Electronic supplementary materials *Mendeleev Commun*., 2015, **25**, 168−170

Asymmetric aldol reactions in ketone/ketone systems catalyzed by ionic liquid-supported C_2-symmetrical organocatalyst

Sergei V. Kochetkov, Alexander S. Kucherenko and Sergei G. Zlotin

List of the Contents

1. Experimental Section

1.1. General Information: The ^{1}H and ^{13}C NMR spectra were recorded by Bruker AM 300 in $CDCI_3$ and $[D_6]$DMSO. The chemical shifts of ^{1}H and ^{13}C were measured relative to Me_4Si or $CDCl_3$, respectively. The high-resolution mass spectra (HRMS) were measured with a Bruker microTOF II spectrometer by using electrospray ionization (ESI). The measurements were taken either in the positive ion mode (interface capillary voltage 4500 V) or in the negative ion mode (3200 V) in the mass range from *m/z* = 50–3000 Da; external or internal calibration was done with electrospray calibrant solution (Fluka). Syringe injection was used for solution in methanol (flow rate 3 μL/min). Nitrogen was applied as a dry gas and the interface temperature was set at 180°C. [1] Elemental analysis was carried out on a microanalyzer Perkin Elmer 2400. The IR spectra (KBr pellets) were recorded by a Specord M82 spectrometer. Silica gel 0.060–0.200 (Acros) was used for column chromatography. The solvents were purified by standard procedures.

1.2. Catalysts preparation

(3*R*,3'*R*,5*S*,5'*S*)-dibenzyl 5,5'-((((1*S*,2*S*)-1,2-diphenylethane-1,2-diyl)bis(azanediyl))-bis-(carbonyl))bis(3-hydroxypyrrolidine-1-carboxylate) (5a).

A solution of ethylchloroformate (2.00 ml, 21 mmol) in THF (10 ml) was added dropwise to a stirred solution of (2*S*)–*N*–((benzyloxy)carbonyl)–4–hydroxylproline **3** (5.56 g, 21 mmol) and Et_3N (2.93 ml, 21 mmol) in THF (60 ml) at 0°C for 15 min. After 30 min, (1*S*,2*S*)-1,2-diphenylethane-1,2-diamine **4a** (2.12 g, 10 mmol) was added to the mixture and the resulting solution was stirred at ambient temperature for 18 h. The precipitate was filtered off and washed successively with water (3×30 ml) and THF (3×30 ml). The resulting white solid was dried under reduced pressure (0.5 Torr) at 50 °C for 2 h to afford amide **5a** as colorless solid. Yield 6.31 g (90%), mp 181-182 °C. $[\alpha]_D^{20}$ −31.47 (*c* 0.17, CH_3CN). ^{1}H NMR (DMSO-d_6): δ = 1.23-1.48 (m, 2H, CH_2CH), 1.65-1.89 (m, 2H, CH_2CH), 3.25-3.40 (m, 4H, CH_2N), 4.08-4.31 (m, 4H,

O*H*, C*H*OH), 4.57-4.70 (m, 1H, C*H*N), 4.95-5.10 (m, 5H, CH_2Ar, C*H*N), 5.34-5.52 (m, 2H, C*H*NH), 7.02-7.45 (m, 20H, *Ar*), 8.21-8.42 (m, 2H, N*H*) ppm. ^{13}C NMR (DMSO-d_6) δ = 38.29, 55.69, 56.05, 59.00, 65.88, 68.46, 126.91, 127.44, 127.74, 128.10, 128.68, 128.33, 136.89, 140.08, 154.14, 171.35 ppm. IR (KBr, cm^{-1}): 3443, 3409, 3308, 3064, 3035, 2946, 1694, 1653, 1539, 1421, 1359 cm^{-1}. $C_{40}H_{42}N_4O_8$. calcd: C 67.97, H 5.99, N 7.93; found: C 68.01, H 6.02, N 7.86. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{40}H_{42}N_4O_8$: 707.3075; found 707.3068.

(3*R*,3'*R*,5*S*,5'*S*)-dibenzyl 5,5'-((((1*R*,2*R*)-1,2-diphenylethane-1,2-diyl)bis(azanediyl))-bis-(carbonyl))bis(3-hydroxypyrrolidine-1-carboxylate) (5b).

Compound **5b** was prepared similarly from **3** and **4b**. Yield 6.80 g (97%), mp 115-116°C. $[\alpha]_D^{20}$ −46.12 (*c* 0.5, CH_3CN). ^{1}H NMR (DMSO-d_6): δ = 1.35-1.66 (m, 2H, CH_2CH), 1.86-2.08 (m, 2H, CH_2CH), 3.35-3.49 (m, 4H, CH_2N), 4.11 (s, 2H, O*H*), 4.15-4.28 (m, 2H, C*H*OH), 4.73-4.85 (m, 1H, C*H*N), 4.95-5.11 (m, 5H, CH_2Ar, C*H*N), 5.11-5.50 (m, 2H, C*H*NH), 7.07-7.45 (m, 20H, *Ar*), 8.35-8.60 (m, 2H, N*H*) ppm. ^{13}C NMR (DMSO-d_6) δ = 38.48, 55.43, 59.10, 66.10, 67.83, 68.48, 126.50, 127.60, 127.77, 127.86, 128.33, 128.33, 137.03, 140.23, 154.53, 171.69 ppm. IR (KBr, cm^{-1}): 3410, 3330, 3063, 3033, 2947, 1671, 1649, 1528, 1421, 1358 cm^{-1}. $C_{40}H_{42}N_4O_8$. calcd: C 67.97, H 5.99, N 7.93; found: C 68.03, H 6.04, N 7.88. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{40}H_{42}N_4O_8$: 707.3075; found 707.3066.

(3*R*,3'*R*,5*S*,5'*S*)-dibenzyl 5,5'-((((1*S*,2*S*)-1,2-diphenylethane-1,2-diyl)bis(azanediyl))-bis(carbonyl))bis(3-((5-bromopentanoyl)oxy)pyrrolidine-1-carboxylate) (6a).

Amide **5a** (5.09 g, 7.2 mmol), 5–bromovaleric acid (2.61 g, 14.4 mmol), DCC (2.97 g, 14.4 mmol), and DMAP (cat.) in CH_2Cl_2 (60 ml) were stirred at 25 °C for 12 h. The precipitate was filtered off and washed with CH_2Cl_2 (3×25 ml). The combined organic washings were evaporated and the residue was purified by column chromatography on silica gel (eluent: $CHCl_3$) to afford the ester **6a** as colorless solid. Yield 5.55 g (75%), mp 118-120 °C. $[\alpha]_D^{20}$ −26.40 (*c* 0.5, CH_3CN). ^{1}H NMR (DMSO-d_6): δ = 1.50-1.88 (m, 10H, CH_2CH, CH_2), 1.90-2.17 (m, 2H,

CH_2CH), 2.22-2.41 (m, 4H, CH_2CO), 3.40-3.65 (m, 8H, CH_2N, CH_2Br), 4.20-4.38 (m, 2H, C*H*O), 4.60-4.71 (m, 1H, C*H*N), 4.95-5.15 (m, 5H, CH_2Ar, C*H*N), 5.35-5.49 (m, 2H, C*H*NH), 7.07-7.40 (m, 20H, *Ar*), 8.31-8.52 (m, 2H, N*H*) ppm. ^{13}C NMR (DMSO-d_6) δ = 24.41, 31.37, 32.45, 34.47, 36.31, 52.49, 56.12, 58.58, 66.10, 72.36, 126.94, 127.43, 127.74, 127.80, 128.08, 128.33, 136.61, 139.88, 153.81, 170.71, 172.15 ppm. IR (KBr, cm^{-1}): 3319, 3063, 3033, 2937, 1735, 1708, 1645, 1518, 1416, 1358 cm^{-1} $C_{50}H_{56}Br_2N_4O_{10}$. calcd: C 58.15, H 5.47, N 5.42; found: C 58.21, H 5.44, N 5.53. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{50}H_{56}Br_2N_4O_{10}$: 1031.2436; found 1031.2423.

(3*R*,3'*R*,5*S*,5'*S*)-dibenzyl 5,5'-((((1*R*,2*R*)-1,2-diphenylethane-1,2-diyl)bis(azanediyl))-bis(carbonyl))bis(3-((5-bromopentanoyl)oxy)pyrrolidine-1-carboxylate) (6b).

Compound **6b** was prepared similarly from **5b**. Yield 5.18 g (70%), mp 147-149 °C. $[\alpha]_D^{20}$ −32.31 (*c* 0.5, CH_3CN). ^{1}H NMR (DMSO-d_6): δ = 1.40-2.00 (m, 10H, CH_2CH, CH_2), 2.21-2.36 (m, 6H, CH_2CH, CH_2CO), 3.45-3.70 (m, 8H, CH_2N, CH_2Br), 4.20-4.37 (m, 2H, C*H*O), 4.75-4.85 (m, 1H, C*H*N), 5.00-5.20 (m, 5H, CH_2Ar, C*H*N), 5.20-5.50 (m, 2H, C*H*NH), 7.05-7.42 (m, 20H, *Ar*), 8.40-8.70 (m, 2H, N*H*) ppm. ^{13}C NMR (DMSO-d_6) δ = 23.01, 31.43, 33.40, 35.38, 36.69, 47.58, 52.63, 58.88, 66.29, 71.80, 127.06, 127.40, 127.59, 127.82, 127.94, 128.29, 136.86, 139.99, 154.24, 170.91, 172.28 ppm. IR (KBr, cm^{-1}): 3326, 3064, 3032, 2933, 1726, 1708, 1647, 1528, 1419, 1355, 1358 cm^{-1} $C_{50}H_{56}Br_2N_4O_{10}$. calcd: C 58.15, H 5.47, N 5.42; found: C 58.19, H 5.42, N 5.49. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{50}H_{56}Br_2N_4O_{10}$: 1031.2436; found 1031.2427.

3,3'-((((3*R*,3'*R*,5*S*,5'*S*)-5,5'-((((1*S*,2*S*)-1,2-diphenylethane-1,2-diyl)bis(azanediyl))bis-(carbonyl))bis(1-((benzyloxy)carbonyl)pyrrolidine-5,3-diyl))bis(oxy))bis(5-oxopentane-5,1-diyl))bis(1-methyl-1H-imidazol-3-ium) bromide (7a).

A mixture of ester **6a** (2.20 g, 2.1 mmol) and 1–methyl–1*H*–imidazole (1.23 g, 15 mmol) was heated at 80 °C for 5 min, cooled to rt and washed thoroughly with Et_2O (5×10 ml). The residue

was dissolved in MeOH (1 ml), then Et_2O (20 ml) was added to the solution. The separated oil was washed with Et_2O (5×10 ml) again and dried under reduced pressure (0.5 Torr) for 1 h to afford bromide **7a** as colorless solid. Yield 2.1 g (84%), mp 95-98 °C. $[\alpha]_D^{20}$ −16.10 (*c* 0.5, CH_3CN). ^{1}H NMR (DMSO-d_6): δ = 1.39-1.70 (m, 6H, CH_2CH, CH_2), 1.70-1.88 (m, 4H, CH_2), 1.95-2.20 (m, 2H, CH_2CH), 2.30-2.42 (m, 4H, CH_2CO), 3.32-3.60 (m, 4H, CH_2N), 3.82 (s, 6H, CH_3), 4.10-4.26 (m, 4H, CH_2N), 4.34-4.60 (m, 2H, C*H*O), 4.69-4.80 (m, 1H, C*H*N), 4.92-5.07 (m, 5H, CH_2Ar, C*H*N), 5.38-5.55 (m, 2H, C*H*NH), 7.04-7.52 (m, 20H, *Ar*), 7.70 (s, 2H, NC*H*CHN), 7.78 (s, 2H, NCHC*H*N), 8.65-8.96 (m, 2H, N*H*), 9.16 (s, 2H, NC*H*N) ppm. ^{13}C NMR (DMSO-d_6) δ = 20.80, 22.92, 28.63, 32.61, 35.70, 36.46, 48.28, 52.57, 56.32, 58.27, 65.82, 72.44, 122.15, 123.54, 126.82, 127.29, 127.53, 127.74, 128.00, 128.30, 136.47, 136.66, 139.98, 153.59, 170.84, 172.09 ppm. IR (KBr, cm^{-1}): 3436, 3213, 3056, 2947, 1732, 1703, 1655, 1537, 1419, 1355 cm^{-1}. $C_{58}H_{68}Br_2N_8O_{10}$. calcd: C 58.20, H 5.73, N 9.36; found: C 58.18, H 5.77, N 9.29. HRMS (ESI): *m/z* $[M]^{2+}$ calcd for $C_{58}H_{68}N_8O_{10}$: 518.2524; found 518.2518.

3,3'-((((3*R*,3'*R*,5*S*,5'*S*)-5,5'-((((1*R*,2*R*)-1,2-diphenylethane-1,2-diyl)bis(azanediyl))bis-(carbonyl))bis(1-((benzyloxy)carbonyl)pyrrolidine-5,3-diyl))bis(oxy))bis(5-oxopentane-5,1-diyl))bis(1-methyl-1H-imidazol-3-ium) bromide (7b).

Compound **7b** was prepared similarly from **6b**. Yield 2.02 g (81%), mp 97-100 °C. $[\alpha]_D^{20}$ −29.96 (*c* 0.5, CH_3CN). ^{1}H NMR (DMSO-d_6): δ = 1.39-1.90 (m, 10H, CH_2CH, CH_2), 2.00-2.35 (m, 6H, CH_2CH, CH_2CO), 3.45-3.70 (m, 4H, CH_2N), 3.82 (s, 6H, CH_3), 4.10-4.20 (m, 4H, CH_2N), 4.22-4.38 (m, 2H, C*H*O), 4.71-4.85 (m, 1H, C*H*N), 5.00-5.50 (m, 7H, CH_2Ar, C*H*N, C*H*NH), 7.04-7.40 (m, 20H, *Ar*), 7.68 (s, 2H, NC*H*CHN), 7.73 (s, 2H, NCHC*H*N), 8.52-8.79 (m, 2H, N*H*), 9.11 (s, 2H, NC*H*N) ppm. ^{13}C NMR (DMSO-d_6): δ = 20.75, 28.61, 32.56, 35.71, 36.62, 48.26, 52.55, 56.83, 58.52, 66.12, 72.42, 122.17, 123.56, 126.65, 126.99, 127.43, 127.66, 128.10, 128.34, 136.47, 136.71, 140.07, 154.10, 170.84, 172.08 ppm. IR (KBr, cm^{-1}): 3433, 3229, 3034, 2946, 1733, 1703, 1529, 1416, 1355 cm^{-1}. $C_{58}H_{68}Br_2N_8O_{10}$. calcd: C 58.20, H 5.73, N 9.36;

found: C 58.16, H 5.78, N 9.27. HRMS (ESI): *m/z* $[M]^{2+}$ calcd for $C_{58}H_{68}N_8O_{10}$: 518.2524; found 518.2519.

3,3'-((((3*R*,3'*R*,5*S*,5'*S*)-5,5'-((((1*S*,2*S*)-1,2-diphenylethane-1,2-diyl)bis(azanediyl))bis-(carbonyl))bis(1-((benzyloxy)carbonyl)pyrrolidine-5,3-diyl))bis(oxy))bis(5-oxopentane-5,1-diyl))bis(1-methyl-1H-imidazol-3-ium) hexafluorophosphate(V) (8a).

A solution of KPF_6 (1.25 g, 6.8 mmol) in water (15 ml) was added to a stirred solution of bromide **7a** (2.00 g, 1.7 mmol) in water (15 ml). The precipitate was filtered off, washed with water (3×15 ml) and dried under reduced pressure (0.5 Torr) for 1 h to afford hexafluorophosphate **8a** as colorless solid. Yield 2.06 g (93%), mp 103-105 °C. $[\alpha]_D^{20}$ −18.30 (*c* 0.5, CH_3CN). ^{1}H NMR (DMSO-d_6): δ = 1.40-1.90 (m, 10H, C*H*$_2$CH, C*H*$_2$), 1.90-2.20 (m, 2H, C*H*$_2$CH), 2.30-2.43 (m, 4H, C*H*$_2$CO), 3.35-3.70 (m, 4H, CH_2N), 3.88 (s, 6H, C*H*$_3$), 4.12-4.35 (m, 6H, C*H*$_2$N, C*H*O), 4.65-4.75 (m, 1H, C*H*N), 4.96-5.13 (m, 5H, C*H*$_2$Ar, C*H*N), 5.35-5.51 (m, 2H, C*H*NH), 7.10-7.40 (m, 20H, *Ar*), 7.73 (d, J=11.0 Hz, 4H, NC*H*C*H*N), 8.30-8.50 (m, 2H, N*H*), 9.10 (s, 2H, NC*H*N) ppm. ^{13}C NMR (DMSO-d_6) δ = 20.75, 28.59, 32.46, 34.96, 35.68, 36.15, 48.32, 52.43, 56.00, 58.60, 66.14, 72.26, 122.15, 123.59, 126.78, 126.92, 127.44, 127.74, 128.09, 128.34, 136.57, 139.70, 153.82, 170.70, 172.10 ppm. IR (KBr, cm^{-1}): 3418, 3325, 3166, 2952, 1734, 1706, 1645, 1521, 1419, 1357, 841, 558 cm^{-1}. $C_{58}H_{68}F_{12}N_8O_{10}P_2$. calcd calcd: C 52.49, H 5.16, N 8.44; found: C 52.41, H 5.14, N 8.46. HRMS (ESI): *m/z* $[M]^{2+}$ calcd for $C_{58}H_{68}N_8O_{10}$: 518.2524; found 518.2516.

3,3'-((((3*R*,3'*R*,5*S*,5'*S*)-5,5'-((((1*R*,2*R*)-1,2-diphenylethane-1,2-diyl)bis(azanediyl))bis-(carbonyl))bis(1-((benzyloxy)carbonyl)pyrrolidine-5,3-diyl))bis(oxy))bis(5-oxopentane-5,1-diyl))bis(1-methyl-1H-imidazol-3-ium) hexafluorophosphate(V) (8b).

Compound **8b** was prepared similarly from **7b**. Yield 2.02 g (91%), mp 90-92 °C. $[\alpha]_D^{20}$ −18.37 (*c* 0.3, CH_3CN). ^{1}H NMR (DMSO-d_6): δ = 1.38-2.00 (m, 10H, C*H*$_2$CH, C*H*$_2$), 2.10-2.36 (m, 6H, C*H*$_2$CH, C*H*$_2$CO), 3.45-3.70 (m, 4H, CH_2N), 3.82 (s, 6H, C*H*$_3$), 4.10-4.20 (m, 4H, C*H*$_2$N), 4.22-

4.35 (m, 2H, C*H*O), 4.73-4.85 (m, 1H, C*H*N), 4.96-5.50 (m, 7H, CH_2Ar, C*H*N, C*H*NH), 7.00-7.45 (m, 20H, *Ar*), 7.70 (d, J=11.0 Hz, 4H, NC*H*C*H*N), 8.45-8.72 (m, 2H, N*H*), 9.09 (s, 2H, NC*H*N) ppm. ^{13}C NMR (DMSO-d_6): δ = 20.74, 28.59, 32.50, 35.69, 48.29, 52.57, 57.05, 58.76, 66.21, 72.42, 122.17, 123.59, 126.69, 127.02, 127.68, 128.17, 128.38, 136.46, 139.77, 154.20, 172.10 ppm. IR (KBr, cm^{-1}): 3412, 3325, 3166, 2949, 1735, 1705, 1525, 1419, 1356, 841, 558 cm^{-1}. $C_{58}H_{68}F_{12}N_8O_{10}P_2$. calcd calcd: C 52.49, H 5.16, N 8.44; found: C 52.43, H 5.13, N 8.48. HRMS (ESI): *m/z* [M]$^{2+}$ calcd for $C_{58}H_{68}N_8O_{10}$: 518.2524; found 518.2518.

3,3'-((((3*R*,3'*R*,5*S*,5'*S*)-5,5'-((((1*S*,2*S*)-1,2-diphenylethane-1,2-diyl)bis(azanediyl))bis-(carbonyl))bis(pyrrolidine-5,3-diyl))bis(oxy))bis(5-oxopentane-5,1-diyl))bis(1-methyl-1H-imidazol-3-ium) hexafluorophosphate(V) (2a).

The hexafluorophosphate **8a** (1.33 g, 1.0 mmol) was dissolved in CH_3OH (20 ml) and Pd/C (100 mg) was added to the solution. The resulting suspension was stirred under H_2 (1 bar) for 9 h, filtered, the filtrate was evaporated under reduced pressure (40 Torr) and the residue was dried *in vacuo* (0.5 Torr) for 2 h to afford catalyst **2a** as light yellow solid. Yield 1.03 g (97%), mp 101-104 °C. $[\alpha]_D^{20}$ −5,97 (*c* 0.5, CH_3CN). ^{1}H NMR (DMSO-d_6): δ = 1.40-1.59 (m, 4H, CH_2), 1.59-2.05 (m, 8H, CH_2, CHCH_2CH), 2.33 (t, J=7.33Hz, 4H, CH_2CO_2), 2.86 (d, J=12.5Hz, 2H, NCH_2), 3.01 (d, J=12.5Hz, 2H, NCH_2), 3.32 (br s, 2H, N*H*), 3.65 (t, J=7.7Hz, 2H, C*H*CO), 3.85 (s, 6H, CH_3), 4.17 (t, 4H, *J*=7.6 Hz, CH_2Im), 5.02 (br s, 2H, C*H*O), 5.29 (d, J=6.6Hz, 2H, C*H*Ph) 7.10-7.28 (m, 10H, *Ar*), 7.72 (d, *J*=15.5 Hz, 4H, NC*H*C*H*N), 8.64 (d, J=7.33 Hz, 2H, N*H*), 9.09 (s, 2H, NC*H*N) ppm. ^{13}C NMR (DMSO-d_6) δ = 20.81, 28.68, 32.68, 35.70, 36.54, 48.41, 52.20, 56.51, 59.16, 75.11, 122.20, 123.60, 127.13, 127.44, 127.90, 128.23, 128.40, 128.61, 136.50, 139.75, 171.68, 172.18 ppm. IR (KBr,cm^{-1}): 3399, 3307, 3171, 2949, 1730, 1658, 1513, 840, 558 cm^{-1}. $C_{42}H_{56}F_{12}N_8O_6P_2$. calcd: C 47.64, H 5.33, N 10.58; found: C 47.59 H 5.30, N 11.02. HRMS (ESI): *m/z* [M]$^+$ calcd for $C_{42}H_{56}N_8O_6PF_6$: 913.3959; found 913.3955; *m/z* [M]$^{2+}$ calcd for $C_{42}H_{56}N_8O_6$: 384.2156; found 384.2155.

3,3'-((((3*R*,3'*R*,5*S*,5'*S*)-5,5'-((((1*R*,2*R*)-1,2-diphenylethane-1,2-diyl)bis(azanediyl))bis-(carbonyl))bis(pyrrolidine-5,3-diyl))bis(oxy))bis(5-oxopentane-5,1-diyl))bis(1-methyl-1H-imidazol-3-ium) hexafluorophosphate(V) (2b).

Compound **2b** was prepared similarly from **8b**. Yield 1.02 g (96%), mp 107-110 °C. $[\alpha]_D^{20}$ −0.4 (*c* 0.5, CH_3CN). ^{1}H NMR (DMSO-d_6): δ = 1.40-1.85 (m, 12H, CH_2, CHCH_2CH), 2.30 (t, J=7.40Hz, 4H, CH_2CO_2), 2.80-3.05 (m, 4H, NCH_2), 3.65-3.75 (m, 2H, C*H*CO), 3.84 (s, 6H, CH_3), 4.18 (t, 4H, *J*=6.6 Hz, CH_2Im), 5.01 (br s, 2H, C*H*O), 5.32 (d, J=5.8Hz, 2H, C*H*Ph) 7.10-7.32 (m, 10H, *Ar*), 7.71 (d, *J*=15.5 Hz, 4H, NC*H*C*H*N), 8.72 (s, 2H, N*H*), 9.10 (s, 2H, NC*H*N) ppm. ^{13}C NMR (DMSO-d_6): δ = 20.89, 28.77, 32.71, 35.79, 36.61, 48.47, 52.02, 56.50, 59.03, 75.13, 122.29, 123.68, 126.94, 127.04, 127.19, 127.93, 127.99, 136.58, 139.84, 171.59, 172.29 ppm. IR (KBr,cm^{-1}): 3400, 3306, 3171, 2940, 1732, 1671, 1522, 841, 558 cm^{-1}. $C_{42}H_{56}F_{12}N_8O_6P_2$. calcd: C 47.64, H 5.33, N 10.58; found: C 47.60 H 5.29, N 10.98. HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{42}H_{56}N_8O_6PF_6$: 913.3959; found 913.3956; *m/z* $[M]^{2+}$ calcd for $C_{42}H_{56}N_8O_6$: 384.2156; found 384.2153.

1.3. General procedure for asymmetric aldol reaction between 9 and 10

A mixture of catalyst **2a** (20 mg, 19 μmol), ketone **10** (95 μmol), AcOH (2.8 μl, 48 μmol, 0.5 equiv. with respect to **10**) and water (3,5 μl, 200 μmol, 2 equiv. with respect to **10**) was cooled to -30°C, then acetone **9** (35 μl, 475 μmol) was added and the reaction mixture was stirred at -30°C for 24 h. Aldol **11** was extracted with Et_2O (2 x 3 ml), the combined extracts were filtered through a silica gel pad (1 g) and evaporated under reduced pressure (15 Torr). Conversions and dr values of aldols **11a-g** were measured by ^{1}H NMR spectroscopy. Compounds **11a** and **11c** were purified by column chromatography (silica gel, EtOAc/*n*-hexane 1:2) to afford corresponding aldols in 93% and 91% yield, respectively. *Ee* values of aldols **11a-g** were determined by HPLC, chiral phases: *Chiralcel OD–H, OJ–H, or Chiralpak AD–H*. NMR spectra and HPLC data for aldols **11a,b,d-g** are available in the cited articles. [2, 3]

Methyl 2-(2-chlorophenyl)-2-hydroxy-4-oxopentanoate (**11c**)

Yield 91%. Colorless oil. R_f = 0.48 (hexan-EtOAc, 2:1). HPLC analysis (OD-H, hexane : *i*-PrOH = 9:1; 220 nm; 0.9 ml/min): t_1=9.48 min (major), t_2=10.43 min (minor). $[\alpha]_D^{20}$ −29.36 (*c* 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 2.35 (s, 3H, C*H*$_3$), 2.71 (d, *J*=20.50Hz, 1H, C*H*$_2$), 3.29 (d, *J*=20.50Hz, 1H, C*H*$_2$), 3.77 (s, 3H, C*H*$_3$), 4.69 (s, 1H, O*H*), 7.20-7.45 (m, 3H, *Ar*), 7.85-7.97 (m, 1H, *Ar*) ppm. ^{13}C NMR ($CDCl_3$): δ = 32.09, 46.36, 53.15, 78.50, 127.40, 127.59, 129.46, 130.36, 130.64, 138.75, 172.58, 211.71 ppm. $C_{12}H_{13}ClO_4$ calcd: C 56.15, H 5.10; found: C 56.47, H 4.98.

1.4. Catalyst recycling

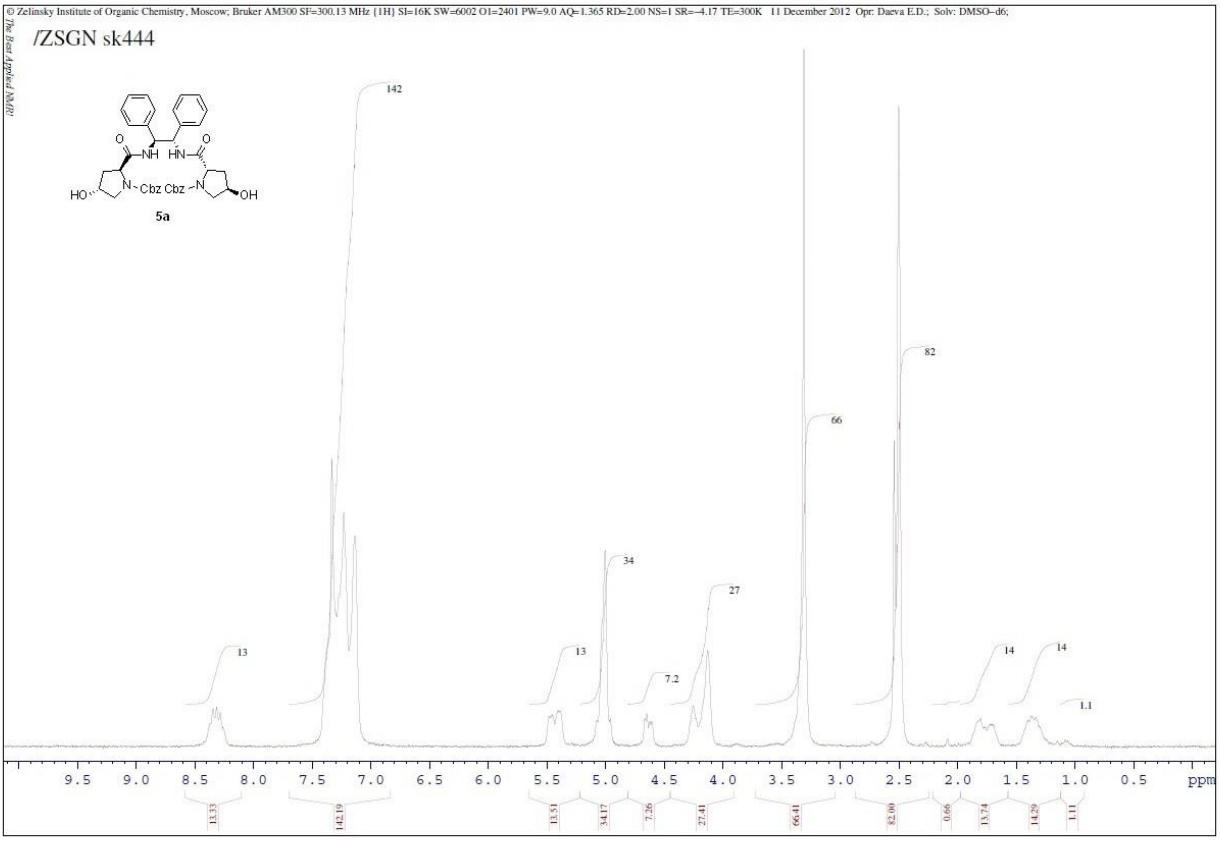
After the extraction of product **11a**, the remaining catalyst **2a** was dried *in vacuo* (1 Torr) for 1 h, fresh portions of corresponding reagents, water and AcOH were added and the reaction was re–performed as described above.

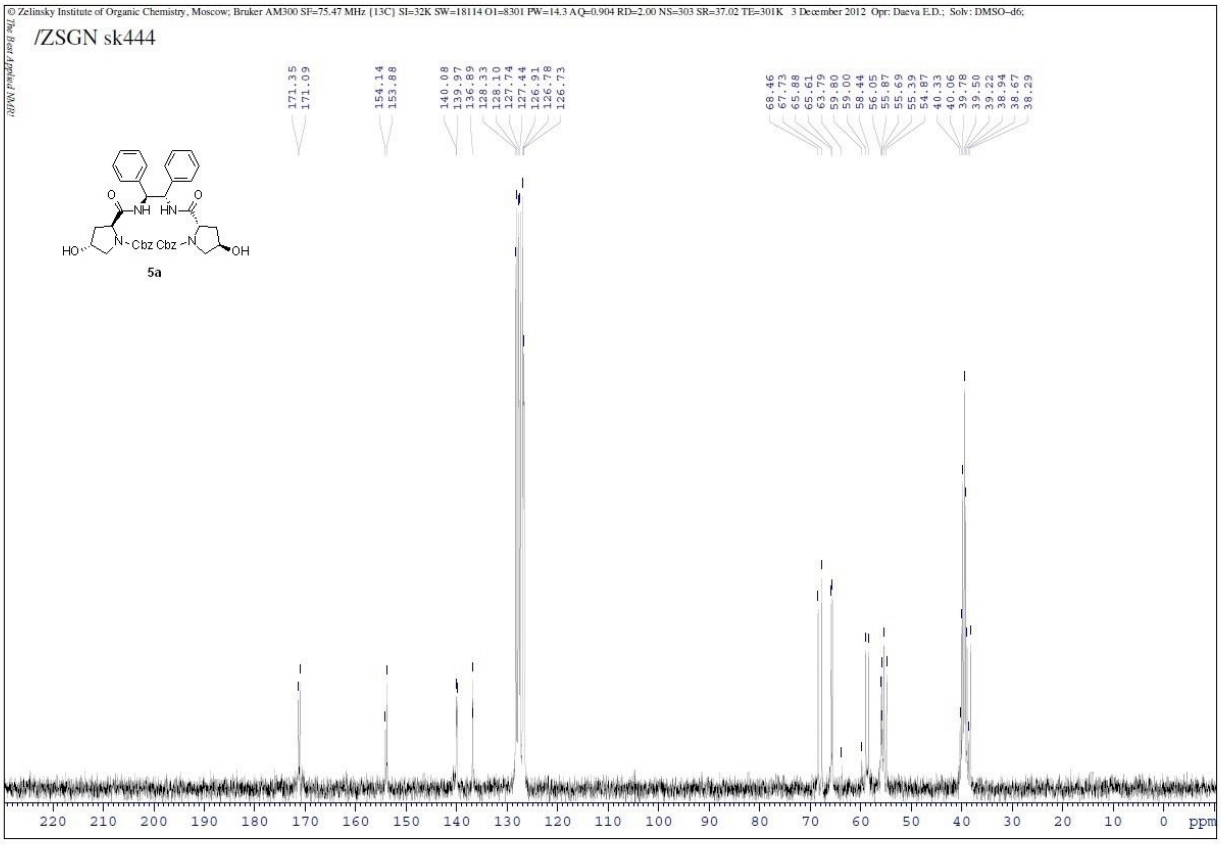
1.5. References

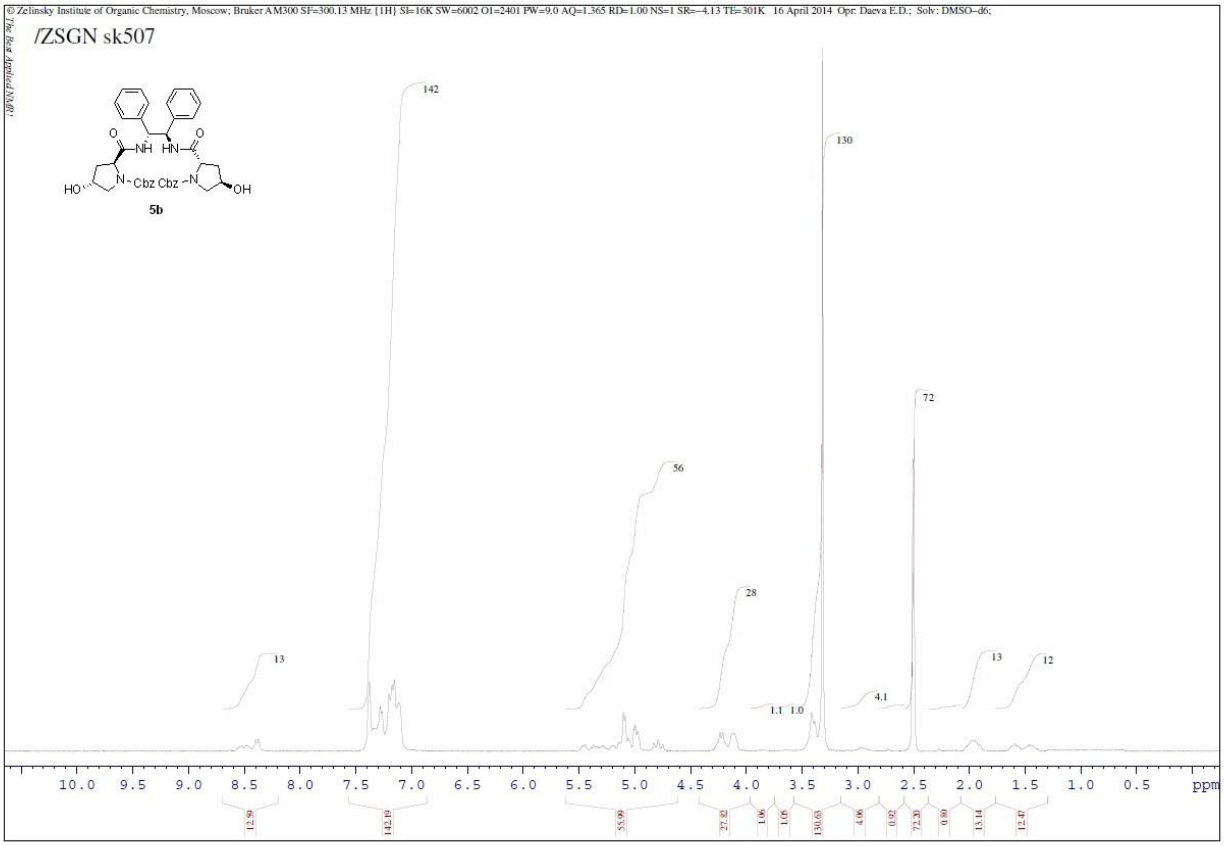
1 P. A. Belyakov, V. I. Kadentsev, A. O. Chizhov, N. G. Kolotyrkina, A. S. Shashkov and V. P. Ananikov, *Mendeleev Commun.*, 2010, **20**, 125.

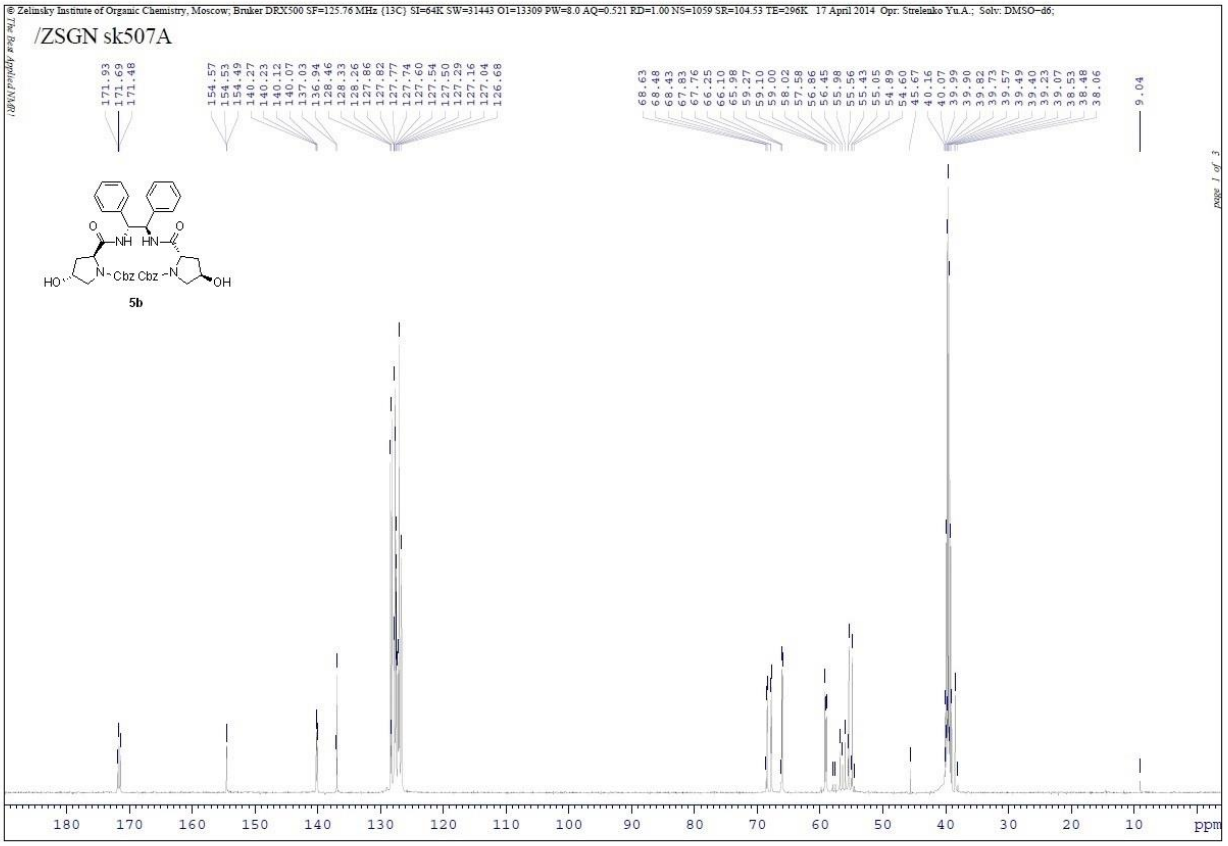
2 F. Wang, Y. Xiong, X. Liu and X. Feng, *Adv. Synth. Catal.*, 2007, **349**, 2665.

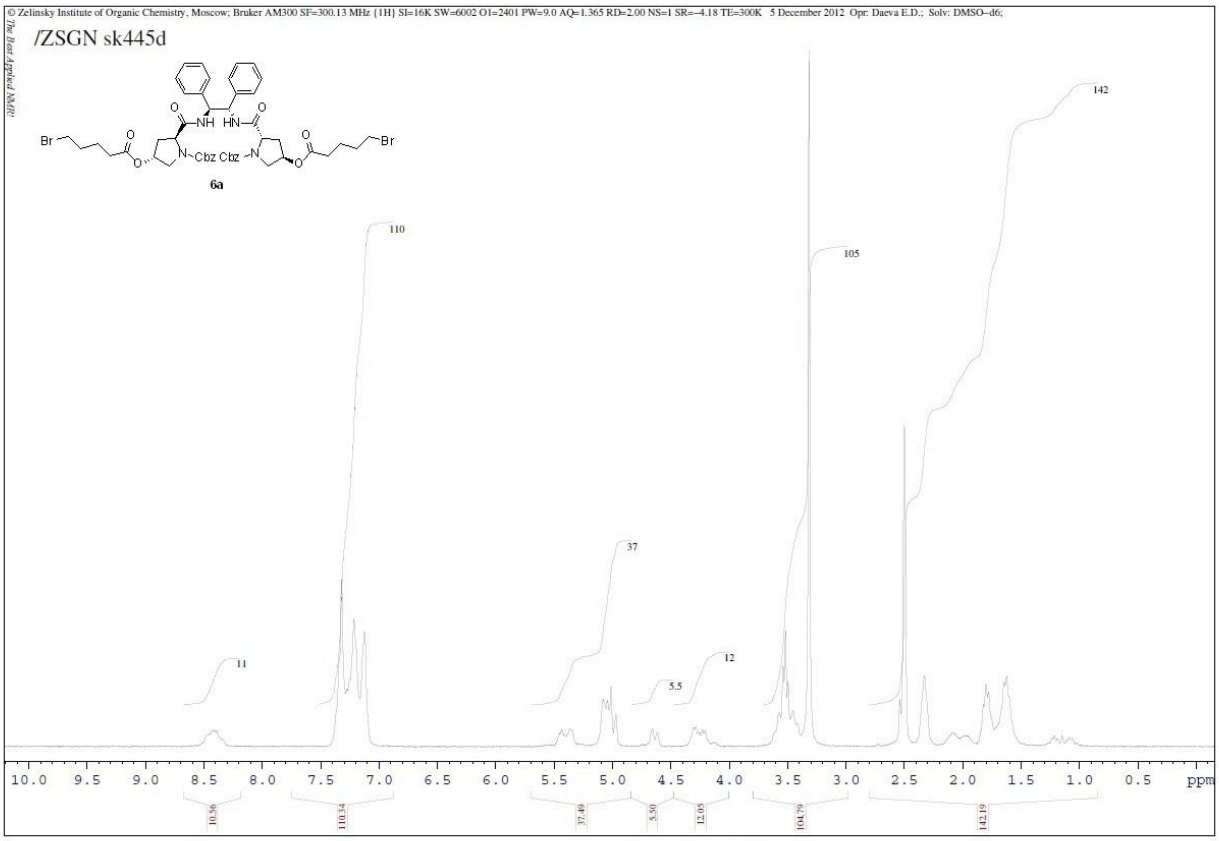
3 (*a*) K. Mikami, Y. Kawakami, K. Akiyama and K. Aikawa, *J. Am. Chem. Soc.*, 2007, **129**, 12950; (*b*) Zh. Tang, L.-F. Cun, X. Cui, A.-Q. Mi, Y.-Zh. Jiang and L.-Z. Gong, *Org. Lett.*, 2006, **8**, 1263; (*c*) J. Liu, Z. Yang, Zh. Wang, F. Wang, X. Chen, X. Liu, X. Feng, Zh. Su and Ch. Hu, *J. Am. Chem. Soc.*, 2008, **130**, 5654; (*d*) C. G. Kokotos, *J. Org. Chem*., 2012, **77**, 1131.

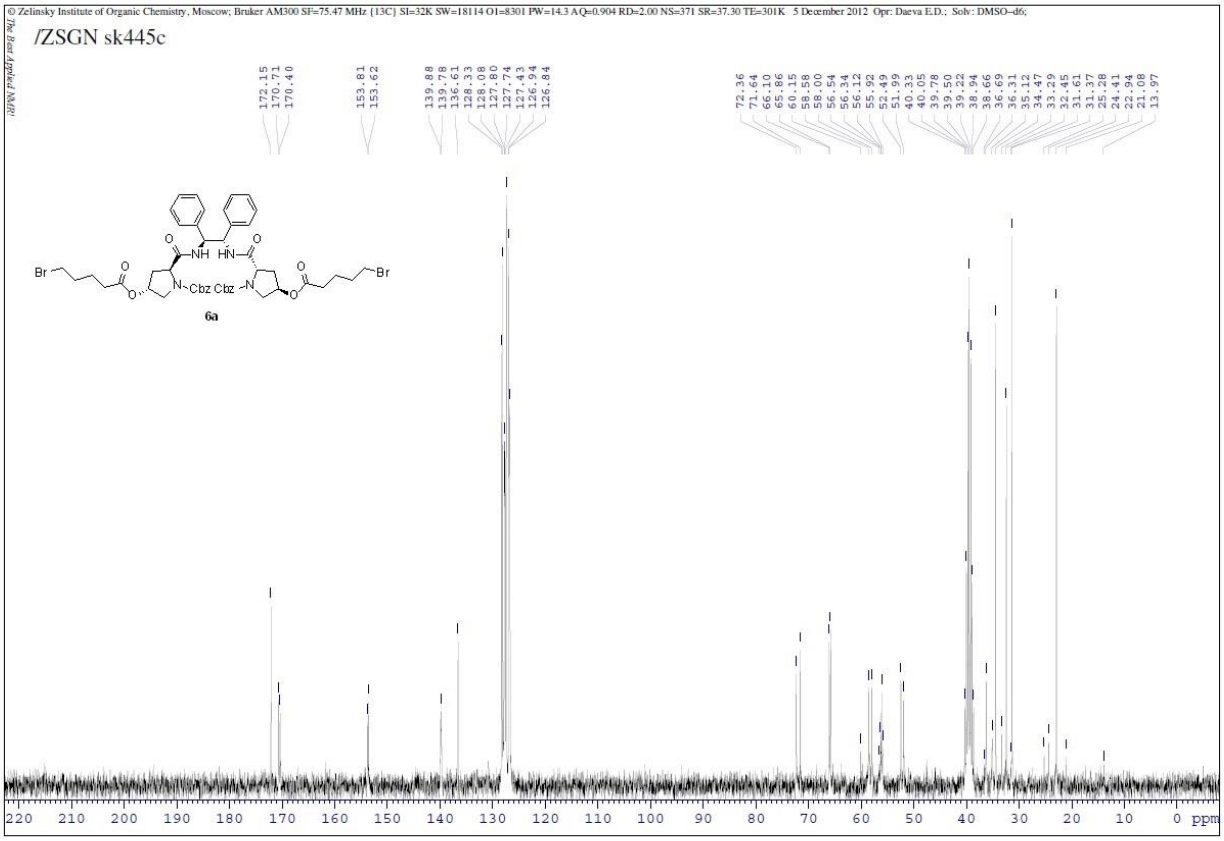

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=16K SW=6002 O1=2401 PW=9.0 AQ=1.365 RD=2.00 NS=1 SR=-4.17 TE=300K 11 December 2012 Opr: Daeva E.D.; Solv: DMSO-d6;
/ZSGN sk444
5a
142
66
82
34
27
13
13
7.2
14
14
1.1
ppm

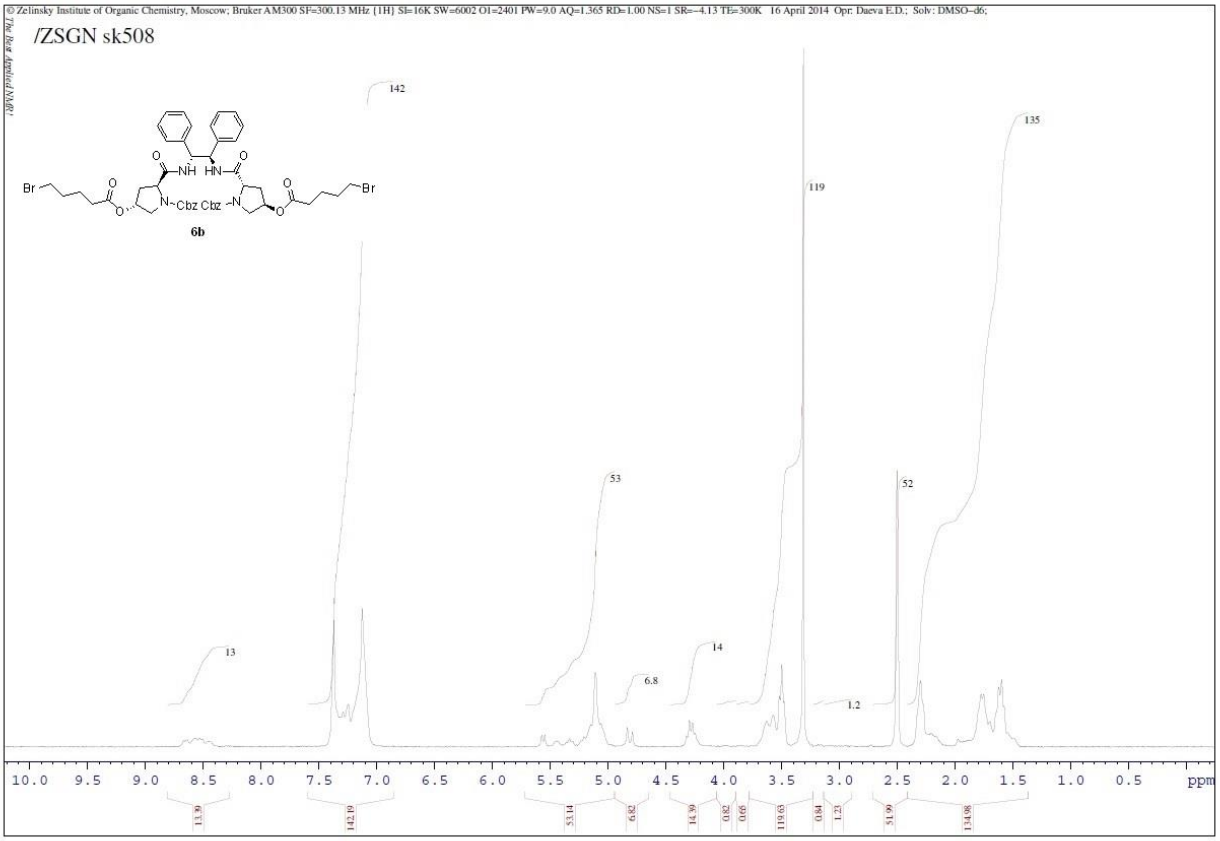

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=14.3 AQ=0.904 RD=2.00 NS=303 SR=37.02 TE=301K 3 December 2012 Opr: Daeva E.D.; Solv: DMSO-d6;
/ZSGN sk444
5a
171.35
171.09
154.14
153.88
140.08
139.97
136.89
128.33
128.10
127.74
127.44
126.91
126.78
126.73
68.46
67.73
65.88
65.61
63.79
59.80
59.00
58.44
56.05
55.87
55.69
55.39
54.87
40.33
40.06
39.78
39.50
39.22
38.94
38.67
38.29
ppm

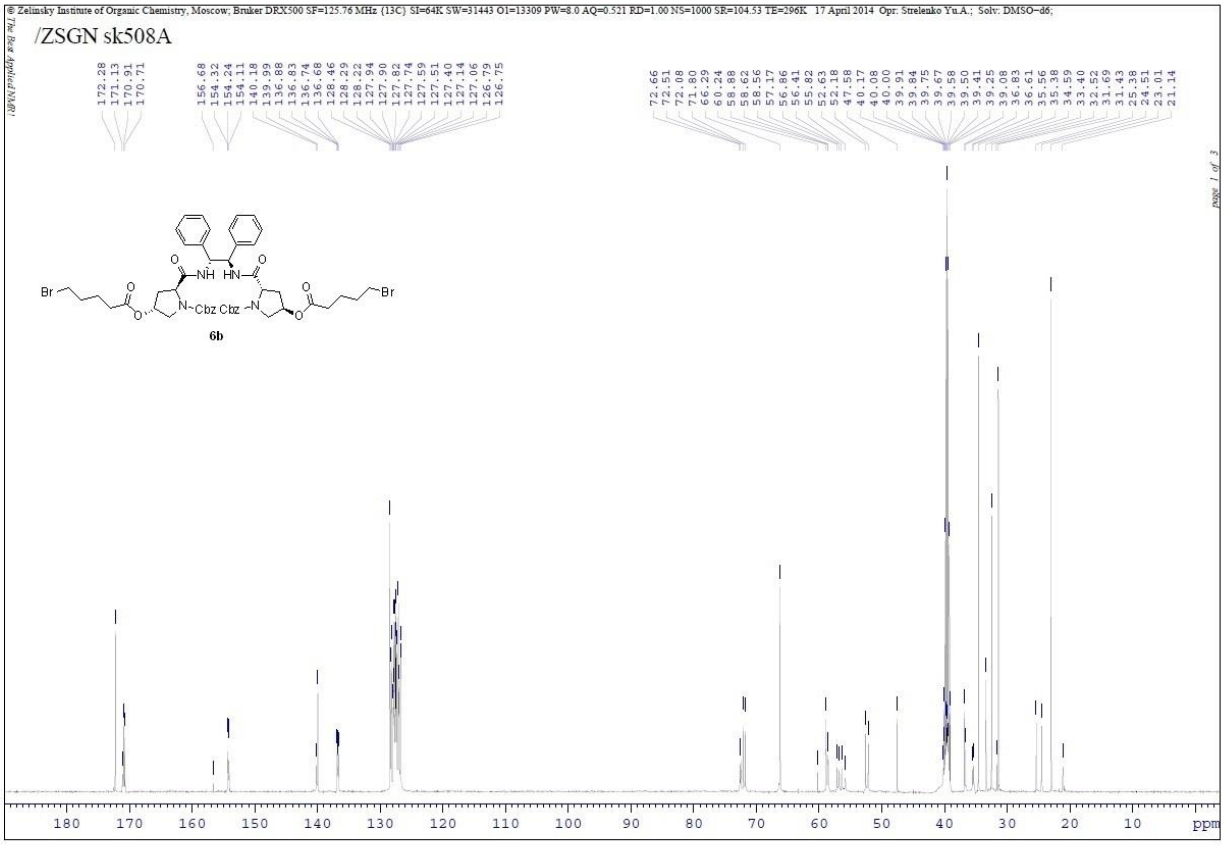

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=16K SW=6002 O1=2401 PW=9.0 AQ=1.365 RD=1.00 NS=1 SR=-4.13 TE=301K 16 April 2014 Opr: Daeva E.D.; Solv: DMSO-d6;
/ZSGN sk507
5b
142
130
72
56
28
13
13
12
4.1
1.1
1.0
ppm

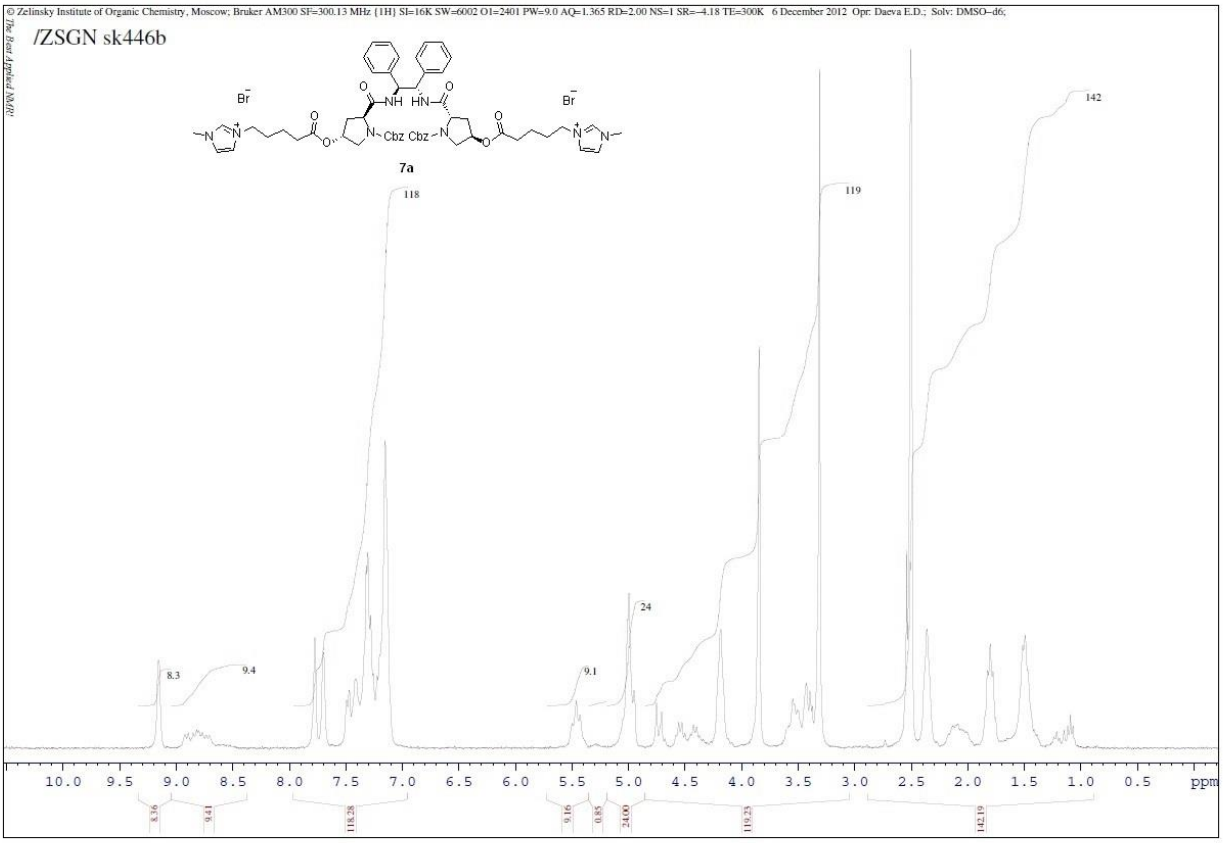

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=125.76 MHz {13C} SI=64K SW=31443 O1=13309 PW=8.0 AQ=0.521 RD=1.00 NS=1059 SR=104.53 TE=296K 17 April 2014 Opr: Strelenko Yu.A.; Solv: DMSO-d6;
/ZSGN sk507A
5b
ppm

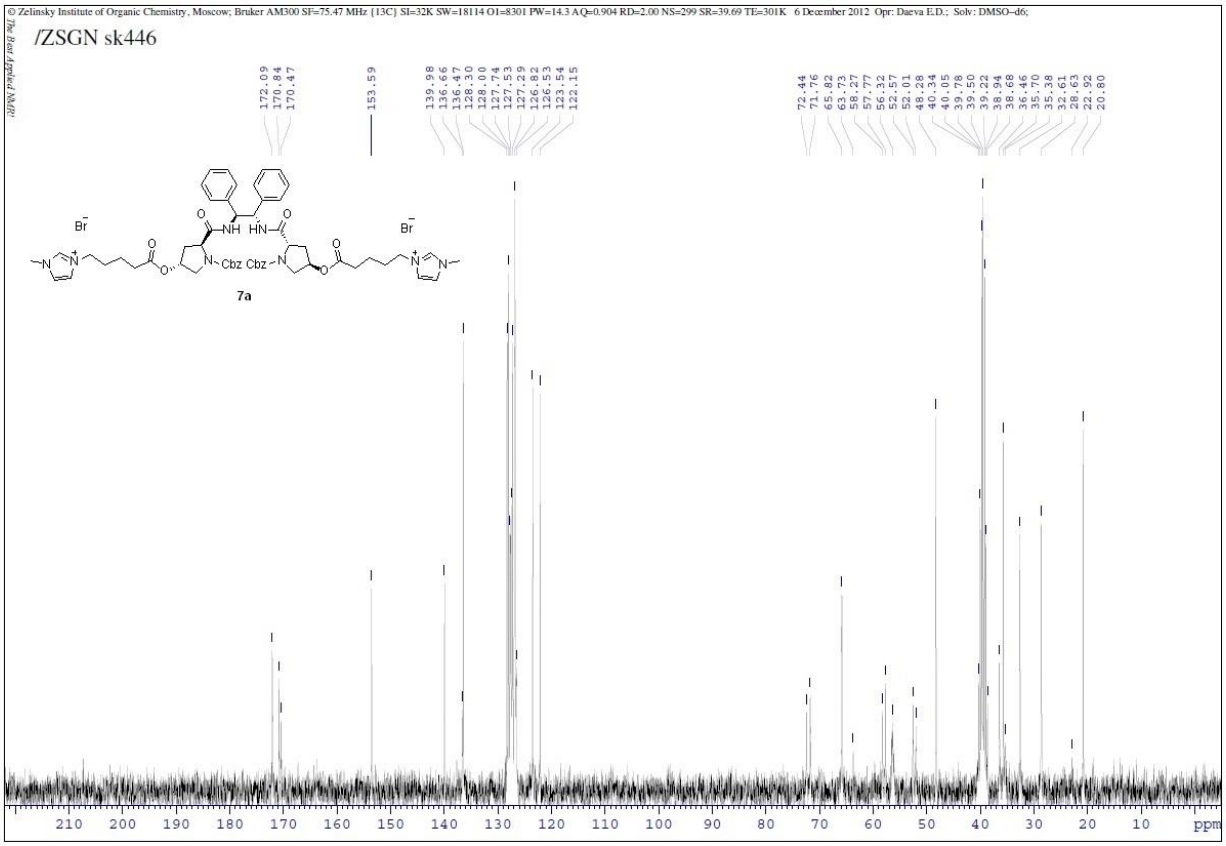

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=16K SW=6002 O1=2401 PW=9.0 AQ=1.365 RD=2.00 NS=1 SR=-4.18 TE=300K 5 December 2012 Opr: Daeva E.D.; Solv: DMSO-d6;
/ZSGN sk445d
6a
142
110
105
37
12
11
5.5
ppm

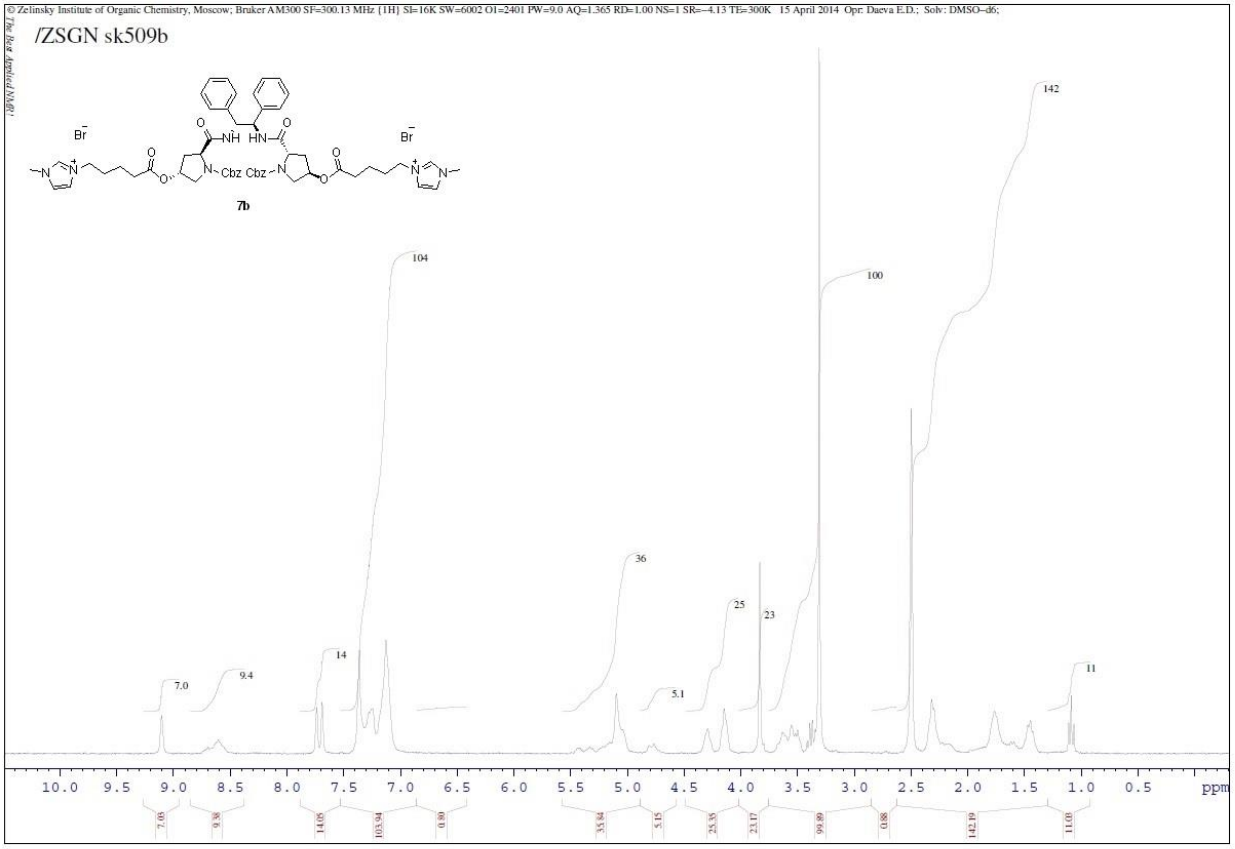

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=14.3 AQ=0.904 RD=2.00 NS=371 SR=37.30 TE=301K 5 December 2012 Opr: Daeva E.D.; Solv: DMSO-d6;
/ZSGN sk445c
6a
ppm

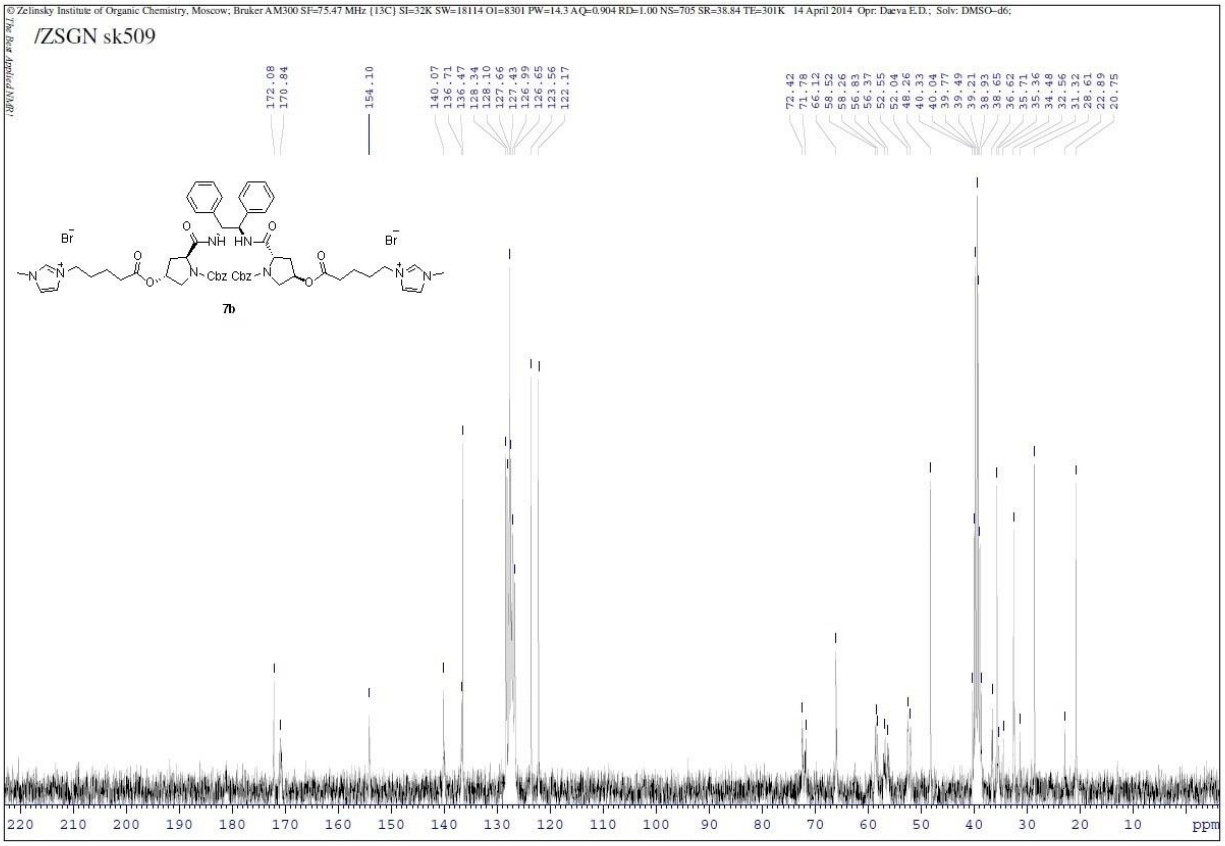

/ZSGN sk508
6b
142
135
119
53
52
14
13
6.8
1.2
ppm

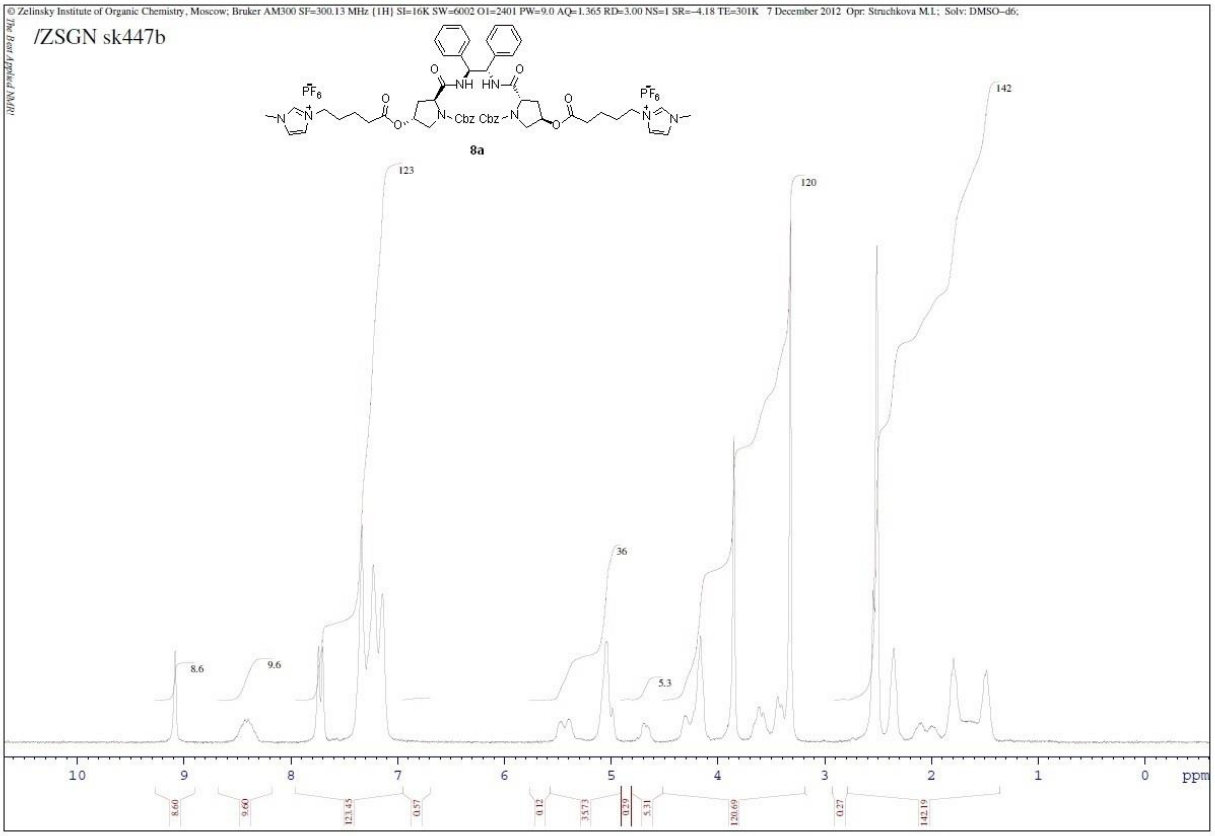

/ZSGN sk508A
6b
ppm

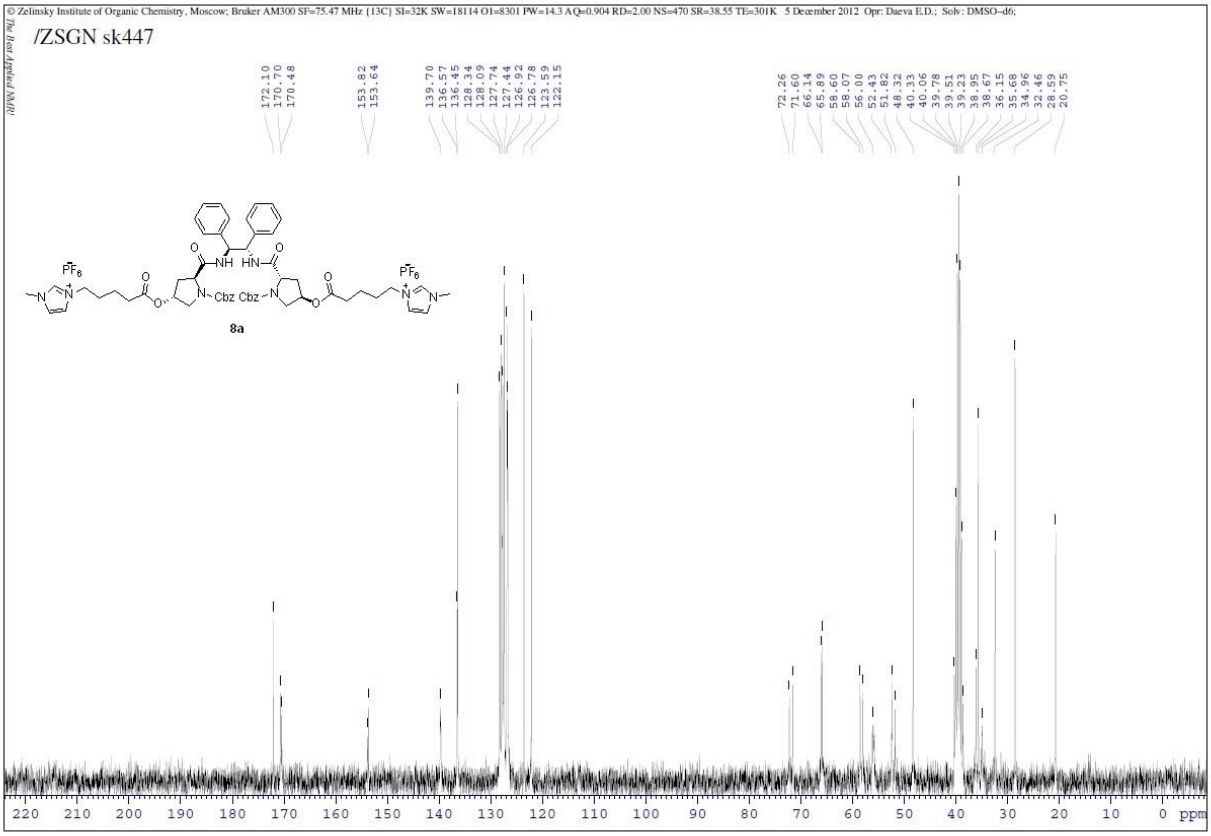

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=16K SW=6002 O1=2401 PW=9.0 AQ=1.365 RD=2.00 NS=1 SR=-4.18 TE=300K 6 December 2012 Opr: Daeva E.D.; Solv: DMSO-d6;
/ZSGN sk446b
7a
118
119
142
24
8.3
9.4
9.1
ppm

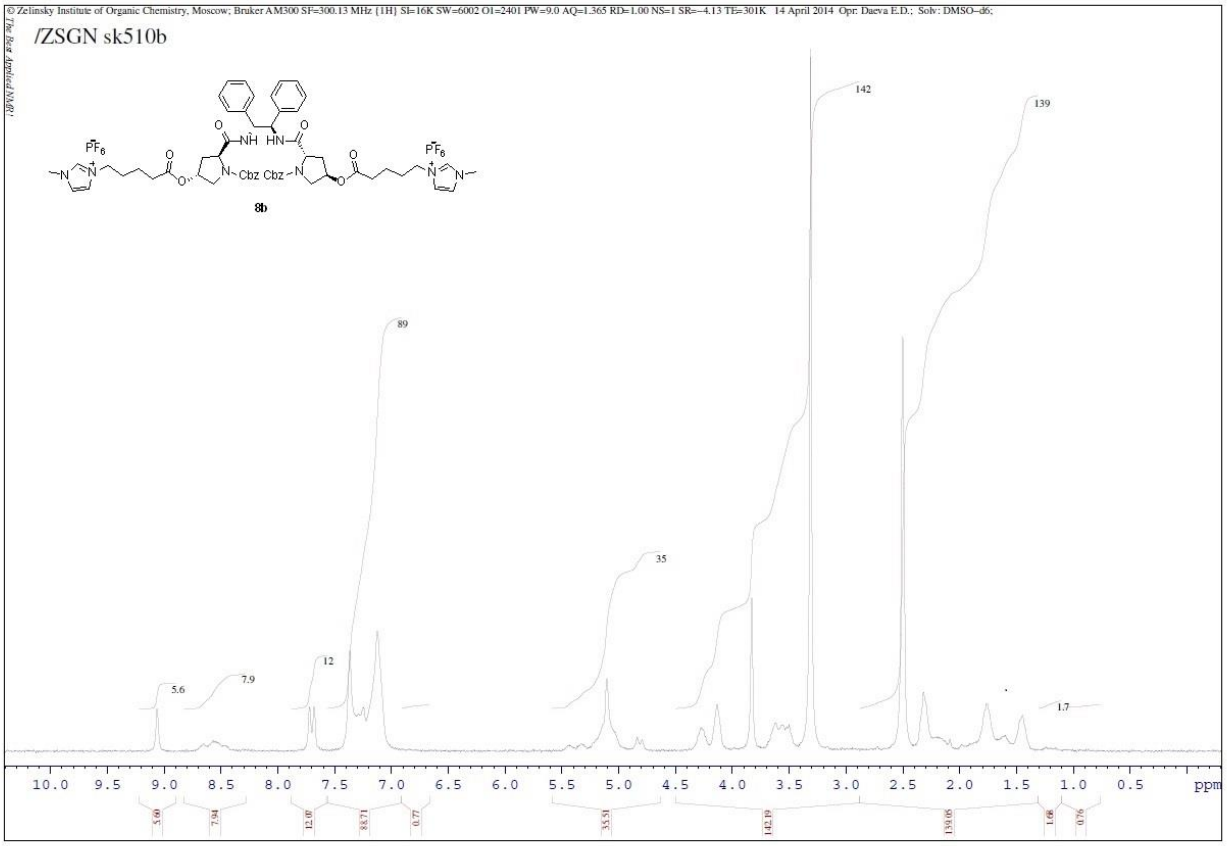

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=14.3 AQ=0.904 RD=2.00 NS=299 SR=39.69 TE=301K 6 December 2012 Opr: Daeva E.D.; Solv: DMSO-d6;
/ZSGN sk446
172.09
170.84
170.47
153.59
139.98
136.66
136.47
128.30
128.00
127.74
127.53
127.29
126.82
126.53
123.54
122.15
72.44
71.76
65.82
63.73
58.27
57.77
56.32
52.57
52.01
48.28
40.34
40.05
39.78
39.50
39.22
38.94
38.68
36.46
35.70
35.38
32.61
28.63
22.92
20.80
7a
ppm

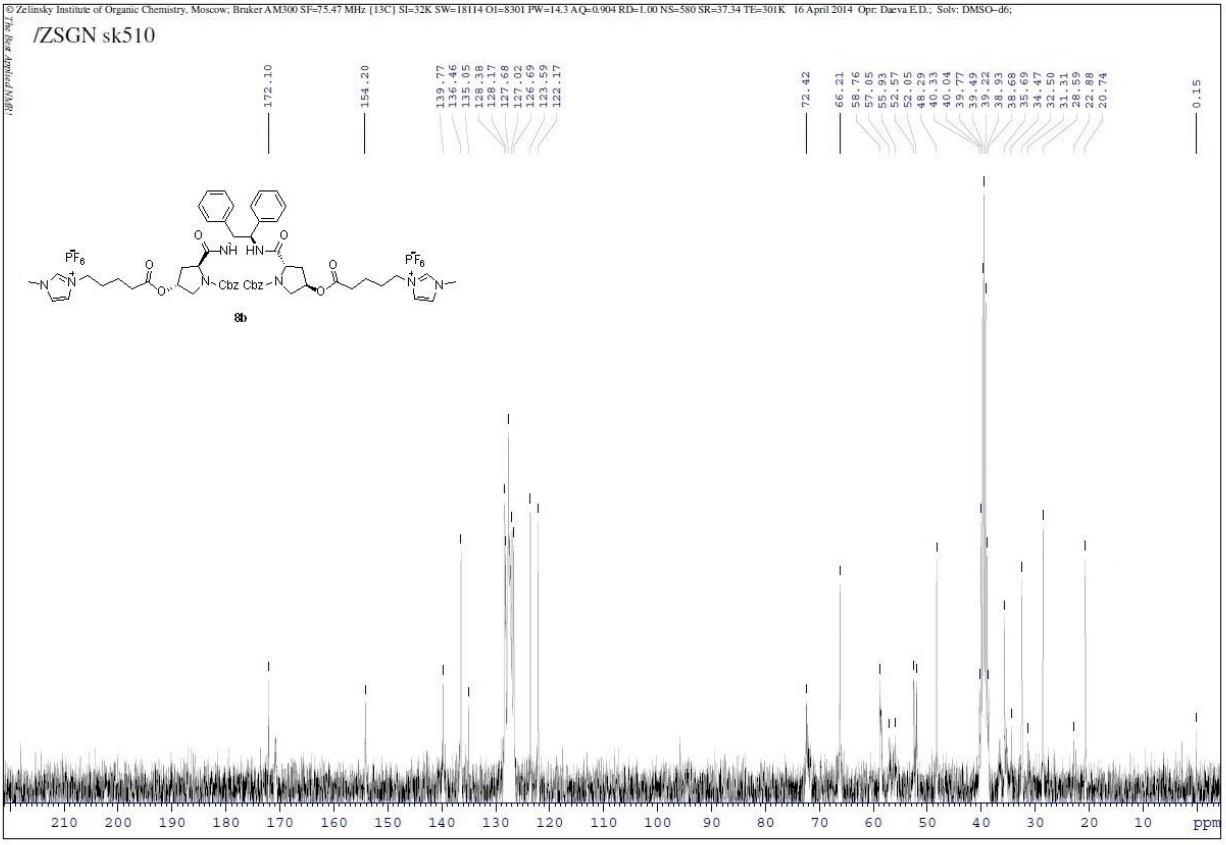

/ZSGN sk509b
7b
142
104
100
36
25
23
14
11
9.4
7.0
5.1
ppm

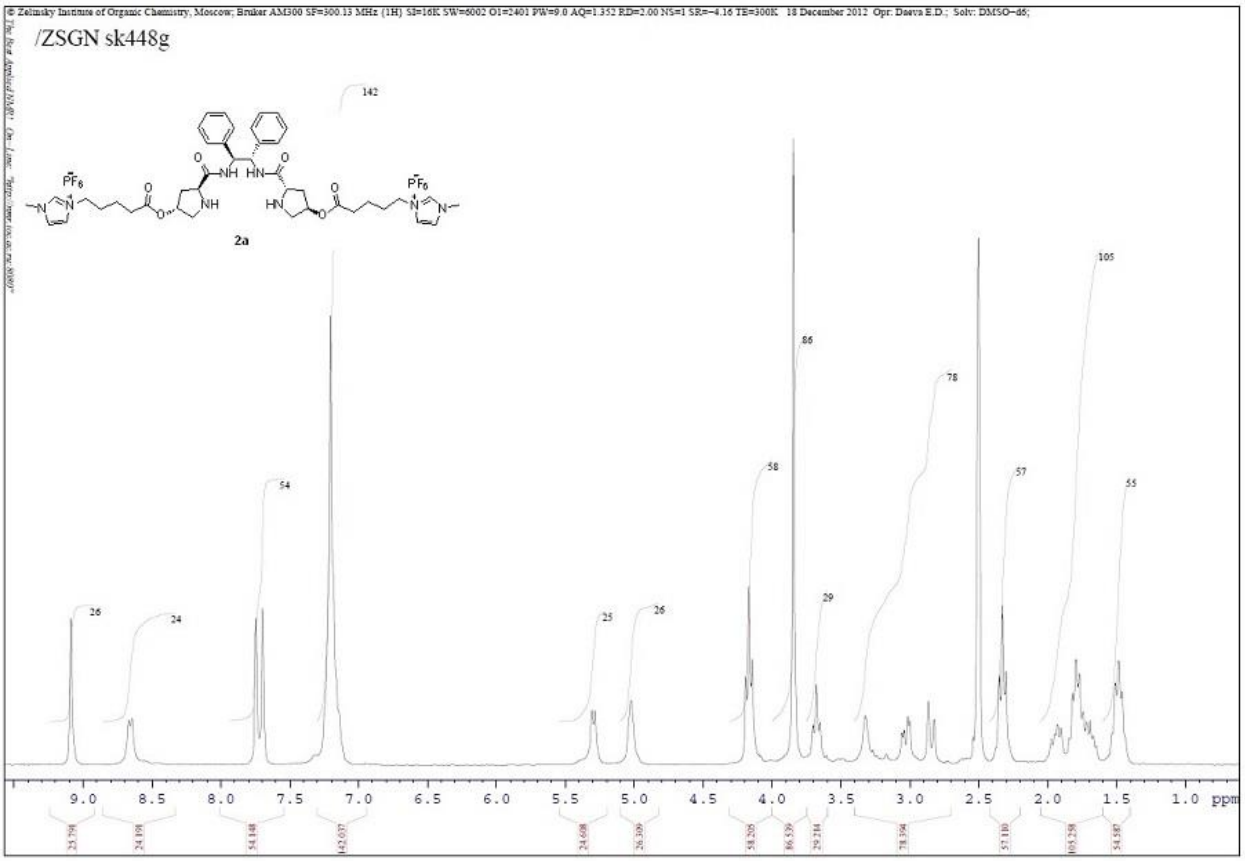

/ZSGN sk509
7b
172.08
170.84
154.10
140.07
136.47
128.34
128.10
127.66
127.43
126.99
126.65
123.56
122.17
72.42
71.78
66.12
58.52
58.26
56.83
56.37
55.55
52.04
48.26
40.33
40.04
39.77
39.49
39.21
38.93
38.65
36.62
35.71
34.56
34.48
32.56
31.32
28.61
22.89
20.75
ppm

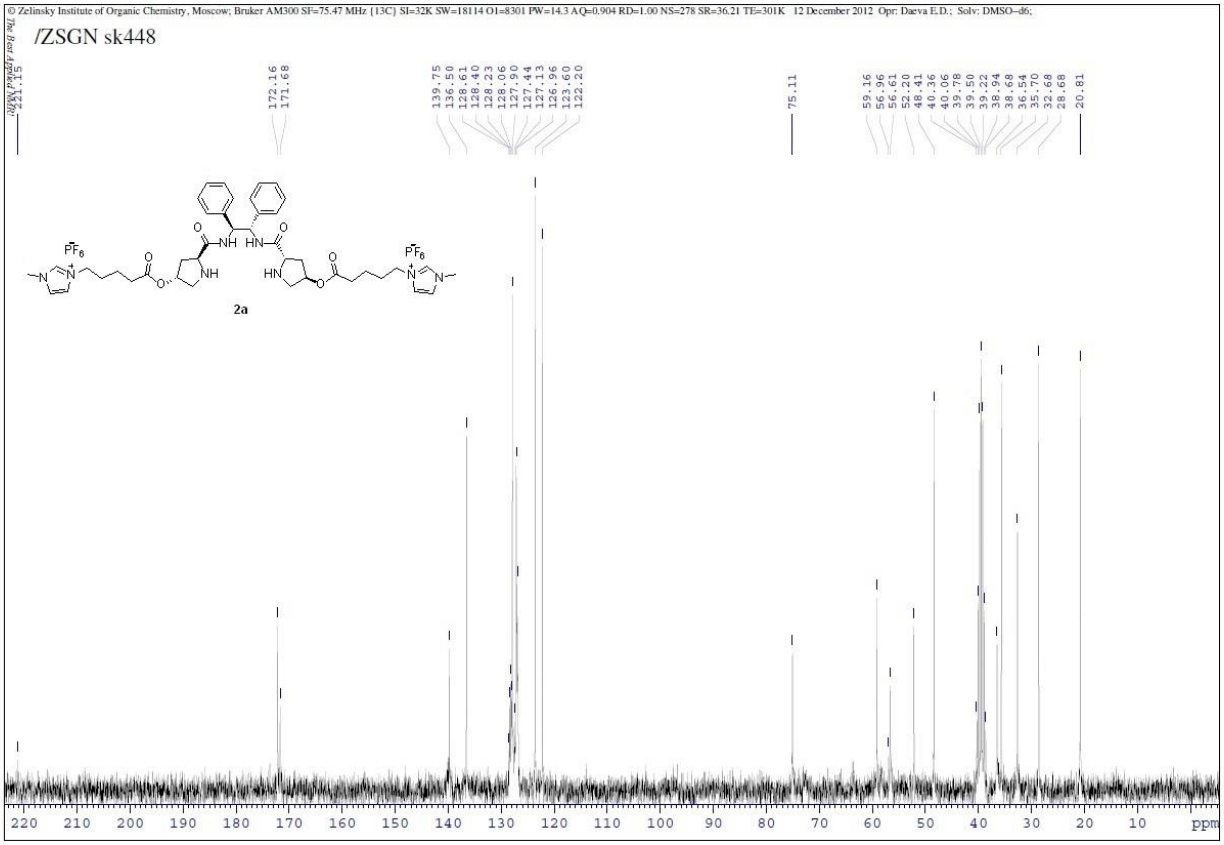

/ZSGN sk447b
8a
142
123
120
36
8.6
9.6
5.3
ppm

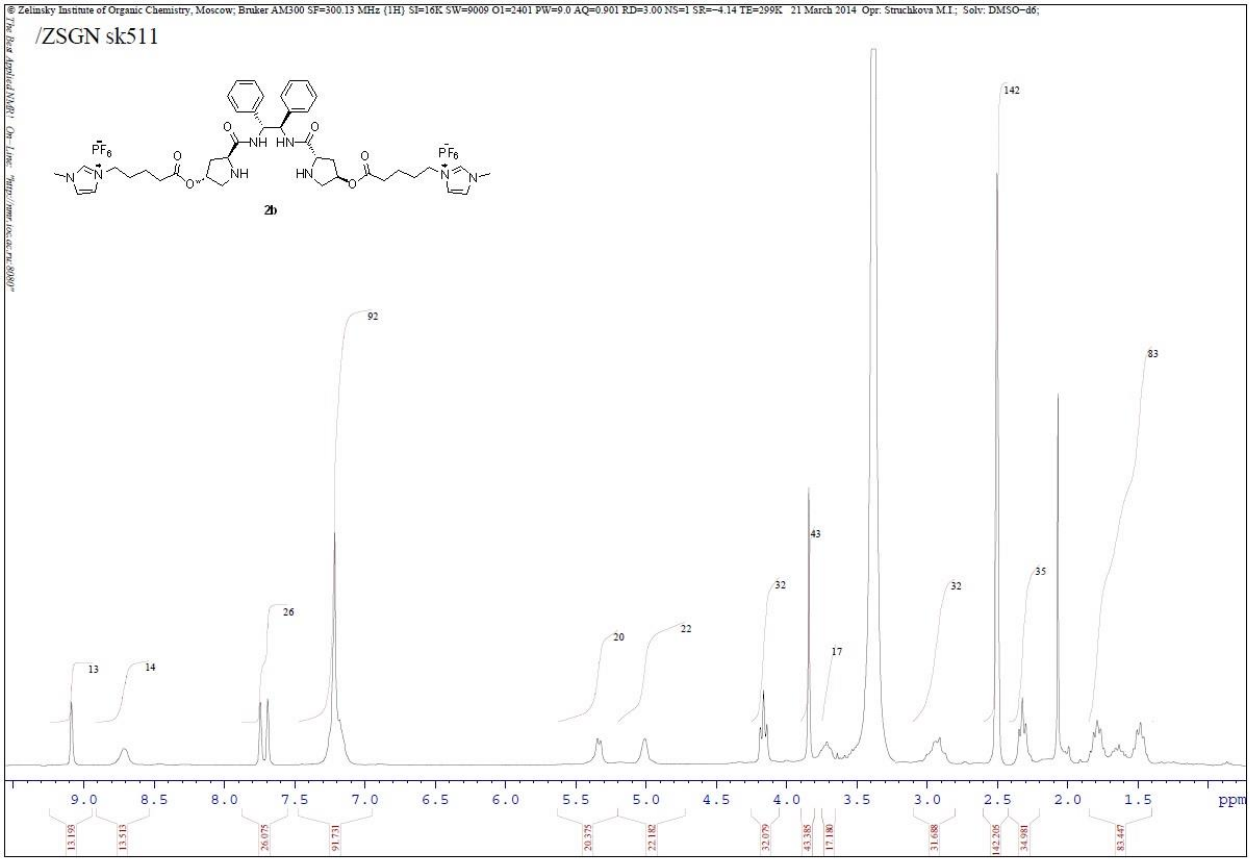

/ZSGN sk447
8a
ppm

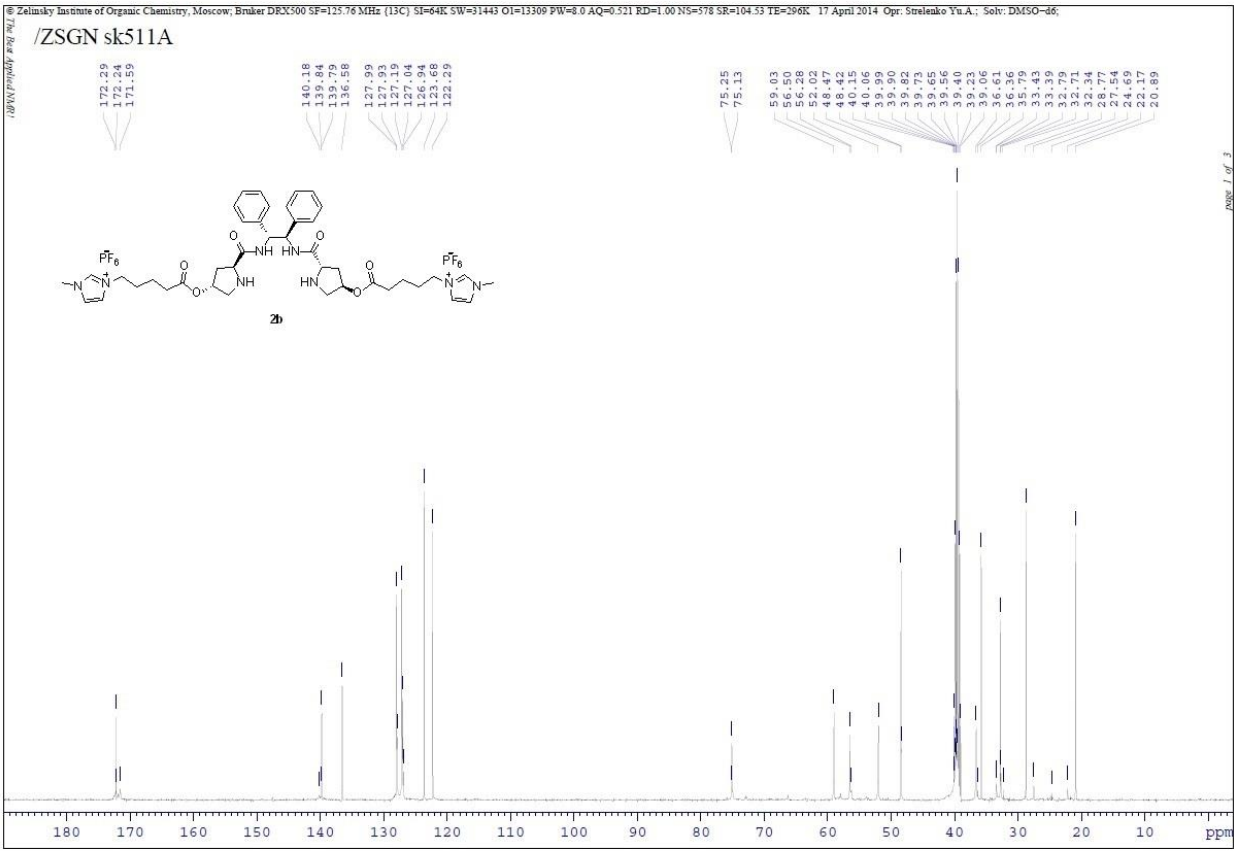

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz [1H] SI=16K SW=6002 OI=2401 PW=9.0 AQ=1.365 RD=1.00 NS=1 SR=-4.13 TE=301K 14 April 2014 Opr: Daeva E.D.; Solv: DMSO-d6;
/ZSGN sk510b
8b
142
139
89
35
12
7.9
5.6
1.7
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

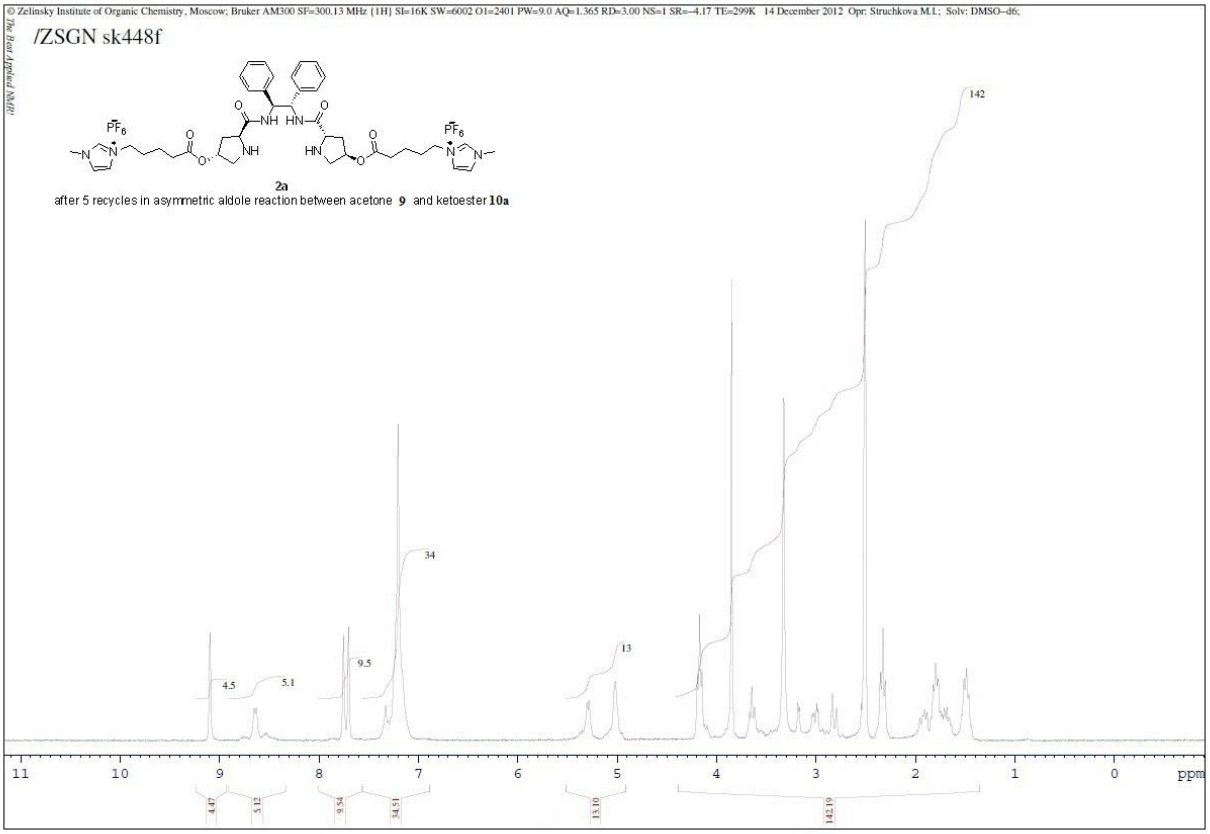

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz [13C] SI=32K SW=18114 OI=8301 PW=14.3 AQ=0.904 RD=1.00 NS=580 SR=37.34 TE=301K 16 April 2014 Opr: Daeva E.D.; Solv: DMSO-d6;
/ZSGN sk510
8b
172.10
154.20
139.77
136.46
135.05
128.38
128.17
127.68
127.02
126.69
123.59
122.17
72.42
66.21
58.76
57.95
55.93
52.57
52.05
48.29
40.33
40.04
39.77
39.49
39.22
38.93
38.68
35.69
34.47
32.56
31.31
28.59
22.88
20.74
0.15
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

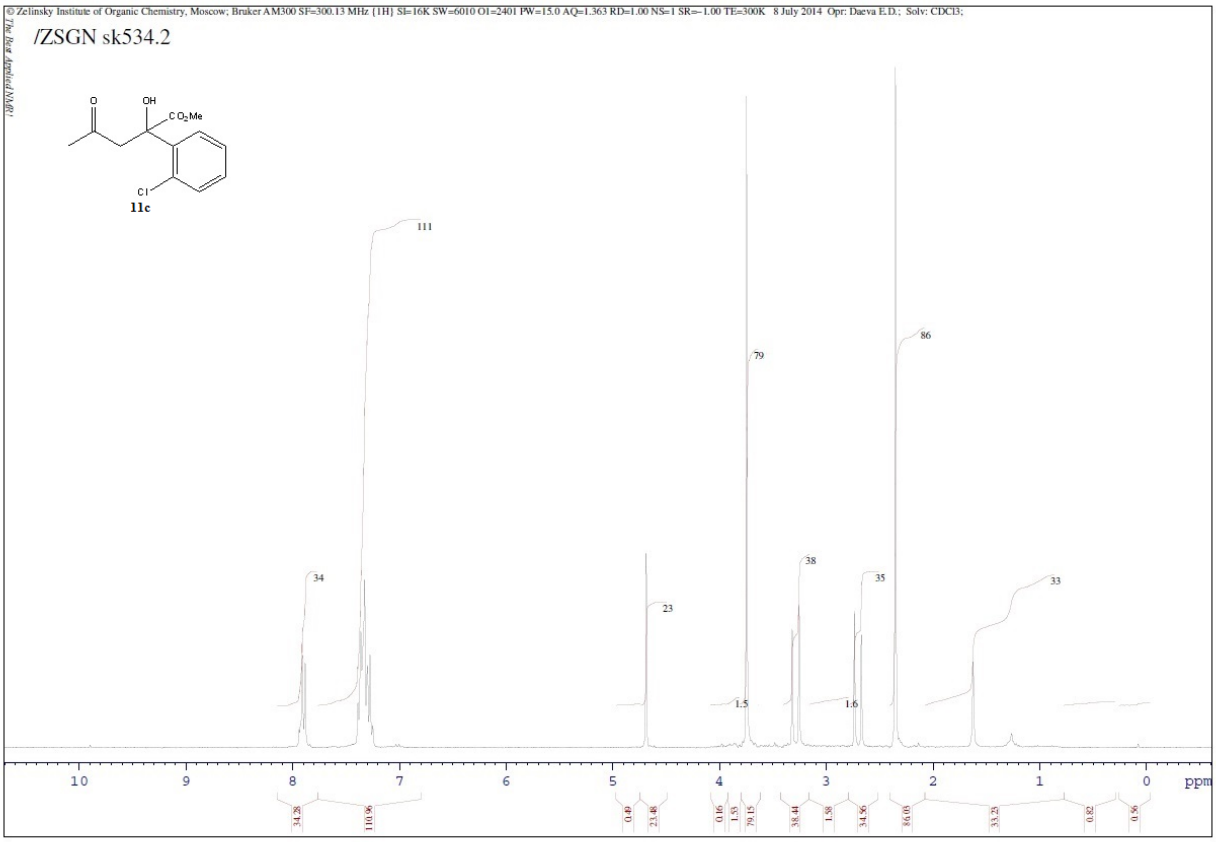

/ZSGN sk448g
2a
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm

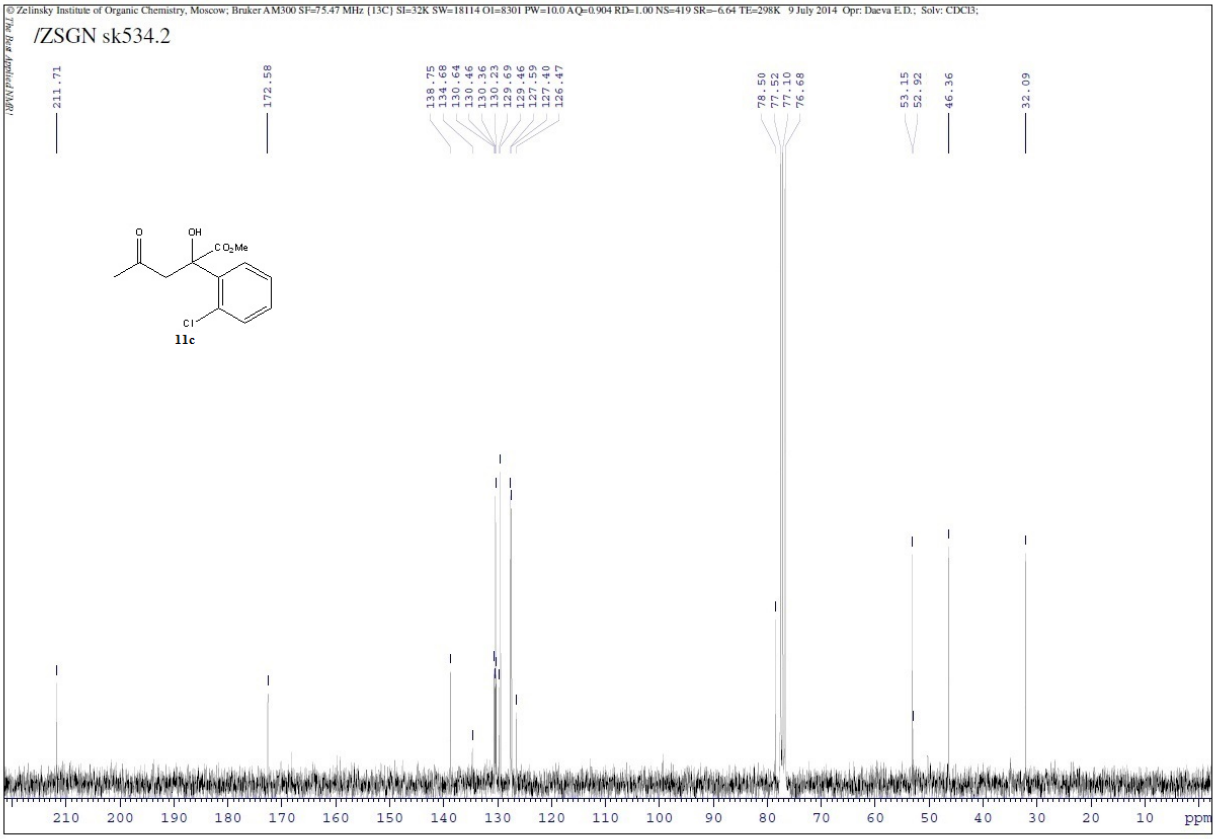

/ZSGN sk448
2a
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


/ZSGN sk511
2b
142
92
83
43
32
32
35
26
20
22
17
13
14
ppm


/ZSGN sk511A
2b
ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=16K SW=6002 O1=2401 PW=9.0 AQ=1.365 RD=3.00 NS=1 SR=-4.17 TE=299K 14 December 2012 Opr: Struchkova M.I.; Solv: DMSO--d6;
/ZSGN sk448f
2a
after 5 recycles in asymmetric aldole reaction between acetone 9 and ketoester 10a
142
34
13
9.5
4.5
5.1
11
10
9
8
7
6
5
4
3
2
1
0
ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=16K SW=6010 O1=2401 PW=15.0 AQ=1.363 RD=1.00 NS=1 SR=-1.00 TE=300K 8 July 2014 Opr: Daeva E.D.; Solv: CDCl3;
/ZSGN sk534.2
11c
111
79
86
38
35
34
33
23
1.5
1.6
10
9
8
7
6
5
4
3
2
1
0
ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz [13C] SI=32K SW=18114 OI=8301 PW=10.0 AQ=0.904 RD=1.00 NS=419 SR=-6.64 TE=298K 9 July 2014 Opr: Daeva E.D.; Solv: CDCl3;
/ZSGN sk534.2
211.71
172.58
138.75
134.68
130.64
130.46
130.36
130.23
129.69
129.46
127.59
127.40
126.47
78.50
77.32
77.00
76.68
53.15
52.92
46.36
32.09
O
OH
CO2Me
Cl
11c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm