

Supporting Information

Heterogeneous Catalysis for the tandem cyclisation of unsaturated alcohols

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1 General Conditions

Amberlyst-15[®] hydrogen form was used as catalyst (from Sigma Aldrich, 216320-25G, Lot # MKBN5224V, P Code 1001537778, CAS 39389-20-3).

All reactions with air or moisture sensitive reagents were conducted in dried glassware under an atmosphere of nitrogen. 3,4-dihydro-2*H*-pyran was used as received without further purification. Tetrahydrofuran (THF) was distilled from sodium/benzophenone, 1,2-dichloroethane (CH₂)₂Cl₂) was dried by distillation over CaH₂. MeCN and MeNO₂ (from Sigma Aldrich, HPLC quality) were used as received without further purification. Solvents for flash and thin layer chromatography [petroleum ether] (PE) and diethyl ether (Et₂O) were used as received without further purification. Reactions were monitored by analytical Thin Layer Chromatography (TLC), which was performed on 0.20 mm precoated silica plates (Silica gel 60, F₂₅₄, Macherey-Nagel). Detection of non UV-active substances was carried out by staining with *p*-anisaldehyde (0.7 mL *p*-anisaldehyde, 1.7 mL acetic acid and 9.5 mL conc. sulfuric acid in 250 mL ethanol), and subsequent heating (heat gun, ca. 150 °C). Separations *via* column chromatography were carried out on a CombiFlash[®]Rf+ (Teledyne Isco, USA), using CHROMABOND[®] Flash columns (Macherey-Nagel GmbH & Co. KG, Germany).

NMR spectra presented (¹H, ¹³C) were recorded on a Bruker AV-500, AV-400 and AV-200 spectrometer at a temperature of 300 K. Chemical shifts (δ) are given in parts per million (ppm) and refer to the residual proton signal of the used solvent. In ¹H-spectra the CDCl₃ residual peak was applied as an internal standard with a chemical shift of 7.26 ppm. The DMSO-d₆ residual peak was applied as an internal standard with a chemical shift of 2.54. ¹³C-spectra were calibrated according to the deuterium-coupled signals of the used solvent

(CDCl₃ = 77.16 ppm, DMSO-d₆ = 40.45 ppm). Spectral splitting patterns are designated as: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), m_c (*centered* multiplet). Infrared spectra were recorded on a Jasco FT/IR-4600 spectrometer. Samples were analyzed directly in substance with the attenuated total reflexion method (ATR). Absorption maxima are reported in wavenumbers (cm⁻¹) and characterised with the following symbols, according to their form and intensity: s (strong), m (medium), w (weak), b (broad). Analytical GC analyses were performed on a Shimadzu GC-2025 capillary gas chromatograph. Analytical GC/MS analyses were performed on a *Shimadzu* QP2010S-MS chromatograph (EI, 70 eV) equipped with a SLB-5ms capillary column (thickness: 0.25 mm, length: 30 m, inside diameter: 0.25 mm). High resolution mass spectrometry (HRMS) was performed on a mass spectrometer LTQ-Orbitrap hybrid Exactive Plus mass spectrometer. Compounds were analyzed in loop injection mode in positive ESI (Electrospray ionization) and APGC (Atmospheric Pressure Gas Chromatography).

2 Experimental Procedures

2.1 Synthesis of the starting materials

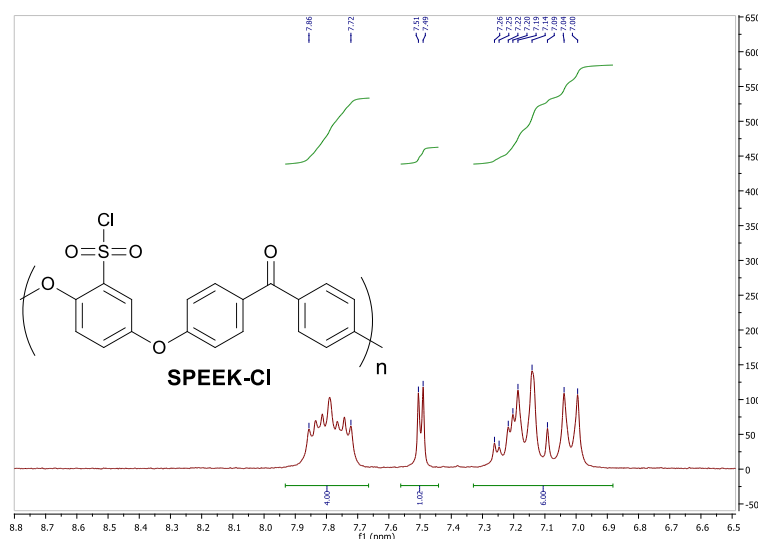
2.1.1 Synthesis of heterogeneous catalyst SPEEK-OH and (SPEEK)₃-Bi

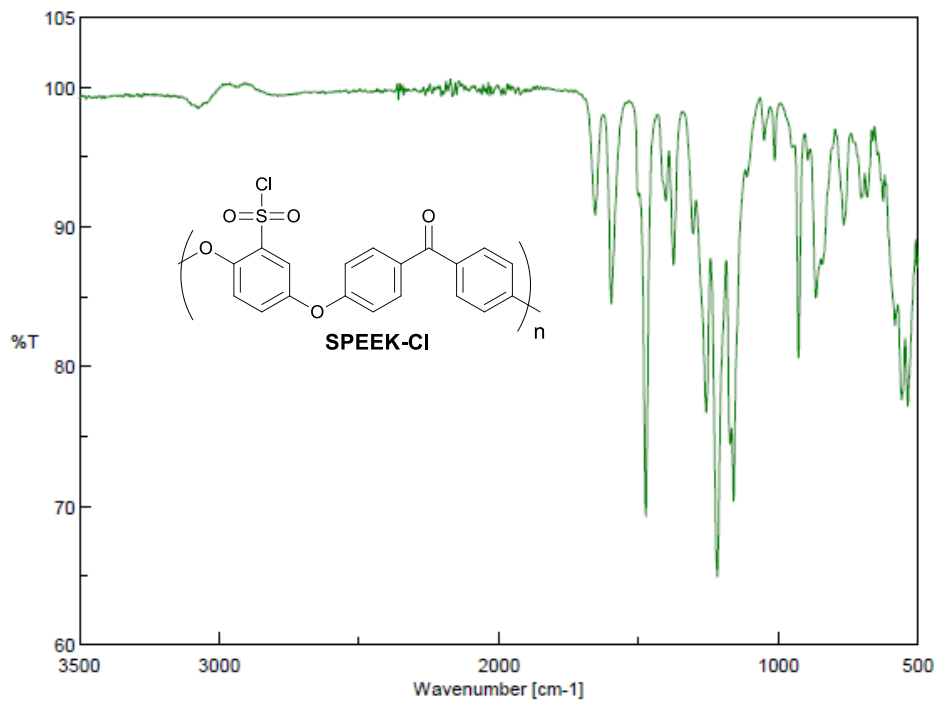
SPEEK-Cl (sulfonation degree 100%) was synthesized from PEEK Solvay KT-820 NT (DP =70) in agreement with the literature.¹

(SPEEK)₃-Bi and SPEEK-OH (sulfonation degree 100%) were synthesized from SPEEK-Cl in agreement with the literature.¹

SPEEK-Cl:

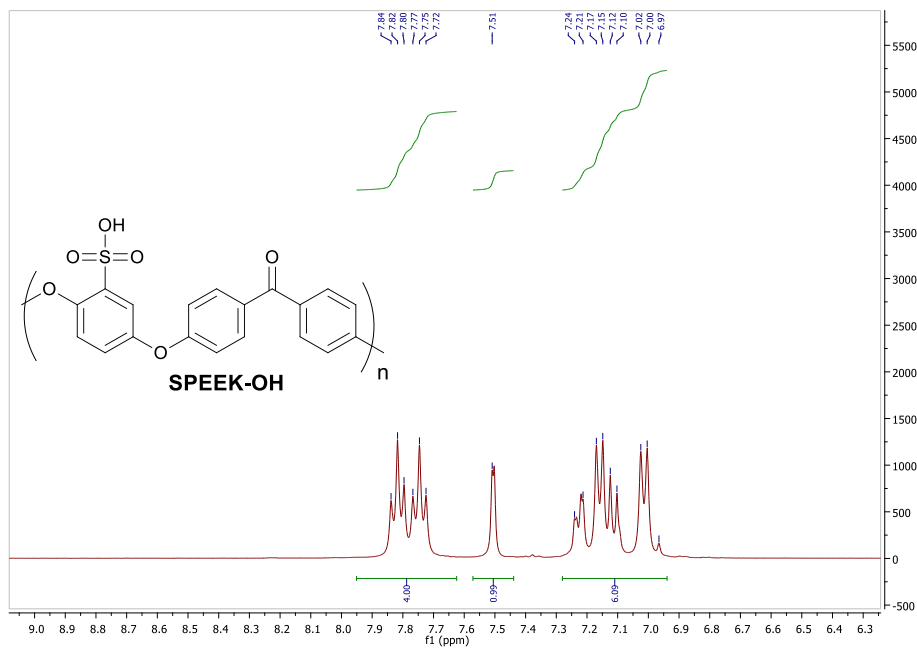
¹H RMN (400 MHz, DMSO-d₆): 7.86-7.72 (m, 4H), 7.51 (d, J = 2.3 Hz, 1H), 7.26-7.00 (m, 6H). IR (cm⁻¹): 1657, 1592, 1465, 1383, 1260, 1222, 1171, 932, 758.

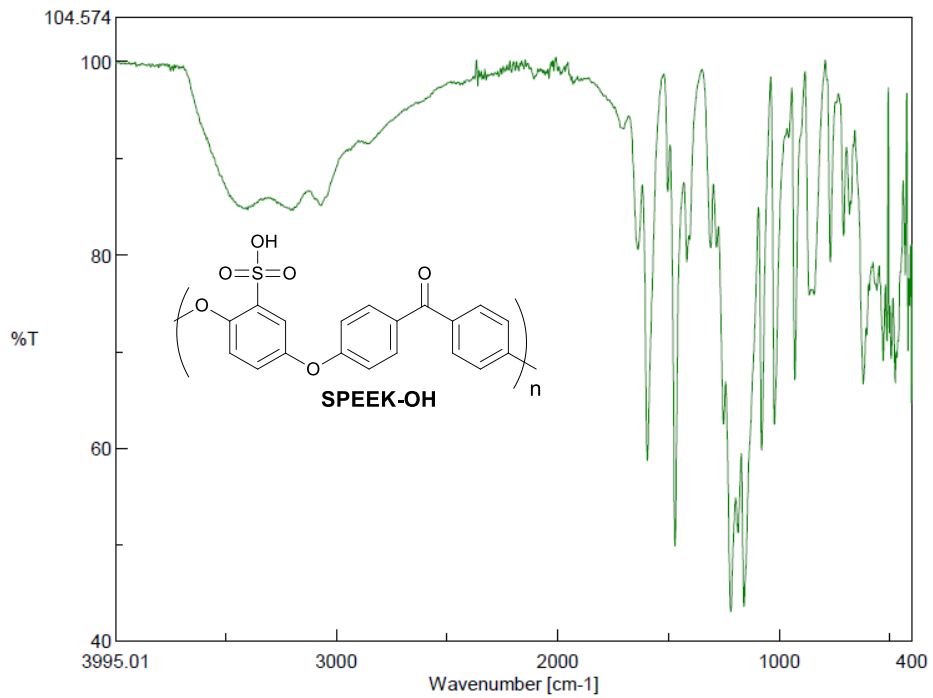




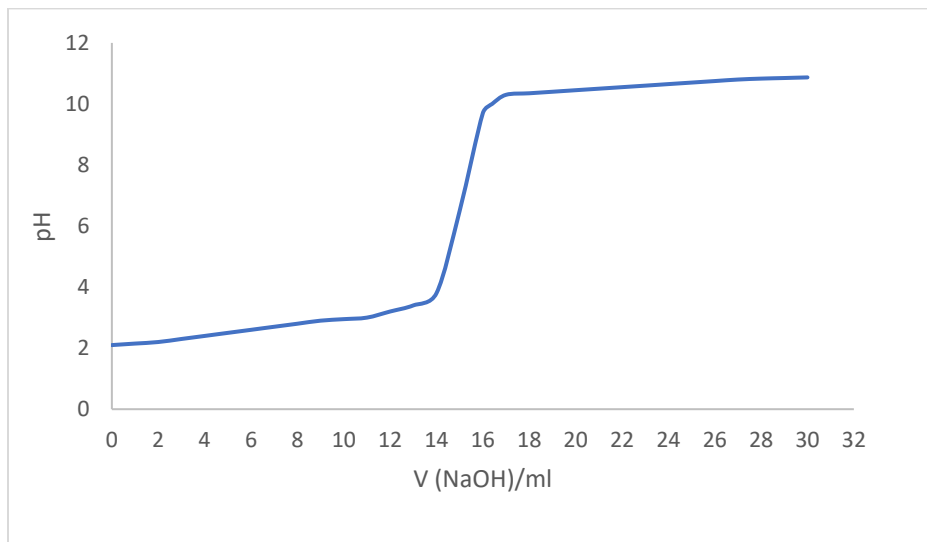
SPEEK-OH:

¹H RMN (400 MHz, DMSO-d₆): δ 7.84-7.72 (m, 4H), 7.51 (d, J = 2.3 Hz, 1H), 7.24-6.97 (m, 6H). IR (cm⁻¹): 3372, 1636, 1601, 1483, 1225, 1170, 1041, 930, 861.



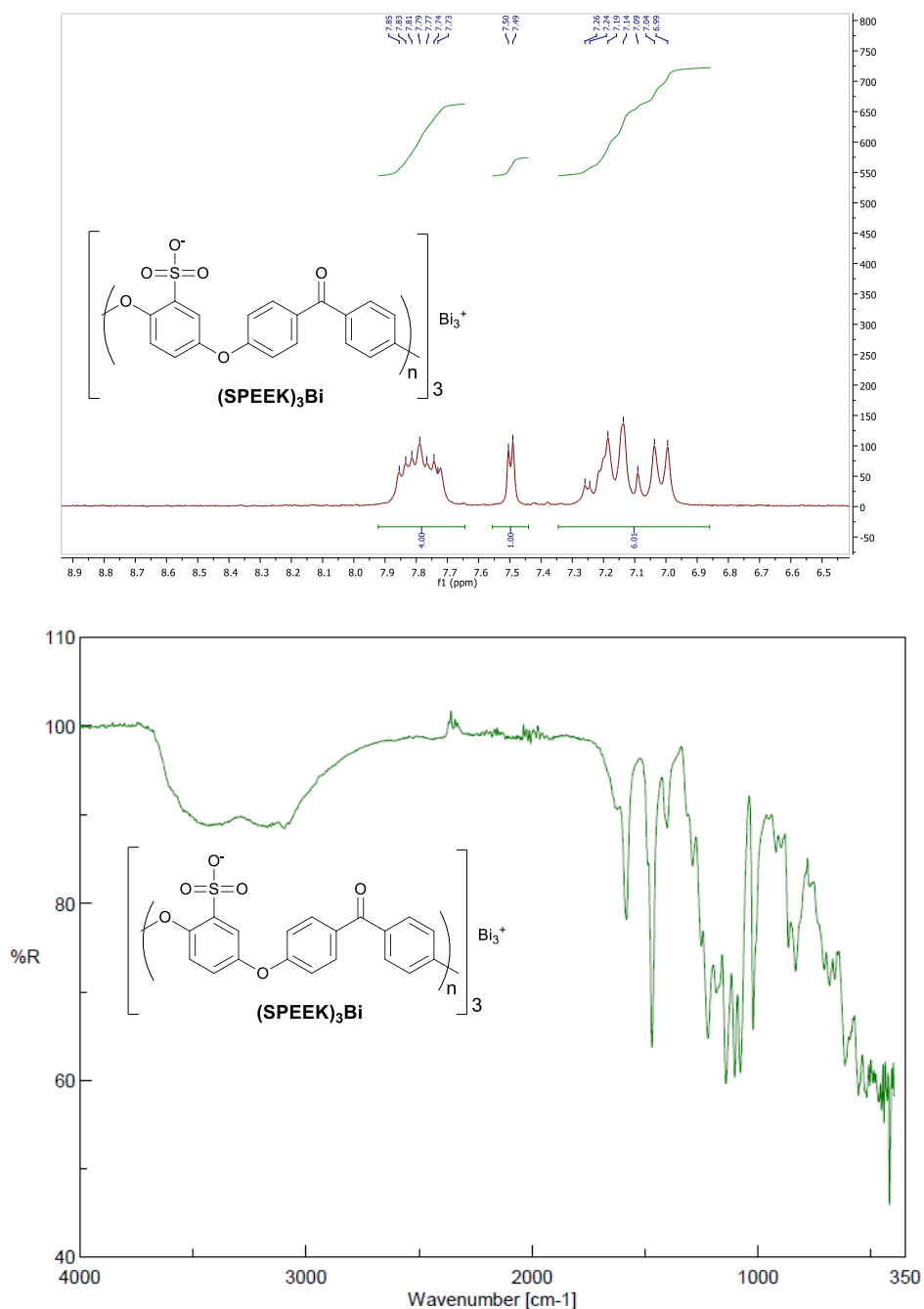


Acid-Base Titration of SPEEK-OH (51 mg, MW = 368 g/mol) in water (NaOH 0,01M):



One function RSO_3H by PEEK monomer

(SPEEK)₃Bi:

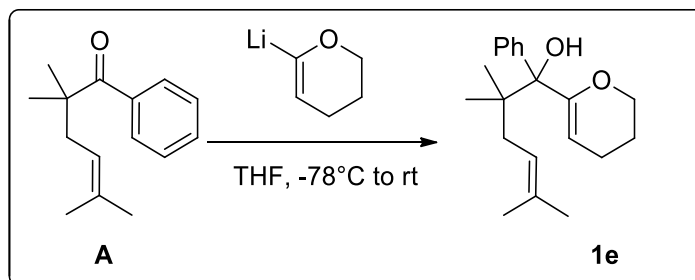


RMN ¹H (400 MHz, DMSO-d₆): 7,85 - 7,73 (m, 4H), 7,50 (d, 1H), 7,26 - 6,99 (m, 6H)
IR (cm⁻¹) : 1625, 1578, 1460, 1222, 1147, 1130, 1088, 1009, 872, 828.

2.1.2 Synthesis of dihydropyranyl derivatives 1a-l

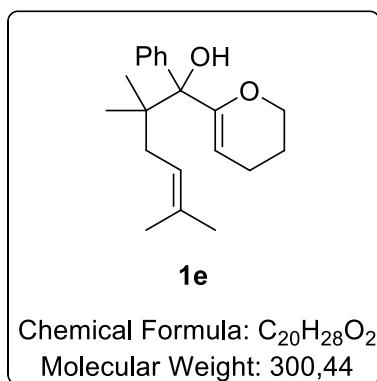
The starting dienols **1a-d**, **1f** and **1g-l** were prepared in agreement with those reported in the literature.²

Synthesis of 1-(3,4-dihydro-2H-pyran-6-yl)-2,2,5-trimethyl-1-phenylhex-4-en-1-ol (1e)



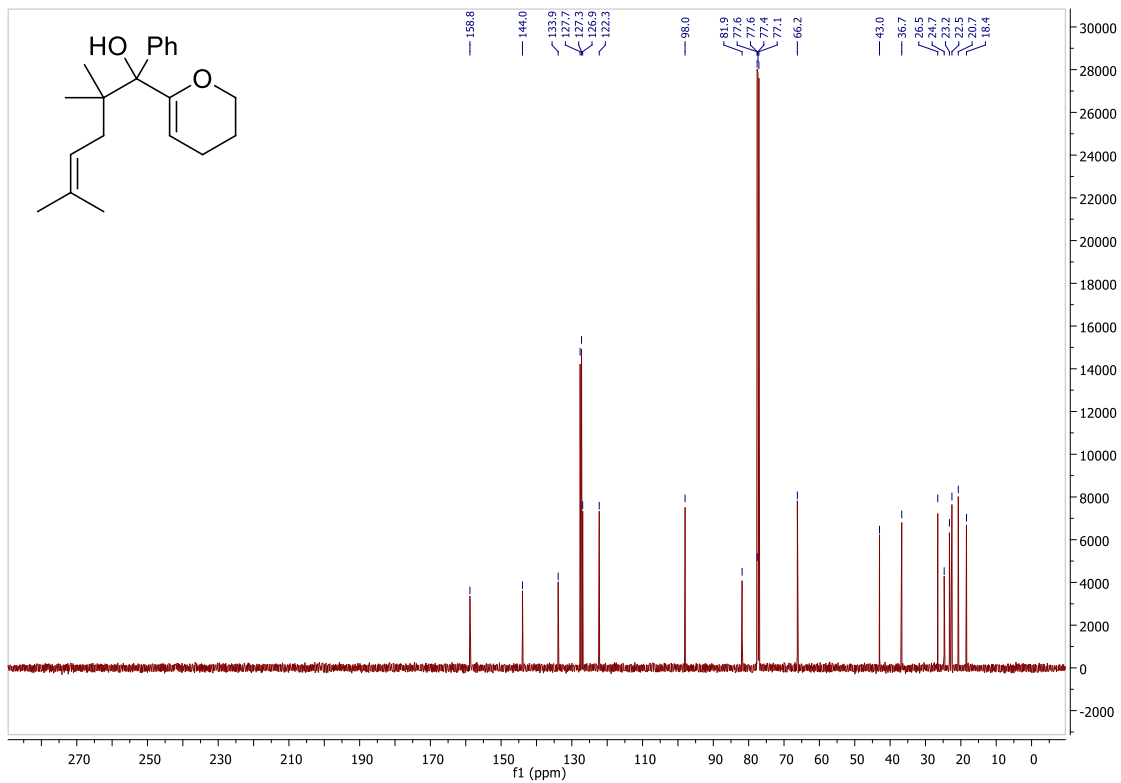
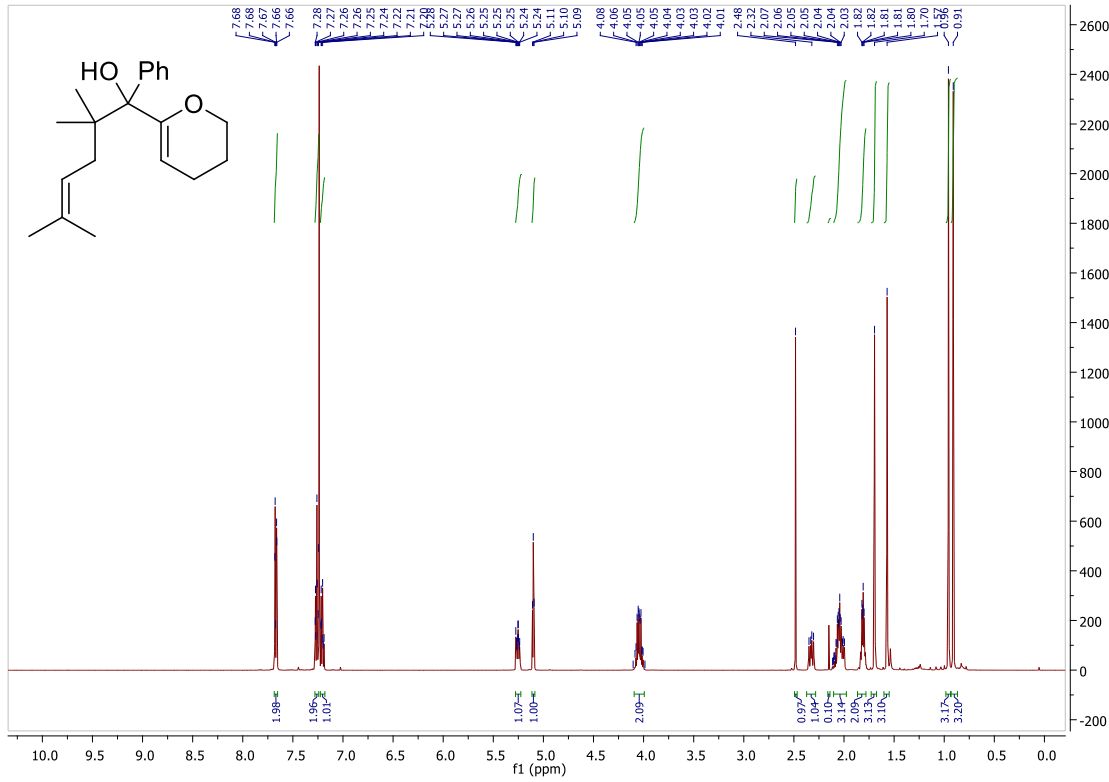
2,2,5-trimethyl-1-phenylhex-4-en-1-one **A** was prepared in agreement with those reported in the literature.³

To a 2 M solution of 3,4-dihydro-2H-pyran (1.2 eq. 0.48 g, 5.60 mmol, 0.47 mL) in anhydrous THF, *tert*-BuLi (1.9 M in pentane, 1.0 – 1.2 eq.) was added dropwise at -78 °C. The mixture was allowed to warm to -5 °C and stirred at this temperature for 3 hours, before being recooled to -78 °C, followed by addition of 2,2,5-trimethyl-1-phenylhex-4-en-1-one **A** (1.0 eq., 1.012 g, 4.68 mmol). The solution was slowly warmed to room temperature and stirred for an additional 2 – 3 hours. Then 5 mL of a saturated aqueous NH₄Cl solution were added, the forming precipitate was dissolved in water and the aqueous phase was extracted with ether (3 × 50 mL). The organic extracts were washed with brine, dried over MgSO₄ and the solvent was removed *in vacuo*. The residue was purified *via* flash column chromatography on Et₃N basified silica gel to afford **1e** in 53 % yield.



The crude product was isolated as a yellow oil (0.74 g, 2.48 mmol, 53%). **1e**: ¹H RMN (CDCl₃): 7.68-7.19 (m, 5H) 5.28-5.24 (t, 1H), 5.11-5.09 (t, 1H), 4.10-.99 (t, 2H), 2.48 (s, 1H, OH), 2.35-2.30 (m, 1H), 2.08-2.01 (q, 2H), 1.82-1.80 (m, 3H), 1.70 (s, 3H) 1.57 (s, 3H), 0.96 (s, 3H), 0.91(s, 3H). ¹³C RMN (50 MHz, CDCl₃): 158.8, 144.0, 133.9, 127.7, 127.3, 126.9, 122.3, 98.0, 81.9, 66.2, 48.0, 36.7, 26.5, 24.7, 23.2, 22.5, 20.7, 18.4. IR (neat): $\tilde{\nu}$ (cm⁻¹) = 3569 (b, OH), 2962 (m), 2930 (m), 2854 (m), 1667 (m), 1449 (m), 1069 (s), 915 (s), 766 (m), 706 (s). ESI-HRMS: m/z calcd. for C₂₀H₂₉O₂

[MH]⁺: 301.2162, found: 301.2161.



2.2 Cyclisation products 2a-h, 3i-l and 4i-l

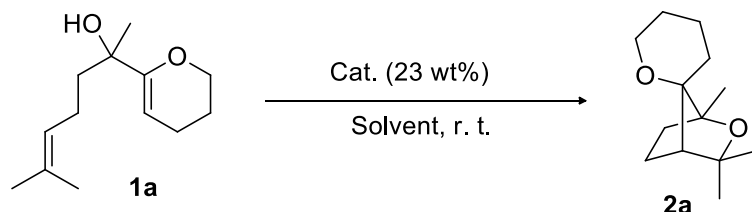
General procedure 1: Amberlyst-15 catalysed cyclisation reaction

Amberlyst-15 was added to a 0.1 M solution of the cyclisation precursor **1a-l** in MeCN at 20 °C and the reaction was followed by GC. Upon completion, the reaction was quenched by addition of a saturated aqueous NaHCO₃ solution. Amberlyst-15 was filtered off. The aqueous phase was extracted with CH₂Cl₂ and the combined organic extracts were washed with brine, dried over MgSO₄ and concentrated *in vacuo*. Purification by column chromatography afforded the corresponding products.

2.2.1 Solvent, temperature and dilution screening for the polycyclisation of **1a**

Influence of the solvent

Table 1. Solvent screening for the cyclisation of **1a** into **2a**.



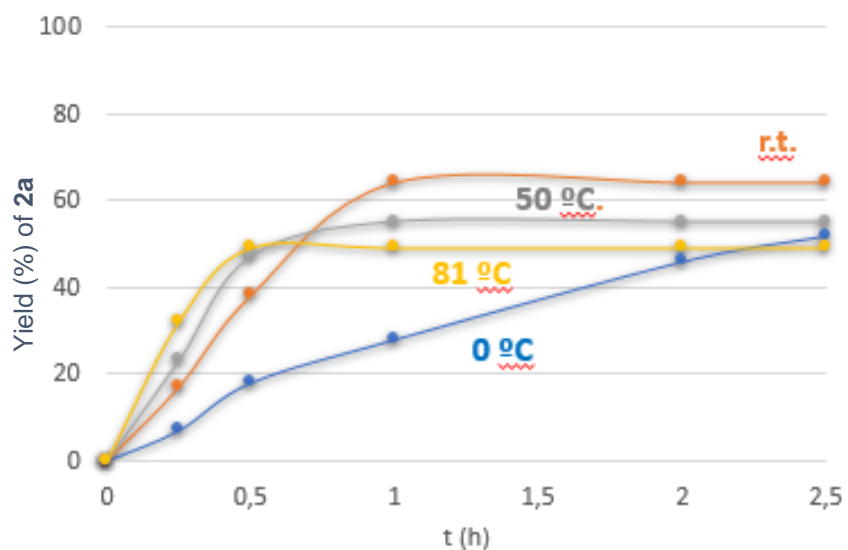
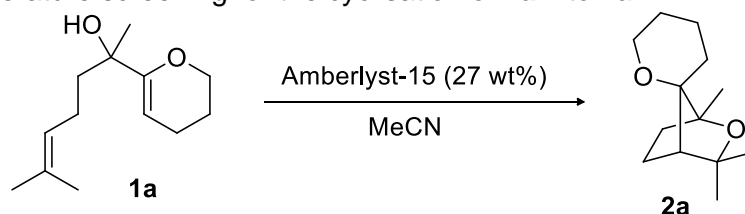
Solvent	t (h)	Conv. 1a	Yield 2a
(CH ₂) ₂ Cl ₂	1	> 95 %	51%
CH _x Cl ₂	1	> 95 %	50%
MeNO ₂	1	> 95 %	52%
Toluene	16	> 95 %	50%
Cyclohexane	16	> 95 %	50%
MeCN	1	> 95 %	63%
MeCN + 20 mol% DIPEA	16	No conversion	-
DMSO	16	No conversion	-

DMF	16	No conversion	-
1,4-dioxan	1	> 95 %	44 %
THF	1	> 95 %	37 %
NMP	16	No conversion	-
H ₂ O	16	No conversion	-

Conditions: Amberlyst-15 (23 wt% with respect to **1a**), 20 °C, [**1a**] = 0,1 M. GC-FID yields were determined using dodecane as internal standard.

Influence of the temperature

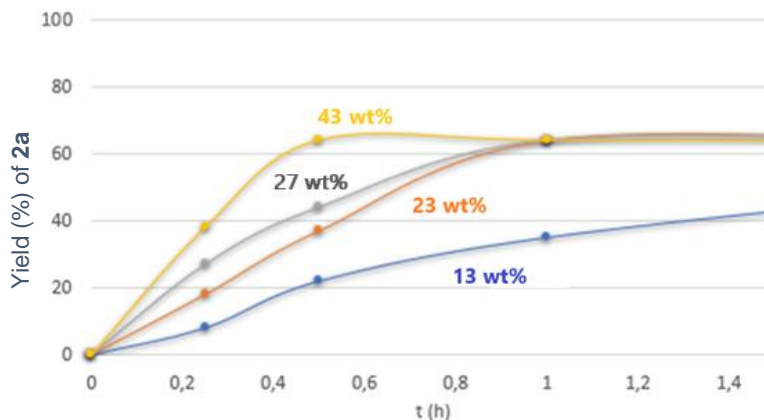
Figure 1. Temperature screening for the cyclisation of **1a** into **2a**.



[**1**] = 0.1M, 27 wt% of Amberlyst-15 with respect to **1a**, MeCN.

Influence of the amount of Amberlyst-15

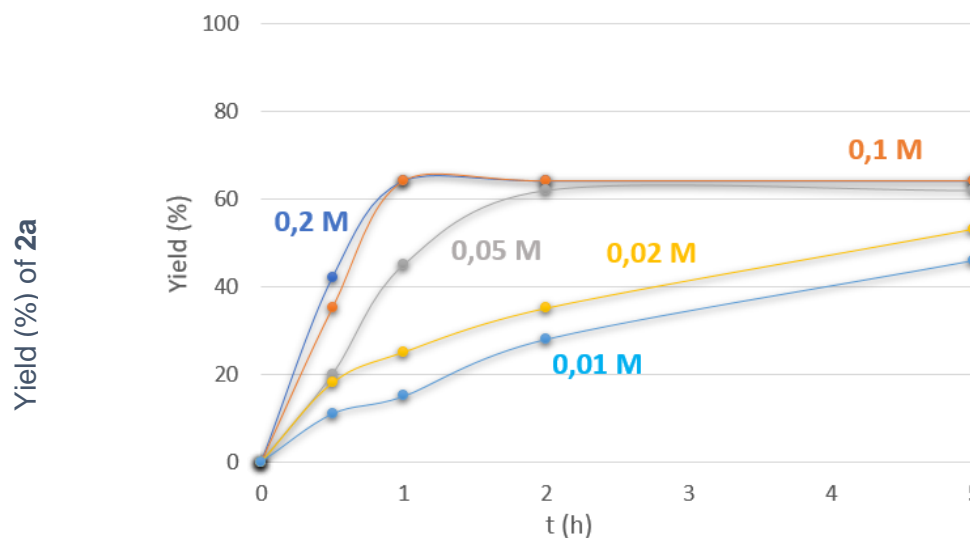
Figure 2. Influence of the catalyst ratio in the cyclisation of **1a** into **2a**.



Conditions: Amberlyst-15 (wt% according to **1a**), **[1]** = 0.1M, 20 °C, MeCN. GC-FID yields were determined using dodecane as internal standard.

Influence of the concentration of **1**

Figure 3. Influence of the concentration of **[1a]**.

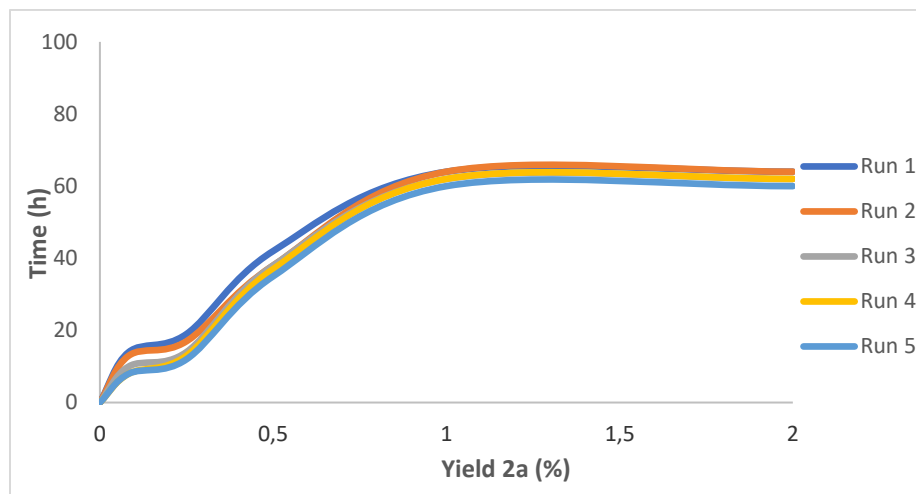


Conditions: Amberlyst-15 (27 wt% with respect to **1a**), 20 °C, MeCN. GC-FID yields were determined using dodecane as internal standard.

Recycling Amberlyst-15 kinetic studies

Recycling Amberlyst-15 Procedure: After cycloisomerisation process, Amberlyst-15 was filtered off, washed with 1N HCl in water, with ethanol 96 %, dried at 101 °C during several hours and reused

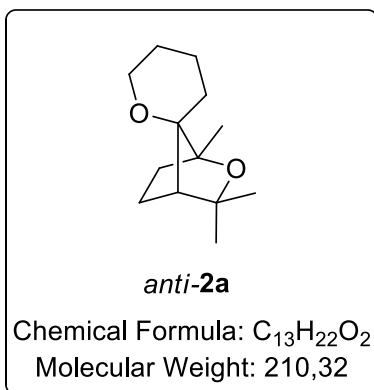
Figure 4. Catalyst recycling test for the polycyclisation of **1a**.



Conditions: MeCN, 20 °C, [1a] = 0.1 M, 27 wt% of Amberlyst-15 with respect to 1a.

2.2.2 Cyclisation products 2a-h

(±)-(1S,4S,7S)-1,3,3-trimethyltetrahydro-2-oxaspiro[bicyclo[2.2.1]heptane-7,2'-pyran] (*anti*-2a)

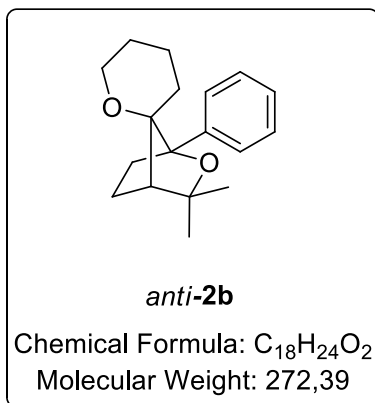


Compound *anti*-2a was synthesized according to **general procedure 1** starting from dienol **1a** (100 mg, 0.47 mmol) in MeCN at room temperature, Amberlyst-15 (27 wt% with respect to **1a**, 0.12 mmol, 37 mg) were added and the mixture was stirred for 1 h. Purification by flash chromatography (PE:Et₂O = 95:5) afforded *anti*-2a (64 mg, 0.30 mmol, 64%) as a pale yellow oil. **¹H-NMR** (500 MHz, CDCl₃): δ [ppm] = 1.03 (s, 3H), 1.20 (s, 3H), 1.21 (s, 3H), 1.46-1.49 (m, 1H), 1.51-1.64 (m, 6H), 1.69- 1.74 (m, 1H), 1.78-1.81 (m, 1H), 2.09-2.11 (m, 1H), 2.33 (bs, 1H), 3.38-3.43 (m_c, 1H), 3.74-3.77 (m, 1H). **¹³C-NMR** (125 MHz,

CDCl₃): δ [ppm] = 15.2, 21.0, 21.3, 26.5, 27.2, 29.2, 29.2, 33.9, 47.0, 64.8, 77.4, 85.3, 86.9.

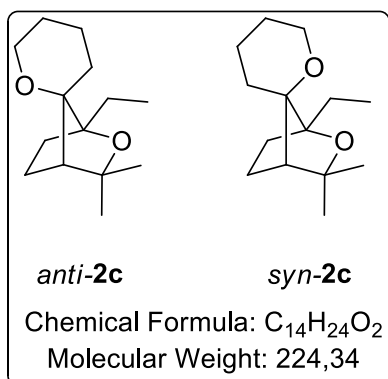
IR (neat): $\tilde{\nu}$ (cm⁻¹) = 2695 (m), 2932 (m), 2857 (w), 1442 (w), 1376 (m), 1200 (m), 1178 (m), 1100 (s), 1074 (s), 989 (s), 909 (s). **APGC-HRMS**: *m/z* calcd. for C₁₃H₂₂O₂ [M]⁺: 210.1624, found: 210.1624. **CAS number**: 2093246-02-5. The experimental data are in accordance with those reported in the literature.¹ **¹H-NMR** (200 MHz, CDCl₃): δ [ppm] = 1.28 (s, 3H), 1.55 (bs, 3H), 1.68 (bs, 3H), 1.55-2.09 (m, 8H), 2.13 (bs, 1H, OH), 4.00 (t, ³J = 5.1 Hz, 2H), 4.79 (t, ³J = 3.8 Hz, 1H), 5.09-5.16 (m_c, 1H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 17.6, 20.0, 22.4, 23.1, 25.7, 25.8, 40.2, 66.3, 73.6, 94.1, 124.5, 131.7, 157.2. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 3464 (b, OH), 2967 (m), 2927 (m), 2850 (m), 1670 (m), 1985 (s), 918 (s). **ESI-HRMS**: *m/z* calcd. for C₁₃H₂₃O₂ [MH]⁺: 211.1693, found: 211.1693. **CAS number**: 1972655-81-4. The experimental data are in agreement with those reported in the literature.²

(±)-(1R,4S,7S)-3,3-dimethyl-1-phenyltetrahydro-2-oxaspiro[bicyclo[2.2.1]heptane-7,2'-pyran] (*anti*-2b)



Compound *anti*-2b was synthesized according to **general procedure 1** starting from dienol **1b** (102 mg, 0.37 mmol) in MeCN at room temperature, Amberlyst-15 (27 wt% with respect to **1b**, 0.09 mmol, 29.43 mg) was added and the mixture was stirred for 4 h. Purification by flash chromatography (PE:Et₂O = 95:5) afforded *anti*-2b (69 mg, 0.26 mmol, 69%) as a white solid. **¹H-NMR** (200 MHz, CDCl₃): δ [ppm] = 7.55 – 7.37 (m, 2H), 7.34 – 7.09 (m, 3H), 3.85 – 3.70 (m, 1H), 3.55 – 3.31 (m, 1H), 2.55 – 2.49 (m, 1H), 2.40 – 2.19 (m, 1H), 2.10 – 1.66 (m, 4H), 1.66 – 1.36 (m, 4H), 1.30 (s, 6H), 1.13 – 0.92 (m, 1H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 139.34, 127.68, 126.76, 126.27, 88.77, 88.53, 77.67, 64.73, 48.43, 35.49, 29.70, 29.51, 27.80, 26.35, 22.12, 21.00. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 2965 (w), 2938 (m), 2859 (w), 1444 (w), 1276 (w), 1092 (m), 1075 (m), 1034 (s), 759 (s), 699 (s). **ESI-HRMS**: *m/z* calcd. for C₁₈H₂₅O₂ [MH]⁺: 273.1855, found: 273.1841. **CAS number**: 1972656-08-8. The experimental data are in agreement with those reported in the literature.²

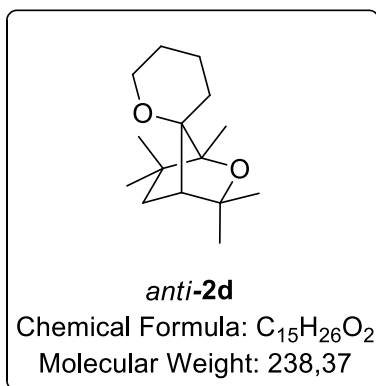
(±)-(1S,4S,7S)-1-ethyl-3,3-dimethyltetrahydro-2-oxaspiro[bicyclo[2.2.1]heptane-7,2'-pyran] (*anti*-2c) and (±)-(1S,4S,7R)-1-ethyl-3,3-dimethyltetrahydro-2-oxaspiro[bicyclo[2.2.1]heptane-7,2'-pyran] (*syn*-2c)



Compounds **2c** were synthesized according to **general procedure 1** starting from dienol **1c** (101 mg, 0.45 mmol) in MeCN at room temperature, Amberlyst-15 (27 wt% with respect to **1c**, 0.11 mmol, 35.4 mg) was added and the mixture was stirred for 2 h. Purification by flash chromatography (PE:Et₂O = 95:5) afforded *anti*-2c (56 mg, 0.25 mmol, 59%) as a pale yellow oil and *syn*-2c (3 mg, 0.013 mmol, 5%) as white crystals. ***Anti*-2c**: **¹H-NMR** (200 MHz, CDCl₃): δ [ppm] = 3.96 – 3.81 (m, 1H), 3.63 – 3.43 (m, 1H), 2.48 (s, 1H), 2.31 – 2.15 (m, 1H), 1.99 – 1.49 (m, 11H), 1.35 (s, 3H), 1.33 (s, 3H), 1.01 (t, ³*J* = 7.5 Hz, 3H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 88.1, 87.43, 77.36, 64.75, 47.19, 30.59, 29.29, 29.26, 27.35, 26.62, 23.02, 21.14, 21.09, 8.69. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 2962 (m), 2934 (m), 2361 (w), 1456 (m), 1377 (m), 1273 (m), 1195 (m), 1175 (m), 1100 (s), 1076 (s), 1042 (s), 973 (s), 910 (s), 884 (s), 856 (s). **CAS number**: 1972656-05-5. ***Syn*-2c**: **¹H-NMR** (200 MHz, CDCl₃): δ [ppm] = 3.92 – 3.76 (m, 1H), 3.53 (td, ³*J* = 11.4, 3.4 Hz, 1H), 2.32 (d, ³*J* = 3.0 Hz, 1H), 1.90 – 1.34 (m, 12H), 1.38 (s, 3H), 1.26 (s, 3H), 0.93 (t, ³*J* = 7.5 Hz, 3H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 88.91, 88.04, 78.75, 64.91, 44.94, 29.95, 28.79, 27.99, 26.50, 22.50, 21.72, 20.95, 8.84. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 2955 (s), 2929 (s), 2849 (m), 2362 (m), 1438 (w), 1354 (w), 1239 (m), 1104 (s), 1078 (s), 1051 (s), 972 (s), 917 (s). **APGC-HRMS**: *m/z* calcd. for C₁₄H₂₅O₂ [M]⁺: 224.1776, found:

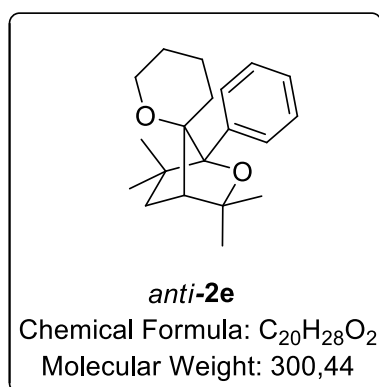
224.1776. **CAS number:** 1972656-04-4. The experimental data are in agreement with those reported in the literature.²

(±)-(1S,4S,7S)-1,3,3,6,6-pentamethyltetrahydro-2-oxaspiro[bicyclo[2.2.1]heptane-7,2'-pyran] (*anti*-2d)

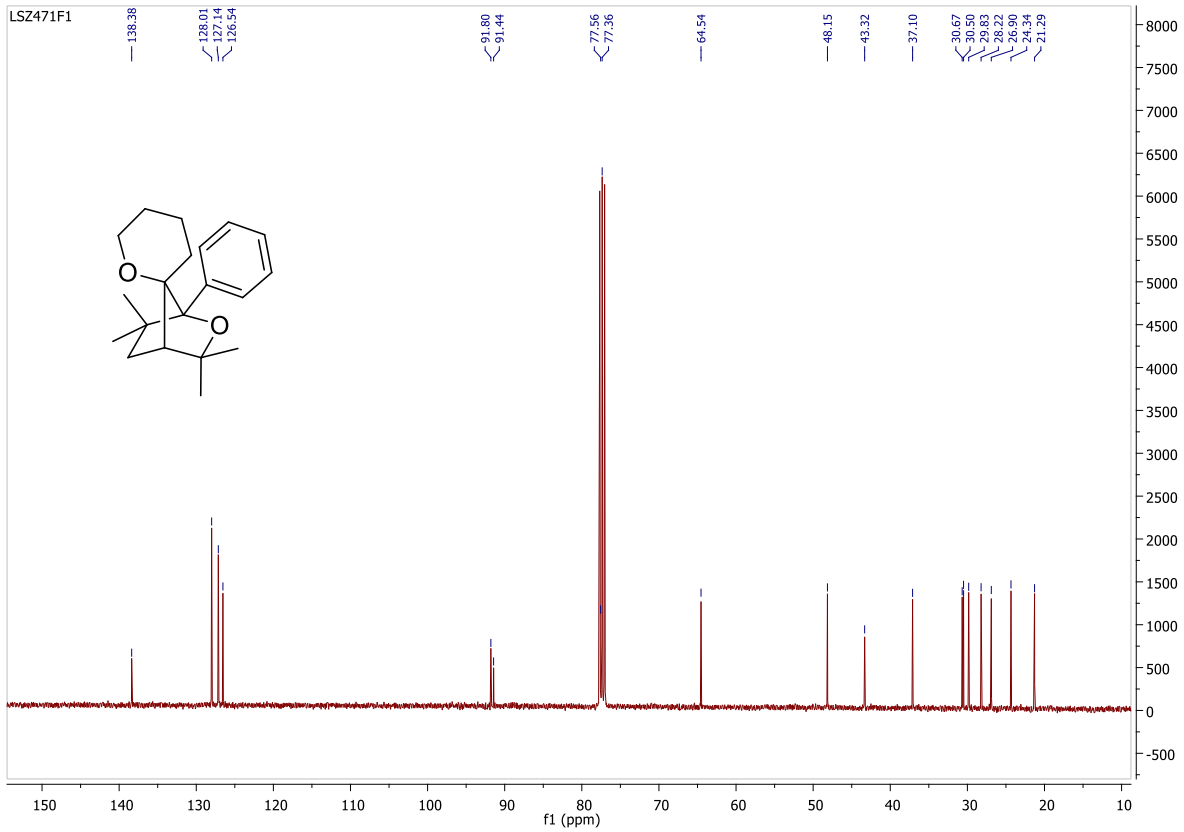
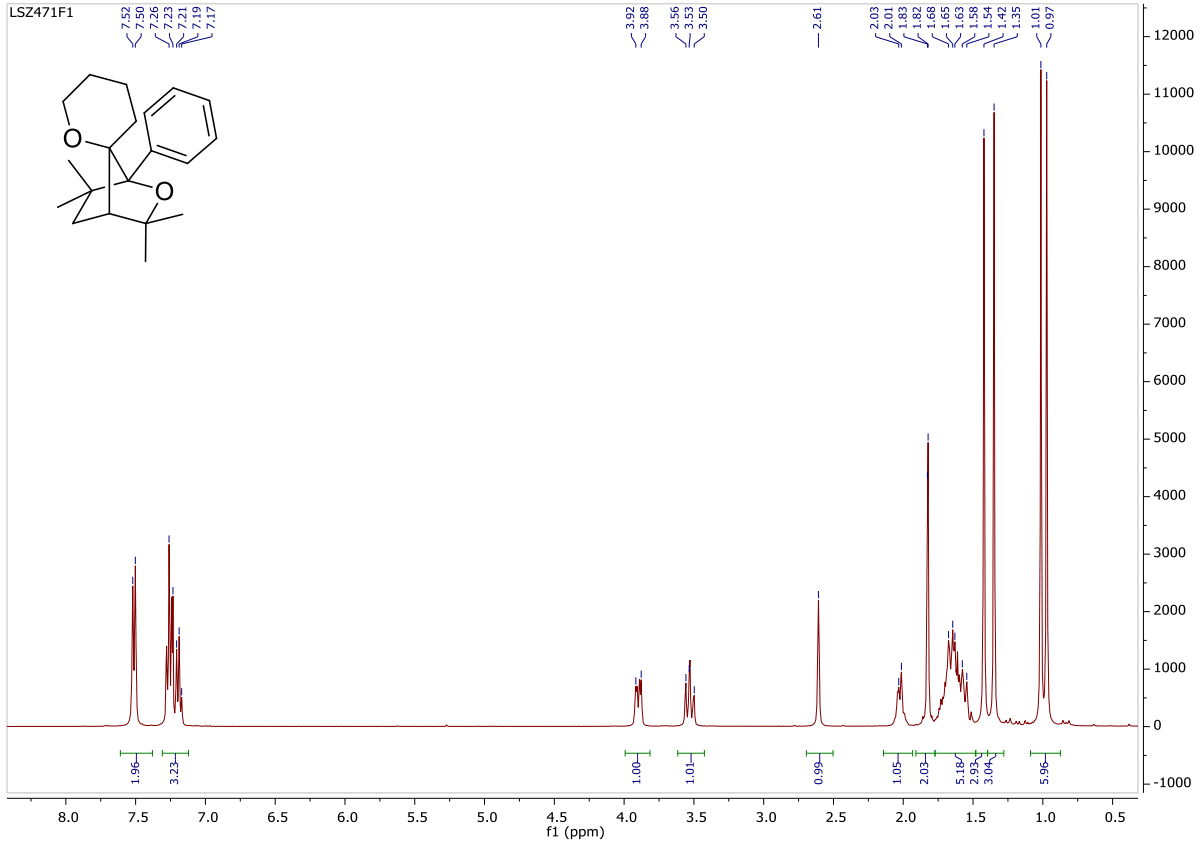


Compound *anti*-2d was synthesized according to **general procedure 1** starting from dienol **1d** (102 mg, 0.43 mmol) in MeCN at room temperature, Amberlyst-15 (27 wt% with respect to **1d**, 0.11 mmol, 33.5 mg) was added and the mixture was stirred for 4 h. Purification by flash chromatography (PE:Et₂O = 95:5) afforded *anti*-2d (59 mg, 0.25 mmol, 58%) as a pale yellow oil. **¹H-NMR** (200 MHz, CDCl₃): δ [ppm] = 3.89 – 3.72 (m, 1H), 3.57 – 3.37 (m, 1H), 2.43 (t, ³J = 2.3 Hz, 1H), 2.27 – 2.15 (m, 1H), 1.86 – 1.51 (m, 7H), 1.32 (s, 3H), 1.31 (s, 3H), 1.12 (s, 3H), 1.10 (s, 3H), 0.97 (s, 3H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 89.52, 88.77, 77.54, 64.25, 47.60, 40.99, 36.57, 30.13, 29.60, 29.12, 27.85, 26.56, 24.33, 21.08, 11.39. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 2934 (m), 2860 (w), 1447 (w), 1375 (m), 1042 (m), 1092 (s), 1082 (s), 1071 (s), 987 (s). **APGC-HRMS**: *m/z* calcd. for C₁₅H₂₇O₂ [MH]⁺: 239.2006, found: 239.2006. **CAS number:** 2093246-03-6. The experimental data are in agreement with those reported in the literature.²

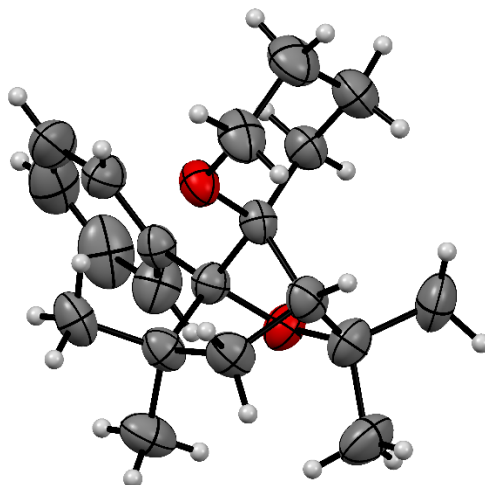
(±)-(1R,2'S,4S)-3,3,6,6-tetramethyl-1-phenyltetrahydro-2-oxaspiro[bicyclo[2.2.1]heptane-7,2'-pyran] (*anti*-2e)



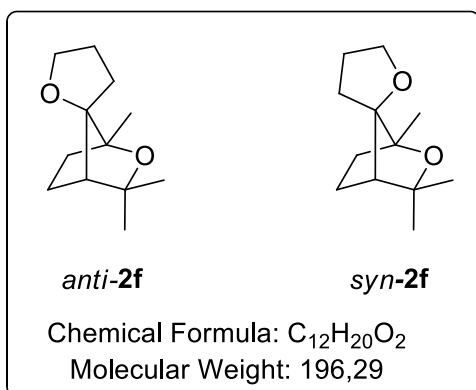
Compound *anti*-2e was synthesized according to **general procedure 1** starting from dienol **1e** (100 mg, 0.33 mmol) in MeCN at room temperature, Amberlyst-15 (27 wt% with respect to **1e**, 0.08 mmol, 26.16 mg) was added and the mixture was stirred for 2 h. Purification by flash chromatography (PE/Et₂O = 95:5) afforded *anti*-2e (72 mg, 0.24 mmol, 72%) as a white solid. **TLC**: R_f = 0.78 (PE/ Et₂O = 95:5), [*p*-anisaldehyde]. **¹H-NMR** (400 MHz, CDCl₃): δ [ppm] = 7.52 – 7.50 (m, 2H), 7.33 – 7.26 (m, 2H), 7.24 – 7.17 (m, 1H), 3.92 – 3.88 (m, 1H), 3.56-3.50 (m, 1H), 2.61 (s, 1H), 2.03 – 2.01 (m, 1H), 1.83-1.82 (d, 2H), 1.68 – 1.54 (m, 5H), 1.42 (s, 3H), 1.35 (s, 3H), 1.01 (s, 3H), 0.97 (s, 3H). **¹³C-NMR** (125 MHz, CDCl₃): δ [ppm] = 138.4, 128.0, 127.1, 126.5, 91.8, 91.4, 64.5, 48.1, 43.3, 37.1, 30.7, 30.5, 29.8, 28.2, 26.9, 24.3, 21.3. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 2960 (w), 2942 (m), 2863 (w), 1450 (w), 1271 (w), 1090 (m), 1077 (m), 1037 (s), 760 (s), 703 (s). **ESI-HRMS**: *m/z* calcd. for C₂₀H₂₉O₂ [MH]⁺: 301.2162, found: 301.2161.



X-ray crystal structure of *anti-2e* (CCDC number 1979084)

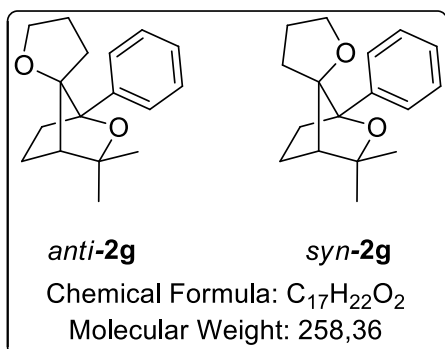


(±)-1*S*,4*S*,7*S*)-1,3,3-trimethyldihydro-3'-*H*-2-oxaspiro[bicyclo[2.2.1]heptane-7,2'-furan] (*anti-2f*) and (±)-1*S*,4*S*,7*R*)-1,3,3-trimethyldihydro-3'-*H*-2-oxaspiro[bicyclo[2.2.1]heptane-7,2'-furan] (*syn-2f*)



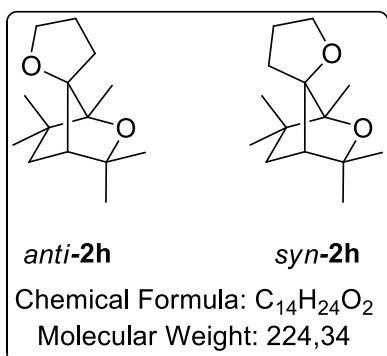
Compounds **2f** were synthesized according to **general procedure 1** starting from dienol **1f** (103 mg, 0.52 mmol) in MeCN at room temperature, Amberlyst-15 (27 wt% with respect to **1f**, 0.13 mmol, 41.2 mg) was added and the mixture was stirred for 2 h. Purification by flash chromatography (PE:Et₂O = 95:5) afforded *anti-2f* (22.1 mg, 0.115 mmol, 22%) as a pale yellow oil and *syn-2f* (52.5 mg, 0.267 mmol, 51%) as a pale yellow oil. *Anti-2f*: ¹H-NMR (500 MHz, CDCl₃): δ [ppm] = 1.07 (s, 3H), 1.22 (s, 3H), 1.25 (s, 3H), 1.48-1.55 (m, 1H), 1.69-1.78 (m, 3H), 1.84-2.05 (m, 4H), 2.22-2.26 (m, 1H), 3.65-3.70 (m, 1H), 3.88-3.91 (m, 1H). ¹³C-NMR (125 MHz, CDCl₃): δ [ppm] = 15.8, 23.1, 27.1, 28.2, 28.4, 29.6, 34.0, 52.6, 67.1, 77.7, 84.8, 94.2. IR (neat): $\tilde{\nu}$ (cm⁻¹) = 2965 (m), 2932 (w), 2871 (w), 1460 (w), 1377 (m), 1175 (m), 1080 (s), 917 (m). **APGC-HRMS**: *m/z* calcd. for C₁₂H₂₁O₂[MH]⁺: 197.1542, found: 197.1532. **CAS number**: 1972656-01-1. *Syn-2f*: ¹H-NMR (500 MHz, CDCl₃): δ [ppm] = 1.12 (s, 3H), 1.25 (s, 3H), 1.43 (s, 3H), 1.45-1.50 (m, 1H), 1.52-1.58 (m, 2H), 1.71-1.78 (m, 3H), 1.80-1.92 (m, 2H), 1.95-2.01 (dt, ³J = 12.4 Hz, 8.1 Hz, 1H), 3.78-3.82 (dt, ³J = 6.6 Hz, 8.1 Hz, 1H), 3.95-3.99 (m, 1H). ¹³C-NMR (125 MHz, CDCl₃): δ [ppm] = 15.3, 21.4, 25.9, 28.1, 28.5, 29.6, 33.1, 51.0, 68.2, 79.3, 85.0, 94.8. IR (neat): $\tilde{\nu}$ (cm⁻¹) = 2965 (m), 2929 (m), 2860 (w), 1457 (w), 1375 (m), 1240 (w), 1121 (w), 1090 (s), 1059 (s), 914 (s). **APGC-HRMS**: *m/z* calcd. for C₁₂H₁₉O₂ [M-H]⁺: 195.1385, found: 195.1398. **CAS number**: 1972656-00-0. The experimental data are in agreement with those reported in the literature.²

(±)-(1R,4S,7S)-3,3-dimethyl-1-phenyldihydro-3'H-2-oxaspiro[bicyclo[2.2.1]heptane-7,2'-furan] (*anti*-2g) and (±)-(1R,4S,7R)-3,3-dimethyl-1-phenyldihydro-3'H-2-oxaspiro[bicyclo[2.2.1]heptane-7,2'-furan] (*syn*-2g)



Compounds **2g** were synthesized according to **general procedure 1** starting from dienol **1g** (101 mg, 0.39 mmol) in MeCN at room temperature, Amberlyst-15 (27 wt% with respect to **1g**, 0.10 mmol, 30.73 mg) was added and the mixture was stirred for 2 h. Purification by flash chromatography (PE:Et₂O = 95:5) afforded *anti*-**2g** (21 mg, 0.081 mmol, 21%) as a pale yellow oil and *syn*-**2g** (63 mg, 0.24 mmol, 62%) as white crystals. *Anti*-**2g**: ¹H-NMR (200 MHz, CDCl₃): δ [ppm] = 7.57 – 7.48 (m, 2H), 7.36 – 7.23 (m, 3H), 3.84 – 3.73 (m, 1H), 3.66 – 3.48 (m, 1H), 2.56 – 2.39 (m, 1H), 2.28 – 1.71 (m, 6H), 1.65 – 1.45 (m, 1H), 1.38 (s, 3H), 1.35 (s, 3H), 0.82 – 0.50 (m, 1H). ¹³C-NMR (50 MHz, CDCl₃): δ [ppm] = 139.15, 127.72, 126.89, 125.72, 96.58, 87.50, 77.94, 67.58, 54.31, 34.71, 30.07, 28.49, 28.41, 26.24, 23.67. IR (neat): $\tilde{\nu}$ (cm⁻¹) = 2968 (m), 2941 (m), 1446 (w), 1271 (w), 1079 (s), 1032 (m), 984 (m), 849 (m), 758 (s), 699 (s). CAS number: 1972656-09-9. *Syn*-**2g**: ¹H-NMR (200 MHz, CDCl₃): δ [ppm] = 7.62 – 7.52 (m, 2H), 7.36 – 7.20 (m, 3H), 3.67 (dt, ³J = 8.1, 7.1 Hz, 1H), 3.42 – 3.29 (m, 1H), 2.44 – 2.28 (m, 1H), 2.07 – 1.52 (m, 10H), 1.38 – 1.33 (m, 3H), 1.26 – 1.10 (m, 1H). ¹³C-NMR (50 MHz, CDCl₃): δ [ppm] = 138.19, 127.81, 127.33, 126.99, 96.59, 87.70, 80.04, 68.19, 52.96, 30.98, 29.85, 28.50, 28.25, 25.01, 21.43. IR (neat): $\tilde{\nu}$ (cm⁻¹) = 2969 (m), 2925 (w), 2862 (w), 1446 (m), 1377 (m), 1084 (m), 1037 (m), 981 (m), 967 (s), 757 (s), 698 (s). APGC-HRMS: *m/z* calcd. for C₁₇H₂₂O₂ [M]⁺: 258.1624, found: 258.1623. CAS number: 1972656-10-2. The experimental data are in accordance with those reported in the literature.²

(±)-(1S,4S,7S)-1,3,3,6,6-pentamethyldihydro-3'H-2-oxaspiro[bicyclo[2.2.1]heptane-7,2'-furan] (*anti*-2h) and (±)-(1S,4S,7R)-1,3,3,6,6-pentamethyldihydro-3'H-2-oxaspiro[bicyclo[2.2.1]heptane-7,2'-furan] (*syn*-2h).

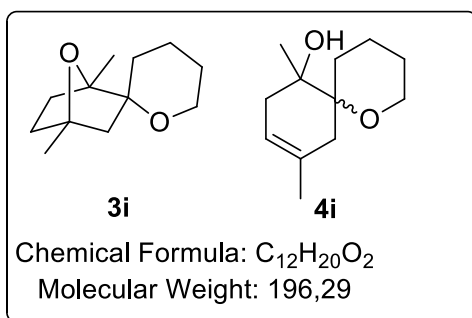


Compounds **2h** were synthesized according to **general procedure 1** starting from dienol **1h** (102 mg, 0.45 mmol) in MeCN at room temperature, Amberlyst-15 (27 wt% with respect to **1h**, 11.4 mmol, 35.7 mg) was added and the mixture was stirred for 2 h. Purification by flash chromatography (PE:Et₂O = 95:5) afforded *anti*-**2h** (17 mg, 0.076 mmol, 17%) as a pale yellow oil and *syn*-**2h** (51 mg, 0.228 mmol, 50%) as a pale yellow oil. *Anti*-**2h**: ¹H-NMR (200 MHz, CDCl₃): δ [ppm] = 3.97 – 3.78 (m, 1H), 3.78 – 3.62 (m, 1H), 2.43 – 2.23 (m, 1H), 2.14 – 1.62 (m, 6H), 1.30 (s, 6H), 1.12 (s, 3H), 1.10 (s, 3H), 0.97 (s, 3H). ¹³C-NMR (50 MHz, CDCl₃): δ [ppm] = 96.29, 87.81, 77.62, 65.84, 52.92, 41.02, 38.24, 31.80, 29.36, 28.69, 26.75, 26.30, 24.12, 11.77. IR (neat): $\tilde{\nu}$ (cm⁻¹) = 2964 (m), 2865 (w), 1451 (w), 1379 (m), 1159 (w), 1077 (s), 978 (w),

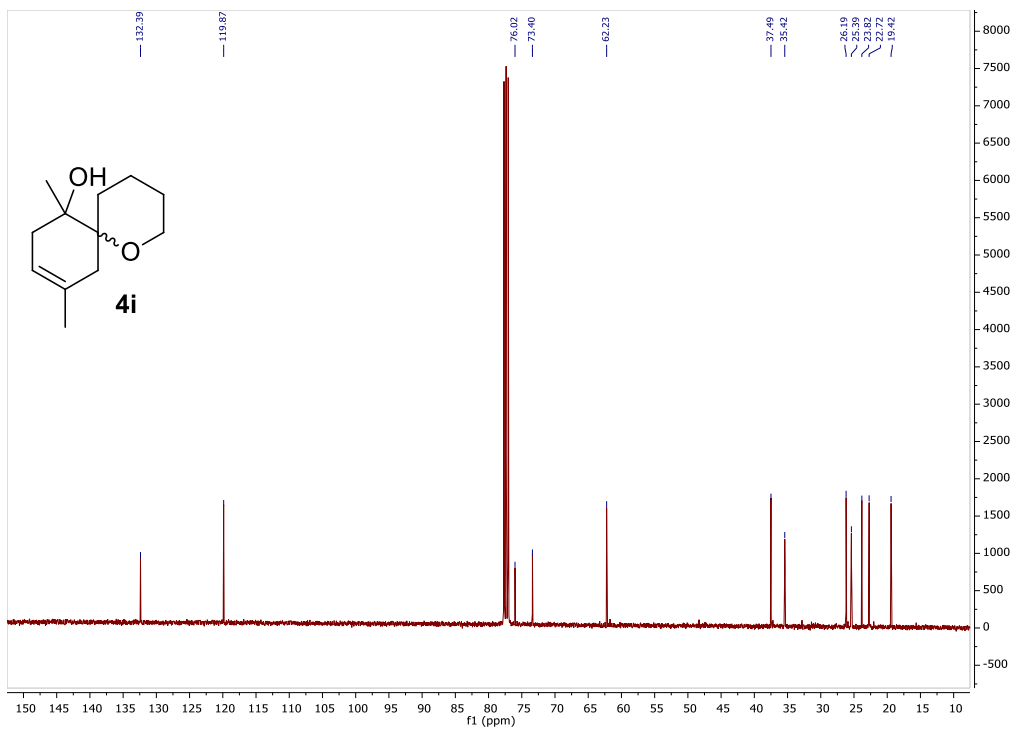
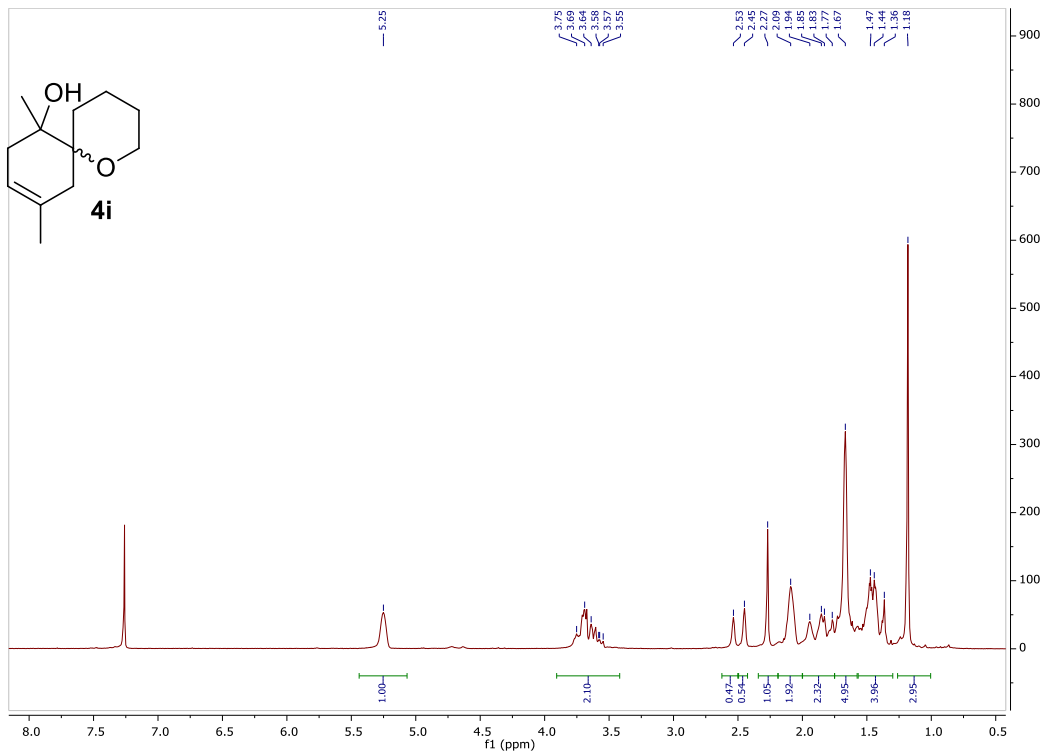
926 (m), 896 (m). **CAS number:** 1972656-13-5. *Syn-2h*: **¹H-NMR** (200 MHz, CDCl₃): δ [ppm] = 3.87 – 3.67 (m, 2H), 2.10 – 1.86 (m, 3H), 1.85 – 1.66 (m, 3H), 1.46 (s, 3H), 1.42 – 1.32 (m, 1H), 1.31 (s, 3H), 1.12 (s, 3H), 1.01 (s, 3H), 0.94 (s, 3H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 95.30, 89.21, 79.24, 65.17, 49.73, 38.88, 37.31, 31.06, 29.35, 28.25, 26.82, 26.07, 24.38, 10.35. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 2955 (m), 2858 (w), 1467 (w), 1374 (m), 1080 (s), 1054 (m), 885 (m). **APGC-HRMS:** *m/z* calcd. for C₁₄H₂₅O₂ [MH]⁺: 225.1855, found: 225.1855. **CAS number:** 1972656-12-4. The experimental data are in agreement with those reported in the literature.²

2.2.3 Cyclisation products 3i-l and 4i-l

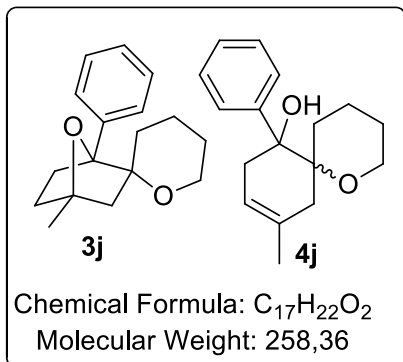
(±)-(1R,2R,4R)-1,4-dimethyltetrahydro-7-oxaspiro[bicyclo[2.2.1]heptane-2,2'-pyran] (**3i**) and (±)-7,10-dimethyl-1-oxaspiro[5.5]undec-9-en-7-ol (**4i**)



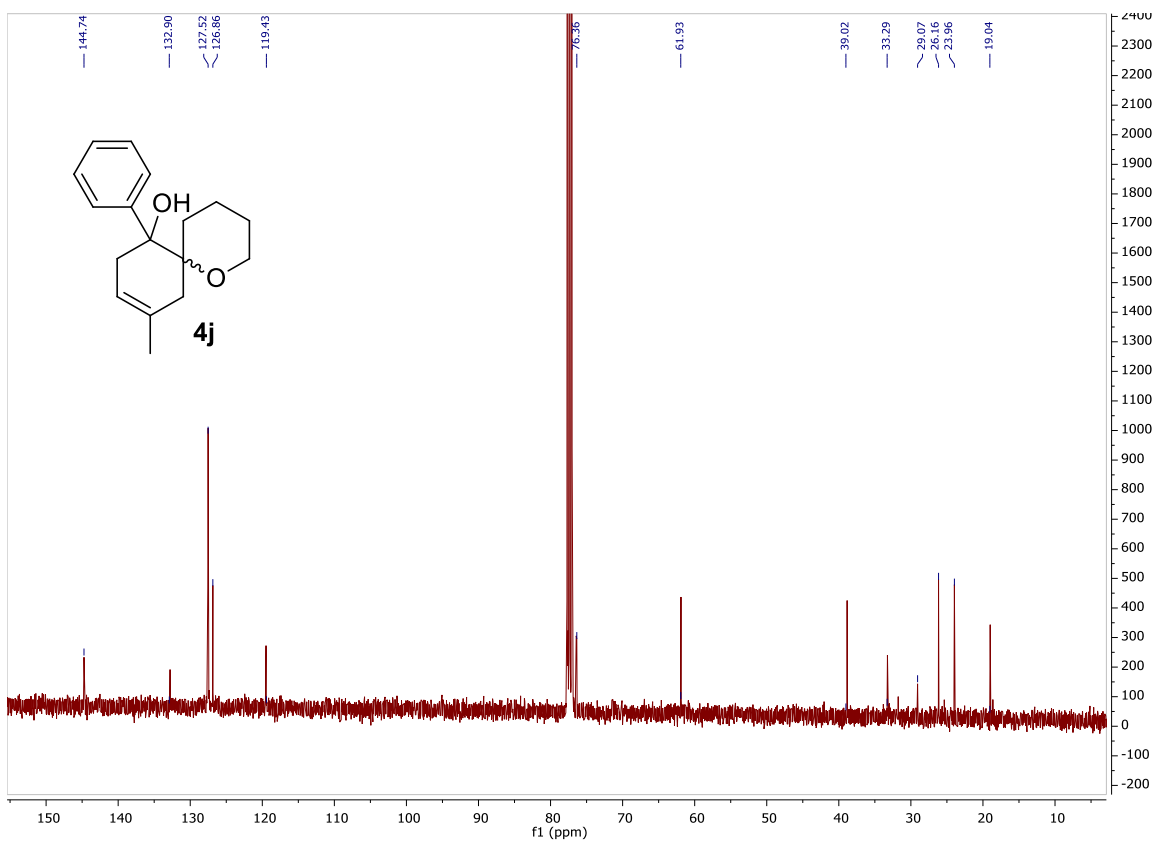
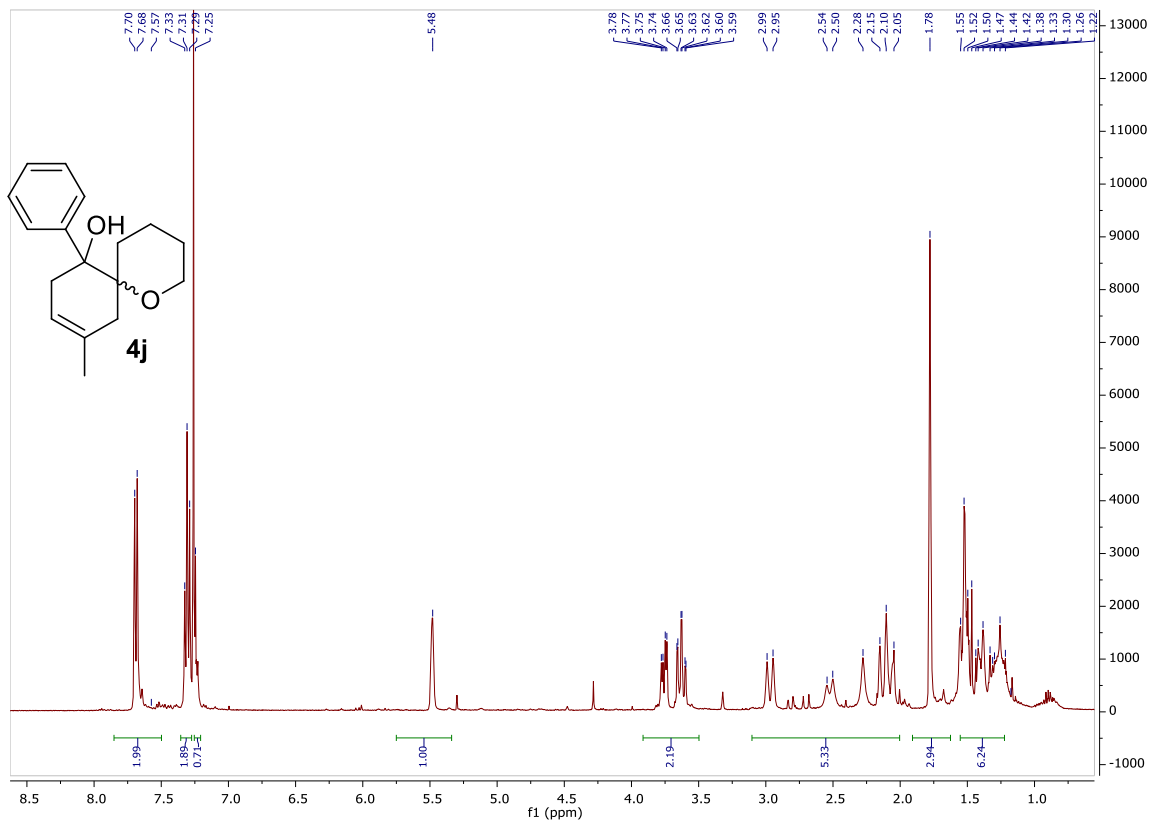
Compound **3i** and **4i** were synthesized according to **general procedure 1** starting from dienol **1i** (100 mg, 0.51 mmol) and Amberlyst-15 (27 wt% with respect to **1i**, 12.7 mmol, 42.2 mg) in MeCN stirred at room temperature for 4 h. Purification by flash chromatography (PE:Et₂O = 95:5) afforded **3i** as a pale yellow oil (12 mg, 0.06 mmol, 12%) and **4i** (34 mg, 0.173 mmol, 34%) as a pale yellow oil. **3i**: **¹H-NMR** (200 MHz, CDCl₃): δ [ppm] = 3.83 (dd, ³J = 11.1, 2.4 Hz, 1H), 3.55 – 3.31 (m, 1H), 2.50 – 2.26 (m, 1H), 1.75 – 1.40 (m, 11H), 1.38 (s, 3H), 1.31 (s, 3H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 87.26, 83.53, 83.22, 65.76, 46.03, 38.12, 32.48, 31.95, 26.25, 22.24, 19.14, 17.20. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 2935 (m), 2860 (w), 1443 (w), 1375 (m), 1233 (m), 1207 (m), 1132 (m), 1083 (s), 1067 (s), 1036 (m), 998 (m), 902 (m), 861 (s). **ESI-HRMS:** *m/z* calcd. for C₁₂H₂₁O₂ [MH]⁺: 197.1537, found: 197.1536. **CAS number:** 2093246-05-8. The experimental data are in agreement with those reported in the literature.² **4i**: **¹H-NMR** (400 MHz, CDCl₃): δ [ppm] = 1.18 (s, 3H), 1.94 – 1.36 (m, 10H), 2.09 (m, 2H), 2.53-2.27 (m, 1H), 2.45 (m, 1H), 3.74-3.55 (m, 2H), 5.25 (m, 1H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 19.39, 22.69, 23.80, 25.34, 26.15, 35.39, 37.27, 62.20, 73.53, 75.90, 119.84, 132.45. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 3467 (b, OH), 2946 (m), 2340 (m), 1444 (m), 1375 (m), 1208 (m), 1146 (m), 1065 (s). **ESI-HRMS:** *m/z* calcd. for C₁₂H₂₁O₂ [MH]⁺: 197.1536, found: 197.1536.



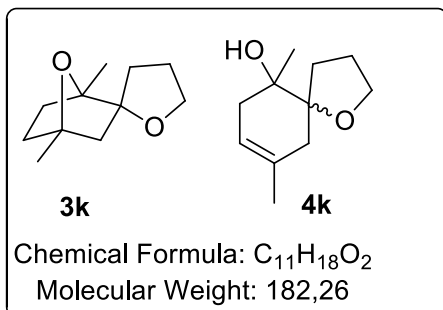
(±)-1S,2R,4R)-4-methyl-1-phenyltetrahydro-7-oxaspiro[bicyclo[2.2.1]heptane-2,2'-pyran] (3j) and (±)-10-methyl-7-phenyl-1-oxaspiro[5.5]undec-9-en-7-ol (4j)



Compound **3j** and **4j** were synthesized according to **general procedure 1** starting from dienol **1j** (100 mg, 0.39 mmol) and Amberlyst-15 (27 wt% with respect to **1j**, 0.1 mmol, 30.4 mg) in MeCN stirred at room temperature for 4 h. Purification by flash chromatography (PE:Et₂O = 95:5) afforded **3j** as a white powder (42 mg, 0.162 mmol, 42%) and **4j** (15 mg, 0.058 mmol, 18%) as a white powder. **3j**: **¹H-NMR** (200 MHz, CDCl₃): δ [ppm] = 7.73 – 7.21 (m, 5H), 4.07 – 3.85 (m, 1H), 3.53 (ddd, ³J = 11.4, 9.0, 4.9 Hz, 1H), 3.18 – 2.85 (m, 1H), 1.97 – 1.32 (m, 10H), 1.60 (s, 3H), 1.04 – 0.76 (m, 1H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 141.26, 127.75, 126.60, 125.78, 91.27, 84.29, 83.67, 65.83, 46.21, 38.00, 33.58, 31.94, 26.05, 22.43, 19.01. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 2941 (m), 2858 (w), 1449 (m), 1121 (m), 1071 (s), 1044 (s), 1021 (s), 988 (m), 761 (s), 701 (s). **ESI-HRMS**: *m/z* calcd. for C₁₇H₂₃O₂ [MH]⁺: 259.1693, found: 259.1693. **CAS number** :1972656-21-5. The experimental data are in agreement with those reported in the literature.² **4j**: **¹H-NMR** (400 MHz, CDCl₃): δ [ppm] = 7.70 – 7.25 (m, 5H), 5.48 (t, 1H), 3.78-3.59 (m, 2H), 2.99 -2.05 (m, 5H), 1.78 (s, 3H), 1.55 – 1.22 (m, 6H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 144.74, 132.90, 127.52, 126.86, 119.73, 76.36, 61.93, 39.02, 33.29, 29.07, 26.16, 23.96, 19.04. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 3508 (OH), 2938 (m), 2857 (w), 2360 (m), 2939 (m), 1493 (m), 1445 (m), 1077 (s), 1045 (s), 908 (m), 758 (s), 700 (s). **ESI-HRMS**: *m/z* calcd. for C₁₇H₂₃O₂ [MH]⁺: 259.1693, found: 259.1690. 1071 (s), 1044 (s), 1021 (s), 988 (m), 761 (s), 701 (s). **ESI-HRMS**: *m/z* calcd. for C₁₇H₂₃O₂ [MH]⁺: 259.1693, found: 259.1693.

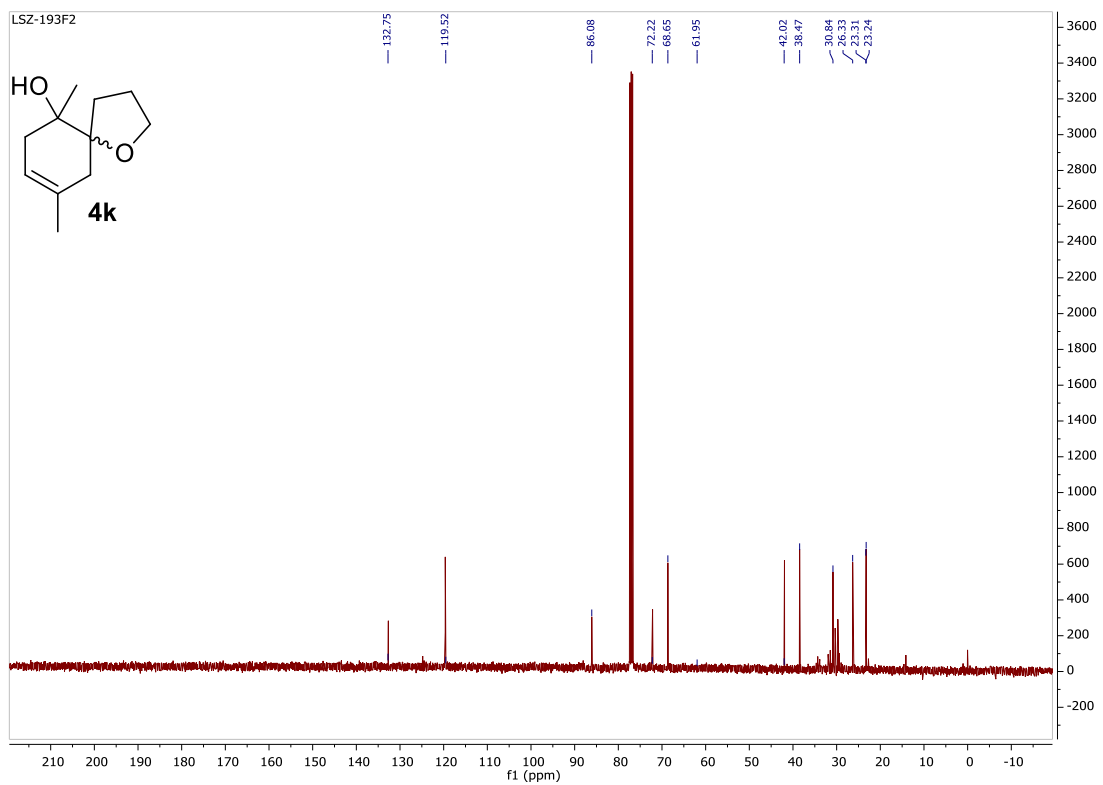
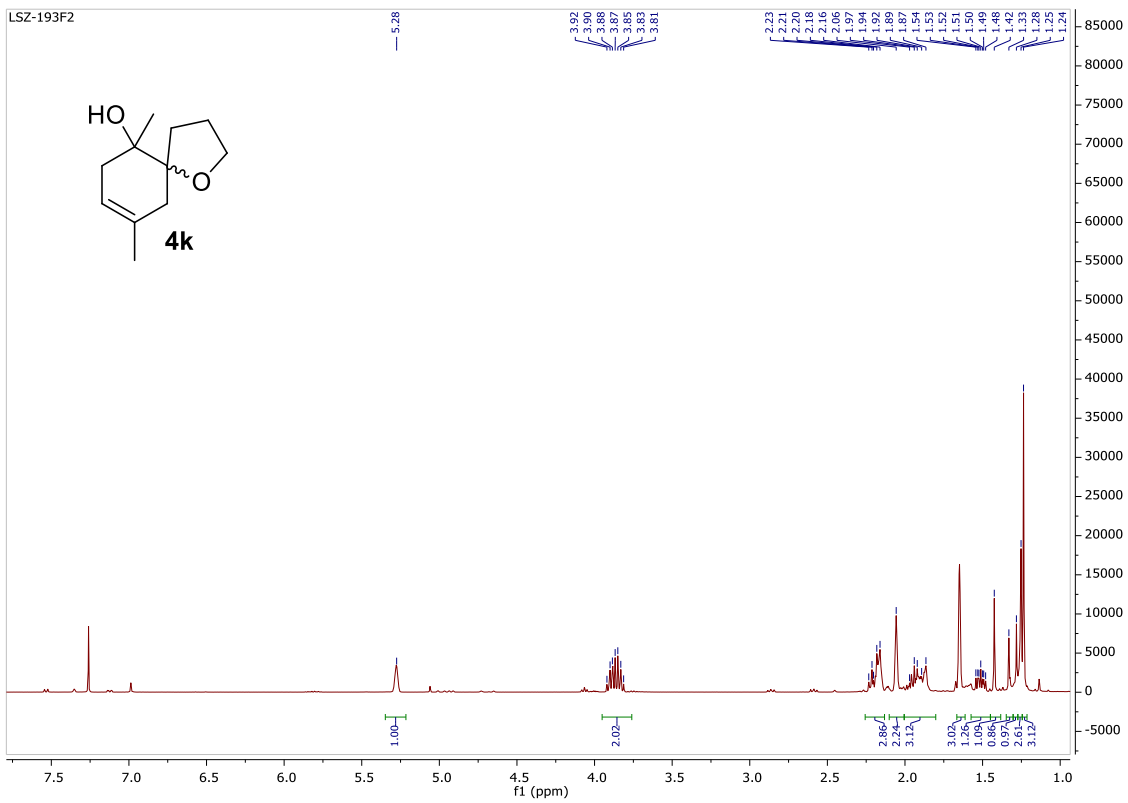


(±)-(1R,2R,4R)-1,4-dimethyldihydro-3'H-7-oxaspiro[bicyclo[2.2.1]heptane-2,2'-furan] (3k) and (±)-6,9-dimethyl-1-oxaspiro[4.5]dec-8-en-6-ol (4k)

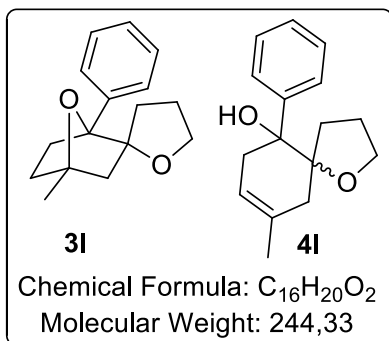


Compound **3k** and **4k** were synthesized according to **general procedure 1** starting from dienol **1k** (101 mg, 0.55 mmol) and Amberlyst-15 (27 wt% with respect to **1k**, 13.8 mmol, 43.5 mg) in MeCN stirred at room temperature for 4 h. Purification by flash chromatography (PE:Et₂O = 95:5) afforded to **3k** as a pale yellow oil (15 mg, 0.083 mmol, 15%) and **4k** (25 mg, 0.138 mmol, 25%) as a pale yellow oil. **3k**: **¹H-NMR** (200 MHz, CDCl₃): δ [ppm] = 3.88 – 3.67 (m, 2H),

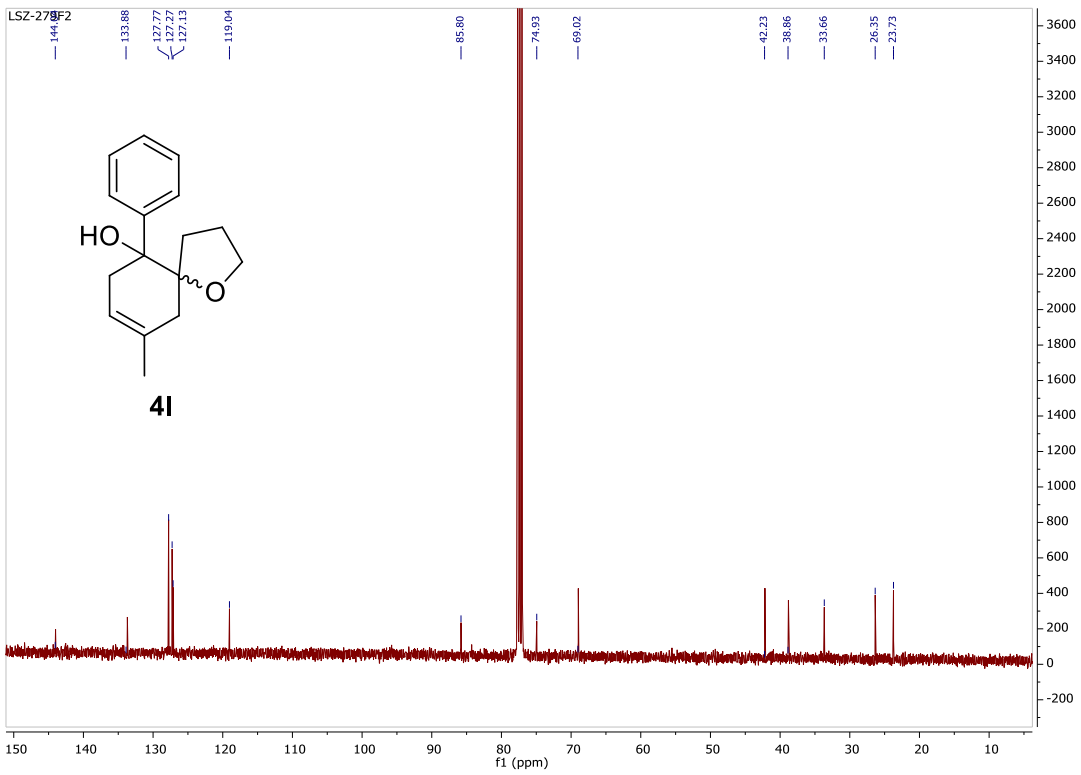
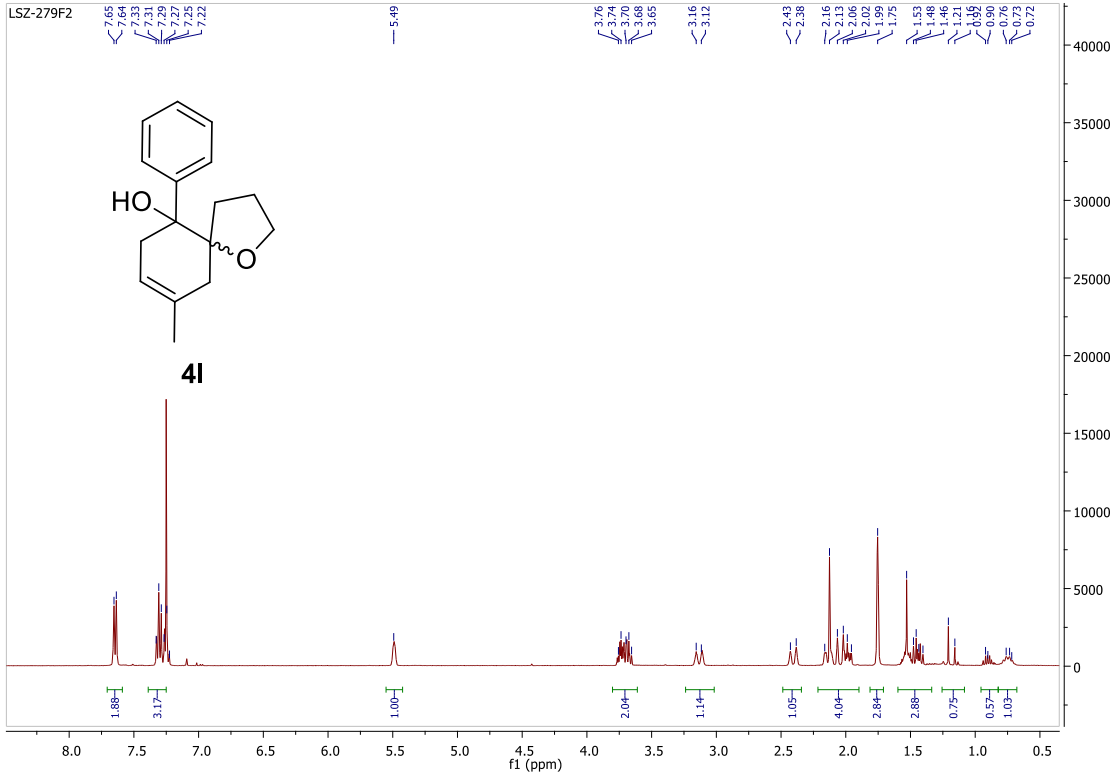
2.38 (ddd, ³J = 11.5, 8.9, 4.5 Hz, 1H), 2.16 (ddd, ³J = 12.1, 7.7, 5.5 Hz, 1H), 1.98 – 1.77 (m, 3H), 1.74 – 1.41 (m, 5H), 1.37 (s, 3H), 1.31 (s, 3H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 90.90, 86.11, 83.63, 67.79, 52.90, 37.74, 36.07, 32.84, 25.81, 21.98, 17.21. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 2966 (m), 2932 (m), 2868 (w), 1445 (w), 1375 (m), 1232 (m), 1126 (m), 1071 (m), 1047 (s), 905 (m), 856 (s). **ESI-HRMS**: *m/z* calcd. for C₁₁H₁₉O₂ [MH]⁺: 183,1385, found: 183,1382. **CAS number**: 1972656-17-9. The experimental data are in agreement with those reported in the literature.² **4k**: **¹H-NMR** (200 MHz, CDCl₃): δ [ppm] = 1.23 (s, 3H), 1.37-1.58 (m, 1H), 1.59-1.72 (m, 3H), 1.82-2.30 (m, 7H), 3.85 (m, 2H), 5.27 (m, 1H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 23.20, 23.25, 26.27, 30.77, 38.41, 41.88, 68.59, 72.09, 86.02, 119.57, 132.59. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 3465 (b, OH), 2967 (m), 2901 (m), 1441 (m), 1366 (m), 1128 (m), 1108 (m), 1065 (s). **ESI-HRMS**: *m/z* calcd. for C₁₁H₁₉O₂ [MH]⁺: 259.1693, found: 259.1690.



(±)-(1S,2R,4R)-4-methyl-1-phenyldihydro-3'H-7-oxaspiro[bicyclo[2.2.1]heptane-2,2'-furan] (3I) and (±)-9-methyl-6-phenyl-1-oxaspiro[4.5]dec-8-en-6-ol (4I)



Compound **3I** and **4I** were synthesized according to **general procedure 1** starting from dienol **1I** (101 mg, 0.41 mmol) and Amberlyst-15 (27 wt% with respect to **1I**, 10.3 mmol, 32.5 mg) in MeCN stirred at room temperature for 4h. Purification by flash chromatography (PE:Et₂O = 95:5) afforded **3I** as a pale yellow oil (40.4 mg, 0.165 mmol, 40%) and **4I** (18 mg, 0.074 mmol, 18%) as a pale yellow oil. **3I**: **¹H-NMR** (200 MHz, CDCl₃): δ [ppm] = 7.53 – 7.17 (m, 5H), 3.85 – 3.56 (m, 2H), 3.04 – 2.83 (m, 1H), 2.02 – 1.37 (m, 8H), 1.49 (s, 3H), 1.18 – 0.96 (m, 1H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 140.90, 127.77, 126.84, 125.79, 92.33, 90.10, 83.64, 68.59, 53.59, 37.58, 37.46, 32.61, 25.56, 22.11. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 2965 (m), 2866 (w), 1446 (m), 1112 (m), 1036 (s), 851 (m), 759 (s), 700 (s). **APGC-HRMS**: *m/z* calcd. for C₁₆H₂₁O₂ [MH]⁺: 245.1542, found: 245,1550. **CAS number**: 1972656-20-4. The experimental data are in agreement with those reported in the literature.² **4I**: **¹H-NMR** (400 MHz, CDCl₃): δ [ppm] = 7.67 – 7.24 (m, 5H), 5.50 (t, 1H), 3.77 – 3.62 (m, 2H), 3.16 – 3.12 (m, 1H), 2.44 – 2.39 (m, 1H), 2.17-1.76 (m, 4H), 1.54 (s, 3H), 1.49-0.72 (m, 3H). **¹³C-NMR** (50 MHz, CDCl₃): δ [ppm] = 144.05, 133.88, 127.77, 127.27, 127.13, 119.04, 85.80, 74.93, 69.02, 42.23, 38.86, 33.66, 26.35, 23.73. **IR** (neat): $\tilde{\nu}$ (cm⁻¹) = 3419 (OH), 2961 (m), 2854, 2358(m), 2337 (w), 1447 (m), 1199 (m), 1034 (s), 825 (m), 752 (s), 701 (s). **ESI-HRMS**: *m/z* calcd. for C₁₆H₂₁O₂ [MH]⁺: 245.1536, found: 245,1535.



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³ S.H. Cai, J.-H. Xie, S. Song, L. Ye, C. Feng and T.P. Loh, *ACS Catalysis* **2016**, 6, 5571-5574.