

Supplementary Information

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On the Reaction of 1-Oxa-4-thiaspiro[4.5]decan-7-one with PhLi. A Reinvestigation

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General. The ^1H and ^{13}C spectra were recorded of samples dissolved in CDCl_3 . The ^1H and ^{13}C spectra were referenced, respectively, to the residual CHCl_3 at δ 7.27 and the central line of CDCl_3 resonance at δ 77.0. The reactions were performed in an atmosphere of dry argon. After aqueous workup, the solvents were removed on a rotovap under reduced pressure at 30 $^\circ\text{C}$. The separations were effected by radial chromatography over silica gel. Mixtures of hexanes and EtOAc were used as the eluent. Et₂O and n-hexane used for the reactions were distilled afresh from LiAlH₄ under argon atmosphere.

Preparation of PhLi: *n*-Butyllithium (2.0 M solution, 1.5 mL) was slowly added to a solution of bromobenzene (0.315 mL, 3.0 mmol) in Et₂O (3 mL) at -70 $^\circ\text{C}$. The resultant solution was stirred at the same temperature for 15 min to give a solution of PhLi (0.67 M).

Addition of PhLi to 1-oxa-4-thiaspiro[4.5]decan-3-one in Et₂O or THF: PhLi (0.76 mL, 0.67 M in Et₂O, 0.51 mmol) was added to a stirred solution of 1-oxa-4-thiaspiro[4.5]decan-3-one (35 mg, 0.203 mmol) in Et₂O or THF (3.2 mL) at -70 $^\circ\text{C}$ and the contents were stirred at the same temperature for 60 min. The reaction was then quenched with MeOH (0.51 mL, 12.5 mmol), diluted with Et₂O, washed with saturated aqueous NH₄Cl and brine, and concentrated afforded the alcohols.

Addition of PhLi to 1-oxa-4-thiaspiro[4.5]decan-3-one in 3:1 mixture of Et₂O and hexane: PhLi (0.76 mL, 0.67 M in Et₂O, 0.51 mmol) was added, all at once, to a stirred solution of 1-oxa-4-thiaspiro[4.5]decan-3-one (35 mg, 0.203 mmol) in Et₂O (2.3 mL) and hexane (1.0 mL) at -70

°C so that the desired solvent composition was eventually 3:1. The contents were stirred at -78 °C for 60 min. The reaction was quenched with MeOH (0.51 mL, 12.5 mmol), diluted with Et₂O, washed with saturated aqueous NH₄Cl and brine, and concentrated to afford the alcohols.

Typical procedure for the reaction of 1-oxa-4-thiaspiro[4.5]decan-3-one with PhMgBr. A 0.18M solution of PhMgBr was prepared from the reaction of Mg powder and bromobenzene in Et₂O at 25 °C. This (0.18 mL) was added to a -70 °C cooled solution of 1-oxa-4-thiaspiro[4.5]decan-3-one (0.015 g, 0.08 mmol) in Et₂O (3 mL). The contents were stirred at -70 °C for 60 min, quenched with MeOH (5 equivalents), and allowed to warm up to 20 °C. The reaction mixture was diluted with Et₂O (10 mL) and washed with saturated aqueous NH₄Cl (1 x 5 mL). The organic solution was dried with anhydrous Na₂SO₄ and the solvent removed on a rotovap under reduced pressure. The residue that could be purified for its components by radial chromatography was filtered through a short column of silica gel.

For the reactions in mixtures of Et₂O and hexane, the Grignard reagent was prepared in Et₂O as usual and its requisite amount added to a solution of 1-oxa-thiaspiro[4.5]decan-3-one in a mixture of Et₂O and hexane. The ratio of the solvents was such that the desired solvent proportion was achieved after all the Grignard solution had been added.

Procedure for the reduction of 1-oxa-4-thiaspiro[4.5]decan-3-one with NaBH₄. NaBH₄ (0.46g, 1.2 mmol) was added to a stirred solution of 1-oxa-4-thiaspiro[4.5]decan-3-one (0.172g, 1 mmol) in MeOH (5 mL) at 0 °C. The resultant was stirred for 30 min when the reaction was found to be complete by TLC. MeOH was removed, the residue was taken with saturated NH₄Cl

(2 mL) and extracted with EtOAc (2 x 5 mL). The organic extract was dried with Na₂SO₄ and filtered. The solvent was removed to obtain a mixture of alcohols.

Procedure for the Reduction of 1-oxa-4-thiaspiro[4.5]decan-3-one with Na(CN)BH₃. A small crystal of methyl orange was added to a solution of 1-oxa-4-thiaspiro[4.5]decan-3-one (0.172g, 1 mmol) in MeOH (1 mL). The solution turned yellow. A few drops of 1N HCl in MeOH were added so that the solution turned red. Now, Na(CN)BH₃ (1.2 mmol) was added in portions. Whenever the color of the reaction mixture started to turn yellow during this addition, drops of HCl were immediately added to restore the red color. After completion of the reaction, it was concentrated and mixed with saturated aqueous NH₄Cl. The products were extracted into EtOAc (2 x 5 mL). The combined extract was dried with Na₂SO₄ and the solvent was removed to obtain a mixture of alcohols.

Procedure for the Reduction of 1-oxa-4-thiaspiro[4.5]decan-3-one with L-Selectride in THF/Toluene. A solution of L-Selectride in THF (1.0 M, 1.5 mL, 1.5 mmol) was added to a stirred solution of 1-oxa-4-thiaspiro[4.5]decan-3-one (0.172g, 1 mmol) in the chosen solvent (2.5 mL) at -70 °C. The stirring was continued at this temperature for 30 min. MeOH (1 mL), 1N NaOH (1 mL) and 30% H₂O₂ (1 mL) were added and the reaction mixture was allowed to warm up to 25 °C and stirred for 30 min. The product was extracted into EtOAc (2 x 5 mL) and the organic extract was washed with brine and dried. The residue obtained from solvent removal was filtered through a silica gel column to furnish a mixture of alcohols.

Procedure for Reduction of 1-oxa-4-thiaspiro[4.5]decan-3-one with DIBAL-H in Toluene.

A solution of DIBAL-H in toluene (1.0M, 1.5 mL, 1.5 mmol) was added to a stirred solution of 1-oxa-4-thiaspiro[4.5]decan-3-one (0.172g, 1 mmol) in toluene (6 mL) at -70 °C. The stirring was continued at this temperature for 30 min and the reaction was quenched with 5% aqueous HCl (3 mL). The products were extracted into EtOAc (2 x 5 mL) followed by washing with brine, drying, removal of the solvents, and filtration of the residue through a short silica gel column to furnish a mixture of alcohols.

1 (liquid). ¹H NMR δ 4.19-4.11 (2H, m), 3.16-3.07 (2H, m), 2.85-2.81 (1H, td, *J* = 14.4, 1.5 Hz), 2.78 (1H, d, *J* = 14.4 Hz), 2.41-2.29 (2H, m), 2.28-2.20 (1H, m), 2.15-2.07 (1H, m), 2.06-1.95 (1H, m), 1.95-1.83 (1H, m). ¹³C NMR δ 207.4, 95.2, 70.2, 55.2, 40.0, 38.3, 33.7, 21.8. Anal. Calcd for C₈H₁₂O₂S: C, 55.78; H, 7.02. Found: C, 55.62; H, 6.90.

2a (mp 94 °C). ¹H NMR δ 7.51-7.21 (5H, m), 4.52 (1H, s), 4.29-4.21 (2H, m), 3.09 (2H, t, *J*=5.8 Hz), 2.33-2.28 (1H, td, *J*=14.4 and 2.4 Hz), 2.27-2.20 (1H, m), 2.19 (1H, d, *J*=1.4 Hz), 2.13-2.03 (1H, m), 1.87-1.71 (4H, m). ¹³C NMR δ 147.5, 128.0, 126.6, 124.4, 94.3, 74.6, 70.7, 49.8, 38.7, 37.6, 32.8, 19.5. Anal. Calcd for C₁₄H₁₈O₂S: C, 67.16; H, 7.25. Found: C, 67.00; H, 7.10.

2b (mp 82 °C). ^1H NMR δ 7.61-7.23 (5H, m), 4.52 (1H, s), 4.19-4.08 (2H, m), 3.09 (2H, t, $J=6.0$ Hz), 2.61 (1H, s), 2.41 (1H, d, $J=14.1$ Hz), 2.24 (1H, d, $J=14.4$ Hz), 2.16 (1H, d, $J=12.6$ Hz), 2.07-1.90 (1H, m), 1.88-1.70 (4H, m). ^{13}C NMR δ 147.5, 128.0, 126.6, 124.4, 94.3, 74.6, 70.7, 49.8, 38.7, 37.6, 32.8, 19.5; Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2\text{S}$: C, 67.16; H, 7.25. Found: C, 67.03; H, 7.12.

4a (liquid). ^1H NMR δ 4.83-4.75 (1H, tt, $J=10.7$ and 4.2 Hz), 4.17 (2H, t, $J=5.9$ Hz), 3.11-3.00 (2H, m), 2.31-2.27 (1H, bd, $J=12.0$ Hz), 2.03 (3H, s), 2.02-1.80 (3H, m), 1.73-1.66 (2H, m), 1.51-1.40 (1H, tq, $J=12.7$ and 3.6 Hz), 1.33-1.22 (1H, dq, $J=12.2$ and 4.2 Hz); ^{13}C NMR δ 170.2, 95.6, 71.8, 69.6, 44.9, 39.0, 33.1, 30.6, 21.3, 21.2. Anal. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_3\text{S}$: C, 55.53; H, 7.46. Found: C, 55.44; H, 7.32.

4b (liquid). ^1H NMR δ 5.00-4.92 (1H, tt, $J=10.2$ and 4.2 Hz), 4.19-4.09 (2H, tq, $J=9.5$ and 5.9 Hz), 3.06 (2H, t, $J=6.1$ Hz), 2.39-2.34 (1H, m), 2.04 (3H, s), 2.01-1.95 (1H, m), 1.95-1.89 (1H, m), 1.86-1.80 (1H, dd, $J=13.2$ and 10.2 Hz), 1.74-1.67 (3H, m), 1.39-1.29 (1H, m). ^{13}C NMR δ 170.3, 93.5, 70.6, 69.9, 44.0, 38.7, 33.3, 30.1, 21.3, 20.8. Anal. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_3\text{S}$: C, 55.53; H, 7.46. Found: C, 55.38; H, 7.25.

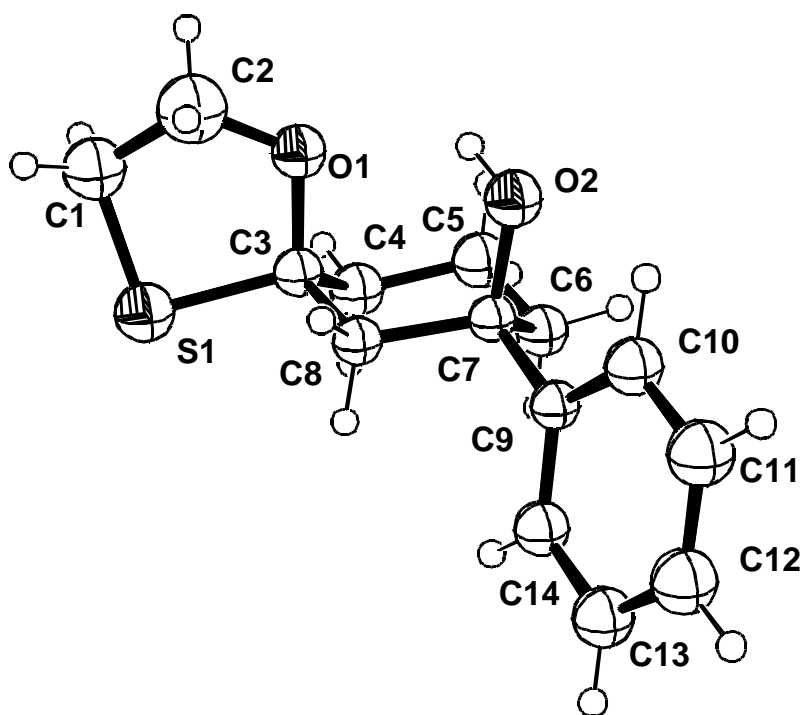


Figure 1. ORTEP plot of **2a**. Selected bond lengths (Å), bond angles (°) and torsion angles (°): S1-C1 1.792(4), S1-C3 1.846(3), O1-C2 1.424(4), O1-C3 1.422(3), O2-C5 1.425(3), C1-S1-C3 91.9(2), C2-O1-C3 110.8(3), S1-C3-O1 104.6(2), O2-C5-C4 109.8(2), O2-C5-C6 105.3(2), O2-C5-C9 110.0(3), S1-C3-C4-C5 $-73.2(3)$, O1-C3-C4-C5 $173.0(2)$, O2-C5-C4-C3 $65.0(3)$, O2-C5-C9-C14 $133.4(3)$, O2-C5-C9-C10 $-49.3(4)$.

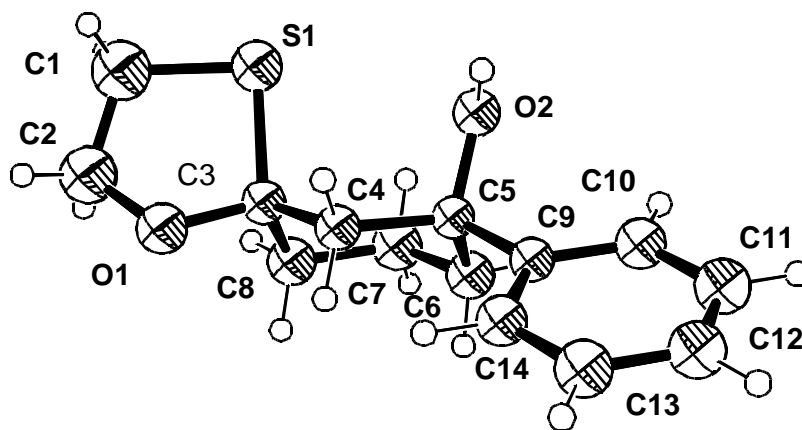


Figure 2. ORTEP plot of **2b**. Selected bond lengths (Å), bond angles (degrees) and torsion angles (degrees): S1-C1 1.782(5), S1-C3 1.851(4), O1-C2 1.384(5), O1-C3 1.422(5), O2-C7 1.431(5), C1-S1-C3 93.1(2), C2-O1-C3 113.1(4), S1-C3-O1 105.6(3), O2-C7-C8 108.7(3), O2-C7-C6 109.3(4), O2-C7-C9 107.4(4), S1-C3-C8-C7 176.1(3), O1-C3-C8-C7 -67.6(5), O2-C7-C8-C3 69.4(5), O2-C7-C9-C14 175.2(4), O2-C7-C9-C10 -6.6(6).

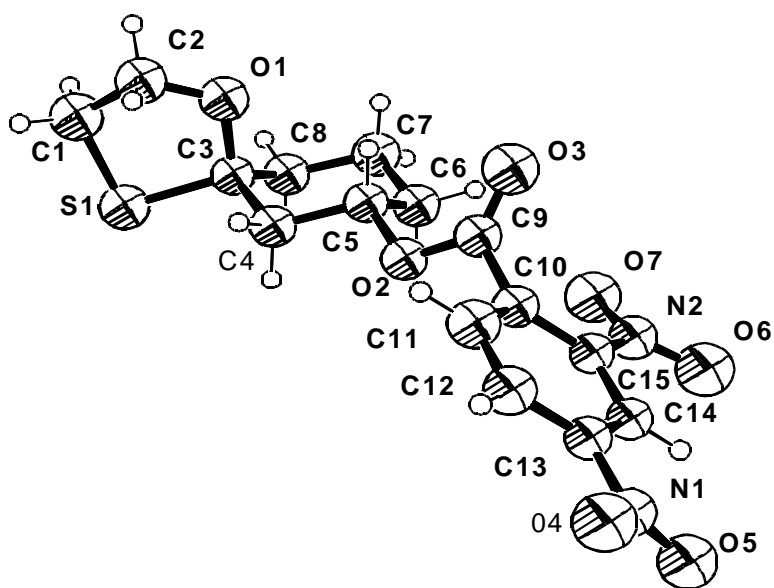


Figure 3. ORTEP plot of **5b**. Selected bond lengths (Å), bond angles (degrees) and torsion angles (degrees): S1-C1 1.804(3), S1-C3 1.852(3), O1-C2 1.387(6), O1-C3 1.419(3), C1-S1-C3 92.18(14), C2-O1-C3 113.60(3), O1-C3-S1 106.16(18), O1-C3-C4-C5 -67.10(3), S1-C3-C4-C5 176.37(18), O2-C5-C4-C3 177.20(2).