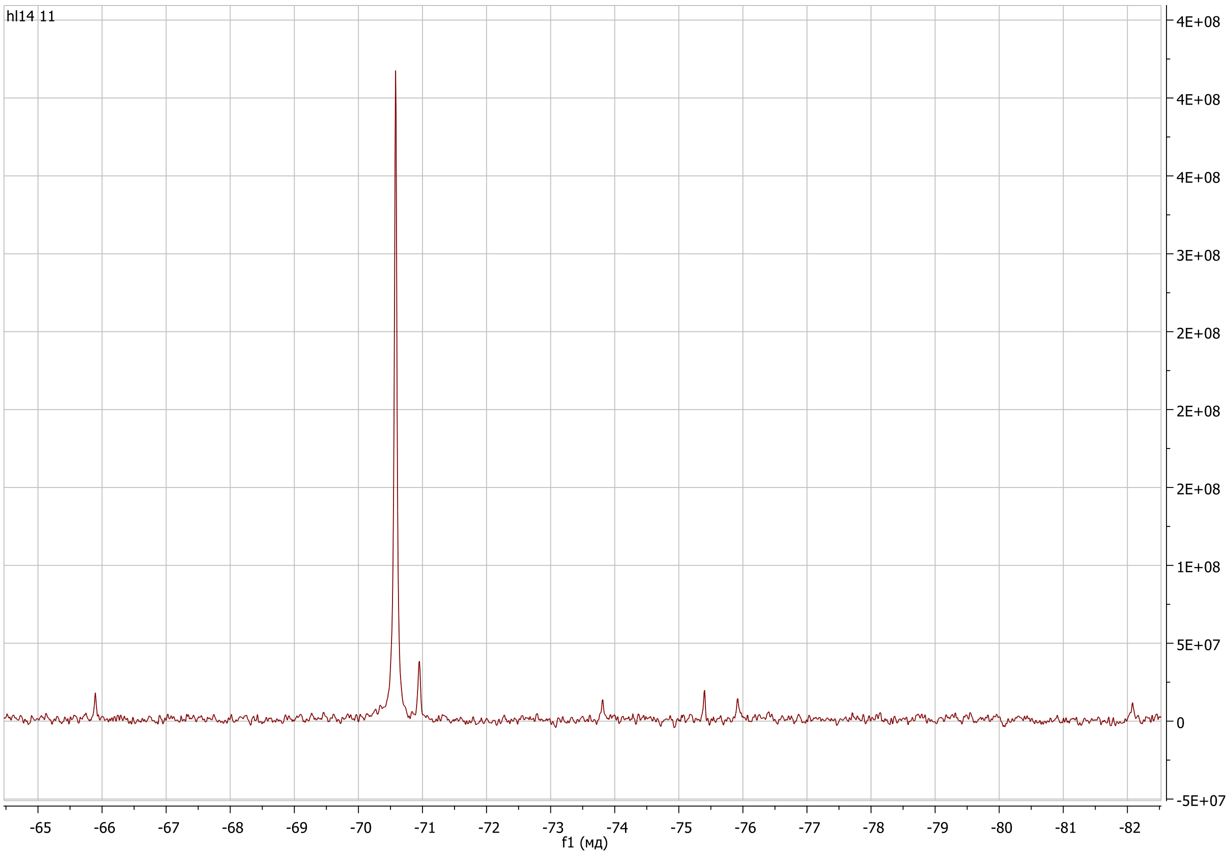


Figure S12. ^{19}F NMR ($CDCl_3$) of complex **5**.

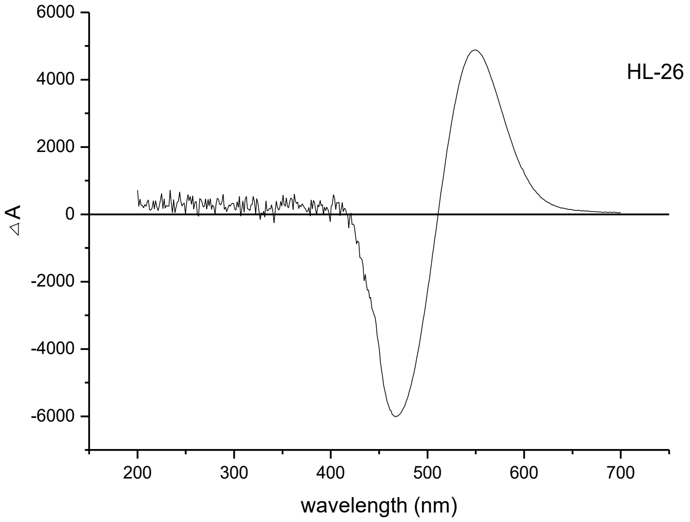


Figure S13. CD spectra of complex **5** ($c = 0.6$ g dm^{-3}, Me_2CO).

HPLC analysis conditions

Liquid chromatography "Stayer" ("Aquilon", Russia) with a hardware-software complex for the automation of the reception and processing of chromatographic data "Ekohrom" was used. The column was CHIRALCEL OJ (250 × 4.6 mm), the eluent was heptane/isopropanol (9:1), the eluent flow rate was 1 ml min^{-1}, the temperature was 25°C, and the ultraviolet (UV) detection wavelength was 254 nm.

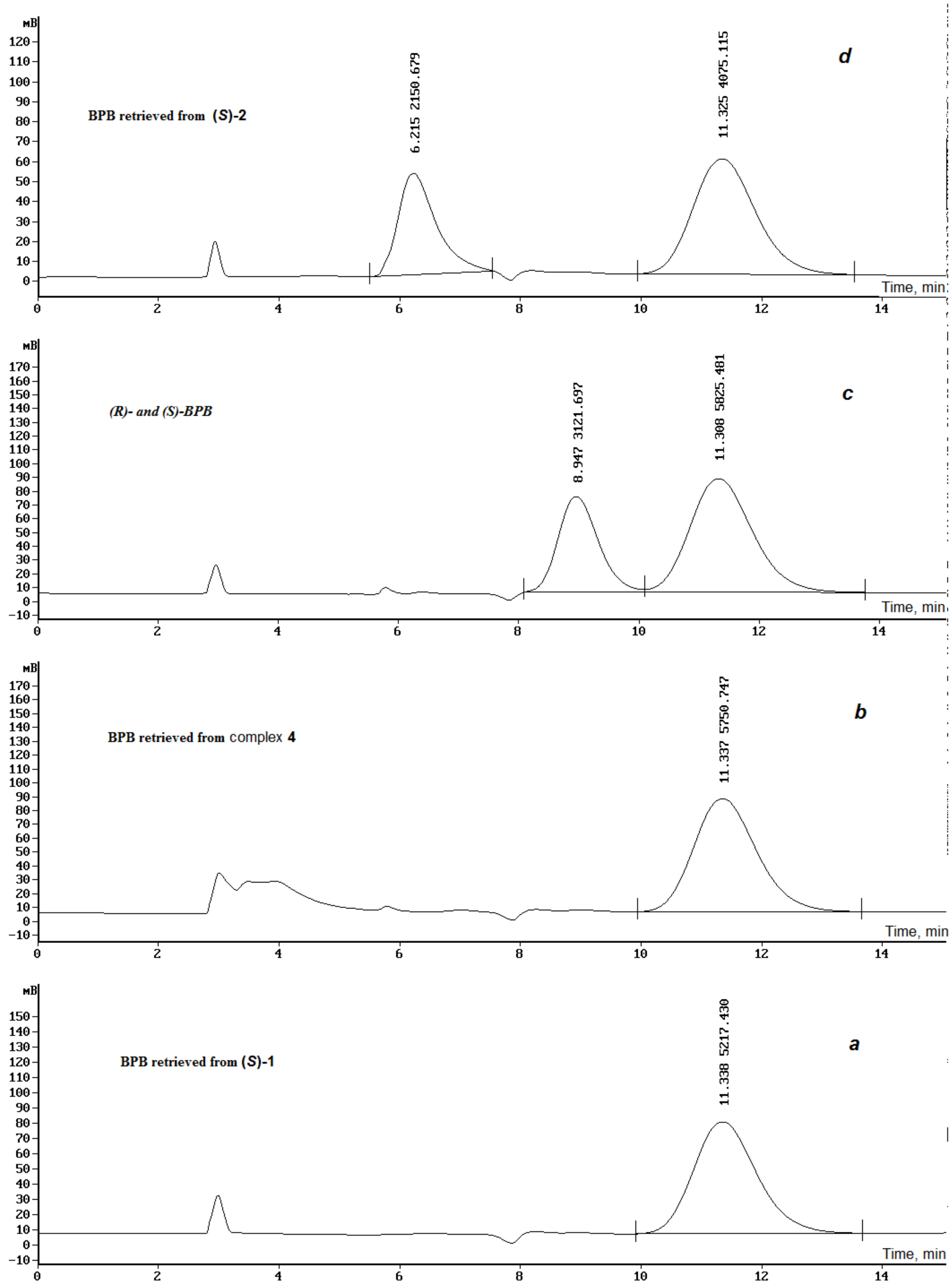


Figure S14. HPLC traces of 2-[(*S*)-*N*-(*N*-benzylprolinoylamino]benzophenone (BPB) recovered from (bottom to top) *a*) the initial (*S*)-**1**, *b*) complex **4**, *c*) an artificial mixture of 31% (*R*)-BPB and 69% (*S*)-BPB, and *d*) complex **2**.