Electronic supplementary materials *Mendeleev Commun.*, 2017, **27**, 473–475

Asymmetric Michael addition of aldehydes to maleimides in primary amine-based aqueous ionic liquid-supported recyclable catalytic system

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

List of the Contents

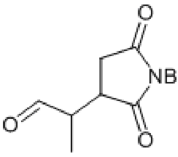
1. General Remarks.

The NMR ^{1}H and ^{13}C spectra were recorded by Bruker AM 300 in $CDCI_3$ and DMSO-d_6. 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. For thin layer chromatographic (TLC) analyses, Merck precoated TLC plates (silica gel 60 F_{254}) were used. Silica gel 0.060 – 0.200 (Acros) was used for column chromatography. The solvents were purified by standard procedures.

2. General procedure for the Michael addition of aldehydes 5 to maleimides 6.

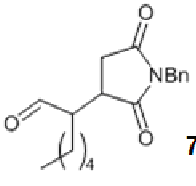
A mixture of aldehyde **5** (354 µmol), maleimide **6** (118 µmol), catalyst **3** (10 mg, 24 µmol), [bmim]BF_4 (200 µl) and water (100 µl) was stirred at ambient temperature for 20 h. Product **7** was extracted with Et_2O (5 x 3 ml), the combined organic extracts were filtered through a silica gel pad (1 g) and evaporated under reduced pressure (15 Torr). Reactant **6** conversions and *dr* values of product **7** were derived from ^{1}H NMR spectroscopy data. Values *ee* of **7** were determined by HPLC (chiral phases: *Chiralcel OD–H or Chiralpak AD–H*, hexane/2-propanol 75/25, 1.0 ml min^{-1}, 220 nm). NMR data for succinimides **7a-c** are available in the literature: (a) Kokotos C. G., *Org. Lett.*, **2013**, *15*, 2406; (b) Yu F.; Jin Zh.; Huang H.; Ye T.; Liang X.; Ye J. *Org. Biomol. Chem.* **2010**, *8*, 4767. Characterization data and preparative yields after flash chromatography for novel compounds **7d-i** are given below.

3. Physical, spectroscopic and chiral HPLC data for new compounds 7d-i



7d

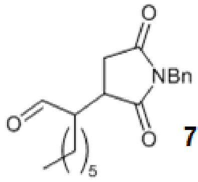
2-(1-Benzyl-2,5-dioxopyrrolidin-3-yl)propanal (**7d**): Light yellow oil. Yield 26 mg (90%), R_f = 0.26 (petroleum ether/EtOAc 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13*/1.31 (d, J=7.5Hz, 3H), 2.35-2.55 (m, 1H), 2.73-3.25 (m, 3H), 4.60-4.80 (m, 2H), 7.22-7.51 (m, 5H), 9.60/9.70* (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.25/11.24*, 31.10/31.72*, 39.43/40.76*, 42.56/42.60*, 46.13/46.57*, 127.88, 128.03, 128.61, 128.70, 135.69, 175.73, 178.11*/178.26, 201.13*/201.47. HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{14}H_{15}NO_3$: 245.1052; found 245,1059. HPLC analysis (*Chiralpak AD-H* column, hexane/2-propanol 75/25, 1.0 mL/min, 220 nm), major diastereomer: t_R (major) 12.8 min, t_R (minor) 31.8 min; minor diastereomer: t_R (major) 14.4 min, t_R (minor) 17.3 min.



7e

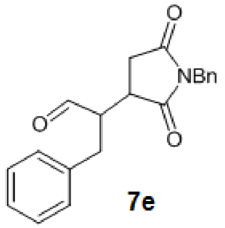
2-(1-Benzyl-2,5-dioxopyrrolidin-3-yl)heptanal (**7e**): Light yellow oil. Yield 32 mg (90%), R_f = 0.3 (petroleum ether /EtOAc 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80-1.00 (m, 3H), 1.10-1.55 (m, 7H), 1.67-1.83*/1.83-2.00 (m, 1H), 2.30-2.55 (m, 1H), 2.65-3.00 (m, 2H), 3.05-3.15*/3.15-3.25 (m, 1H), 4.60-4.75 (m, 2H), 7.20-7.45 (m, 5H), 9.57/9.70* (s, 1H). ^{13}C NMR (75 MHz,

$CDCl_3$): δ = 13.94, 22.26*/22.38, 25.85*/26.28, 27.02/27.24*, 31.53/31.62*, 31.83, 38.82*/39.11, 42.54/42.57*, 51.15/52.12*, 127.81, 127.99, 128.57, 128.64, 128.80, 135.66*/135.74, 175.73*/175.80, 178.28*/178.68, 201.56*/201.82. HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{18}H_{23}NO_3$: 301.1678; found 301.1666. HPLC analysis (*Chiralpak AD-H* column, hexane/2-propanol 95/5, 1.0 mL/min, 220 nm), major diastereomer: t_R (major) 7.3 min, t_R (minor) 28.8 min; minor diastereomer: t_R (major) 12.5 min, t_R (minor) 11.2 min.



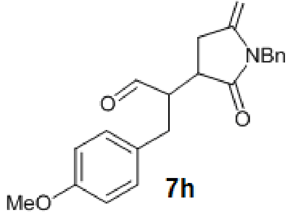
7f

2-(1-Benzyl-2,5-dioxopyrrolidin-3-yl)octanal (**7f**): Light yellow oil. Yield 34 mg (92%), R_f = 0.3 petroleum ether /EtOAc 2:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.80-1.00 (m, 3H), 1.12-1.55 (m, 9H), 1.68-1.85*/1.85-2.00 (m, 1H), 2.32-3.53 (m, 1H), 2.65-3.02 (m, 2H), 3.06-3.15*/3.15-3.26 (m, 1H), 4.60-4.75 (m, 2H), 7.20-7.46 (m, 5H), 9.56/9.71* (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.02, 22.55, 25.93*/26.34, 27.34/27.57*, 29.09/29.19*, 31.41/31.53*, 31.84, 38.83*/39.13, 42.56/42.59*, 51.16/52.14*, 127.83, 128.01, 128.58, 128.59, 128.66, 128.82, 135.67*/135.76, 175.74*/175.80, 178.29*/178.68, 201.56*/201.82. HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{19}H_{25}NO_3$: 315.1834; found 315.1840. HPLC analysis (*Chiralpak AD-H* column, hexane/2-propanol 95/5, 1.0 mL/min, 220 nm), major diastereomer: t_R (major) 6.3 min, t_R (minor) 25.5 min; minor diastereomer: t_R (major) 11.5 min, t_R (minor) 10.2 min.



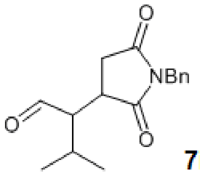
7e

2-(1-Benzyl-2,5-dioxopyrrolidin-3-yl)-3-phenylpropanal (**7g**): Light yellow oil. Yield 35 mg (92%), R_f = 0.45 (*n*-hexane/EtOAc 2:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.45 (dd, *J*=6.70Hz, *J*=17.5Hz, 1H), 2.75-3.25 (m, 4H), 4.58-4.75 (m, 2H), 7.05-7.60 (m, 10H), 9.65/9.75* (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.76*/29.54, 30.81*/31.10, 31.60*/31.72, 46.13/46.57*, 52.56/52.93*, 126.68, 126.86, 126.78, 127.80-128.70, 135.69, 138.62, 178.11/178.26*, 178.26, 201.41/201.47*. HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{20}H_{19}NO_3$: 321.1365; found 321.1361. HPLC analysis (*Chiralpak AD-H* column, hexane/2-propanol 85/15, 1.0 mL/min, 220 nm), major diastereomer: t_R (major) 25.8 min, t_R (minor) 35.3 min; minor diastereomer: t_R (major) 31.2 min, t_R (minor) 39.8 min.



7h

2-(1-Benzyl-2,5-dioxopyrrolidin-3-yl)-3-(4-methoxyphenyl)propanal (**7h**): Light yellow oil. Yield 38 mg (93%), R_f = 0.4 (*n*-hexane/EtOAc 2:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.31-2.52 (m, 1H), 2.70-3.18 (m, 5H), 3.85 (s, 3H), 4.55-4.70 (m, 2H), 6.95-7.60 (m, 9H), 9.60/9.72* (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.90*/30.36, 31.20*/32.10, 32.62/32.85*, 45.73, 52.36/52.57*, 55.57, 114.13, 126.62, 126.77, 126.88, 127.63, 128.03, 128.68, 130.26, 130.91, 136.61, 157.62, 178.22/176.36*, 201.61/201.69*. HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{21}H_{21}NO_4$: 351.1471; found 351.1479. HPLC analysis (*Chiralpak AD-H* column, hexane/2-propanol 85/15, 1.0 mL/min, 220 nm), major diastereomer: t_R (major) 26.6 min, t_R (minor) 34.7 min; minor diastereomer: t_R (major) 32.9 min, t_R (minor) 37.4 min.



7i

2-(1-Benzyl-2,5-dioxopyrrolidin-3-yl)-3-methylbutanal (**7i**): Light yellow oil. Yield 34 mg (21%),[#] R_f = 0.28 (petroleum ether/EtOAc 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.03*/1.05 (d, J=6.8Hz, 3H), 1.1*/1.2 (d, J=6.8Hz, 3H), 2.15-2.98 (m, 4H), 3.05-3.15 (m, 1H), 4.60-4.75 (m, 2H), 7.20-7.45 (m, 5H), 9.20/9.33* (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.98*/21.02, 21.16/21.56*, 27.72/28.05*, 32.34/32.97*, 37.98/38.19*, 42.61, 57.04/58.48*, 127.83, 128.01, 128.57, 128.60, 128.67, 128.90, 135.65*/135.81, 175.47*/175.99, 178.27*/179.23, 202.62*/202.90. HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{16}H_{19}NO_3$: 273.1365; found 273.1371. HPLC analysis (*Chiralpak AD-H* column, hexane/2-propanol 75/25, 1.0 mL/min, 220 nm), major diastereomer: t_R (major) 15.6 min, t_R (minor) 28.8 min; minor diastereomer: t_R (major) 16.7 min, t_R (minor) 18.0 min. [#]For product characterization experiment with a five-fold loading of the reagents was performed.

4. Larger scale synthesis of 7a

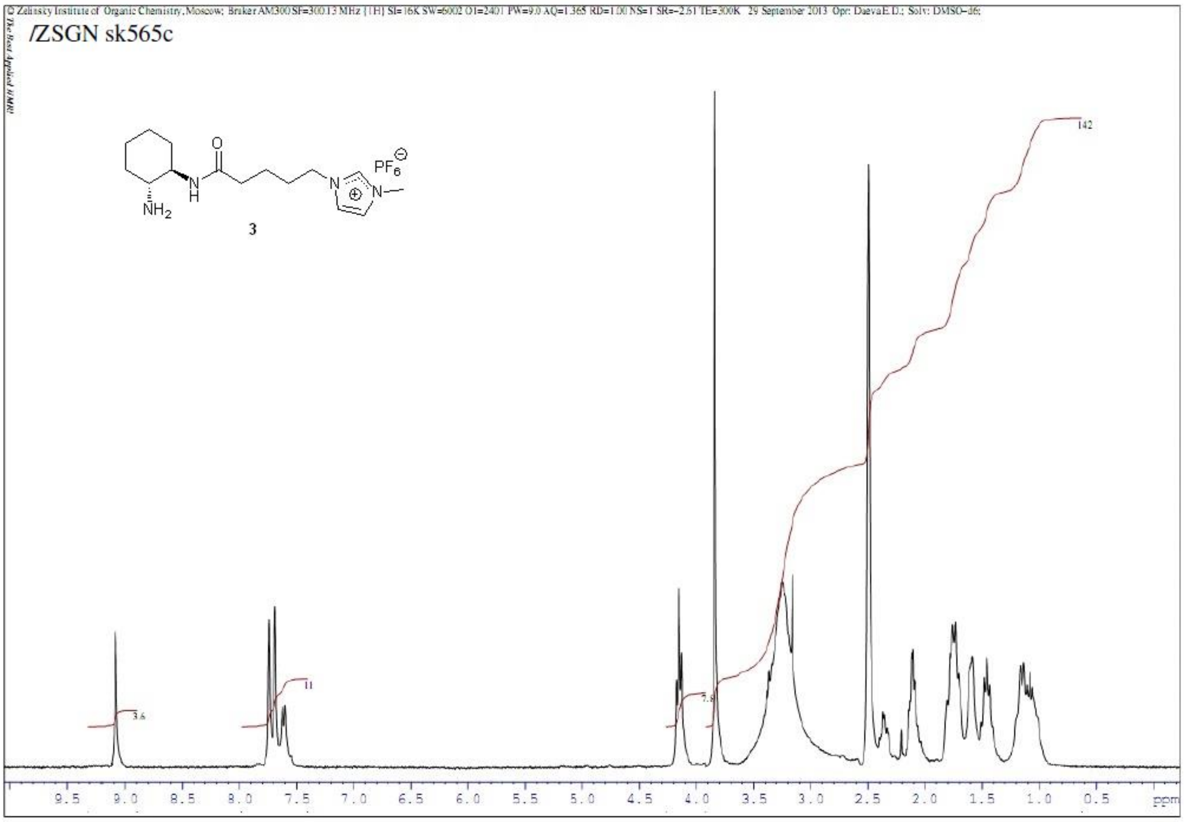
A mixture of isobutyraldehyde **5a** (0.162 ml, 1.77 mmol), *N*-phenylmaleimide **6a** (102 mg, 0.59 mmol), catalyst **3** (50 mg, 0.12 mmol), [bmim]BF_4 (1 ml) and water (0.5 ml) was stirred at ambient temperature for 20 h. Product **7a** was extracted with Et_2O (5 x 6 ml), the combined organic extracts were evaporated under reduced pressure (15 Torr). The product was purified by column chromatography. Yield of **7a** was 130 mg (90 %).

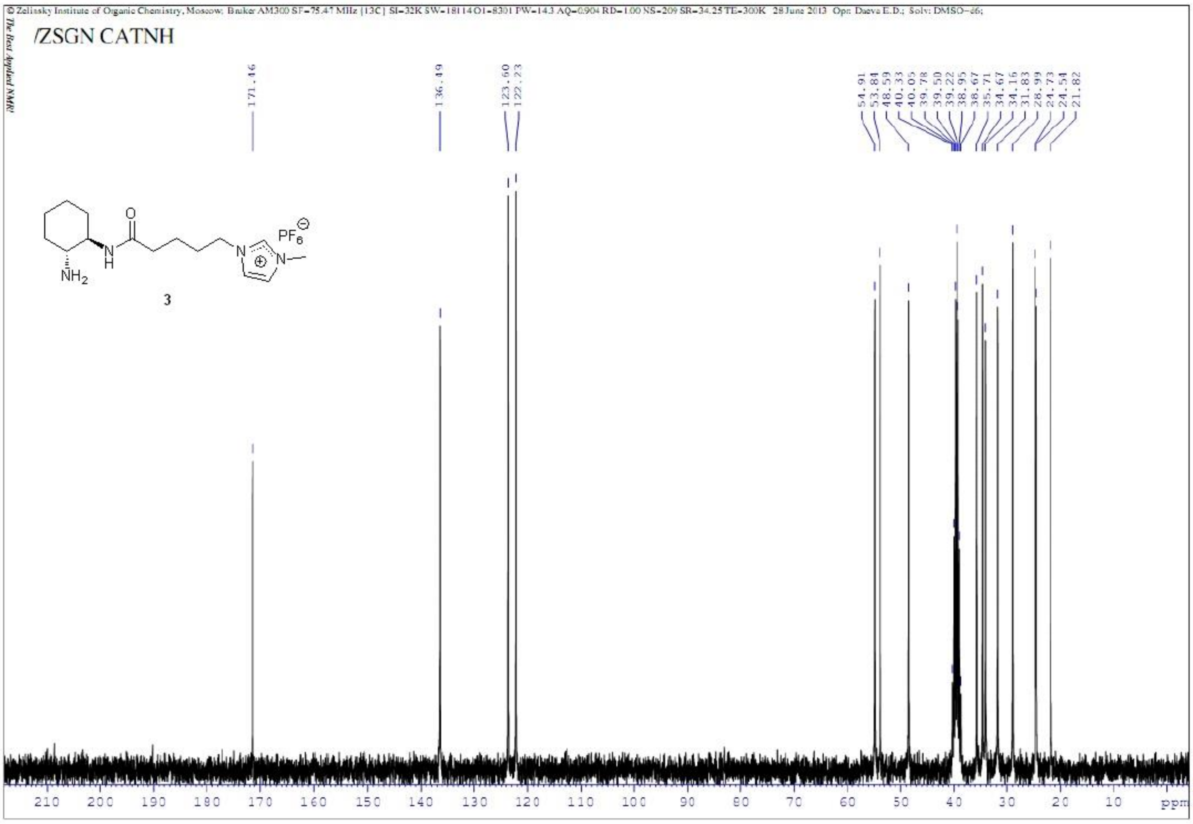
5. General procedure for catalyst recycling

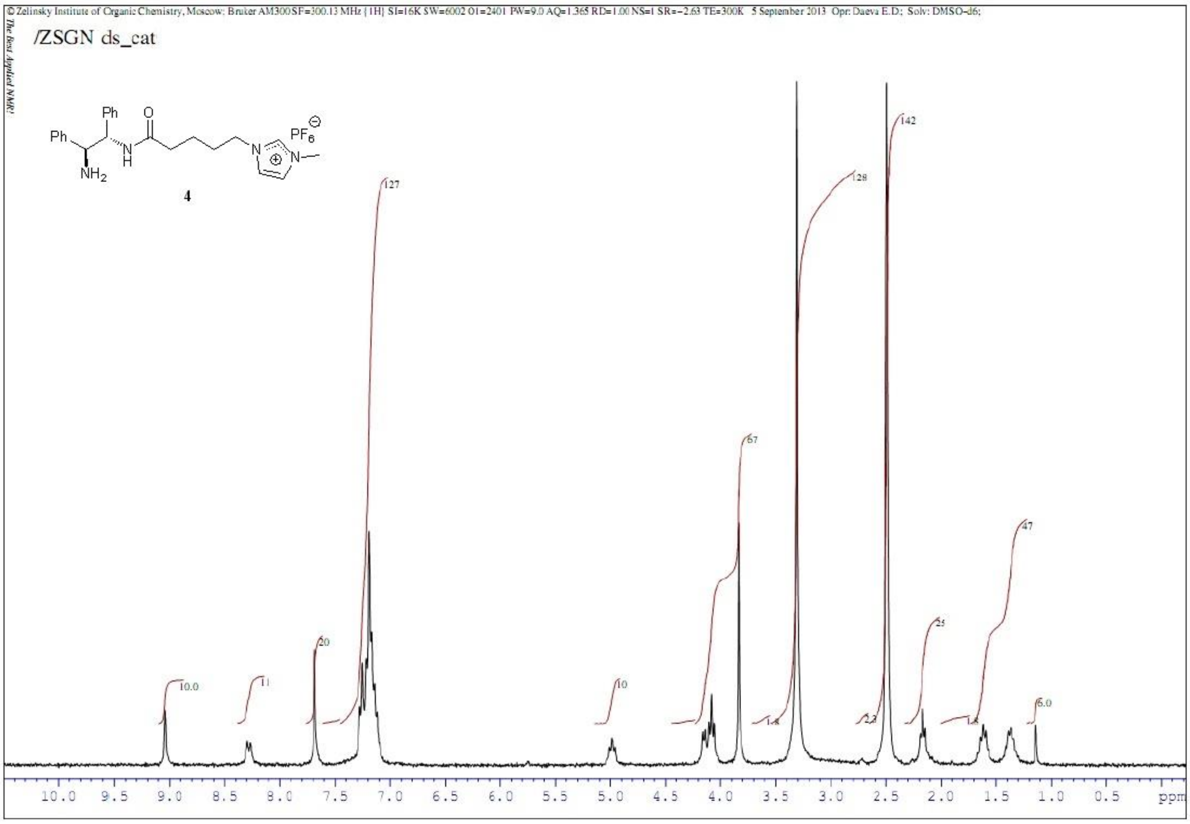
After extraction of product **7a**, the residue (catalyst **1**/IL/H_2O) was dried *in vacuo* (20 Torr) for 15 min, fresh portions of starting compounds were added and the reaction was re-performed as described above.

6. Pictures of ^{1}H and ^{13}C NMR spectra of compounds 3 and 4

Compounds **3** and **4** were prepared as described in [Adv. Synth. Catal. **2012**, *354*, 3078-3086].



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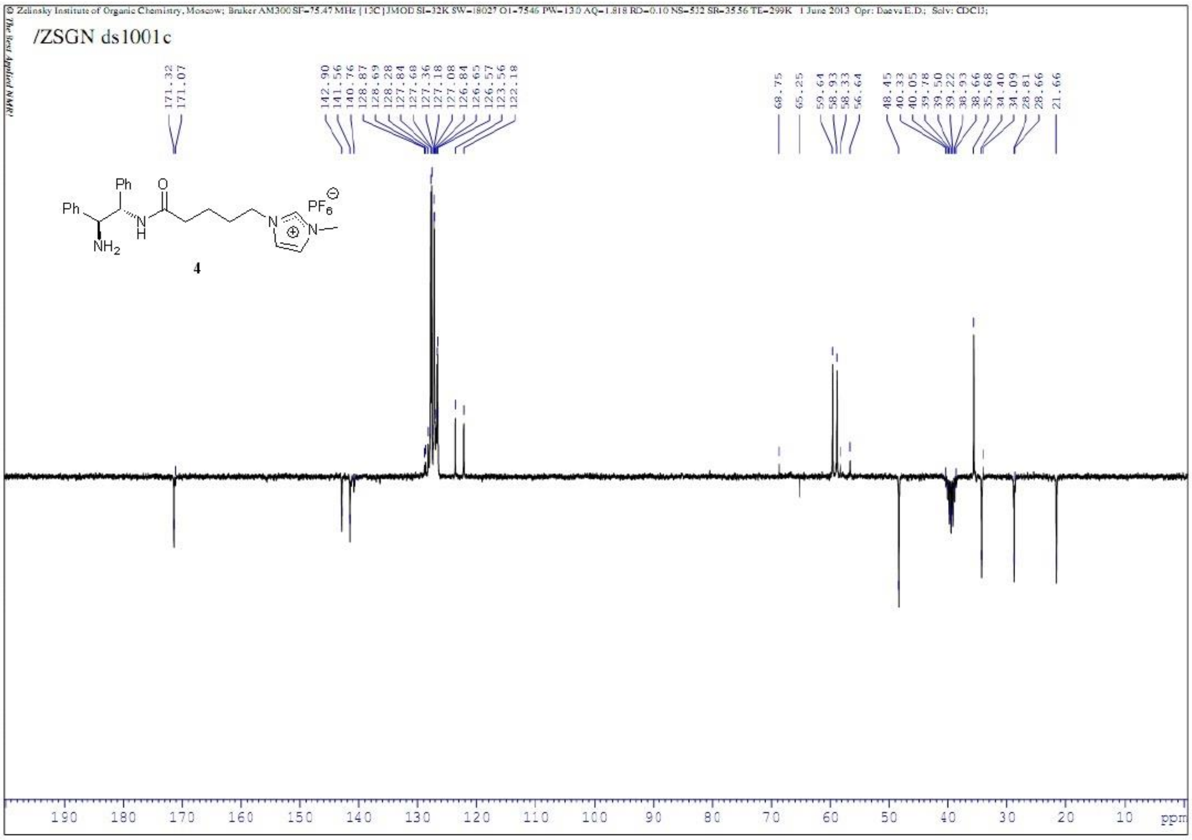
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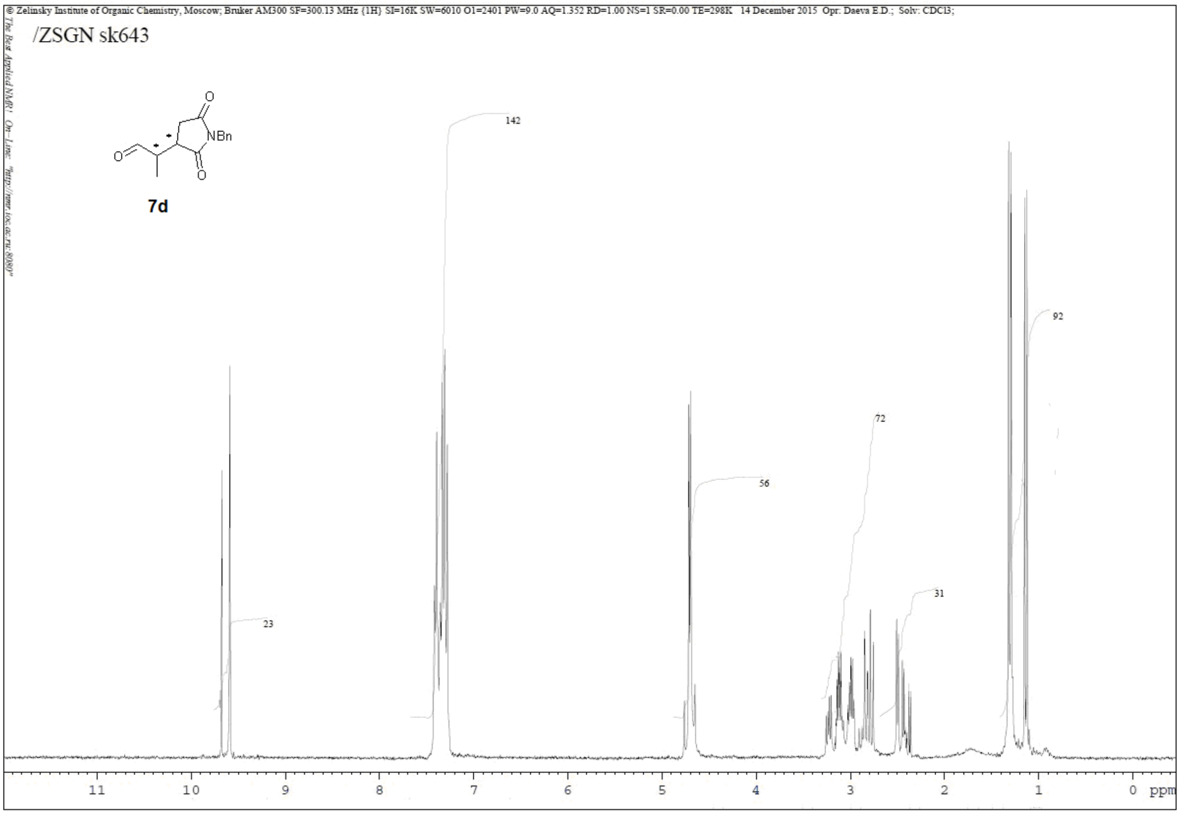
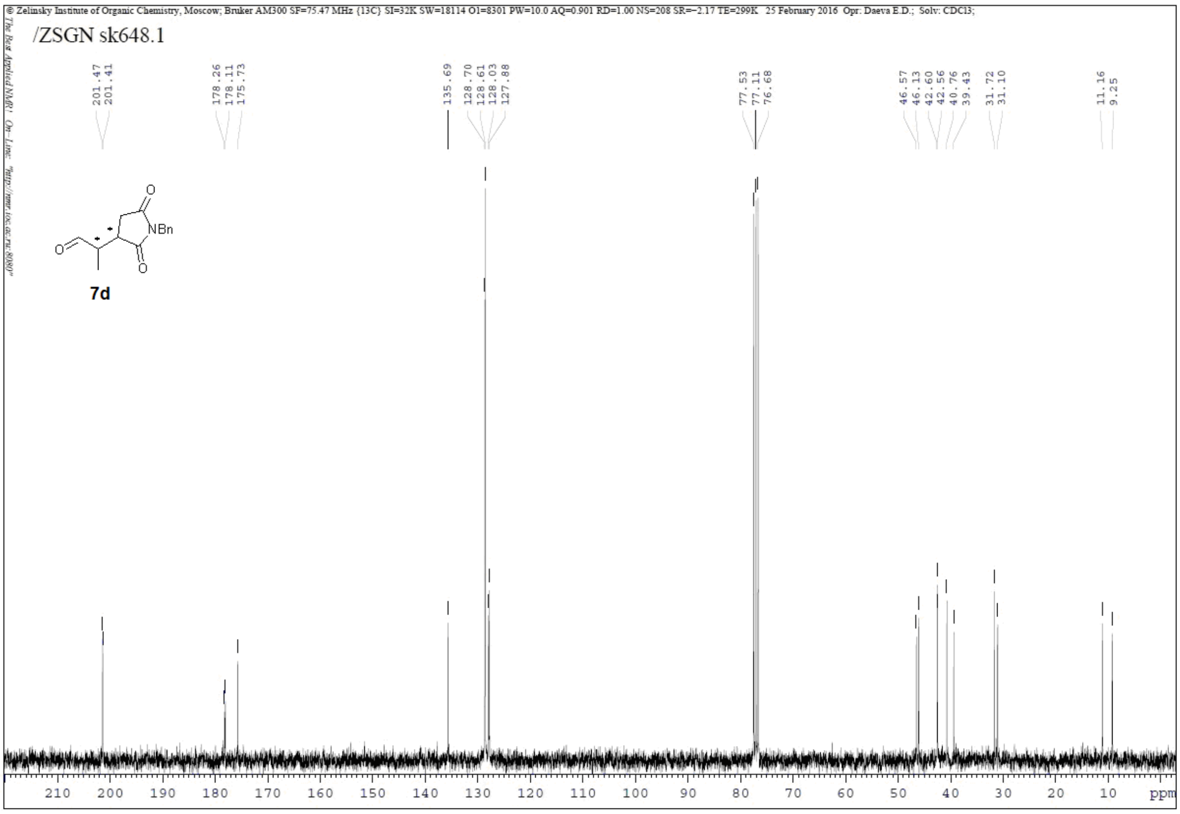
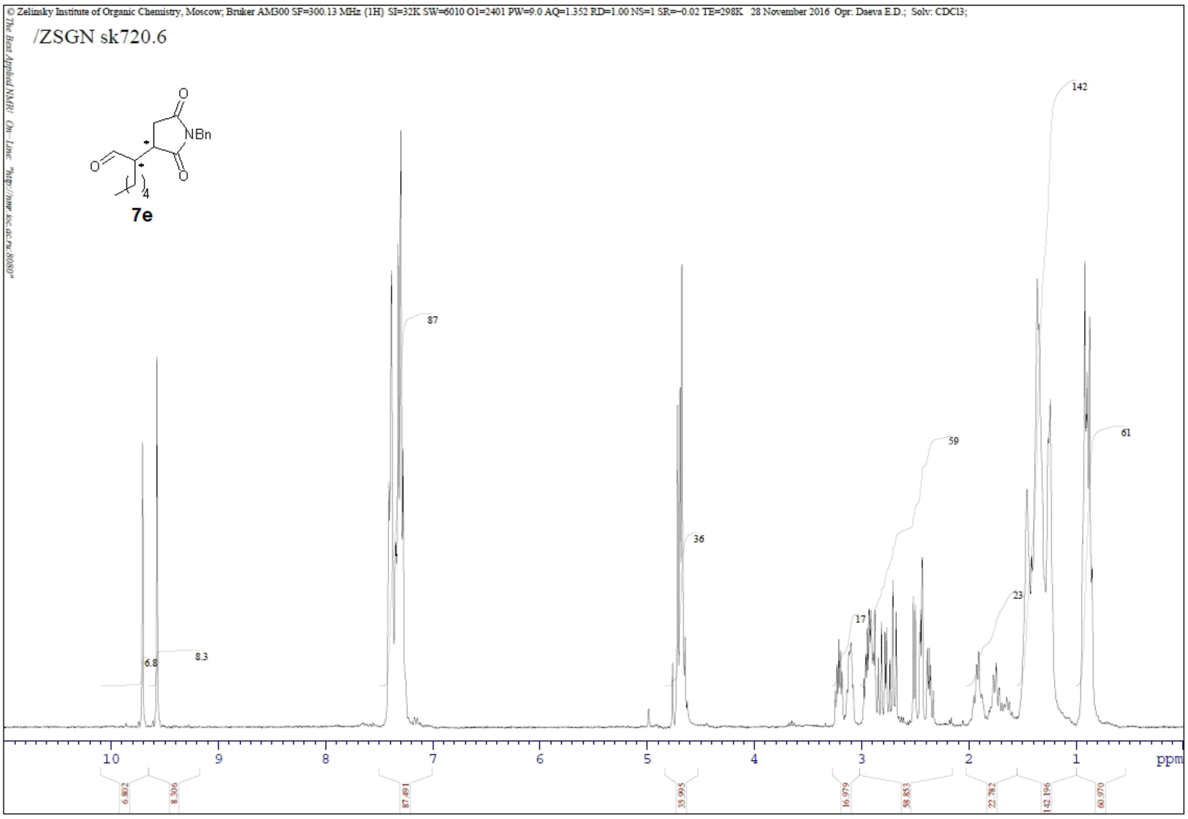
7. ^{1}H and ^{13}C NMR spectra of new compounds 7d-i



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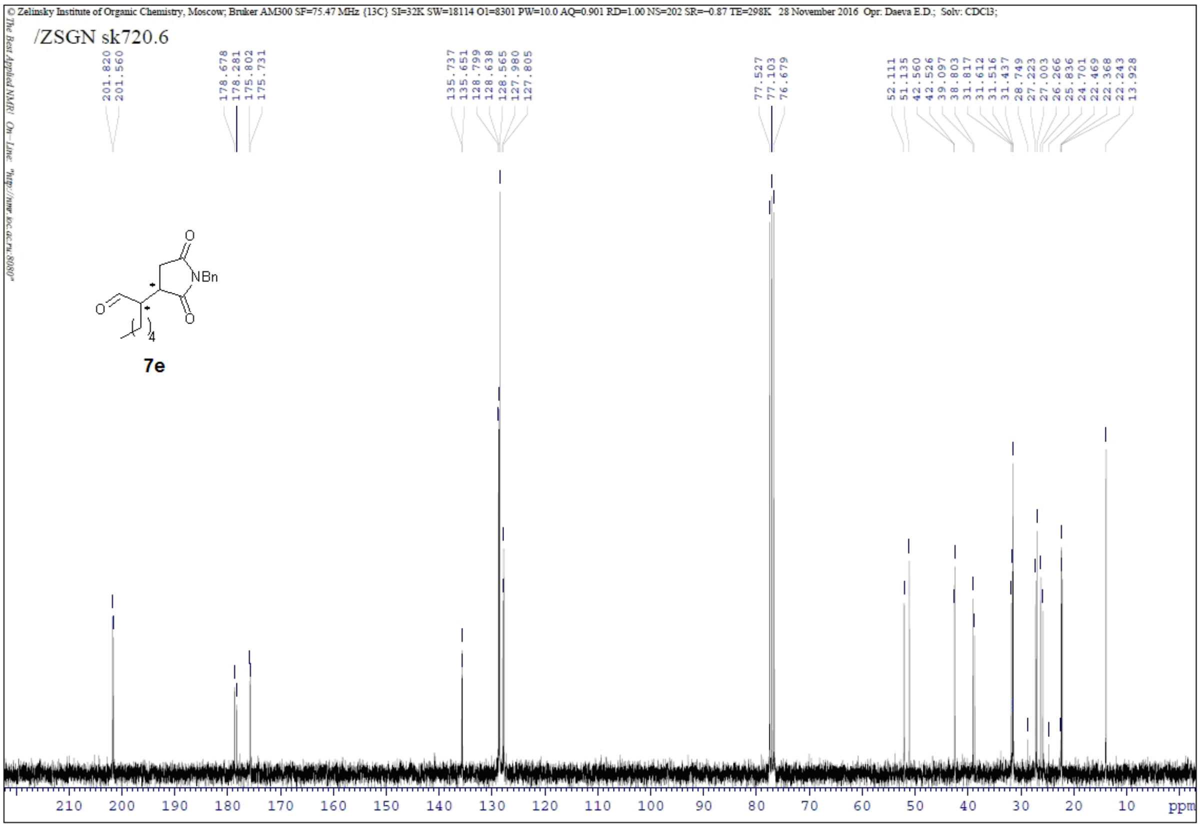
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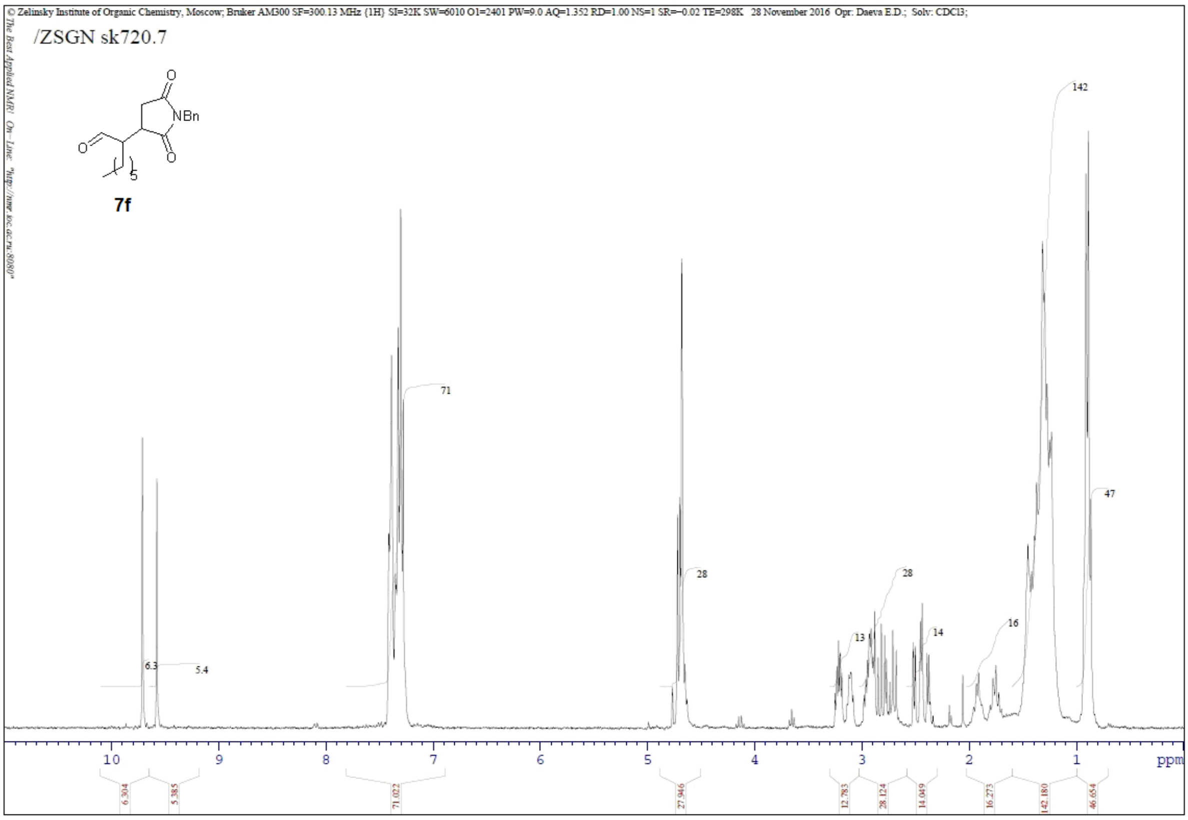
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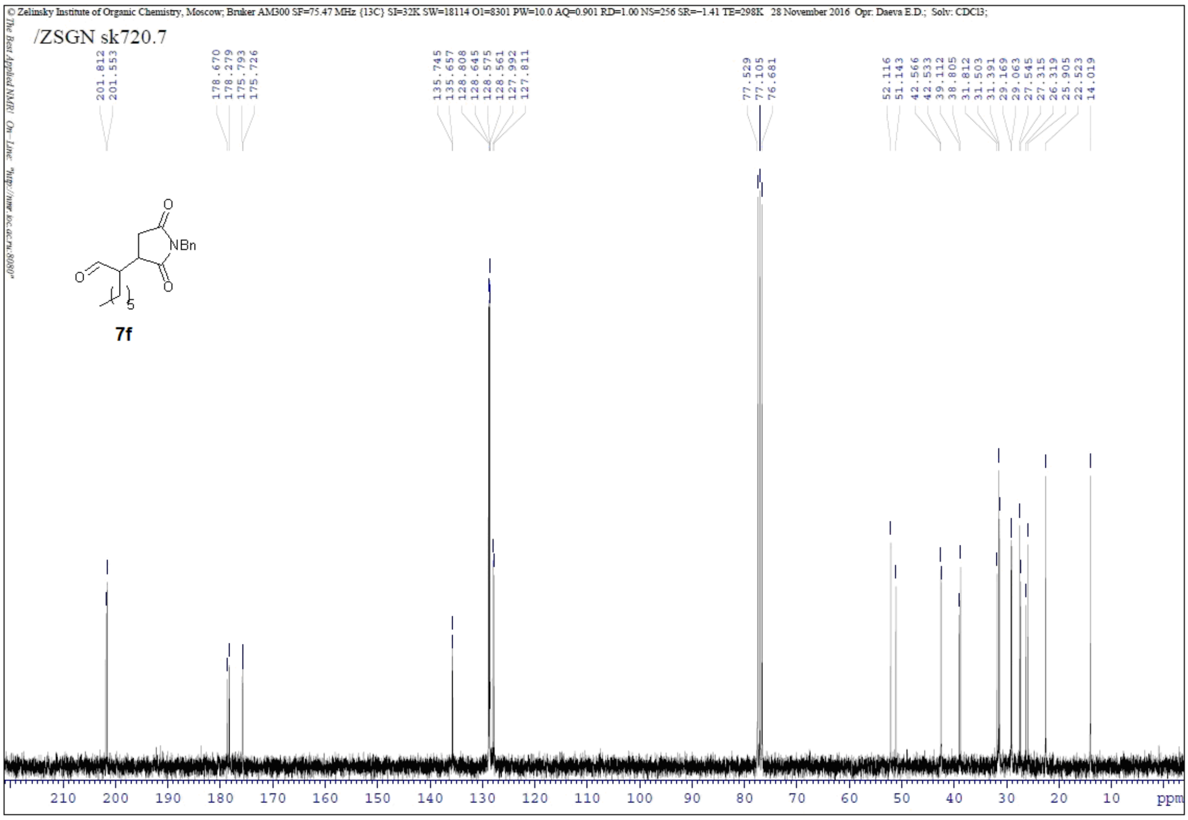
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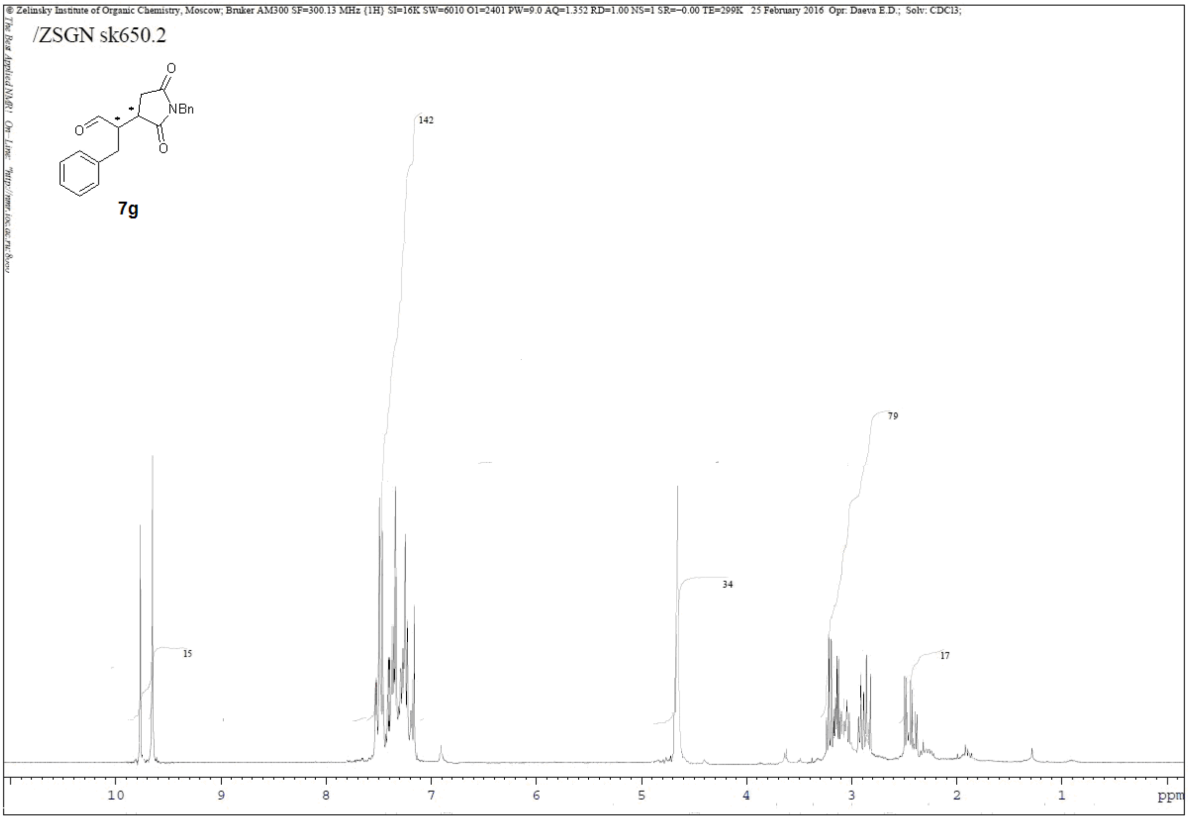
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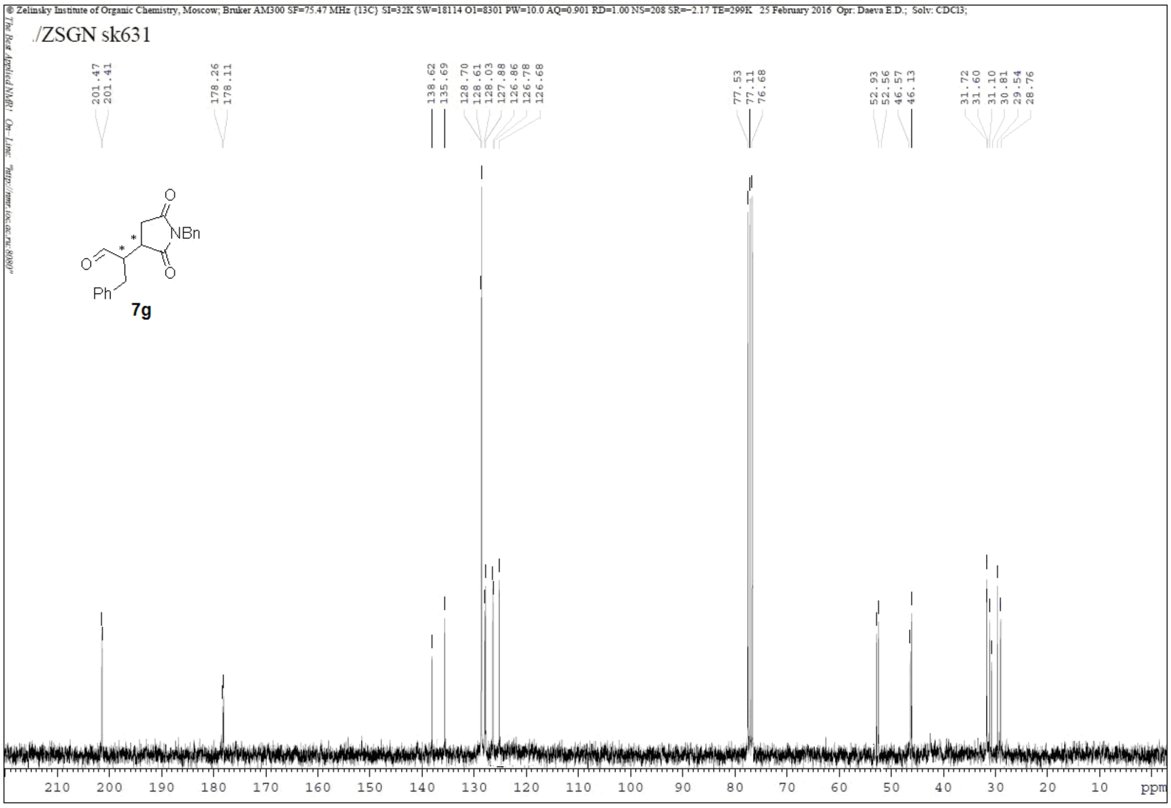
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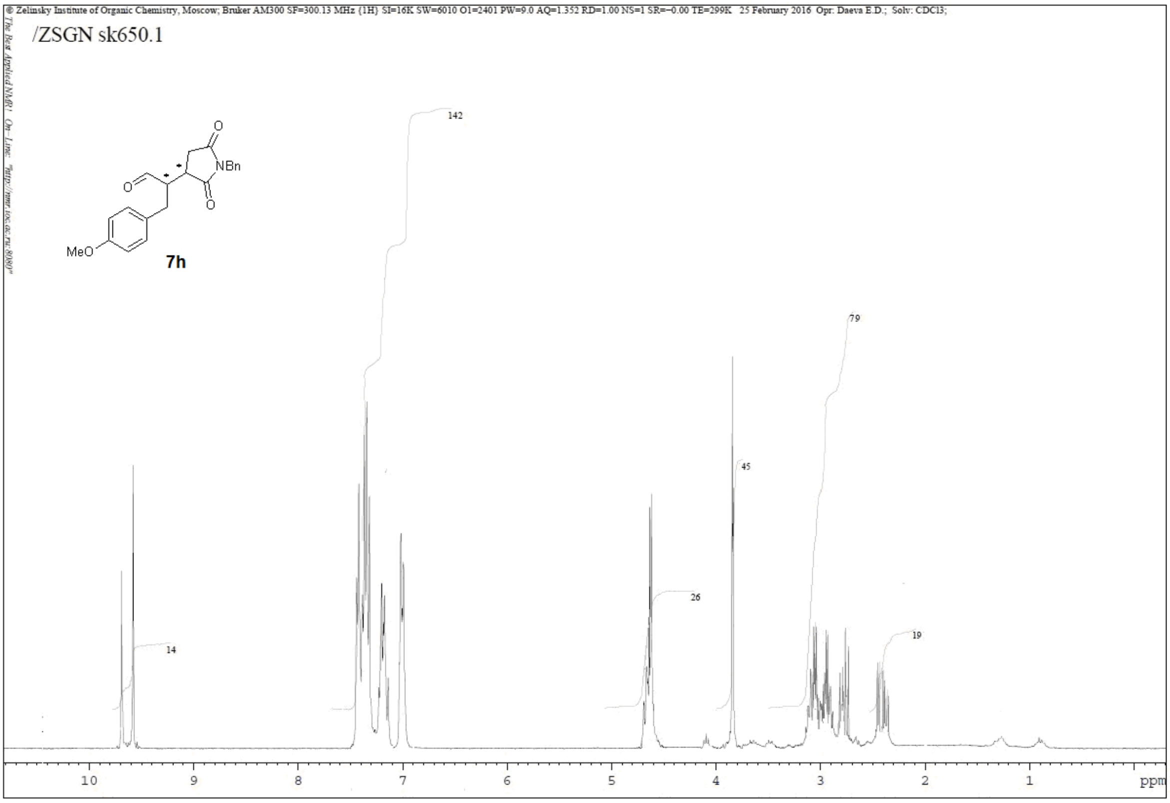
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O
O
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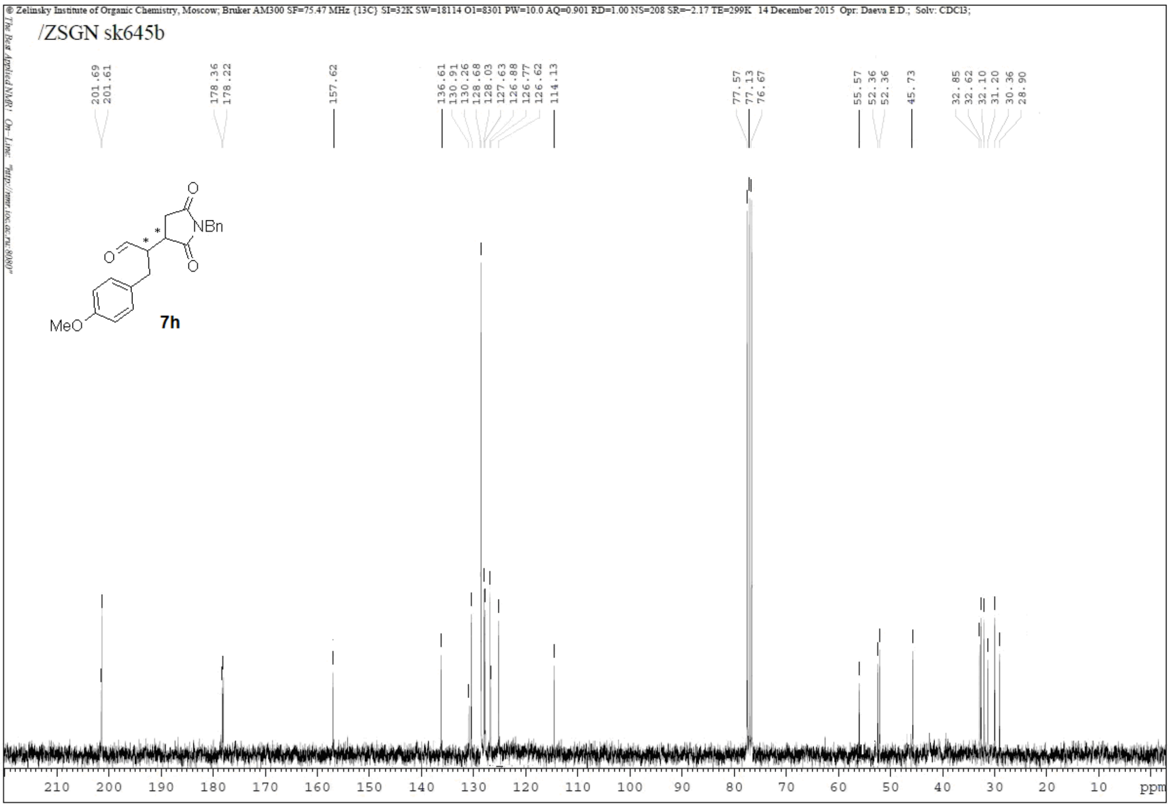
© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=10.0 AQ=0.901 RD=1.00 NS=208 SR=-2.17 TE=299K 14 December 2015 Opr: Daeva E.D.; Solv: CDCl3;
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126.62
114.13
77.57
77.13
76.67
55.57
52.36
52.36
45.73
32.85
32.62
32.10
31.20
30.36
28.90
O
NBn
O
O
MeO
*
*
7h
210
200
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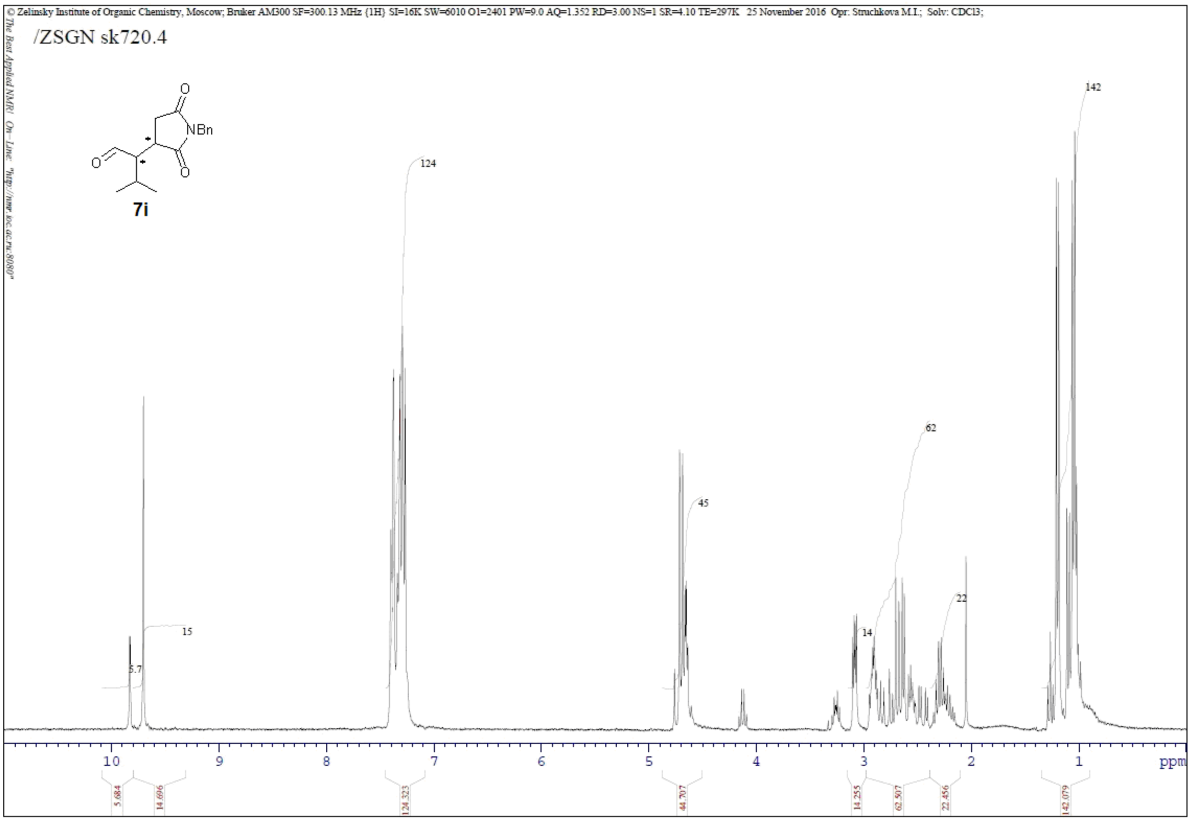
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The Best Applied NMR! On-Line: "http://nmr.ioc.ac.ru:8080"
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NBn
O
O
7i
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45
14
62
22
142
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9
8
7
6
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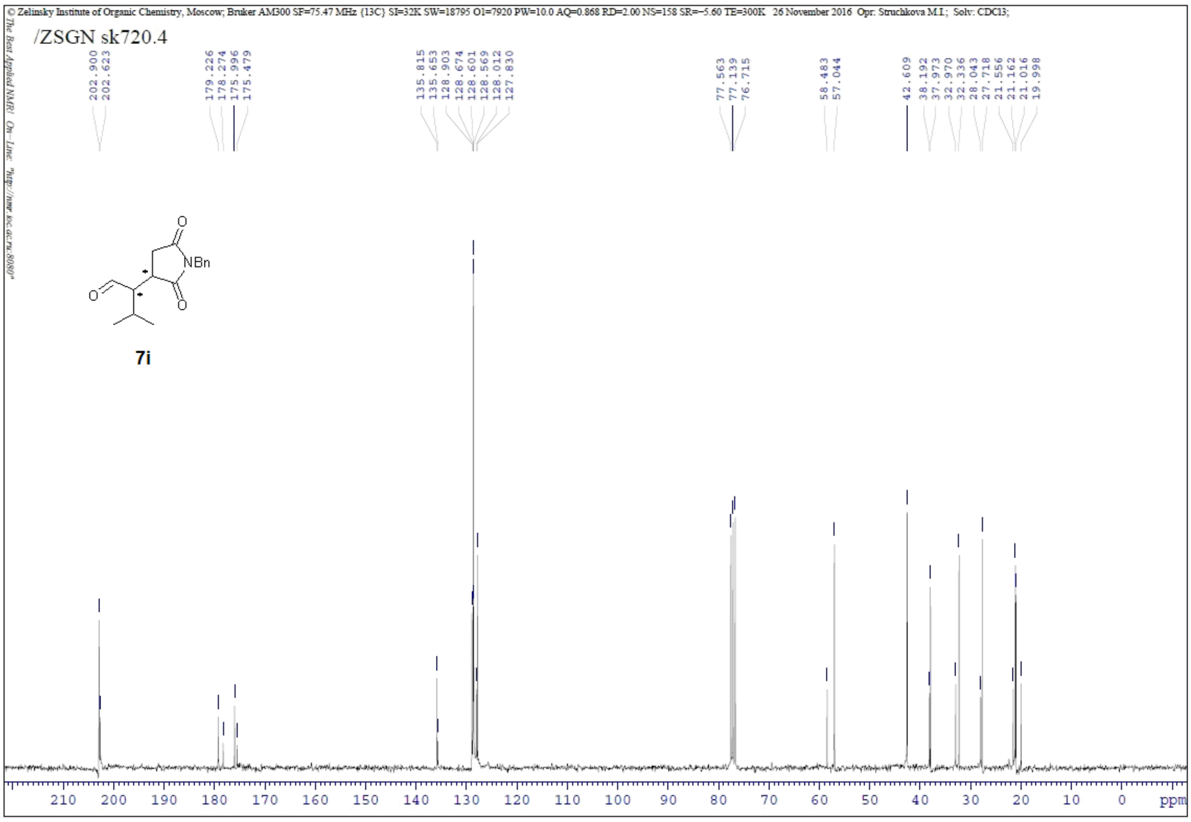
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The Best Applied NMR! On-Line: "http://nmr.ioc.ac.ru:8080"
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77.139
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57.044
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32.336
28.043
27.718
21.556
21.162
21.016
19.998
O
NBn
O
O
7i
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm