**Iterative Approach to Polycyclic Ethers based on Stereoselective Oxonium Ylide [2,3]-Shifts**

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**Supporting Information**

**General.** Reactions were carried out in flame-dried glassware under a positive nitrogen atmosphere unless otherwise stated. Transfer of anhydrous solvents and reagents was accomplished with oven-dried syringes or cannula. Solvents were distilled before use: methylene chloride from calcium hydride, tetrahydrofuran and diethylether from sodium/benzophenone ketyl, toluene from sodium metal. Ethereal diazomethane was prepared from Diazald according to literature procedures.1 Thin layer chromatography was performed on glass plates precoated with 0.25mm Kieselgel 60 F 254 (Merck). Flash chromatography columns were packed with 230-400 mesh silica gel (Merck). Radial chromatography was carried out on a Chromatotron 7924T (Harrison Research) with plates prepared using silica gel 60 F 254 with gypsum binder (EM) on glass rotors. Proton nuclear magnetic resonance spectra (1H NMR) were recorded at 300 MHz or 500 MHz and coupling constants (J) are reported in Hertz (Hz). Carbon nuclear magnetic resonance spectra (13C NMR) were recorded at 75 MHz or 125 MHz and are reported (ppm) relative to the center line of the triplet from chloroform-d (77.26 ppm).

![Scheme 1](image)

**Scheme 1; Synthesis of 9.**

**2-Methoxy-2-allyl-3-hydroxytetrahydropyran.** 2-Allyl-3-hydroxytetrahydropyran was prepared via a variation of a McDonald procedure.2 t-Butyllithium (100 mL, 170 mmol, 1.1 eq) was added via cannula to a vigorously stirring solution of dihydropyran (14.0 mL, 154 mmol) in THF (28.3 mL) at -78°C. The mixture was then carefully allowed to warm to -30°C. When all of the yellow-orange precipitate had dissolved the solution was allowed to warm to 0°C and stirred for 1 h. The solution was then cooled to -78°C, added via cannula to Cul (14.9 g, 78.5 mmol, 0.51 eq) in THF (60 mL), in a three neck flask equipped with an addition funnel charged with allyl bromide (5.07 mL, 58.5 mmol, 0.38 eq) in THF (39...
mL), at -78°C. The mixture was stirred for 1 h and the allyl bromide solution was then added drop-wise
over 15 min. After the addition was complete, the solution was stirred at -78°C for 1 h and then allowed
to warm to room temperature and stirred for an additional 3 h. The reaction was diluted with Et₂O (100
mL) and quenched with a 30% NH₄OH saturated with NH₄Cl solution (100 mL). The resulting slurry
was allowed to stir for 1 h and then sit undisturbed until two layers formed. The aqueous phase was
extracted with Et₂O (200 mL) and the combined organic phase was washed with a 30% NH₄OH saturated
with NH₄Cl solution (300 mL), dried with anhydrous MgSO₄, concentrated to a small volume (~20 mL)
and immediately dissolved in MeOH (146 mL) cooled to 0°C. After slow, careful addition of mCPBA
(18.8 g, 76.1 mmol) the reaction was stirred until completion as determined by TLC (1 h) and then diluted
with Et₂O (130 mL). The reaction was then carefully quenched with sat. NaHCO₃/ice mixture (200 mL).
The aqueous phase was extracted with Et₂O (2x100 mL). The combined organic phase was washed with
equal volumes of sat. NaHCO₃, brine, dried over anhydrous MgSO₄, filtered, and concentrated. The
residue was purified by flash chromatography to yield 7.87 g of 2-methoxy-2-allyl-3-hydroxytetrahydropyran
as a mixture of diastereomers (78% over two steps). R₆ 0.22, 0.28 (30% EtOAc/Hexanes) Major diastereomer: R₆ 0.22, (30% EtOAc/Hexanes); ¹H NMR (500 MHz, CDCl₃) δ
5.94-5.08 (m, 1H), 5.19-5.09 (m, 2H), 3.58-3.44 (m, 3H), 3.28 (s, 3H), 2.57-2.46 (m, 2H), 1.85-1.78 (m,
2H), 1.73-1.57 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 133.8, 118.3, 99.8, 69.9, 60.8, 47.8, 38.1, 28.3,
25.4.

(2R*, 3S*)-2-Allyl-3-hydroxypropanoic Acid. To a solution of Et₃SiH (36.5 mL, 228 mmol, 5 eq) and
2-methoxy-2-allyl-3-hydroxytetrahydropyran (7.86 g, 45.7 mmol) in CH₂Cl₂ (152 mL) and CH₃CN (152
mL) at 0°C was added BF₃·OEt₂ (11.6 mL, 91.5 mmol, 2 eq). The reaction was stirred for 3 h and poured
into a sat NaHCO₃/ice mixture (200 mL). The aqueous phase was then extracted with CH₂Cl₂ (2x100
mL) and the combined organic phase was washed with brine (300 mL), dried over anhydrous MgSO₄,
filtered, concentrated and purified by flash chromatography to yield 5.16 (80%) of 9 as a colorless oil. R₆
0.14 (30% EtOAc/Hexanes); IR (neat) 3405, 2936, 2852, 1096 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ
5.92 (dddd, J=17.1, 10.1, 7.1, 7.1 Hz, 1H), 5.15-5.06 (m, 2H), 3.93-3.86 (m, 1H), 3.41-3.28 (m, 2H), 1.85-1.78 (m,
2H), 2.63-2.53 (m, 1H), 2.33-2.23 (m, 1H), 1.23-1.20 (m, 3H), 1.72-1.71 (m, 3H), 1.46-1.33 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 135.4, 117.1, 81.9, 70.5, 67.9, 37.2, 33.0, 25.8.

2-((2R*, 3S*)-3-Hydroxypropan-2-yl)acetic Acid. Ozone was bubbled into a solution of 9
(2.037 g, 14.35 mmol) in CH₂Cl₂ (100 mL) and MeOH (18 mL) at -78°C until the solution turned a
persistent blue color. The solution was then allowed to stir for 30 min. Argon was bubbled into the
solution until it was colorless, after which the cooling bath was removed and argon was bubbled until the reaction mixture reached r.t.. The reaction mixture was then concentrated and the residue was dissolved in 88% formic acid (10.8 mL) and 30% H₂O₂ (5.6 mL) and heated to 70°C for 8 h. The reaction mixture was then concentrated and the residue was dissolved in Et₂O (150 mL) and extracted with 1 M KOH (3x20 mL). The combined basic aqueous phase was washed with Et₂O (60 mL). The aqueous phase was then acidified with 3 N HCl until pH=1-2 and saturated with NaCl. The aqueous phase was extracted with EtOAc (8x100 mL). The combined organic phase was dried over anhydrous MgSO₄, filtered, concentrated and placed under high vacuum overnight to afford 1.95 g (85%) of 10 as a thick brown oil. 

![Chemical structure of 10](image)

**2-((2R*, 3S*)-3-Allyloxypyran-2-yl)acetic Acid.** The acid 10 (2.28 g, 14.3 mmol) was dissolved in THF (20 mL) and then added via cannula to a vigorously stirring mixture of NaH (1.03 g, 42.8 mmol, 3 eq) in THF (5 mL) at 0°C. After 10 min, allyl bromide was added via syringe (1.24 mL, 14.3 mmol, 1 eq) and the mixture was heated to reflux. After 10 h, the reaction was cooled to r.t., diluted with Et₂O (15 mL), quenched with water (10 mL) and the aqueous phase was then washed with Et₂O (30 mL), acidified with 3 N HCl until the pH=1-2, and then extracted with Et₂O (8x50 mL). The combined organic phase was dried over anhydrous MgSO₄, filtered, and concentrated to afford 2.67 g (95%) of 11 as a thick yellow oil. 

![Chemical structure of 11](image)

**HRMS (FAB, m-1) for C₁₀H₁₅O₄ calcd 199.0970, found: m/z 199.0974.**
1-Diazo-3-((2R*, 3S*)-3-allyloxypyran-2-yl)propan-2-one. Freshly distilled oxalyl chloride (0.22 mL, 2.45 mmol, 1.2 eq) was added to a solution of acid 11 (409 mg, 2.05 mmol) in CH₂Cl₂ (14 mL). One drop of DMF was added (gas evolution) and the reaction was stirred at r.t. for 4 h. The mixture was then added via cannula to a freshly prepared solution of CH₂N₂ (~8 mmol) in Et₂O (30 mL) at -10°C. After stirring at -10°C for 60 min, the ice bath was removed and the reaction mixture was allowed to warm to r.t. and stirred for an additional 60 min. The reaction was quenched with water (20 ml) and the resulting biphasic solution was stirred until no further gas evolution was evident. The aqueous phase was extracted with Et₂O (2x30 ml). The combined organic phase was washed with brine (80 ml), dried over anhydrous Na₂SO₄, filtered, concentrated and purified by radial chromatography (4mm plate, solvent ramp: 100 mL each of 20%, 30%, 40%, 50%, 60% Et₂O/Hexanes) to yield 307 mg (67%) of 2 as a yellow oil. R_f 0.15 (50% Et₂O /Hexanes); IR (neat) 3082, 2939, 2856, 2102, 1736, 1640, 1097 cm⁻¹; ¹H NMR (500MHz, CDCl₃) δ 5.87 (dddd, J = 17.2, 10.4, 5.6, 5.5 Hz, 1H), 5.35 (br s, 1H), 5.25 (dddt, J = 17.1, 1.7, 1.7, 1.7 Hz, 1H), 5.16 (dddt, J = 10.4, 1.2, 1.2, 1.2 Hz, 1H), 4.10 (dddt, J = 12.6, 5.4, 1.4, 1.4 Hz, 1H), 3.9 (dddt, J = 12.6, 5.7, 1.3, 1.3 Hz, 1H), 3.87-3.82 (m, 1H), 3.57 (dddt, J = 9.1, 9.0, 3.1 Hz, 1H), 3.35 (dddt, J = 11.6, 8.8, 2.9 Hz, 1H), 3.07 (dddt, J = 10.7, 9.1, 4.5 Hz, 1H), 2.85 (dddt, J = 14.5, 2.9 Hz, 1H), 2.41 (app br s, 1H), 2.27-2.17 (m, 1H), 1.71-1.59 (m, 2H), 1.36 (dddt, J = 12.7, 12.7, 10.7, 4.9 Hz, 1H); ¹³C NMR (125MHz, CD₂Cl₂) δ 193.5, 135.7, 116.8, 78.5, 77.2, 69.9, 68.2, 55.3, 44.7, 29.7, 25.8; Anal. Calcd for C₁₁H₁₆N₂O₃: C, 58.91, H, 7.19. Found, C, 59.28, H, 7.20.

Representative procedure for catalytic decomposition of diazoketones. To a mixture of CH₂Cl₂ or toluene (0.01 M) and catalyst was added via cannula or syringe pump a solution of the diazoketone (0.1 M in CH₂Cl₂ or toluene). When the addition was complete the reaction was monitored by TLC and concentrated upon consumption of the diazoketone. The reaction mixture was purified by radial or flash chromatography.

Decomposition of diazoketone 2 with Rh₂(OAc)₄. To a mixture of CH₂Cl₂ (15 mL, 0.015 M) and Rh₂(OAc)₄ (3 mg, 0.007 mmol, 3 mol %) heated to reflux was added via syringe pump (addition time 3h) a solution of diazoketone 2 (50 mg, 0.22 mmol) in CH₂Cl₂ (0.8 mL). When the addition was complete the reaction mixture was concentrated. Flash chromatography yielded 12 mg (25%) of ketone 7 and 14 mg (32%) of an inseparable mixture of 5a/b (5a/b: 5/1 determined by GC).

Decomposition of diazoketone 2 with Cu(tfacac)₂. To a mixture of CH₂Cl₂ (102 mL, 0.01 M) and Cu(tfacac)₂ (19 mg, 0.05 mmol, 5 mol %) heated to reflux was added via cannula a solution of
diazoketone 2 (230 mg, 1.02 mmol) in CH₂Cl₂ (10 mL). When the addition was complete (5 min) the reaction was monitored by TLC and, upon consumption of the diazoketone (120 min), the reaction was cooled to r.t. and a solution of 30% NH₄OH saturated with NH₄Cl (50 mL) was added. The aqueous phase was extracted with CH₂Cl₂ (2x50 mL), the combined organic phase was dried with anhydrous MgSO₄, filtered and concentrated. Purification by flash chromatography (silica gel, 3 cm x 18 cm column, solvent ramp: 200 mL each of 20%, 30%, 50%, 60% Et₂O/Hexanes) yielded 10 mg (5%) of 7 and 162 mg (80%) of an inseparable mixture of 5a/b (5a/b: 1/30 determined by GC).

(1S*, 3R*, 6R*)-3-Allyl-2,7-dioxabicyclo[4.4.0]decan-4-one (5a). Rᵣ 0.38 (30% EtOAc/Hexanes); IR (neat) 2945, 2854, 1724, 1641, 1097 cm⁻¹; ¹H NMR (500MHz, CDCl₃) δ 5.85 (dd, J=17.1, 10.3, 6.8, 6.8 Hz 1H), 5.16-5.15 (m, 1H), 5.12-5.11 (m, 1H), 3.96-3.92 (m, 1H), 3.85 (dd, J=7.6, 4.3 Hz 1H), 3.45-3.39 (m, 1H), 3.37-3.30 (m, 2H), 2.89 (dd, J=15.8, 5.0 Hz 1H), 2.64 (app br s, 1H), 2.50-2.41 (m, 1H), 2.39-2.32 (m, 1H), 2.22-2.05 (m, 1H), 1.80-1.75 (m, 2H), 1.57-1.49 (m, 1H); ¹³C NMR (125MHz, CDCl₃) δ 205.4, 134.2, 117.6, 83.1, 77.5, 77.1, 67.7, 45.6, 33.8, 29.3, 25.3.

(1S*, 3S*, 6R*)-3-Allyl-2,7-dioxabicyclo[4.4.0]decan-4-one (5b). Rᵣ 0.38 (30% EtOAc/Hexanes); IR (neat) 3077, 2944, 2855, 1722, 1641, 1091 cm⁻¹; ¹H NMR (500MHz, CDCl₃) δ 5.78 (dd, J=14.2, 9.6, 9.6, 7.1 Hz 1H), 5.16-5.15 (m, 1H), 5.13-5.12 (m, 1H), 4.09 (dd, J=9.8, 5.4 Hz, 1H), 3.95-3.94 (m, 1H), 3.50 (dd, J=10.7, 9.2, 4.5 Hz, 1H), 3.44-3.38 (m, 1H), 3.34 (dd, J=11.7, 9.3, 5.5 Hz, 1H), 2.85 (dd, J=16.4, 5.5, 1.1 Hz, 1H), 2.61 (dd, J=14.4, 9.6, 7.1, 1.2, 1.2 Hz, 1H), 2.45 (dd, J=16.4, 11.7 Hz, 1H), 2.39 (dd, J=14.5, 6.7, 5.3, 1.2, 1.2 Hz, 1H), 2.13-2.08 (m, 1H), 1.81-1.76 (m, 2H), 1.53-1.45 (m 1H); ¹³C NMR (125MHz, CDCl₃) δ 207.7, 132.9, 118.6, 81.8, 76.8, 70.1, 67.8, 43.7, 34.5, 29.4, 25.5.

(1S*, 6R*)-6-Allyloxy-2-oxabicyclo[4.3.0]nonan-8-one (7). Rᵣ 0.34 (30% EtOAc/Hexanes); IR (neat) 2934, 2860, 1750, 1095 cm⁻¹; ¹H NMR (300MHz, CDCl₃) δ 5.83 (dd, J=17.2, 10.4, 5.6 Hz, 1H), 5.22 (dd, J=17.2, 1.7, 1.7, 1.7 Hz, 1H), 5.13 (dd, J=10.4, 1.5, 1.5 Hz, 1H), 3.99-3.83 (m, 4H), 3.46-3.38 (m, 1H), 2.73 (dd, J=18.5, 4.9, 1.3 Hz, 1H), 2.56 (dd, J=18.3, 1.3 Hz, 1H), 2.30 (dd, J=17.9, 1.1 Hz, 1H), 2.20-2.17 (m, 1H), 2.19 (dd, J=17.8 Hz, 1H), 1.83-1.69 (m, 3H); ¹³C NMR (75MHz, CDCl₃) δ 216.2, 135.0, 116.6, 80.0, 77.5, 67.1, 62.9, 44.8, 41.8, 28.8, 23.5.

Epimerization and reduction of 5a/b. One pot procedure: Catalytic DBU (1 drop) was added to mixture of 5a/b (142 mg, 0.72 mmol, 5a/b: 1/30) in THF (3.6 mL). The reaction was monitored by GC and stirred until no further change in epimer ratio was observed (16 h). The reaction was cooled to 0°C and LiAlH₄ was added (14 mg, 0.36 mmol), and the reaction was stirred until complete consumption of
the ketone was evident by TLC. The reaction was quenched with 1:1 Na₂SO₄:10H₂O:Celite and the resulting slurry was stirred for 30 min. Anhydrous MgSO₄ was added and the slurry stirred for and additional 30 min. The slurry was then filtered, concentrated and the products separated by flash chromatography to afford 12a (95 mg, 67%) and 12b (14 mg, 10%).

Two pot procedure: Catalytic DBU (1 drop) was added to a mixture of 5a/b (307 mg, 1.57 mmol, 5a/b: 1/30) in toluene (15 mL, 0.1 M). The reaction was heated to reflux and monitored by GC until no further no further change in epimer ratio was observed (5 h). The mixture was then condensed and passed through a short pad of silica gel (3 cm in a disposable pipette) eluting with 50% Et₂O/Hexanes. The solution was then concentrated to yield 301 mg (98%) of a mixture of 5a/b enriched in 5a. The mixture was dissolved in THF, cooled to 0°C and LiAlH₄ (30 mg, 0.8 mmol) was added, the reaction was then allowed to stir until complete consumption of the ketone was evident by TLC. The reaction was quenched with 1:1 Na₂SO₄:10H₂O:Celite and the resulting slurry was stirred for 30 min. Anhydrous MgSO₄ was added and the slurry stirred for and additional 30 min. The slurry was then filtered, concentrated and the products separated by flash chromatography (silica gel, 2 cm x 28 cm column, solvent ramp: 100 mL each of 40%, 50%, 60%, 70% Et₂O/Hexanes) to afford 261 mg, (86%) of 12a (84% from 5a/b) and 37 mg (12%) of 12b.

(1S*, 3R*, 4S*, 6R*)-3-Allyl-2,7-dioxabicyclo[4.4.0]decan-4-ol (12a). Rf 0.12 (30% EtOAc/Hexanes); IR (neat) 3435, 3075, 2943, 2868, 1103, 1066, cm⁻¹; ¹H NMR (500MHz, CDCl₃) δ 5.94 (dddd, J=17.1, 10.1, 6.9, 6.9 Hz, 1H), 5.15 (dddd, J=17.2, 1.5, 1.5, 1.5 Hz, 1H), 5.09-5.07 (m, 1H), 3.92-3.88 (m, 1H), 3.50 (ddd, J=10.7, 9.4, 4.5 Hz, 1H), 3.44-3.38 (m, 1H), 3.34 (ddd, J=11.7, 9.3, 5.5 Hz, 1H), 3.02-2.95 (m, 2H), 2.58-2.53 (m, 1H), 2.36-2.03 (m, 2H), 2.07-2.03 (m, 1H), 1.76-1.68 (m, 2H), 1.63 (br s, 1H), 1.51-1.37 (m 2H); ¹³C NMR (125MHz, CDCl₃) δ 135.7, 117.7, 82.1, 78.4, 77.5, 70.5, 68.5, 39.6, 37.4, 29.9, 26.2; Anal. Calcd for C₁₁H₁₈O₃: C, 66.64, H, 9.15. Found, C, 66.37, H, 9.19.

(1S*, 3S*, 4S*, 6R*)-3-Allyl-2,7-dioxabicyclo[4.4.0]decan-4-ol (12b). Rf 0.08 (30% EtOAc/Hexanes); ¹H NMR (500MHz, CDCl₃) δ 5.68 (dddd, J=17.1, 10.1, 7.1, 7.1 Hz, 1H), 5.17-5.08 (m, 2H), 4.08 (ddd, J=11.0, 5.5, 5.5 Hz, 1H), 3.99 (ddd, J=15.7, 5.4, 5.4 Hz, 1H), 3.93-3.89 (m, 1H), 3.59-3.50 (m, 1H), 3.17 (ddd, J=10.9, 9.2, 4.3 Hz, 1H), 2.98 (ddd, J=11.6, 9.3, 4.4 Hz, 1H), 2.59-2.53 (m, 1H), 2.43-2.38 (m, 1H), 2.14 (ddd, J=11.5, 4.5, 4.5 Hz, 1H), 1.95-1.92 (m, 1H), 1.75-1.61 (m, 4H), 1.40-1.32 (m, 1H); ¹³C NMR (125MHz, CDCl₃) δ 135.2, 117.2, 77.6, 76.2, 69.1, 68.2, 68.1, 34.4, 29.5, 28.8, 25.9.

Oxidation of 12b. TPAP (30 mg, 0.086 mmol, 6 mol %) was added to a mixture of NMO (388 mg, 3.31 mmol), 12b (285 mg, 1.44 mmol), crushed and oven dried 4Å molecular sieves, and CH₂Cl₂
(9.56 mL, 0.15 M). After 10 min the reaction was complete as ascertained by TLC, the mixture was filtered and condensed. The resulting oil was passed through a short pad of silica gel (2 cm in a disposable pipette) eluting with 50% Et₂O/Hexanes and condensed to yield 248 mg (88%) of pure 5b.

**2-((1S*, 3R*, 4S*, 6R*)-4-Hydroxy-2,7-dioxabicyclo[4.4.0]decan-3-yl)acetic Acid.** Ozone was bubbled into a solution of 12a (489 mg, 2.47 mmol) in CH₂Cl₂ (17.3 mL) and MeOH (3.3 mL) at -78°C until the solution turned a persistent blue color. The solution was then allowed to stir for 30 min. Argon was bubbled into the solution until it was colorless, after which the cooling bath was removed and argon was bubbled until the reaction mixture reached r.t.. The reaction mixture was then concentrated and the residue was dissolved in 88% formic acid (1.85 mL) and 30% H₂O₂ (0.96 mL) and heated to 70°C for 8 h. The reaction mixture was again concentrated and the residue was dissolved in Et₂O (20 mL) and extracted with 1 M KOH (3x5 mL). The combined basic aqueous phase was washed with Et₂O (15 mL). The aqueous phase was then acidified with 3N HCl until pH=1-2 and saturated with NaCl. The aqueous phase was extracted with EtOAc (8x20 mL). The combined organic phase was dried over anhydrous MgSO₄, filtered, concentrated and placed under high vacuum for 12 h to afford 453 mg (85%) of the product as a white solid. Alternatively, the crude reaction mixture can be purified directly after the oxidation by concentration followed by flash chromatography (silica gel, solvent ramp: 100 mL each of 2.5%, 5%, 7.5%, 10% MeOH/CH₂Cl₂/20 drops glacial HOAc). Rf 0.25 (5% MeOH/CH₂Cl₂/2 drops glacial HOAc in 10 mL); mp 149-153°C; IR (KBr) 3433, 2960, 1724, 2858, 1690 cm⁻¹; ¹H NMR (500MHz, d₆-acetone) δ 10.6 (br s, 1H), 3.98-3.88 (br s, 1H), 3.81-3.78 (m, 1H), 3.55 (ddd, J=9.1, 9.1, 2.7 Hz, 1H), 3.37 (ddd, J=10.8, 9.4, 4.5 Hz, 1H), 3.33-3.28(m, 1H), 2.96-2.88 (m, 2H), 2.87 (dd, J=15.7, 2.8 Hz, 1H), 2.26 (dd, J=15.7, 9.3 Hz, 1H), 2.55-2.22 (m, 1H), 1.94-1.91 (m, 1H), 1.66, 1.59 (m, 2H), 1.44 (ddd, J=11.2, 11.2, 11.2 Hz, 1H), 1.38-1.30 (m, 1H); ¹³C NMR (125MHz, d₆-acetone) δ 173.5, 80.7, 79.1, 78.2, 70.1, 68.5, 40.5, 38.5, 30.5, 26.7; HRMS (FAB, m-1) for C₁₀H₁₅O₅ calcd 215.0920, found: m/z 215.0912.

**2-((1S*, 3R*, 4S*, 6R*)-4-Allyloxy-2,7-dioxabicyclo[4.4.0]decan-3-yl)acetic Acid.** 2-((1S*, 3R*, 4S*, 6R*)-4-hydroxy-2,7-dioxabicyclo[4.4.0]decan-3-yl)acetic acid (25 mg, 0.12 mmol) was dissolved in DME (0.3 mL) and then added via cannula to a mixture of KH (40 mg of 35% dispersion in mineral oil, 0.35 mmol, 3eq, washed with hexanes prior to addition) in DME (0.3 mL) at 0°C. After 10
min, allyl bromide was added (11 µL, 0.13 mmol, 1.1 eq). The reaction was carefully quenched after 4 h with water (0.3 mL). The organic phase was extracted with 1 N KOH (0.3 mL) and the combined aqueous phase was then washed with Et₂O (2 mL), acidified with 3 N HCl until the pH=1-2, and then extracted with Et₂O (8x2 mL). The combined organic phase was dried over anhydrous MgSO₄, filtered, and concentrated to afford 24 mg (80%) of 13 as a golden oil. If a small amount of the bicyclic hydroxy-acid remains, the two acids can be separated by flash chromatography (silica gel, solvent ramp: 100 mL each of 2.5%, 5%, 7.5%, 10% MeOH/CH₂Cl₂/20 drops glacial HOAc). Rₜ 0.55 (5% MeOH/CH₂Cl₂/2 drops glacial HOAc in 10 mL); IR (neat) 3100, 2944, 2871, 1712, 1098 cm⁻¹; ¹H NMR (500MHz, CDCl₃) δ 10.6 (br s, 1H), 5.87 (dddd, J=16.3, 10.3, 5.9, 5.9 Hz, 1H), 5.26 (ddddd, J=17.3, 1.6, 1.6, 1.6 Hz, 1H), 5.18 (ddddd, J=10.3, 1.2, 1.2, 1.2 Hz, 1H), 4.12 (ddddd, J=12.5, 5.4, 1.2, 1.2 Hz, 1H), 3.94-3.89 (m, 2H), 3.69 (dddd, J=8.9, 8.9, 3.8 Hz, 1H), 3.39-3.34 (m, 1H), 3.22 (dd, J=10.9, 9.3, 4.5 Hz, 1H), 3.08 (ddd, J=11.1, 8.9, 4.5 Hz, 1H), 2.95 (ddd, J=11.5, 8.9, 4.2 Hz, 1H), 2.88 (dd, J=15.6, 3.8 Hz, 1H), 2.50 (dd, J=15.7, 8.2 Hz, 1H), 2.48-2.45 (m, 1H), 2.07-2.04 (m, 1H), 1.72-1.68 (m, 2H) 1.47-1.35 (m, 2H); ¹³C NMR (125MHz, CDCl₃) δ 177.4, 134.6, 117.7, 77.9, 77.2, 76.7, 76.0, 69.9, 68.0, 37.9, 35.4, 29.3, 25.4; HRMS (FAB, m/z) for C₁₃H₁₉O₅ calcd 255.1233, found: m/z 255.1234.

1-Diazo-3-((1S*, 3R*, 4S*, 6R*)-4-allyloxy-2,7-dioxabicyclo[4.4.0]decan-3-yl)propan-2-one.

Isobutylchloroformate (70 µL, 0.53 mmol, 1.0 eq) was added to a mixture of triethylamine (74 µL, 0.53 mmol, 1.0eq) and 13 (137 mg, 0.53 mmol) in Et₂O (2.12 mL). The reaction was heated to reflux for 2.5 h then filtered and added via cannula to a solution of CH₂N₂ (~4mmol) in Et₂O (~12 mL) at 0°C. The reaction was allowed to stand for 12 h and then diluted with Et₂O (12 mL) and carefully quenched with 0.1 M HOAc (10 mL) until gas evolution ceased. The organic phase was then washed with sat. NaHCO₃ (20 mL). The aqueous phase was extracted with Et₂O (10mL) and the combined organic phase was washed with brine (30 mL), dried over anhydrous MgSO₄, filtered, concentrated and purified by flash chromatography (silica gel, 2 cm x 12 cm column, 30% EtOAc/hexanes) to yield 58 mg (44%) of 14 as a yellow solid. Rₜ 0.13 (30% EtOAc/Hexanes); IR (KBr) 3124, 2954, 2852, 2104, 1635, 1097 cm⁻¹; ¹H NMR (500MHz, CDCl₃) δ 5.86 (ddddd, J=16.3, 10.4, 5.0, 5.0 Hz, 1H), 5.34 (br s, 1H), 5.34-5.22 (m, 1H), 5.17-5.15 (m, 1H), 4.12-4.08 (m, 1H), 3.92-3.87 (m, 2H), 3.65 (ddd, J=8.9, 8.9, 2.8 Hz, 1H), 3.37-3.32 (m, 1H), 3.19 (ddd, J=10.6, 9.3, 4.4 Hz, 1H), 3.03 (ddd, J=11.1, 8.9, 4.4 Hz, 1H), 2.92 (ddd, J=11.6, 8.9, 4.3 Hz, 1H), 2.81 (app br d, J=14.8 Hz, 1H), 2.45 (ddd, J=11.6, 4.4, 4.4 Hz, 1H), 2.47-2.36 (s, br 1H), 2.04-2.01 (m, 1H) 1.72-1.66 (m, 2H), 1.44-1.32 (m, 2H); ¹³C NMR (125MHz, CD₂Cl₂, -25°C) δ 193.2,
134.9, 117.1, 77.8, 77.4, 76.5, 75.8, 69.8, 67.9, 55.5, 43.8, 35.4, 29.3, 25.5; HRMS (FAB, m+1) for C\textsubscript{14}H\textsubscript{21}N\textsubscript{2}O\textsubscript{4} calcd 281.1501, found: m/z 281.1501.

Tris(pyran) 15b (α-isomer): To a solution of CH\textsubscript{2}Cl\textsubscript{2} (12.5 mL, 0.01 M) and Cu(tfacac)\textsubscript{2} (2 mg, 5 mol %) heated to reflux, was added via cannula a solution of diazoketone 14 (35 mg, 0.13 mmol, in 2 mL of CH\textsubscript{2}Cl\textsubscript{2}) over 5 min. When the addition was complete, the reaction was monitored by TLC and upon consumption of the diazoketone (120 min), the reaction was cooled to r.t. and a solution of 30% NH\textsubscript{2}OH saturated with NH\textsubscript{4}Cl (10 mL) was added. The aqueous phase was extracted with CH\textsubscript{2}Cl\textsubscript{2} (2x10 mL), the combined organic phase was dried with anhydrous MgSO\textsubscript{4}, filtered and concentrated. The reaction mixture was purified by flash chromatography (silica gel, 2 cm x 12 cm column, solvent ramp: 100 mL each of 10%, 20%, 30%, 40% Et\textsubscript{2}O/Hexanes) to afford 25 mg (80%) of 15b as a white solid. R\textsubscript{f} 0.30 (50% Et\textsubscript{2}O/Hexanes); mp 84-85°C; IR (KBr) 2955, 2874, 1722, 1107, 1021 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (500MHz, CD\textsubscript{2}Cl\textsubscript{2}) \textsuperscript{δ} 5.78 (dddd, J=17.0, 10.2, 6.9, 6.9 Hz, 1H), 5.16-5.10 (m, 2H), 4.04 (ddd, J=9.8, 5.5, 0.6 Hz, 1H), 3.91-3.86 (m, 1H), 3.56 (ddd, J=11.1, 9.3, 4.5 Hz, 1H), 3.43 (ddd, J=11.7, 9.4, 5.6 Hz, 1H), 3.39-3.34 (m, 1H), 3.10-3.05 (m, 2H), 2.82 (ddd, J=16.3, 5.5, 1.1 Hz, 1H), 2.60 (ddd, J=14.5, 9.7, 7.2, 1.2, 1.2 Hz, 1H), 2.45 (ddd, J=16.4, 11.7, 0.6 Hz, 1H), 2.36 (ddd, J=14.9, 6.9, 5.5, 1.4, 1.4 Hz, 1H), 2.28 (ddd, J=11.4, 3.9, 3.9 Hz, 1H), 2.06-2.00 (m, 1H) 1.77-1.67 (m, 2H) 1.55-1.38 (m, 2H); \textsuperscript{13}C NMR (125MHz, CD\textsubscript{2}Cl\textsubscript{2}) \textsuperscript{δ} 207.4, 133.6, 118.4, 81.7, 78.5, 77.6, 76.7, 69.6, 68.5, 43.9, 36.1, 34.8, 29.8, 26.1; HRMS (EI) for C\textsubscript{14}H\textsubscript{20}O\textsubscript{4} calcd 252.1362, found; m/z 252.1369.

Tris(pyran) 15a (β-isomer): Catalytic DBU (1 drop) was added to 15b (22 mg, 0.087 mmol) in toluene (0.9 mL, 0.1 M). The reaction was heated to reflux and monitored by GC until no further change in epimer ratio was observed (6 h). The mixture was then cooled to r.t., condensed and passed through a short pad of silica gel (2 cm in a disposable pipette) eluting with 50% Et\textsubscript{2}O/Hexanes. The solution was then concentrated to yield 20 mg (91%) of a mixture of 15a/b enriched in 15a as a white solid (15a/b: 10/1 determined by GC). R\textsubscript{f} 0.36 (30% EtOAc/Hexanes); mp 88-94°C; IR (KBr) 2955, 2861, 1723, 1098, 1023 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (500MHz, CDCl\textsubscript{3}) \textsuperscript{δ} 5.84 (dddd, J=17.0, 10.2, 6.7, 6.7 Hz, 1H), 5.13 (ddd, J=17.6, 2.4, 2.4, 2.4 Hz, 1H) 5.08-5.05 (m, 1H), 3.96-3.92 (m, 1H), 3.83 (dd, J=7.4, 4.3 Hz, 1H), 3.46-
3.37 (m, 3H), 3.13-3.06 (m, 2H), 2.92 (dd, J = 15.5, 4.9 Hz, 1H), 2.68-2.61 (m, 1H), 2.49-2.32 (m, 3H), 2.09-2.04 (m, 1H), 1.78-1.72 (m, 2H), 1.63-1.56 (m, 1H), 1.49-1.40 (m, 1H); $^{13}$C NMR (75MHz, CD$_2$Cl$_2$) $\delta$205.2, 134.8, 117.5, 83.1, 78.4, 77.5, 77.2, 76.4, 68.4, 45.6, 36.0, 34.2, 29.7, 26.1.

![Chemical structure](image)

**Tris(pyran) 16a.** LiAlH$_4$ (2 mg, 0.04 mmol) was added to a solution of 15a/b (19 mg, 0.075 mmol) in THF (0.75 mL, 0.1 M) cooled to 0°C. The reaction was then allowed to stir until complete consumption of the starting material was evident by TLC. The reaction was quenched with 1:1 Na$_2$SO$_4$·10H$_2$O:Celite and the resulting slurry was stirred for 30 min. Anhydrous MgSO$_4$ was added and the slurry stirred for and additional 30 min. The slurry was then filtered, concentrated and the products separated by flash chromatography (silica gel, 2 cm x 10 cm column, solvent ramp: 100 mL each of 50%, 60%, 70%, 80%, 90% Et$_2$O/Hexanes) to afford 18 mg (94%) of 16a as a white solid and 1 mg (5%) of an isomer. R$_f$ 0.32 (100% Et$_2$O); IR (KBr) 3391, 2939, 2852, 1113, 1088 cm$^{-1}$; $^1$H NMR (500MHz, CDCl$_3$) $\delta$ 5.95 (dddd, $J$=17.2, 10.1, 6.9, 6.9 Hz, 1H), 5.17-5.13 (m, 1H), 5.10-5.08 (m, 1H), 3.93-3.90 (m, 1H), 3.54-3.48 (m, 1H), 3.38 (ddd, $J$=11.4, 11.4, 4.0 Hz, 1H), 3.18 (ddd, $J$=9.2, 6.9, 4.2 Hz, 1H), 3.12-2.99 (m, 4H), 2.58-2.53 (m, 1H), 2.40-2.28 (m, 3H), 2.08-2.05 (m, 1H), 1.76-1.69 (m, 2H), 1.61 (app br d, 1H), 1.54-1.39 (m, 3H); $^{13}$C NMR (75MHz, CD$_2$Cl$_2$) $\delta$ 135.7, 117.1, 82.0, 78.7, 77.8, 77.2, 77.0, 69.9, 68.4, 39.2, 36.9, 36.1, 29.8, 26.1; HRMS (EI) for C$_{14}$H$_{22}$O$_4$ calcd 254.1518, found; m/z 254.1508.

3 Compound 8 was also prepared using Rousseau’s method and is in excellent agreement with published data.