SUPPORTING INFORMATION

1-{(1*S*,2*S*,4*R*)-7,7-Dimethyl-1-[(pyrrolidin-1-yl)methyl]bicyclo[2.2.1]heptan-2-yl}-1*H*-benzo[*d*]imidazole

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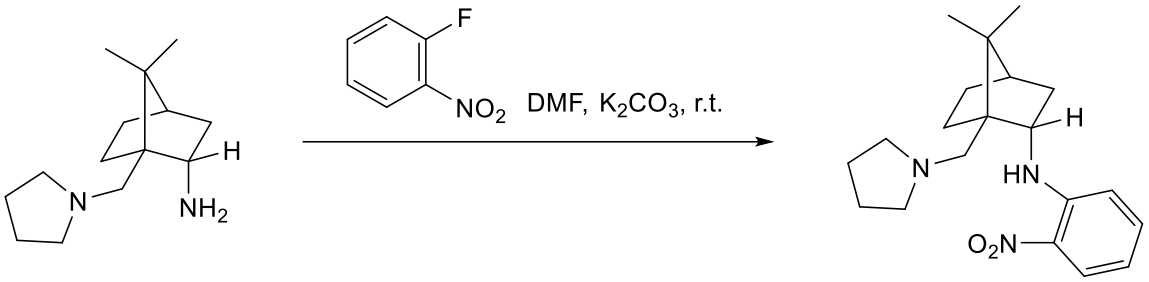
1. Materials and methods, syntheses, and characterization

Solvents for extractions and chromatography were of technical grade and were distilled prior to use. Extracts were dried over technical grade anhydrous Na_2SO_4. Melting points were determined on a Kofler micro hot stage and on SRS OptiMelt MPA100 – Automated Melting Point System (Stanford Research Systems, Sunnyvale, California, United States). The NMR spectra were obtained on a Bruker UltraShield 500 plus (Bruker, Billerica, Massachusetts, United States) at 500 MHz for ^{1}H and 126 MHz for ^{13}C nucleus, using $CDCl_3$ with TMS as the internal standard, as solvents. Mass spectra were recorded on an Agilent 6224 Accurate Mass TOF LC/MS (Agilent Technologies, Santa Clara, California, United States), IR spectra on a Perkin-Elmer Spectrum BX FTIR spectrophotometer (PerkinElmer, Waltham, Massachusetts, United States). Column chromatography (CC) was performed on silica gel (Silica gel 60, particle size: 0.035-0.070 mm (Sigma-Aldrich, St. Louis, Missouri, United States)). All the commercially available chemicals used were purchased from Sigma-Aldrich (St. Louis, Missouri, United States). Catalytic hydrogenation was performed on a Parr Pressure Reaction Hydrogenation Apparatus (Moline, IL, USA). The optical rotation of optical active substances was measured on a Perkin Elmer 241 MC Polarimeter (PerkinElmer, Waltham, MA, USA) equipped with a Na lamp (sodium emission lines at 589.0 nm) at 20°C.

(1*S*,2*S*,4*R*)-7,7-Dimethyl-1-(pyrrolidin-1-ylmethyl)bicyclo[2.2.1]heptan-2-amine (**1**)[1] was prepared following the literature procedure.

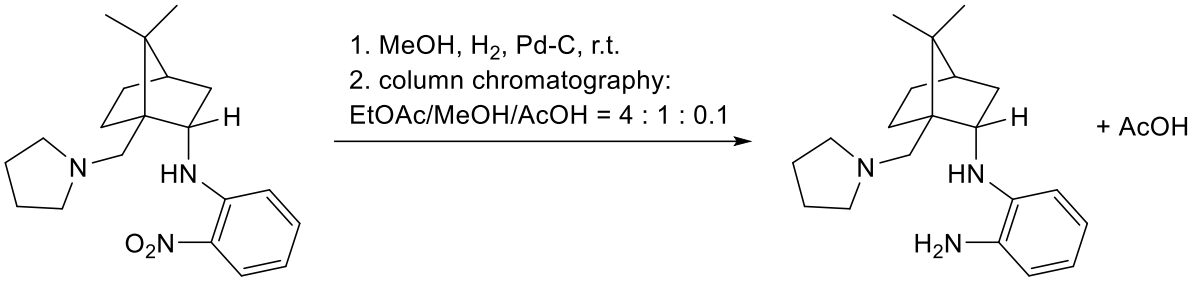
Synthesis of (1*S*,2*S*,4*R*)-7,7-dimethyl-*N*-(2-nitrophenyl)-1-(pyrrolidin-1-ylmethyl)bicyclo[2.2.1]heptan-2-amine (2)



1 **2**

A mixture of (1*S*,2*S*,4*R*)-7,7-dimethyl-1-(pyrrolidin-1-ylmethyl)bicyclo[2.2.1]heptan-2-amine (**1**) (1.75 mmol, 343 mg), 1-fluoro-2-nitrobenzene (1.75 mmol, 0.185 mL), K_2CO_3 (1.75 mmol, 0.242 g), and DMF (5 mL) was stirred at 25°C for 24 h. Volatile component were evaporated *in vacuo*. The residue was purified by column chromatography (EtOAc). Fractions containing the product **2** were combined and volatile components evaporated *in vacuo*. Yield: 553 mg (1.61 mmol, 92%) of yellow solid; mp = 83.5–85.3°C. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.95 (*s*, 3H); 1.02 (*s*, 3H); 1.01 – 1.06 (*m*, 1H); 1.24 (*ddd*, *J* = 4.4, 9.5, 12.3 Hz, 1H); 1.58 – 1.68 (*m*, 3H); 1.68 – 1.84 (*m*, 4H); 2.23 (*ddd*, *J* = 4.1, 9.5, 13.5 Hz, 1H); 2.38 – 2.49 (*m*, 4H); 2.69 (*q*, *J* = 7.3 Hz, 2H); 2.82 (*d*, *J* = 13.4 Hz, 1H); 3.81 (*d*, *J* = 10.1 Hz, 1H); 6.57 (*ddd*, *J* = 1.3, 6.9, 8.4 Hz, 1H); 6.71 (*dd*, *J* = 1.3, 8.9 Hz, 1H); 7.35 (*ddd*, *J* = 1.7, 6.9, 8.7 Hz, 1H); 8.14 (*dd*, *J* = 1.7, 8.7 Hz, 1H); 9.01 (*s*, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$): δ 19.40, 20.23, 24.08, 26.66, 28.14, 38.28, 45.28, 48.43, 52.25, 56.73, 58.33, 58.48, 114.60, 115.41, 126.94, 132.46, 135.61, 145.90.

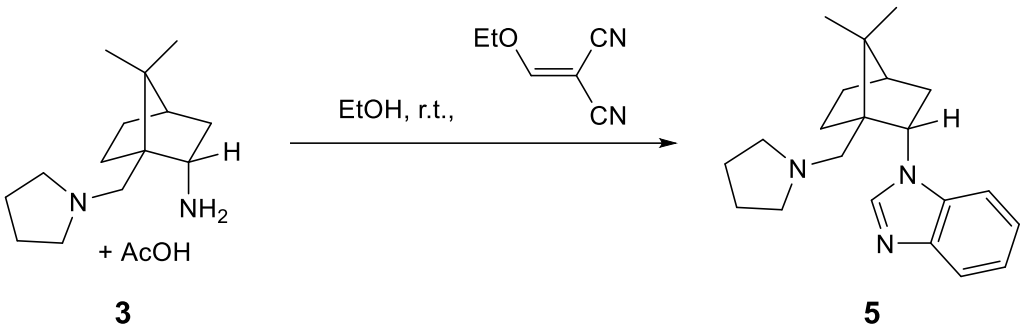
Synthesis of N^1-((1*S*,2*S*,4*R*)-7,7-dimethyl-1-(pyrrolidin-1-ylmethyl)bicyclo[2.2.1]heptan-2-yl)benzene-1,2-diamine (3)



2 **3**

A mixture of (1*S*,2*S*,4*R*)-7,7-dimethyl-*N*-(2-nitrophenyl)-1-(pyrrolidin-1-ylmethyl)bicyclo-[2.2.1]heptan-2-amine (**2**) (0.83 mmol, 285 mg), Pd-C (ω = 10%, 20 mg), and MeOH (5 mL) was shaken in a Paar shaker hydrogenation apparatus in H_2 atmosphere (3 bar) at 25°C for 6 h. The reaction mixture was filtrated to remove Pd-C, volatile components were evaporated *in vacuo*. The residue was purified by column chromatography (Silica Gel 60; EtOAc/MeOH/AcOH = 4 : 1 : 0.1). Fractions containing the product **3** were combined and volatile components evaporated *in vacuo*. Yield: 262 mg (0.70 mmol, 85%, acetic acid to amine **3** in a 1 : 1 ratio) of colorless oil. ν_{max} 3378, 2954, 2877, 2791, 1616, 1571, 1507, 1441, 1416, 1389, 1354, 1323, 1254, 1231, 1156, 1069, 1037, 910, 868, 777, 740, 695, 670 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.95 (*s*, 3H); 0.98 – 1.03 (*m*, 1H); 1.02 (*s*, 3H); 1.33 (*ddd*, *J* = 4.6, 9.5, 12.4 Hz, 1H); 1.62 – 1.69 (*m*, 1H); 1.71 (*t*, *J* = 4.6 Hz, 1H); 1.79 – 1.88 (*m*, 5H); 1.99 (*s*, 3H); 2.41 – 2.57 (*m*, 2H); 2.88 (*d*, *J* = 2.5 Hz, 2H); 2.94 (*br s*, 2H); 3.12 (*br s*, 2H); 3.71 (*ddd*, *J* = 1.8, 3.9, 9.6 Hz, 1H); 6.18 (*br s*, 4H); 6.49 (*dd*, *J* = 1.3, 7.6 Hz, 1H); 6.62 – 6.67 (*m*, 2H); 6.71 (*ddd*, *J* = 2.7, 6.2, 7.7 Hz, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$): δ 19.33, 20.16, 22.93, 23.76, 26.34, 28.27, 38.34, 45.03, 49.77, 51.13, 56.93, 57.01, 60.65, 112.16, 115.23, 118.59, 119.04, 136.11, 136.25, 176.69.

Synthesis of 1-((1*S*,2*S*,4*R*)-7,7-dimethyl-1-(pyrrolidin-1-ylmethyl)bicyclo[2.2.1]heptan-2-yl)-1*H*-benzo[*d*]imidazole (5)

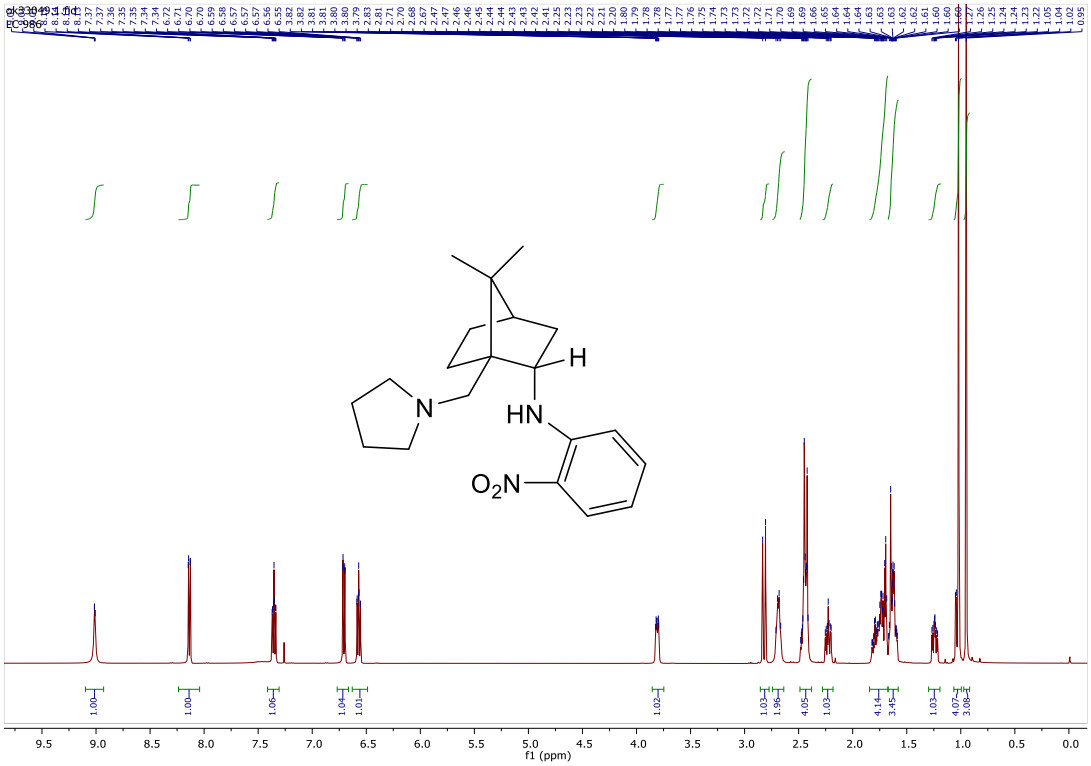


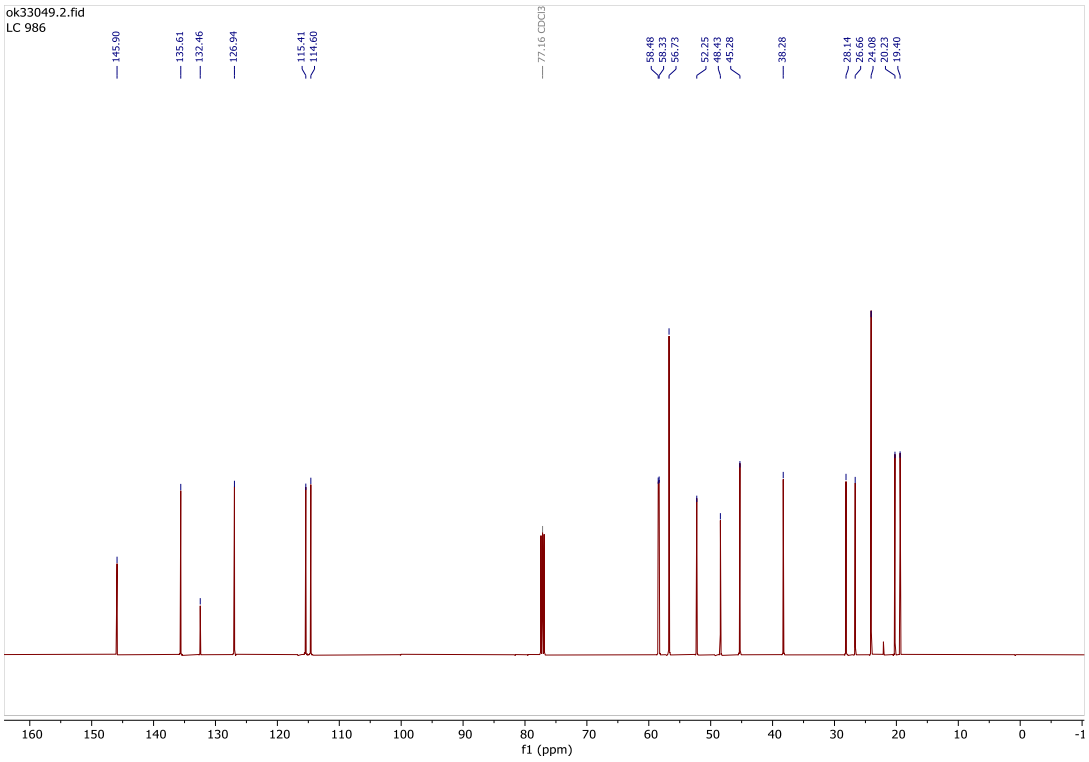
3 **5**

A mixture of N^1-((1*S*,2*S*,4*R*)-7,7-dimethyl-1-(pyrrolidin-1-ylmethyl)bicyclo[2.2.1]heptan-2-yl)benzene-1,2-diamine (**3**) (157 mg, 0.42 mmol; acetic acid to amine **3** in a 1 : 1 ratio) and 2-(ethoxymethylene)malononitrile (61 mg, 0.50 mmol) in dichloromethane (2 mL) was stirred at 25°C for 24 h. Volatile components were evaporated *in vacuo*. The residue was purified by column chromatography (Silica Gel 60; EtOAc/petroleum ether = 3 : 1). Fractions containing the product **5** were combined and volatile components evaporated *in vacuo*. Yield: 118 mg (0.365 mmol, 87%) of colorless semisolid. $[\alpha]_D^{r.t.}$ = –55.9 (0.16, MeOH). EI-HRMS: *m/z* = 324.2429 (MH^+); $C_{21}H_{29}N_3$ requires: *m/z* = 324.2434 (MH^+); ν_{max} 2958, 2781, 2192, 1613, 1562, 1482, 1456, 1420, 1390, 1370, 1351, 1329, 1284, 1225, 1196, 1111, 1073, 1009, 907, 888, 797, 783, 766, 737, 643 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.98 – 1.10 (*m*, 2H); 1.06 (*s*, 3H); 1.17 (*s*, 3H); 1.17 – 1.26 (*m*, 2H); 1.56 – 1.66 (*m*, 2H); 1.73 – 1.83 (*m*, 1H); 1.86 (*t*, *J* = 4.5 Hz, 1H); 1.89 – 2.01 (*m*, 3H); 2.03 – 2.09 (*m*, 1H); 2.14 – 2.24 (*m*, 2H); 2.36 (*d*, *J* = 13.1 Hz, 1H); 2.59 – 2.69 (*m*, 1H); 2.78 (*d*, *J* = 13.2 Hz, 1H); 4.86 (*ddd*, *J* = 2.4, 5.0, 11.9 Hz, 1H); 7.19 – 7.25 (*m*, 2H); 7.39 – 7.44 (*m*, 1H); 7.71 – 7.77 (*m*, 1H); 8.17 (*s*, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$): δ 19.41, 20.79, 23.50, 27.00, 28.52, 37.42, 45.03, 50.85, 54.00, 55.64, 57.07, 59.81, 111.64, 119.62, 121.82, 121.96, 135.87, 142.22, 142.72.

2. NMR spectra

(1*S*,2*S*,4*R*)-7,7-dimethyl-N-(2-nitrophenyl)-1-(pyrrolidin-1-ylmethyl)bicyclo[2.2.1]heptan-2-amine (2)





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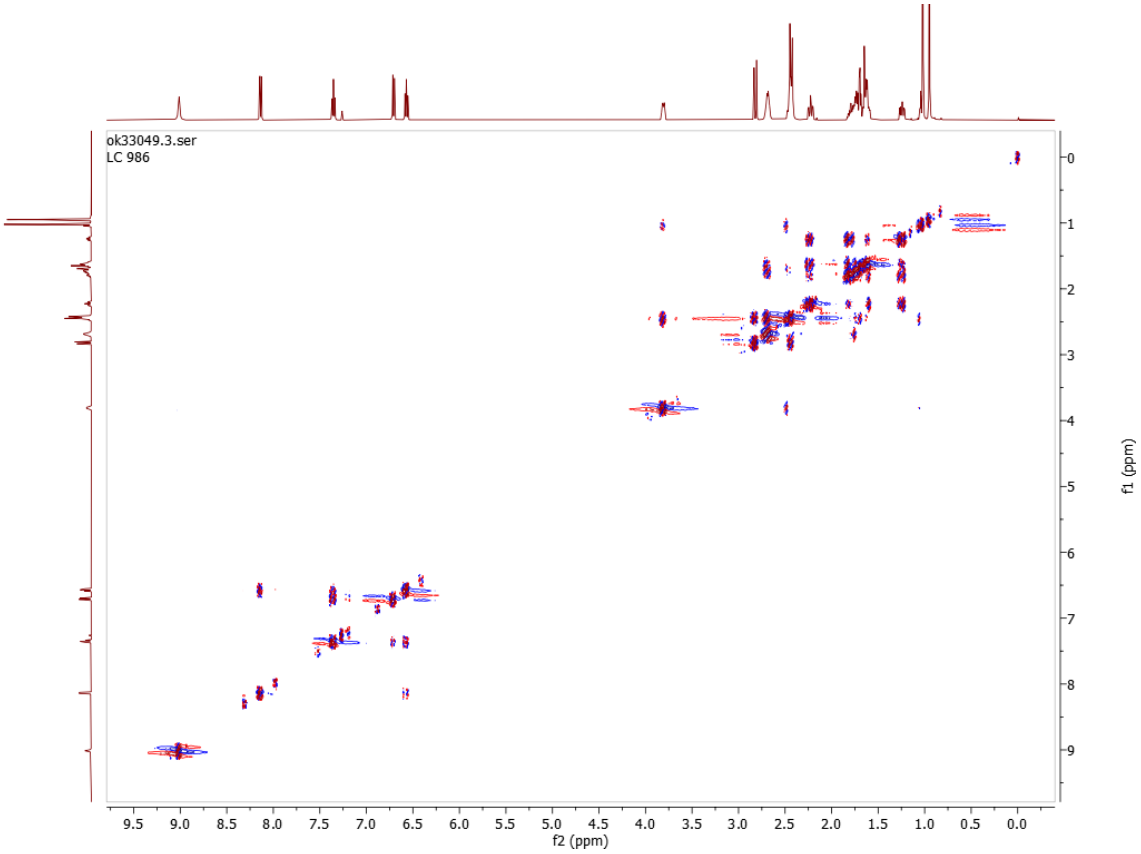
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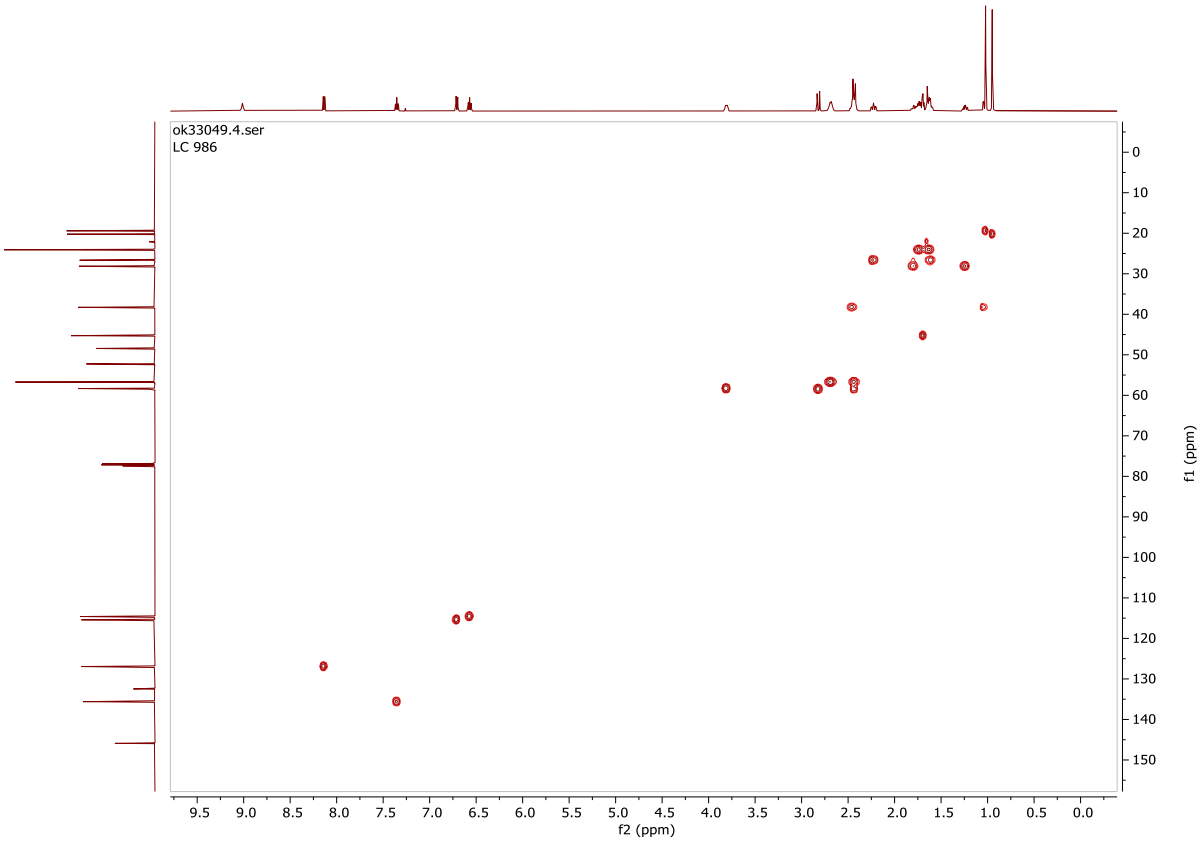
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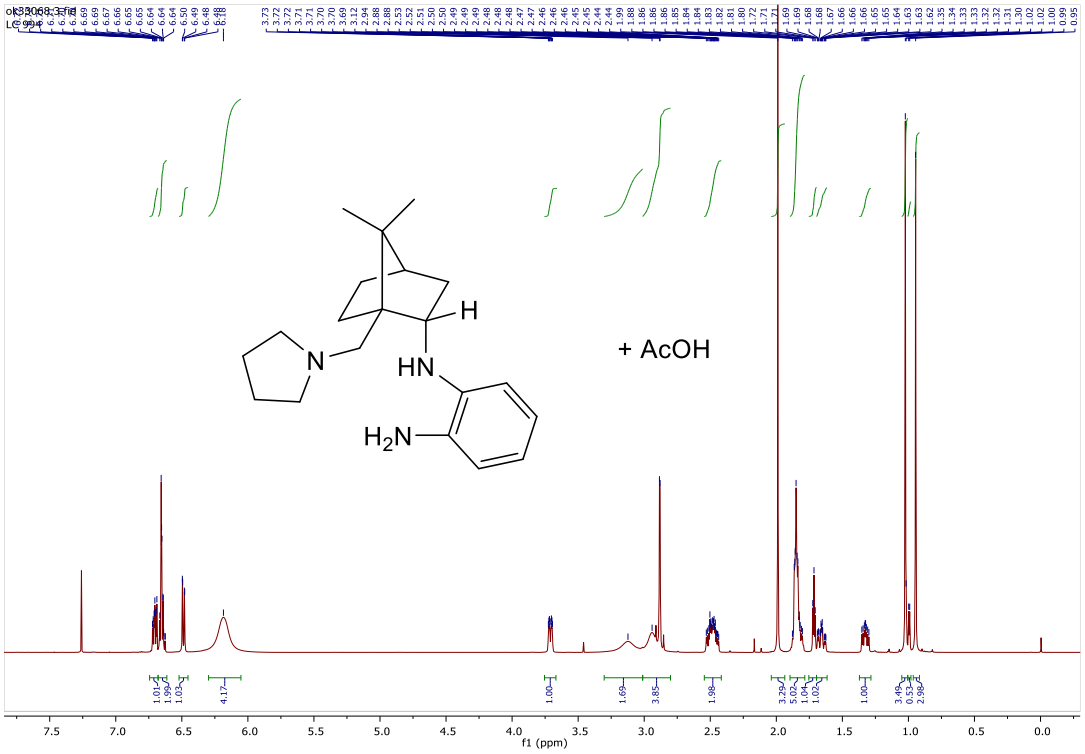
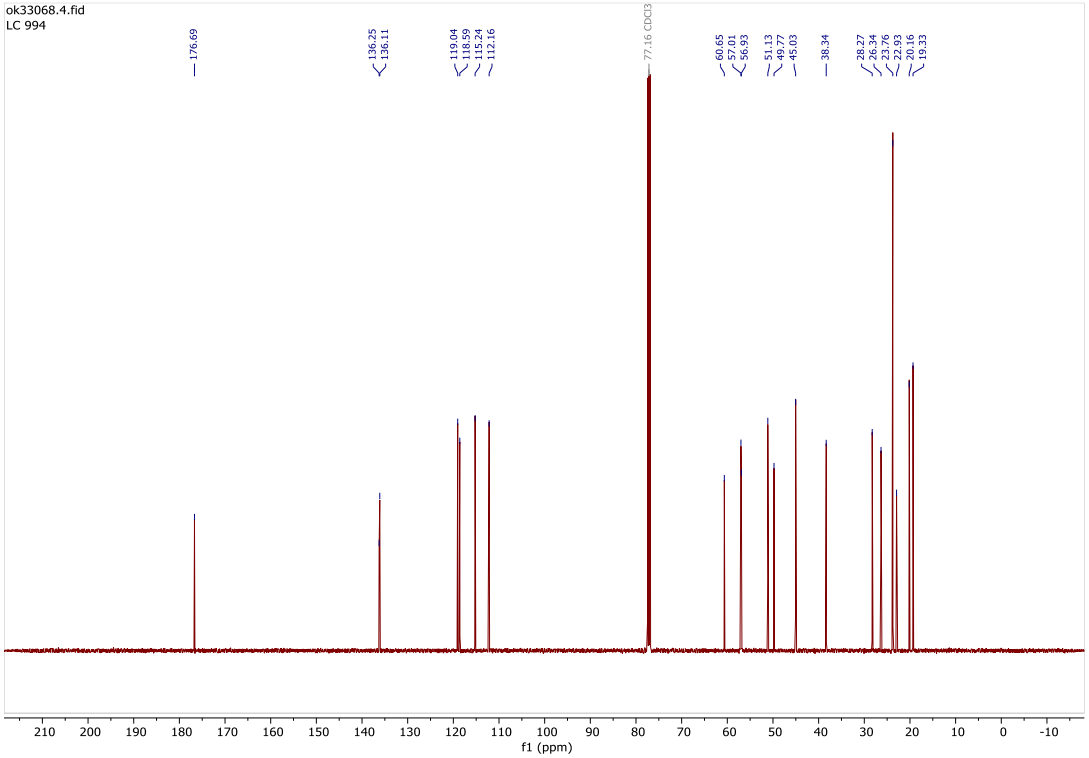
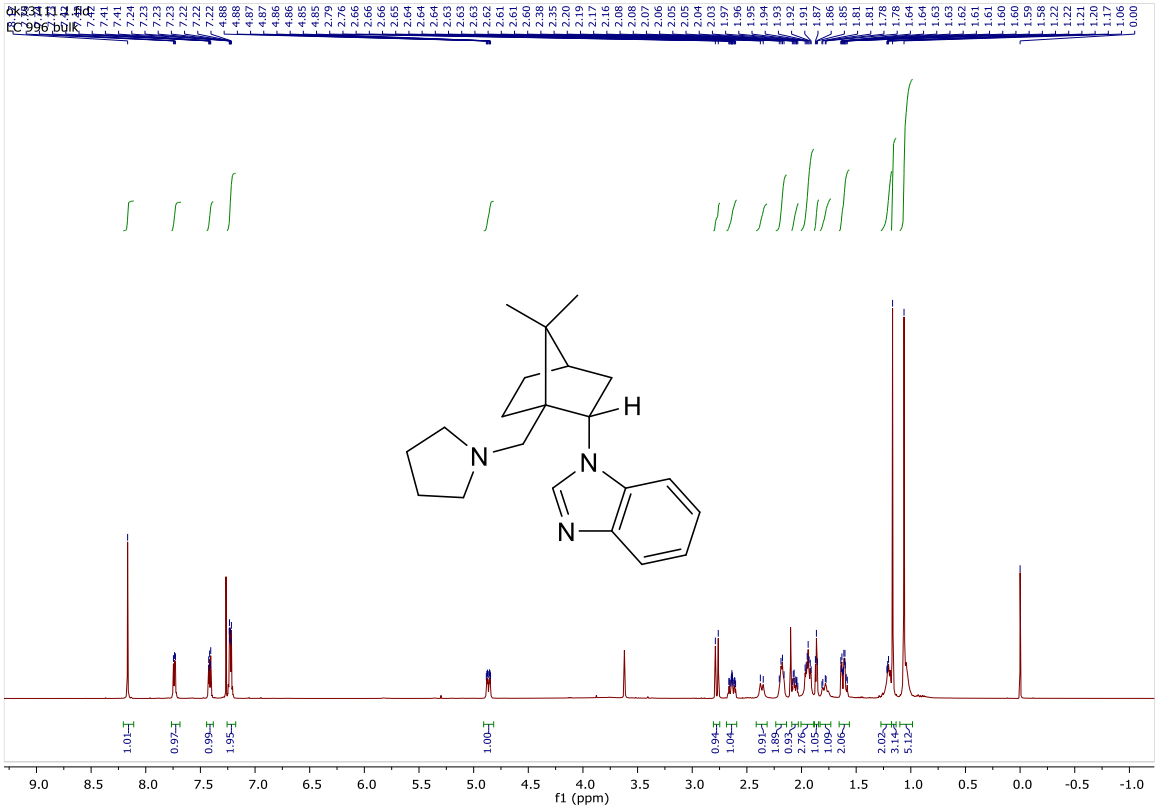
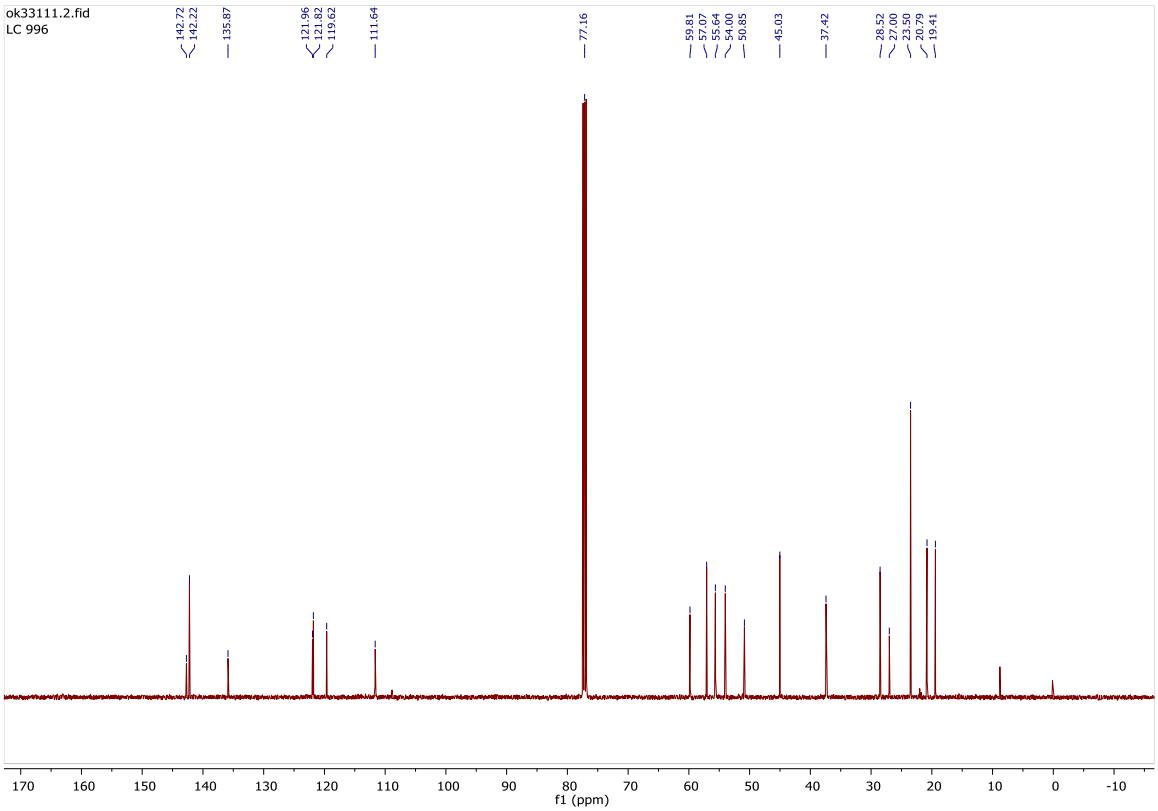
N^1-((1*S*,2*S*,4*R*)-7,7-Dimethyl-1-(pyrrolidin-1-ylmethyl)bicyclo[2.2.1]heptan-2-yl)benzene-1,2-diamine (3) + acetic acid (1 : 1 ratio)





1-((1*S*,2*S*,4*R*)-7,7-Dimethyl-1-(pyrrolidin-1-ylmethyl)bicyclo[2.2.1]heptan-2-yl)-1*H*-benzo[*d*]imidazole (5)





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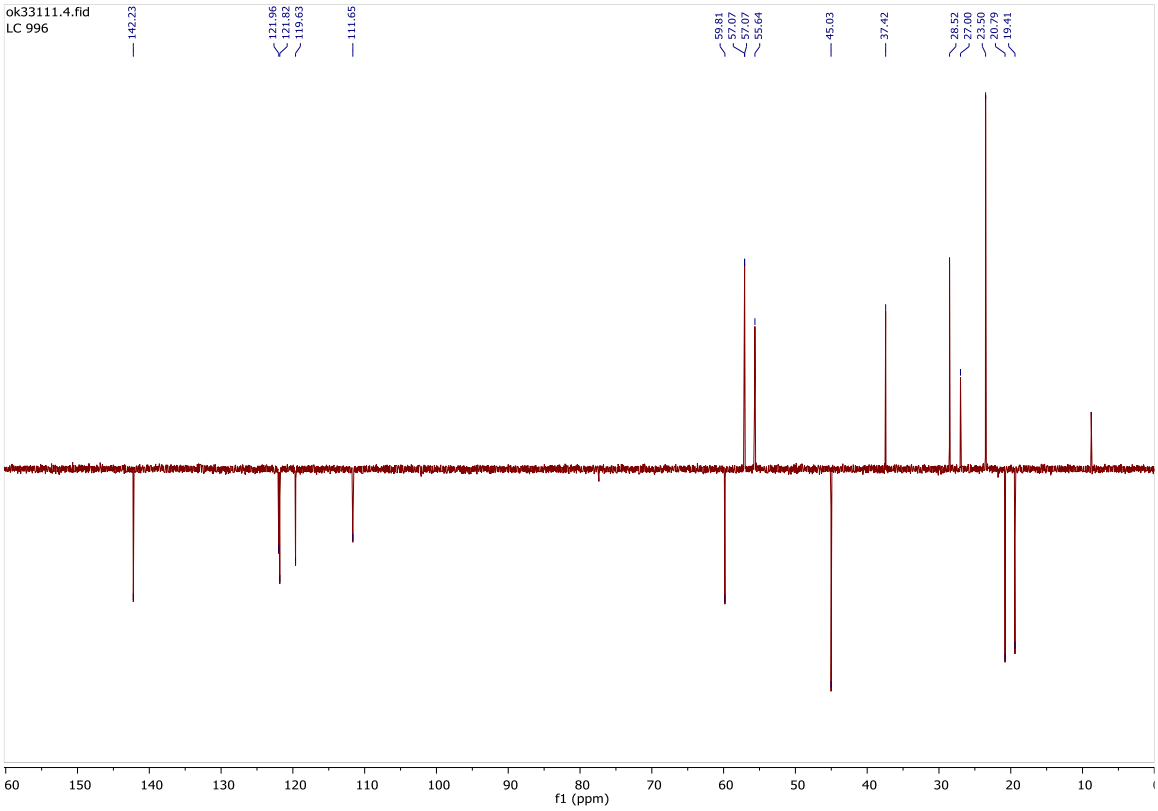

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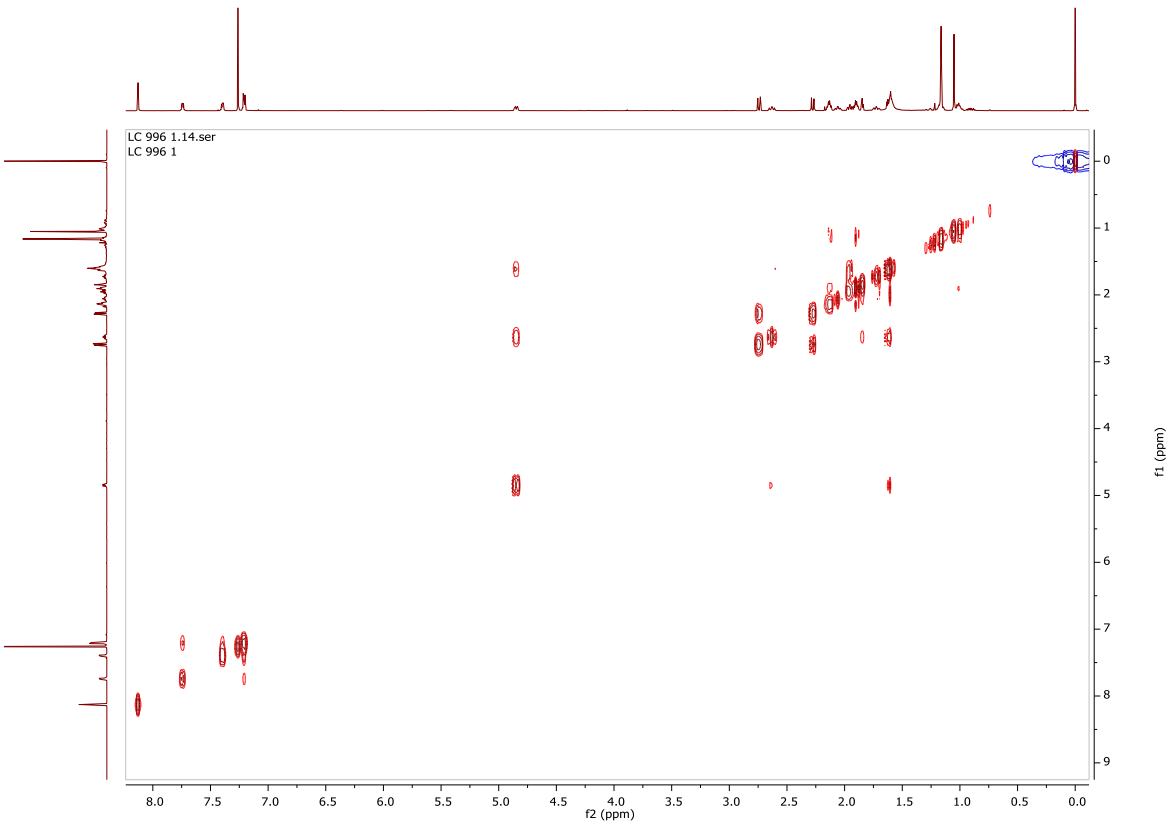

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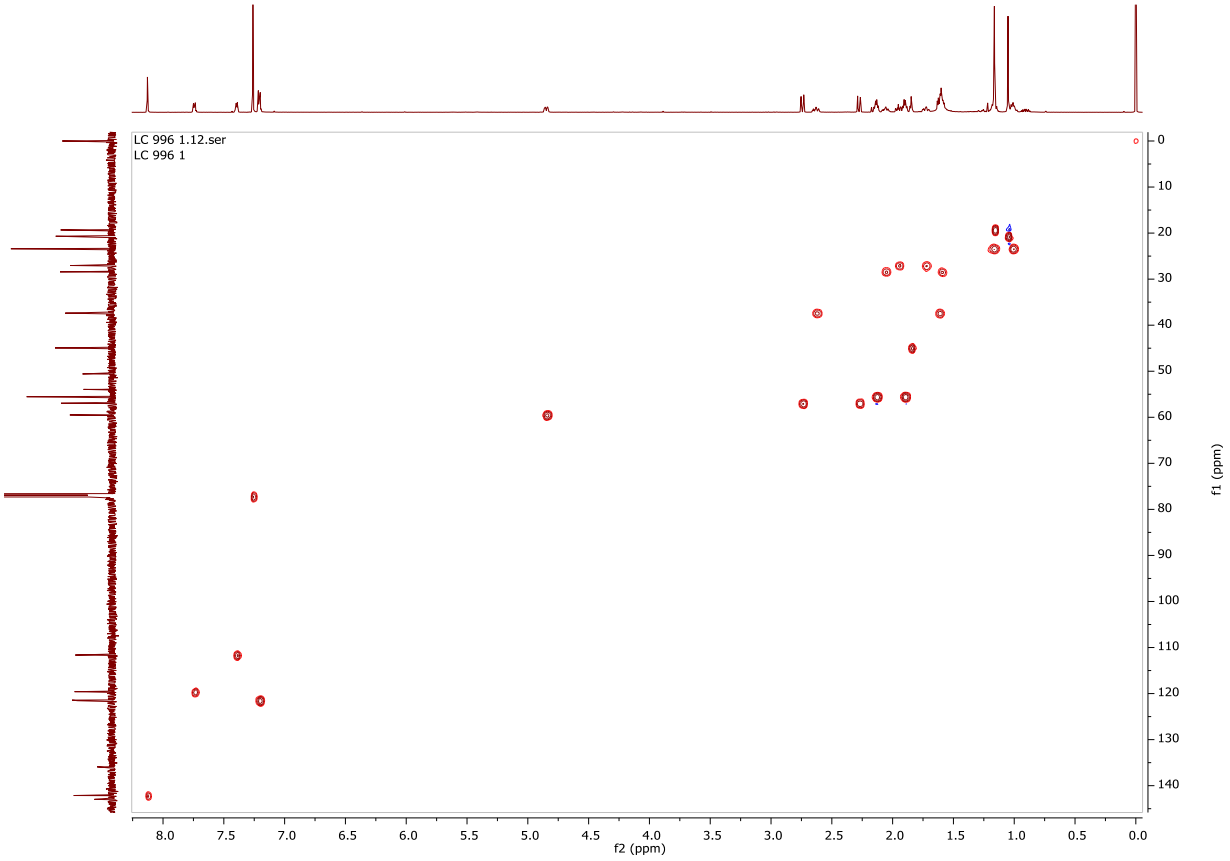
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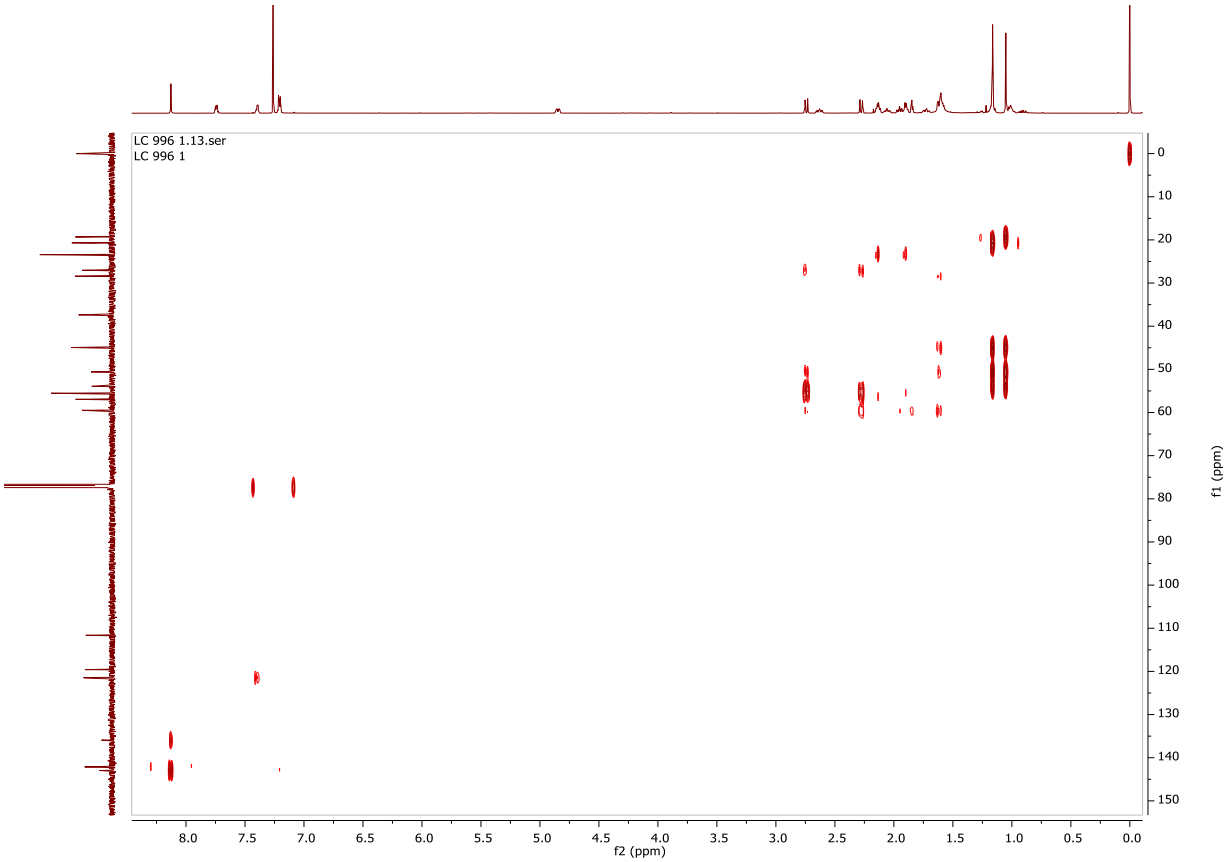
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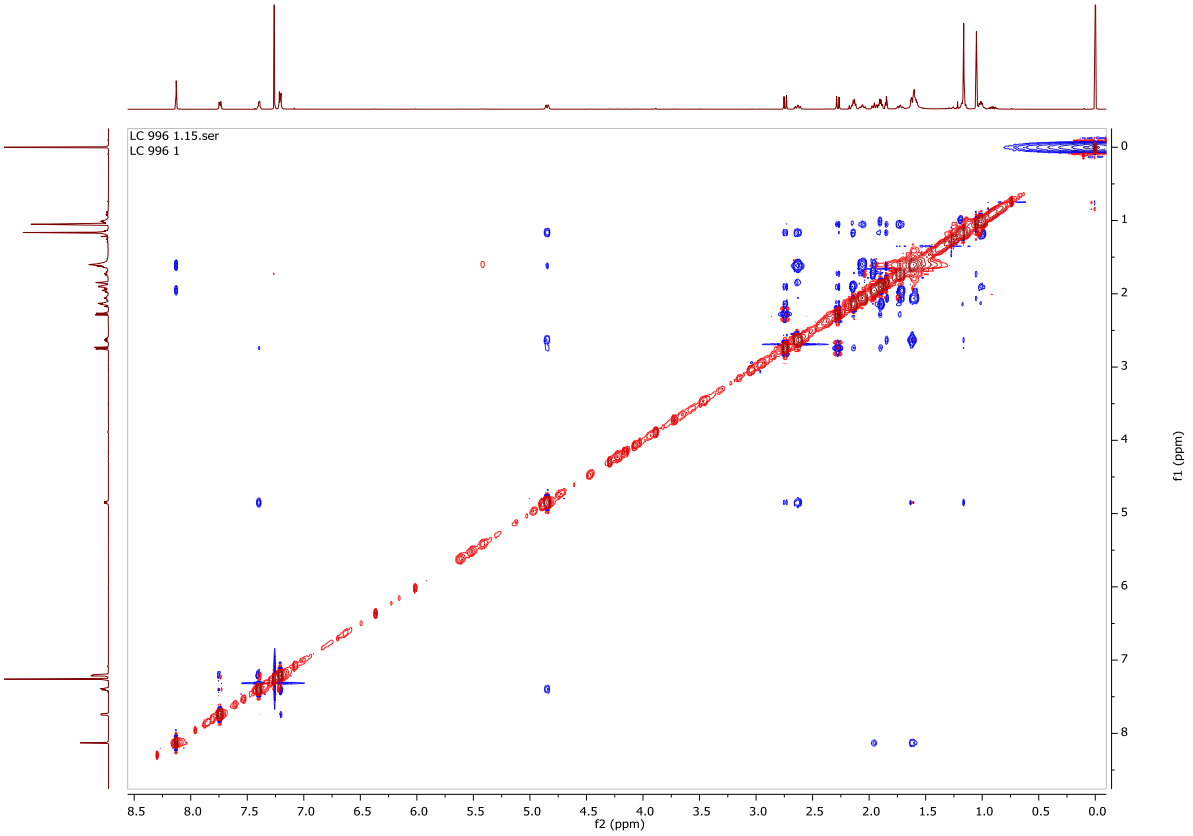
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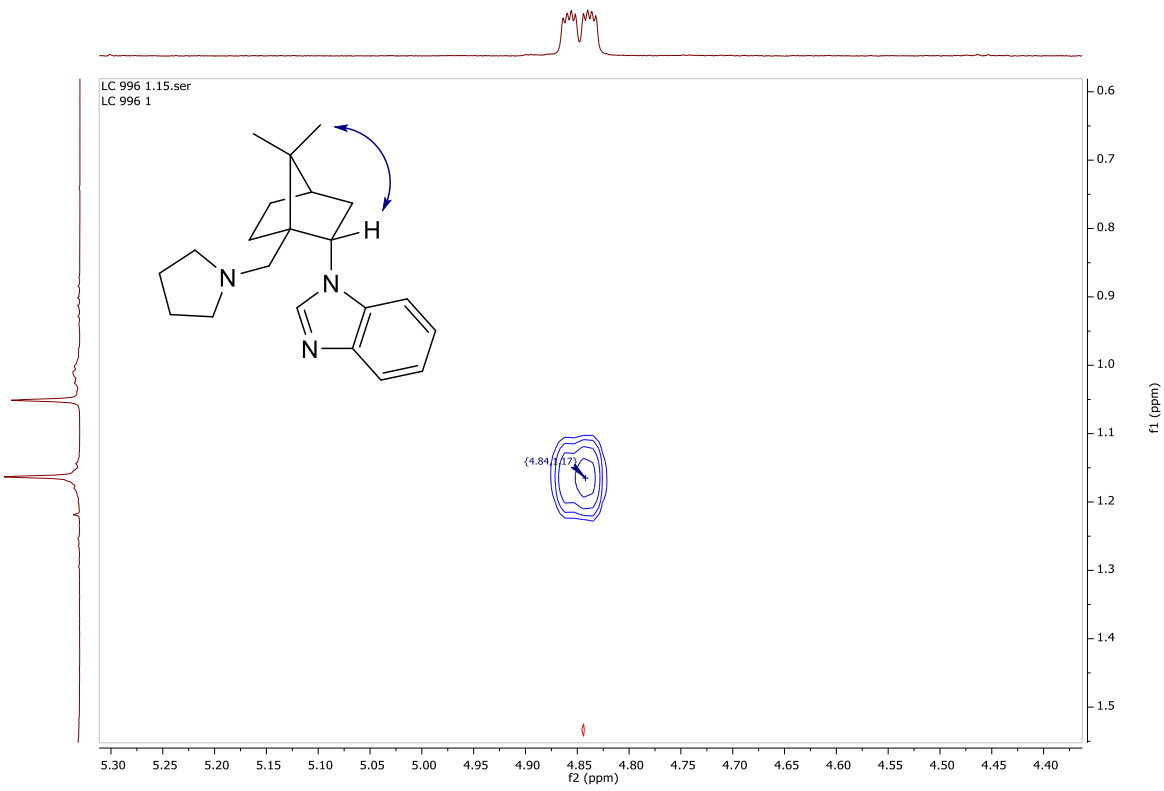
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H
N
N
N
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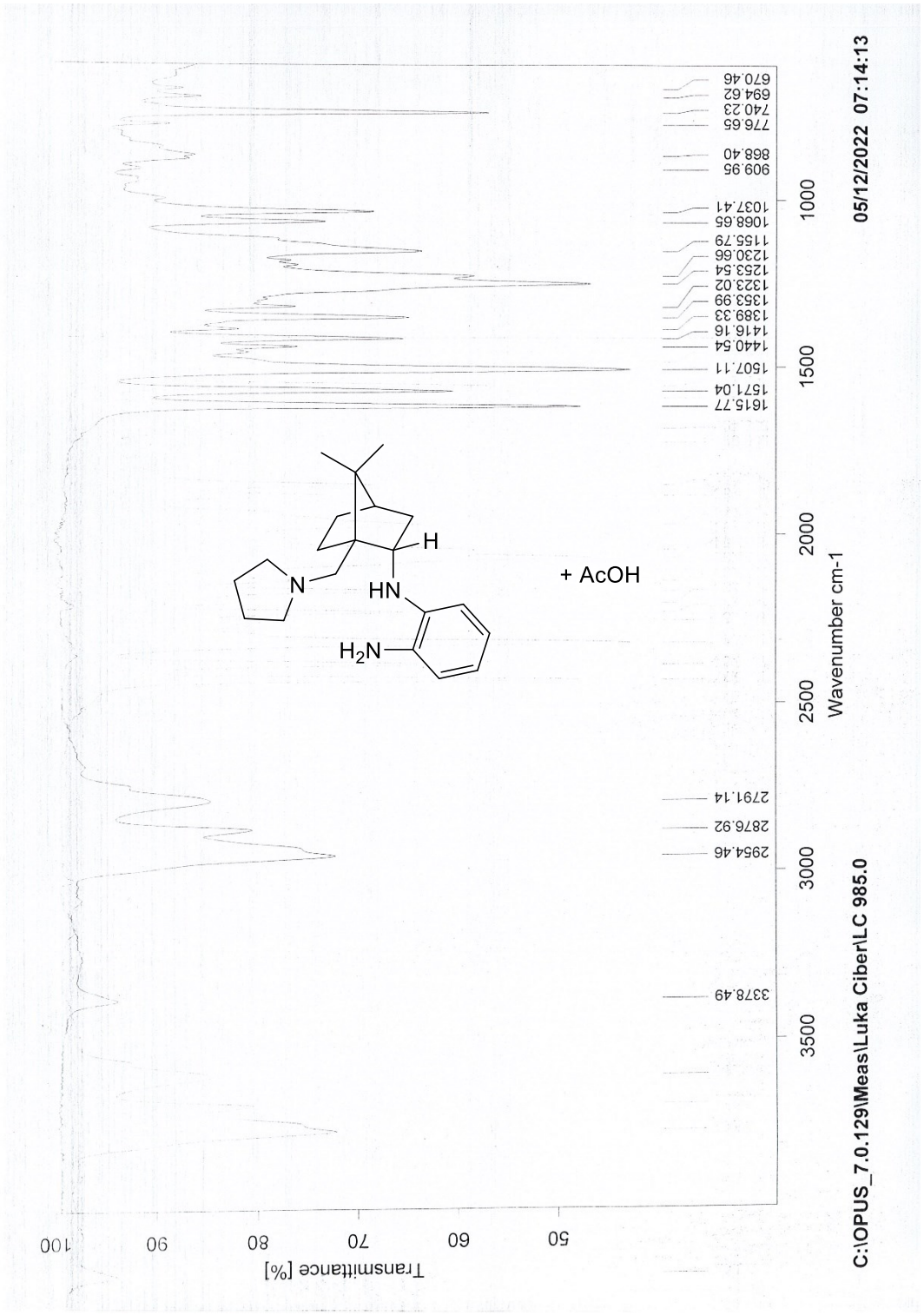
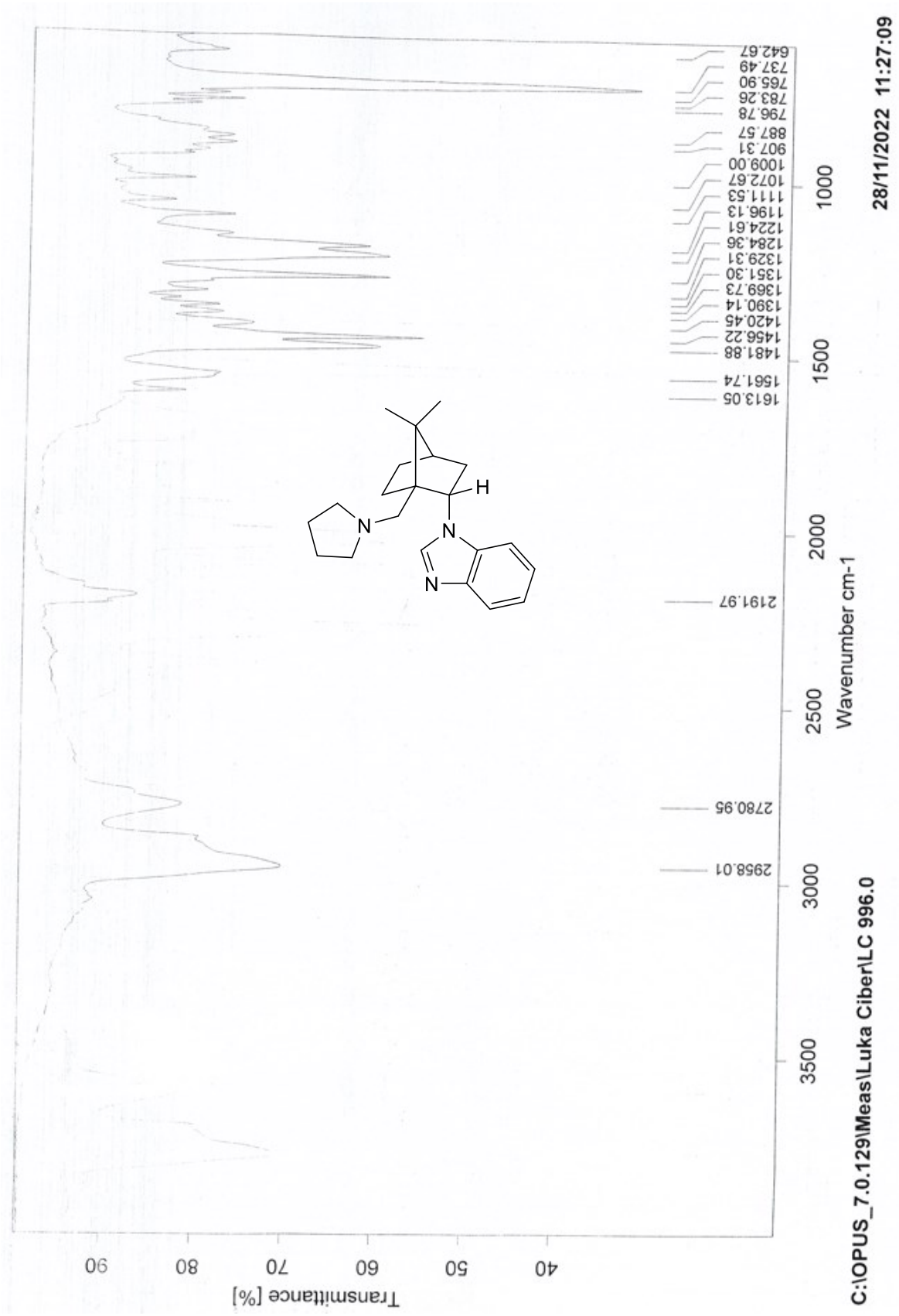
f2 (ppm)
f1 (ppm)

3. IR spectra

***N*^{1}-((1*S*,2*S*,4*R*)-7,7-Dimethyl-1-(pyrrolidin-1-ylmethyl)bicyclo[2.2.1]heptan-2-yl)benzene-1,2-diamine (3) + acetic acid (1 : 1 ratio)**



1-((1*S*,2*S*,4*R*)-7,7-Dimethyl-1-(pyrrolidin-1-ylmethyl)bicyclo[2.2.1]heptan-2-yl)-1*H*-benzo[*d*]imidazole (5)



4. MS spectra

1-((1*S*,2*S*,4*R*)-7,7-Dimethyl-1-(pyrrolidin-1-ylmethyl)bicyclo[2.2.1]heptan-2-yl)-1*H*-benzo[*d*]imidazole (5)

Qualitative Compound Report

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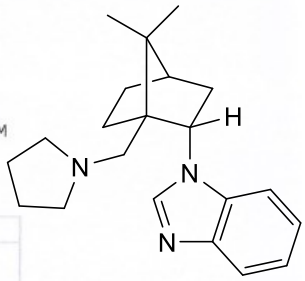
IRM Calibration Status	Success	**DA Method**	Damijana.m
Comment			



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Compound Identification Results

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324.2429	324.2407	-2.1	C18 H32 N2 O3	(M+H)+	
324.2429	324.2394	-3.5	C16 H30 N5 O2	(M+H)+	
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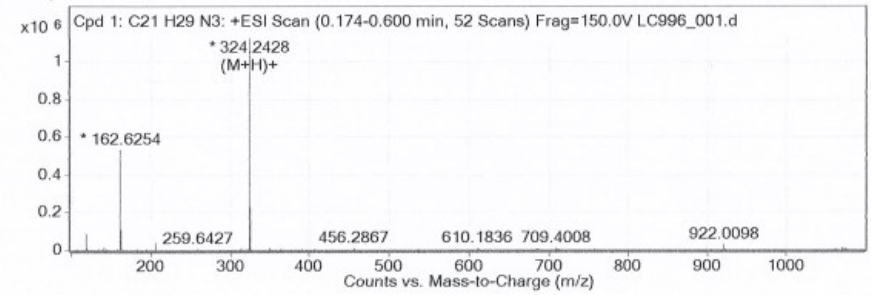
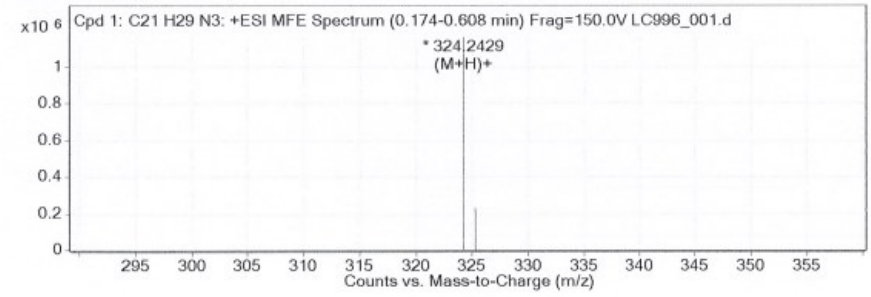
MS Spectrum



MFE MS Zoomed Spectrum



--- End Of Report ---

5. References

[1] S. Ričko, J. Svete, B. Štefane, A. Perdih, A. Golobič, A. Meden, U. Grošelj, 1,3-Diamine-Derived Bifunctional Organocatalyst Prepared from Camphor, *Adv. Synth. Catal.* **2016**, *358*, 3786–3796, https://doi.org/10.1002/adsc.201600498.