Continuous Pd-Catalyzed Carbonylative Cyclization Using Iron Pentacarbonyl as a CO Source

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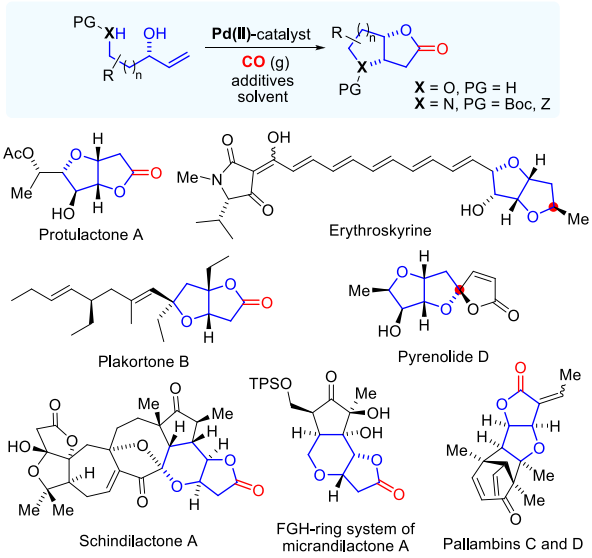
ABSTRACT: This work discloses a continuous flow carbonylation reaction using iron pentacarbonyl as source of CO. The described transformation using this surrogate was designed for use in commonly accessible flow equipment. Optimized conditions were applied to a scalable synthesis of the natural compound isolated from perianal glandular pheromone secretion of the African civet cat. In addition, a flow Pd-catalyzed carbonylation of aryl halides was successfully reported.

INTRODUCTION

Domino reaction processes in organic chemistry have become popular strategies in synthesis laboratories. The growing interest in the preparation of structurally complex and biologically active compounds has led to an expanding effort in the development and use of these approaches.[1] Since its discovery, the domino palladium catalyzed carbonylative process cyclization has been proven as a robust and stereoselective transformation for the synthesis of various bicyclic lactones.[2] Moreover, its chemical tolerance to many functional groups has been demonstrated in various complex natural product syntheses (Scheme 1).[3] Despite the benefits of this domino transformation, there are certain drawbacks that inhibit its common application. One of the main objections being the use of toxic carbon monoxide gas, which is not detectable by human senses. While many modifications of the reaction conditions for this cyclization have appeared over the last years,[4] new approaches are always beneficial, especially one using surrogates for CO gas. For comparison, several methods have been developed to carry out normal carbonylation reactions of aryl halides[5] without the direct use of gaseous CO.[6] For example, using metal carbonyls[7] also or several other CO surrogates[8]. Some of these methods have been also transferred to flow reactors.

Scheme 1. Pd(II)-Catalyzed Carbonylative Cyclization



Indeed continuous-flow methodology has become an important concept of contemporary chemistry for a more sustainable reaction processing. It also facilitates the development of synthetic routes requiring the safe handling of toxic agents and minimizing excess waste.[9] Recent attention has focused on carbonylation reactions of aryl/alkene halides utilizing the benefits arising from the use of flow techniques. To date, several types of the continuous flow for Pd-catalyzed carbonylation have been reported (Figure 1).

Generally, there are two main methods for the introduction of carbon monoxide into the reaction stream depending on which type of flow equipment is used. In 2011, we have developed the flow-approach for carbonylation of aryl and alkenyl iodides employing a tube-in-tube reactor with porous gas-permeable Teflon AF-2400 membrane (Figure 1, I.a).[10] More commonly used methods for precise feeding of CO into a reaction stream employs an in-line mass flow controller (Figure 1, I.b).[11]

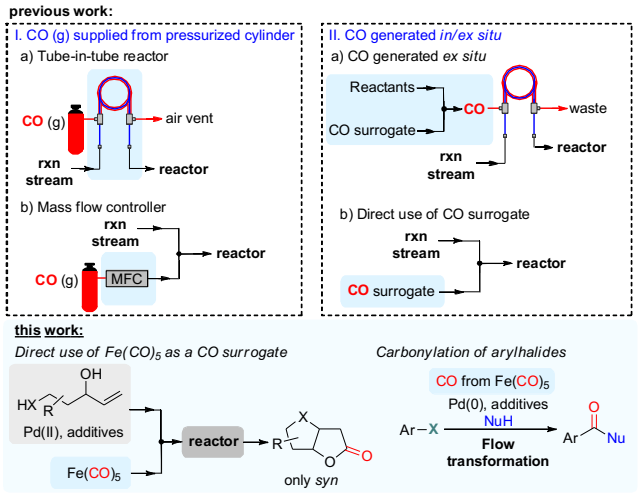


Figure 1. Carbonylations in Microflow Systems

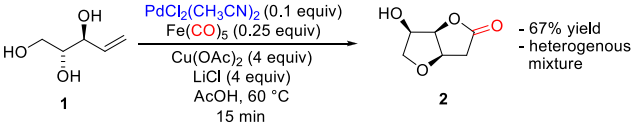
In both cases, the carbon monoxide gas is supplied from a pressurized cylinder. In addition, there are a few continuous-flow transformations utilizing CO surrogates. Hydrolysis of oxalyl chloride using an aqueous NaOH solution leads to *in situ* generation of carbon monoxide, which can then be passed through tube-in-tube reactor to enrich a reaction stream.[12] Similar specialized reactors equipped with a CO gas permeable PTFE inner tube have also been successfully tested in Pd-catalyzed carbonylation using formic acid as an alternative CO source (Figure 1, II.a).[13] Alcázar, De Borggraeve et al.[14] also described continuous-flow transformation using 2,4,6-trichlorophenyl formate as a CO surrogate method (Figure 1, II.b). The limitation of this CO surrogate is the formation of the corresponding trichlorophenol esters, which requires an additional processing step for modification.

RESULTS AND DISCUSSION

In the course of a program directed towards CO gas-free carbonylation,[15] we have developed a new protocol for Pd-catalyzed carbonylation reactions based on the use of iron pentacarbonyl.[15c-d] However, this transformation has its limitations in upscaling. The instant release of gaseous CO after the addition of $Fe(CO)_5$ to reaction mixture causes over-pressure in the reaction flask. *In situ* generation of carbonyl species from $Fe(CO)_5$ directly in the reaction mixture offers excellent opportunities for carrying out this reaction in a continuous mode. Here we report a flow update of homogenous Pd-catalyzed carbonylation reaction using iron pentacarbonyl as a CO surrogate.

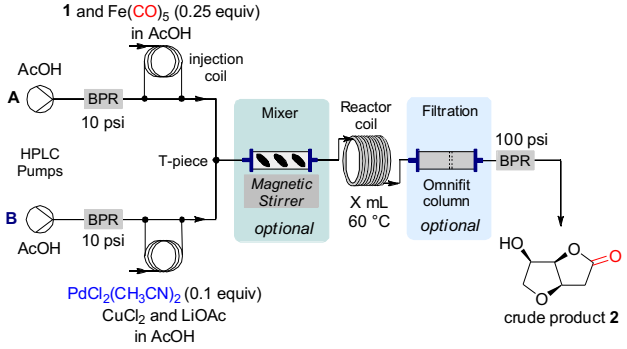
Firstly, we investigated the conditions used for common batch Pd-catalyzed cyclocarbonylation of (amino)alkenols. (Scheme 2).

Scheme 2. Batch Pd(II)-Catalyzed Cyclocarbonylation of pent-4-en-1,2,3-triol 1



Usually, this batch transformation of unsaturated triol **1** under optimized reaction conditions employs 0.25 equiv of liquid $Fe(CO)_5$ which corresponds to 1.25 equiv of CO. However, the reaction cycle necessitates the use of 4 equiv of $Cu(OAc)_2$ and 4 equiv of LiCl as a reoxidation system for $PdCl_2(CH_3CN)_2$ catalyst. Nevertheless, the reaction mixture results in a heterogenous mixture in acetic acid. Full conversion of substrate within 15 minutes is indicated by a color change of the reaction mixture from green to pale brown.[15d] Direct use of these conditions to flow system was not possible due to the insolubility of reagents. Adjustment of the reaction components was, however, necessary. We began the optimization of flow reaction with Pd-catalyzed oxycarbonylation of pent-4-en-1,2,3-triol **1**. Triol **1** was selected as a model substrate for the initial study due to its moderate reactivity compared to other previously used unsaturated alcohols. Firstly, the reoxidation system had to be altered to form a soluble complex in acetic acid. Thus, changing the ratio of Cu(II) and Li(I) salts from 1:1 to 1:2 resulted in the formation of 0.25 M green and homogenous solution at room temperature in acetic acid. We could now focus on further optimization of flow reaction conditions (Table 1).[16]

Table 1. Optimization of Flow Reaction Conditions



entry	reox. system[a] (equiv)	scale (mmol /M[b])	flow rate A/B (mL/min)	reactor (mL) rxn time (min)	mixer / filter.	yield (%)
1[c]	4	0.3/0.4	0.08/0.55	6/10	- / -	-
2	3	0.4/0.6	0.08/0.55	6/10	- / -	33
3	2.5	0.5/0.7	0.08/0.55	6/10	- / -	55
4[d]	3	0.4/0.6	0.08/0.55	6/10	- / -	32
5[e,f]	3	1.8/0.6	0.1/0.7	8/10	+ / -	47
6[e,f]	3	1.8/0.6	0.07/0.47	8/15	+ / -	56
7[e,f]	3	2.2/0.6	0.11/0.75	26/30	+ / -	58
8[g]	3	2.2/0.6	0.22/1.5	26/15	+ / +	56
9[g]	3.5	1.9/0.5	0.22/1.5	26/15	+ / +	59
10[g,h]	3.5	1.9/0.5	0.22/1.5	26/15	+ / +	63

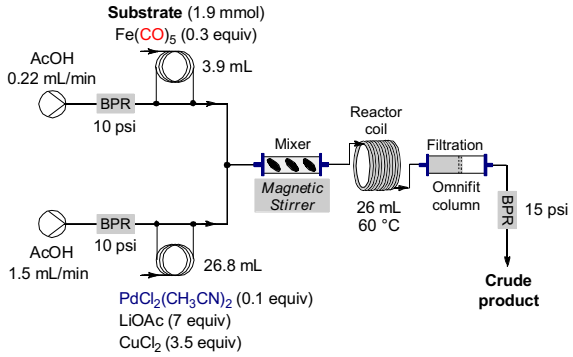
[a]X equiv of reoxidation system corresponds to X equiv of $CuCl_2$ and 2X equiv of LiOAc (0.25 M solution of $CuCl_2$ in AcOH). [b]Concentration of substrate in AcOH. [c]Problems with the isolation of product due to the large amount of salts. [d]Reaction performed at 40 °C. [e]Final BPR was excluded. [f]Segmented flow was observed. [g] BPR (15 psi) at the end of flow system was used. [h]0.3 equiv of $Fe(CO)_5$ was used.

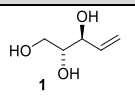
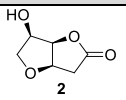
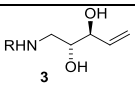
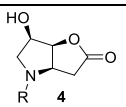
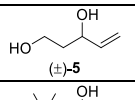
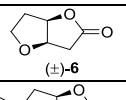
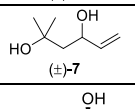
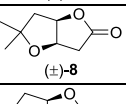
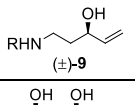
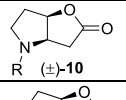
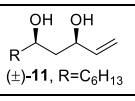
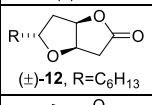
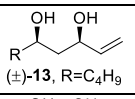
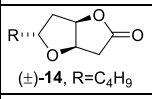
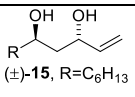
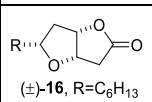
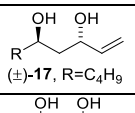
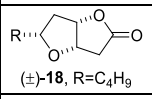
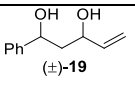
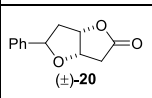
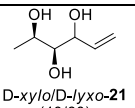
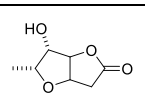
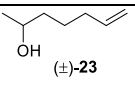
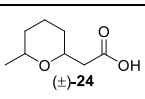
For these experiments a two reaction stream reactor set-up was devised. The reagents were loaded into the injection coils and pumped through a T-piece directly to 1/8-inch HPLC-tube reactor using Knauer Azura HPLC pumps. In some cases, mixer[17] and filtration units were incorporated into the flow system. Optimization reactions were conducted by altering the temperature, the size of the reactor to adjust reaction times and the amount of reoxidant/$Fe(CO)_5$. The results show that the best

conditions for flow reaction were using 3.5 equiv of $CuCl_2$, 7.0 equiv of LiOAc, 0.3 equiv of $Fe(CO)_5$ and 0.1 equiv of Pd(II) catalyst (Table 1, entry 10) (0.3 equiv of $Fe(CO)_5$ corresponds to 1.5 theoretical amount of CO).

The optimal flow system involved HPLC column with frit as a filtration unit to avoid blocking of final back-pressure regulator (BPR) with solid and an in-line mixer for better agitation of two input streams. The reaction time was 15 min at 1.72 mL/min combined flow (26 mL reactor) and the product **1** was isolated after MPLC purification in 63% yield similarly to batch experiment.

Table 2. Continuous Flow Pd(II)-Catalyzed Carbonylation of Alkenols and Aminoalkenols using $Fe(CO)_5$



entry	substrate	product	yield (%)	
			flow	batch[lit.]
1	 **1**	 **2**	63	67[15d]
2	 **3**	 **4**	65 (**4a**, R=Boc) 50 (**4b**, R=Cbz) 62 (**4c**, R=Ts)	74[15d] 27[15d] 64[15d]
3	 (±)-**5**	 (±)-**6**	82	80[15d]
4	 (±)-**7**	 (±)-**8**	83	72[15d]
5	 (±)-**9**	 (±)-**10**	71 (**10a**, R=Boc) 77 (**10b**, R=Cbz) 81 (**10c**, R=Ts)	95[15d] 88[4b] 90[4b]
6	 (±)-**11**, R=C_6H_{13}	 (±)-**12**, R=C_6H_{13}	62	67[18]
7	 (±)-**13**, R=C_4H_9	 (±)-**14**, R=C_4H_9	77	75[19]
8	 (±)-**15**, R=C_6H_{13}	 (±)-**16**, R=C_6H_{13}	39	67[18]
9	 (±)-**17**, R=C_4H_9	 (±)-**18**, R=C_4H_9	54	75[19]
10	 (±)-**19**	 (±)-**20**	46 (*exo*) 15 (*endo*)	N.A.
11	 D-*xylo*/D-*lyxo*-**21** (40/60)	 D-*ido*/D-*galacto*-**22** (60/40)	61	N.A.
12	 (±)-**23**	 (±)-**24**	88	80[20]

With this optimized flow setup, we examined the Pd-catalyzed carbonylation of different alkenols and aminoalkenols (Table 2). Unsaturated alcohols as substrates were available from our previous study[15d, 18-20] and prepared by identical preparative procedures (see Experimental section).

By applying the optimized conditions, non-complex lactones **2**, **4**, **6**, **8**, **10** and **20** were isolated after the MPLC purification in similar yields compared to batch experiments (Table 2, entries 1-5 and 10). We also prepared the Hagen´s gland lactones **12** and **14** in 62 and 77% yield, respectively (Table 2, entries 6 and 7).[18,19] Substrate **21** was transformed using the flow chemistry system into lactone **22** that had been previously used in the formal synthesis of pyrenolide D (61% yield, Table 2, entry 11).[3a] To prove the versatility and effectiveness of this flow transformation, longer run experiments were investigated using substrates **7** and **23**. The flow system was adjusted for direct pumping of the reagent solutions *via* Azura HPLC pumps. Also, substrates and $Fe(CO)_5$ were pumped separately to the system. A higher amount of LiOAc (10.5 equiv) in these experiments was used to prevent precipitation of the reoxidation salt in the stock solution. Following 193 min long experiment using substrate **7** provided product **8** (2.66 g) in 83% yield.[21] Similarly, a large scale synthesis of the natural compound isolated from perianal glandular pheromone secretion of the African civet cat. (1.52 g) using this system was accomplished. The product (±)-*syn*-**24** was isolated after 172 min long run in 53% yield (Figure 2).

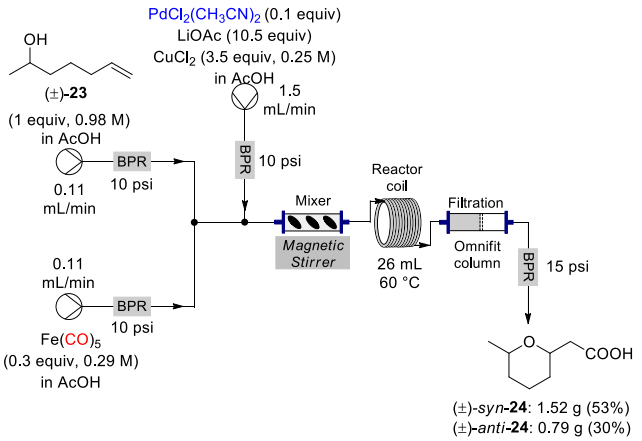


Figure 2. Large scale flow synthesis of natural compound (±)-*syn*-**24**

The above results suggest the protocol may be applied to Pd-catalyzed carbonylative couplings of aryl halides. The conditions for Pd-catalyzed aminocarbonylation of *p*-iodoanisole are based on our previously reported study[22] and applied in flow carbonylation using $Fe(CO)_5$ as a CO surrogate (Figure 3). This transformation after few optimization experiments readily provided expected product in 64% yield.

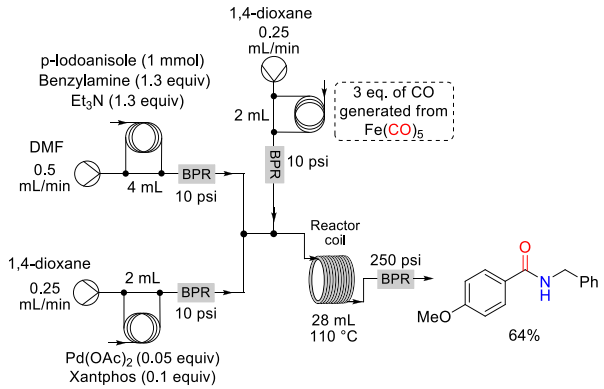


Figure 3. Preliminary flow chemistry setup for aminocarbonylation reactions of aryl iodides.

CONCLUSION

In summary, we have demonstrated the compatibility of iron pentacarbonyl as a CO surrogate for carbonylation reactions in a flow reactor. We have shown the Pd-catalyzed cyclocarbonylation reactions of unsaturated alcohols and aminoalcohols using $Fe(CO)_5$ in a continuous microflow system. The robust process proceeds in readily constructed tube-reactor providing lactones in good yields comparable with batch experiments. The ability to scale-up these reactions in flow in a contained environment, is an advantage in providing access to these useful lactonic building block precursors.

EXPERIMENTAL SECTION

General information

Commercial materials which were obtained from Sigma-Aldrich, Acros Organics, Alfa Aesar or Fisher Scientific were used without further purification. Reactions were monitored using TLC on silica gel. Compound purification was affected by flash chromatography. All solvents were distilled before use. Hexanes refer to the fraction boiling at 60-65 ^{o}C. Flash column liquid chromatography (FLC) was performed on silica gel Kieselgel 60 (15-40 μm, 230-400 mesh) and analytical thin-layer chromatography (TLC) was performed on aluminium plates pre-coated with either 0.2 mm (DC-Alufolien, Merck) or 0.25 mm silica gel 60 F254 (ALUGRAM® SIL G/UV254, Macherey-Nagel). Analyzed compounds were visualized by UV fluorescence and by dipping the plates in an aqueous H_2SO_4 solution of cerium sulphate/ammonium molybdate followed by charring with a heat gun. Melting points were obtained using a Boecius apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on either 300 (75) MHz MercuryPlus or 600 (151) MHz Unity Inova spectrometers from Varian. Chemical shifts (δ) are quoted in ppm and are referenced to the tetramethylsilane (TMS), $CDCl_3$ or DMSO-d_6 as internal standard. FTIR spectra were obtained on a Nicolet 5700 spectrometer (Thermo Electron) equipped with a Smart Orbit (diamond crystal ATR) accessory, using the reflectance technique (4000-400 cm^{-1}). High resolution mass spectra (HRMS) were recorded on an OrbitrapVelos mass spectrometer (Thermo Scientific, Waltham, MA, USA; Bremen, Germany) with a heated electrospray ionization (HESI) source. The mass spectrometer was operated with full scan (50–2000 amu) in positive or negative FT mode (at a resolution of 100,000). The sample was dissolved in methanol and infused via syringe pump at a rate of 5 mL/min. The heated capillary was maintained at 275 °C with a source heater temperature of 50 °C and the sheath, auxiliary and sweep gases were at 10, 5 and 0 units, respectively. Source voltage was set to 3.5 kV.

General procedure for flow carbonylation reactions

General method 1: Injection coil A (3.9 mL, PTFE tubing, 1/8" o.d., 1/16" i.d.) was loaded with a solution of substrate (1.90 mmol, 1 equiv) and $Fe(CO)_5$ (75 μL, 0.57 mmol, 0.3 equiv) in glacial AcOH. Injection coil B (26.8 mL, PTFE tubing, 1/8" o.d., 1/16" i.d.) was loaded with a solution of $CuCl_2$ (0.89 g, 6.64 mmol, 3.5 equiv), LiOAc (0.88 g, 13.27 mmol, 7 equiv) and $PdCl_2(CH_3CN)_2$ (0.05 g, 0.19 mmol, 0.1 equiv) in glacial AcOH. These reaction mixtures were pumped using HPLC pumps (Knauer Azura 4.1S with 10 mL pump head) at 0.22 mL/min and 1.5 mL/min flowrate and mixed at a T-piece. Mixing of both streams was performed by installed magnetic mixer. Subsequently, combined reaction solutions were directed to a reactor (25.7 mL, PTFE tubing, 1/8" o.d., 1/16" i.d) heated in 60 °C water bath. The installation of backpressure regulators (2 × 10 psi) in front of the T-piece was used to ensure unidirectional flow through the heating coil (reactor). On exiting the heating coils, the product flow stream was directed through a glass Omnifit column (15 mm i.d. × 100 mm length) with filter to remove any solids. A backpressure regulator (15 psi) was placed immediately after the glass Omnifit column to prevent out-gassing of the dissolved CO from the solvent mixture. The product stream was then collected into a round bottom flask. The reaction mixture was then concentrated *in vacuo* and the residue was purified by MPLC.

General method 2: A solution of substrate (0.98 M in AcOH, stream A) and the solution of $Fe(CO)_5$ (0.29 M in AcOH, stream B) were pumped using HPLC pumps (Knauer Azura 4.1S with 10 mL pump head) at 0.11 mL/min flowrate and mixed together in T-piece. The combined streams were united with a third solvent stream C (solution of $CuCl_2$ (0.25 M), LiOAc (0.74 M) and $PdCl_2(CH_3CN)_2$ (0.007 M) in AcOH, 1.5 mL/min, pumped by HPLC pump Knauer Azura 4.1S with 10 mL pump head) via a second T-piece. Mixing of streams was performed by installed magnetic mixer. Subsequently, the combined reaction solutions were directed to a reactor (25.7 mL, PTFE tubing, 1/8" o.d., 1/16" i.d.) heated in 60 °C water bath. The installation of backpressure regulators (3 × 10 psi) in front of the T-piece was used to ensure unidirectional flow through the heating coils (reactor). On exiting the heating coil (reactor), the product flow stream was directed through a glass Omnifit column (15 mm i.d. × 100 mm length) with filter to remove any solids. A backpressure regulator (15 psi) was placed immediately after the glass Omnifit column to prevent out-gassing of the dissolved CO from the solvent mixture. The product stream was then collected into a round bottom flask. The reaction mixture was then concentrated *in vacuo* and the crude product was purified by MPLC.

General method 3: A solution of substrate (0.98 M in AcOH, stream A) and the solution of $Fe(CO)_5$ (0.25 M in AcOH, stream B) were pumped using HPLC pumps (Knauer Azura 4.1S with 10 mL pump head) at 0.32 mL/min flowrate and mixed together in T-piece. The combined streams were united with a third stream C (solution of $CuCl_2$ (0.25 M), LiOAc (0.51M) and $PdCl_2(CH_3CN)_2$ (0.007 M) in AcOH, 4.36 mL/min, pumped by HPLC pump Knauer Azura 4.1S with 10 mL pump head) via a second T-piece. Mixing of streams was performed by installed

magnetic mixer. Subsequently, the combined reaction solutions were directed to a reactor (15 mL, PTFE tubing, 1/8" o.d., 1/16" i.d.) heated in 80 °C water sonication bath. The installation of backpressure regulators (3 × 45 psi) in front of the T-piece was used to ensure unidirectional flow through the heating coils (reactor). On exiting the heating coil (reactor), the product flow stream was directed through a glass Omnifit column (15 mm i.d. × 100 mm length) with filter to remove any solids. A backpressure regulator (45 psi) was placed immediately after the glass Omnifit column to prevent out-gassing of the dissolved CO from the solvent mixture. The product stream was then collected into a round bottom flask. The reaction mixture was then concentrated *in vacuo* and the crude product was purified by MPLC.

(1R,5R,8R)-8-Hydroxy-2,6-dioxabicyclo[3.3.0]octan-3-one (**2**). The title compound was prepared according to general method 1 from triol **1** (224 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 40/60 then isocratic hexanes/EtOAc: 40/60) provided desired lactone **2** (172 mg, 63%, white solid). All physical and spectral data were in good agreement with the literature.[23] R_f = 0.20 (hexanes/EtOAc, 2:3); mp 76.5-77.0 °C, lit.[24] mp 77.0-79.0 °C; $[\alpha]_D^{20}$ +87.8 (*c* 1.10, $CHCl_3$); IR (ATR) ν_{max} 3363, 1763, 1144, 1041, 588 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ_H 4.98 (t, *J* = 4.9 Hz, 1H, H-1), 4.76 (ddd, *J* = 6.7, 4.9, 1.5 Hz, 1H, H-5), 4.42 (ddd, *J* = 6.9, 6.0, 4.9 Hz, 1H, H-8), 3.93 (dd, *J* = 9.0, 6.0 Hz, 1H, H-7_a), 3.67 (dd, *J* = 9.0, 6.9 Hz, 1H, H-7_b), 2.92 (dd, *J* = 18.6, 6.7 Hz, 1H, H-4_a), 2.58 (dd, *J* = 18.6, 1.5 Hz, 1H, H-4_b) ppm; ^{13}C NMR{^1H} (75 MHz, CD_3OD) δ_c 178.3, 84.7, 78.4, 72.6, 71.9, 37.4 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_6H_9O_4$: 145.0501, Found: 145.0496, $[M+Na]^+$ Calcd. for $C_6H_8NaO_4$: 167.0320, Found: 167.0315.

(1S,5R,8R)-8-Hydroxy-6-tert-butyloxycarbonyl-2-oxa-6-azabicyclo[3.3.0]octan-3-one (**4a**). The title compound was prepared according to general method 1 from aminodiol **3a** (412 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 50/50 then isocratic hexanes/EtOAc: 50/50) provided desired lactone **4a** (300 mg, 65%, white solid). All physical and spectral data were in good agreement with the literature.[15d] R_f = 0.20 (hexanes/EtOAc, 1:1); mp 128.1-128.4 °C; $[\alpha]_D^{20}$ -80.7 (*c* 0.48, $CHCl_3$); IR (ATR) ν_{max} 3367, 2980, 1774, 1670, 1403 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, mixture of rotamers) δ_H 4.96-4.92 (m, 1H, H-1), 4.51-4.38 (m, 2H, H-5 and H-8), 3.90-3.80 (m, 1H, H-7_a), 3.37-3.20 (m, 1H, H-7_b), 2.84-2.70 (m, 2H, H-4), 2.41 (br s, 1H, OH), 1.46 (s, 9H, $C(C\underline{H}_3)_3$) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$, mixture of rotamers) δ_C 175.7, 175.4, 153.9, 153.3, 82.5, 81.9, 80.9, 70.6, 69.9, 55.9, 50.1, 49.9, 36.7, 36.1, 28.8 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{11}H_{18}NO_5$: 244.1185, Found: 244.1179, $[M+Na]^+$ Calcd. for $C_{11}H_{17}NNaO_5$: 266.1004, Found: 266.0999, $[M+K]^+$ Calcd. for $C_{11}H_{17}KNO_5$: 282.0744, Found: 282.0738.

(1S,5R,8R)-6-Benzyloxycarbonyl-8-hydroxy-2-oxa-6-azabicyclo[3.3.0]octan-3-one (**4b**). The title compound was prepared according to general method 1 from aminodiol **3b** (477 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 40/60 then isocratic hexanes/EtOAc: 40/60) provided desired lactone **4b** (263 mg, 50%, orange solid). All physical and spectral data were in good agreement with the literature.[25] R_f = 0.20 (hexanes/EtOAc, 2:3); mp 107.1-107.6 °C, lit.[26] mp 108-109 °C; $[\alpha]_D^{20}$ -66.8 (*c* 1.69, $CHCl_3$); IR (ATR) ν_{max} 3446, 1776, 1690, 1417, 1096 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, mixture of rotamers) δ_H 7.40-7.30 (m, 5H, H_{Ar}), 5.18-5.07 (m, 2H, PhC$\underline{H}_2$), 4.92 (dd, *J* = 5.7, 4.4 Hz, 1H, H-1), 4.56-4.46 (m, 1H, H-5), 4.40-4.34 (m, 1H, H-8), 3.91-3.85 (m, 1H, H-7_a), 3.44-3.30 (m, 1H, H-7_b), 3.08 (br s, 1H, OH), 2.93-2.67 (m, 2H, H-4) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$, mixture of rotamers) δ_C 175.6, 175.3, 154.6, 154.1, 136.1, 128.8, 128.7, 128.5, 128.4, 128.2, 82.4, 81.8, 70.6, 69.9, 67.8, 67.6, 56.4, 55.9, 50.5, 50.0, 36.7, 36.0 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{14}H_{16}NO_5$: 278.1029, Found: 278.1023, $[M+Na]^+$ Calcd. for $C_{14}H_{15}NNaO_5$: 300.0848, Found: 300.0844.

(1S,5R,8R)-8-Hydroxy-6-tosyl-2-oxa-6-azabicyclo[3.3.0]octan-3-one (**4c**). The title compound was prepared according to general method 1 from aminodiol **3c** (515 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 60/40 then isocratic hexanes/EtOAc: 60/40) provided desired lactone **4c** (350 mg, 62%, white solid). All physical and spectral data were in good agreement with the literature.[15d] R_f = 0.20 (hexanes/EtOAc, 2:3); mp 141.9-142.4, lit.[15d] mp 140-141 °C; IR (ATR) ν_{max} 3419, 1757, 1341, 1160, 537 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.71 (d, *J* = 8.1 Hz, 2H, H_{Ar}), 7.36 (d, *J* = 8.1 Hz, 2H, H_{Ar}), 4.80 (dd, *J* = 6.5, 4.5 Hz, 1H, H-1), 4.40 (td, *J* = 6.5, 4.2 Hz, 1H, H-5), 4.08 (td, *J* = 6.3, 4.5 Hz, 1H, H-8), 3.58 (dd, *J* = 11.3, 6.3 Hz, 1H, H-7_a), 3.36 (dd, *J* = 11.3, 6.3 Hz, 1H, H-7_b), 2.92-2.87 (m, 2H, H-4), 2.45 (s, 3H, CH_3) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 174.6, 144.7, 134.5, 130.3, 127.4, 81.7, 70.4, 57.6, 52.1, 36.9, 21.7 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{13}H_{16}NO_5S$: 298.0749, Found: 298.0745, $[M+Na]^+$ Calcd. for $C_{13}H_{15}NNaO_5S$: 320.0569, Found: 320.0564.

rac-7,7-Dimethyl-2,6-dioxabicyclo[3.3.0]octane-3-one (**(±)-8**). The title compound was prepared according to general method 1 from diol **(±)-7** (247 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 60/40 then isocratic hexanes/EtOAc: 60/40) provided desired lactone **(±)-8** (245 mg, 83%, colorless oil). According to general method 2 in 193 min. long run 2.656 g (83%) of **(±)-8** was obtained. According to general method 3 in 180 min. long run 7.014 g (80%) of **(±)-8** was obtained.All physical and spectral data were in good agreement with the literature.[15d] R_f = 0.20 (hexanes/EtOAc, 3:2); IR (ATR) ν_{max} 2973, 1170, 1154, 1065, 904 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.05 (ddd, *J* = 5.9, 4.7, 2.1 Hz, 1H, H-5), 4.73 (td, *J* = 4.7, 1.7 Hz, 1H, H-1), 2.75 (dd, *J* = 18.3, 4.7 Hz, 1H, H-8_a), 2.67 (dd, *J* = 18.3, 1.7 Hz, 1H, H-8_b), 2.20 (dd, *J* = 14.5, 2.1 Hz, 1H, H-4_a), 2.13 (dd, *J* = 14.5, 5.9 Hz, 1H, H-4_b), 1.34 (s, 3H, CH_3), 1.26 (s, 3H, CH_3) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 175.9, 86.1, 83.2, 77.5, 45.0, 37.3, 29.3, 28.7 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_8H_{13}O_3$: 157.08647, Found: 157.08598, $[M+Na]^+$ Calcd. for $C_8H_{12}NaO_3$: 179.06841, Found: 179.06795.

rac-2,6-Dioxabicyclo[3.3.0]octane-3-one (**(±)-6**). The title compound was prepared according to general method 1 from diol **(±)5** (194 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 50/50 then isocratic hexanes/EtOAc: 50/50) provided desired lactone **(±)-6** (199 mg, 82%, colorless oil). All physical and spectral data were in good agreement with the literature.[27] R_f = 0.20 (hexanes/EtOAc, 1:1); IR (ATR) ν_{max} 1766, 1181, 1066, 1026, 828 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.15-5.07 (m, 1H, H-1), 4.69 (ddd, *J* = 5.8, 4.5, 0.7 Hz, 1H, H-5), 4.01-3.88 (m, 2H, H-7), 2.77 (dd, *J* = 18.7, 5.8 Hz, 1H, H-4_a), 2.66 (dd, *J* = 18.7, 0.7 Hz, 1H, H-4_b), 2.37-2.26 (m, 1H, H-8_a), 2.27-2.07 (m, 1H, H-8_b) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 175.9, 84.4, 78.2, 67.1, 36.4, 33.2 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd.

for:$C_6H_9O_3$: 129.0552, Found: 129.0546, $[M+Na]^+$ Calcd. for $C_6H_8NaO_3$: 151.0371, Found: 151.0366.

rac-6-(tert-Butyloxycarbonyl)-2-oxa-6-azabicyclo[3.3.0]octan-3-one (**(±)-10a**). The title compound was prepared according to general method 1 from amino alcohol **(±)-9a** (382 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 60/40 then isocratic hexanes/EtOAc: 60/40) provided desired lactone **(±)-10a** (306 mg, 71%, white solid). All physical and spectral data were in good agreement with the literature.[28] R_f = 0.20 (hexanes/EtOAc, 3:2); mp 108.3-108.7, lit.[28] mp 109-110 °C; IR (ATR) ν_{max} 1768, 1681, 1409, 1163, 770 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, mixture of rotamers) δ_H 5.05 (br s, 1H, H-1), 4.49-4.39 (m, 1H, H-5), 3.82-3.65 (m, 1H, H-7_a), 3.35 (td, J = 11.1, 6.1 Hz, 1H, H-7_b), 2.90-2.67 (m, 2H, H-4), 2.29 (dd, J = 14.2, 6.1 Hz, 1H, H-8_a), 2.09-1.96 (m, 1H, H-8_b) 1.46 (s, 9H, C(C$\underline{H}_3$)$_3$) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$, mixture of rotamers) δ_C 176.0, 175.6, 153.9, 153.3, 84.3, 83.3, 80.7, 58.0, 44.4, 44.1, 36.8, 36.0, 30.8, 30.3, 28.6. ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{11}H_{18}NO_4$: 228.1236, Found: 228.1230, $[M+Na]^+$ Calcd. for $C_{11}H_{17}NNaO_4$: 250.1055, Found: 250.1050, $[M+K]^+$ Calcd. for $C_{11}H_{17}KNO_4$: 266.0795, Found: 266.0789.

rac-6-Benzyloxycarbonyl-2-oxa-6-azabicyclo[3.3.0]octan-3-one (**(±)-10b**)The title compound was prepared according to general method 1 from amino alcohol **(±)-9b** (446 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 50/50 then isocratic hexanes/EtOAc: 50/50) provided desired lactone **(±)-10b** (381 mg, 77%, pale yellow solid). All physical and spectral data were in good agreement with the literature.[29] R_f = 0.20 (hexanes/EtOAc, 1:1); mp 99.0-99.5, lit.[29] mp 100-101 °C; IR (ATR) ν_{max} 1762, 1697, 1419, 1111, 734 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, mixture of rotamers) δ_H 7.40-7.30 (m, 5H, H_{Ar}), 5.19-5.08 (m, 3H, H-1, PhC$\underline{H}_2$), 4.54-4.45 (m, 1H, H-5), 3.91-3.76 (m, 1H, H-7_a), 3.43 (td, J = 11.1, 6.2 Hz, 1H, H-7_b), 2.94-2.69 (m, 2H, H-4), 2.32 (dd, J = 14.1, 6.2 Hz, 1H, H-8_a), 2.11-1.98 (m, 1H, H-8_b) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$, mixture of rotamers) δ_C 175.6, 175.2, 154.4, 154.0, 136.3, 128.8, 128.7, 128.5, 128.3, 128.3, 128.2, 84.1, 83.1, 67.6, 67.4, 58.5, 57.9, 44.7, 44.3, 36.7, 35.8, 30.8, 30.4. ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{14}H_{16}NO_4$: 262.1079, Found: 262.1074, $[M+Na]^+$ Calcd. for $C_{14}H_{15}NNaO_4$: 284.0899, Found: 284.0893, $[M+K]^+$ Calcd. for $C_{14}H_{15}KNO_4$: 300.0638, Found: 300.0633.

rac-6-Tosyl-2-oxa-6-azabicyclo[3.3.0]octan-3-one (**(±)-10c**). The title compound was prepared according to general method 1 from amino alcohol **(±)-9c** (485 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 50/50 then isocratic hexanes/EtOAc: 50/50) provided desired lactone **(±)-10c** (433 mg, 81%, white solid). All physical and spectral data were in good agreement with the literature.[30] R_f = 0.20 (hexanes/EtOAc, 1:1); mp 131.9-132.5, lit.[30] mp 133-134 °C; IR (ATR) ν_{max} 1773, 1335, 1156, 973, 573 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.75-7.68 (m, 2H, H_{Ar}), 7.35 (dd, J = 8.6, 0.7 Hz, 2H, H_{Ar}), 4.96 (td, J = 5.4, 1.4 Hz, 1H, H-1), 4.37 (ddd, J = 6.6, 5.4, 1.3 Hz, 1H, H-5), 3.58 (ddd, J = 11.3, 8.6, 2.7 Hz, 1H, H-7_a), 3.53-3.42 (m, 1H, H-7_b), 2.96 (dd, J = 18.7, 1.3 Hz, 1H, H-4_a), 2.84 (dd, J = 18.7, 6.6 Hz, 1H, H-4_b), 2.45 (s, 3H, CH_3), 2.25-2.13 (m, 1H, H-8_a), 1.83-1.68 (m, 1H, H-8_b) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 174.9, 144.4, 134.9, 130.0, 127.3, 83.5, 60.1, 47.0, 36.8, 31.3, 21.7 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{13}H_{16}NO_4S$: 282.0800, Found: 282.0795, $[M+Na]^+$ Calcd. for $C_{13}H_{15}NNaO_4S$: 304.0620, Found: 304.0614, $[M+K]^+$ Calcd. for $C_{13}H_{15}KNO_4S$: 320.0359, Found: 320.0353.

D-ido/D-galacto-7-methyl-8-hydroxy-2,6-dioxabicyclo[3.3.0]octan-3-one (**22**). The title compounds were prepared according to general method 1 from mixture of (2*R*,3*S*,4*S*)-hex-5-ene-2,3,4-triol and (2*R*,3*S*,4*R*)-hex-5-ene-2,3,4-triol (ratio 40:60) (251 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 40/60 then isocratic hexanes/EtOAc: 40/60) provided desired lactones D-*ido*/D-*galacto* **(22)** as inseparable mixture (183 mg, 61%, ratio: 60:40 from ^1H NMR, white solid). All physical and spectral data of **D-*ido* 22** were in good agreement with the literature.[31] R_f = 0.20 (hexanes/EtOAc, 2:3); mp 136.8-137.3, lit.[31] mp 138-140 °C; IR (ATR) ν_{max} 3344, 1767, 1138, 1040, 822 cm^{-1}; **D-*ido* (22)**: ^1H NMR (300 MHz, $CDCl_3$) δ_H 4.98 (dd, J = 10.6, 4.9 Hz, 1H, H-1), 4.95-4.89 (m, 1H, H-5), 4.25-4.22 (m, 1H, H-8), 4.14 (qd, J = 6.3, 2.8 Hz, 1H, H-7), 2.81-2.58 (m, 2H, H-4), 2.01 (s, 1H, OH), 1.30 (t, J = 6.3 Hz, 3H, CH_3) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 175.8, 88.1, 76.3, 76.0, 75.5, 36.0, 13.1 ppm; **D-*galacto* (22)**: ^1H NMR (300 MHz, $CDCl_3$) δ_H 4.95-4.89 (m, 1H, H-1), 4.59 (td, J = 6.1, 3.1 Hz, 1H, H-5), 4.28-4.25 (m, 1H, H-8), 3.95 (qd, J = 6.3, 4.2 Hz, 1H, H-7), 2.81-2.58 (m, 2H, H-4), 2.01 (s, 1H, OH), 1.30 (t, J = 6.3 Hz, 3H, CH_3) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 175.4, 83.5, 79.0, 75.8, 72.1, 36.2, 14.0 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_7H_{11}O_4$: 159.0657, Found: 159.0653, $[M+Na]^+$ Calcd. for $C_7H_{10}NaO_4$: 181.0477, Found: 181.0472.

rac-(1R,5R,7S)-7-Phenyl-2,6-dioxabicyclo[3.3.0]octane-3-one (**(±)-exo-20**) and *rac-(1R,5R,7R)-7-Phenyl-2,6-dioxabicyclo[3.3.0]octane-3-one* (**(±)-endo-20**). The title compounds were prepared according to general method 1 from diol **(±)-19** (338 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 75/25 then isocratic hexanes/EtOAc: 75/25) provided desired lactones **(±)-exo-20** (178 mg, 46%, orange oil) and **(±)-endo-20** (58 mg, 15%, orange oil). All physical and spectral data of **(±)-exo-20** were in good agreement with the literature.[32] **(±)-exo-20**: R_f = 0.20 (hexanes/EtOAc, 7:3); IR (ATR) ν_{max} 1774, 1171, 1059, 944, 754 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.41-7.27 (m, 5H, H_{Ar}), 5.24 (t, J = 4.8 Hz, 1H, H-1), 5.13 (dd, J = 10.6, 4.8 Hz, 1H, H-7), 5.05 (ddd, J = 5.8, 4.8, 1.6 Hz, 1H, H-5), 2.91-2.79 (m, 2H, H-4), 2.71 (dd, J = 14.2. 4.8 Hz, 1H, H-8_a), 2.10-1.98 (m, 1H, H-8_b) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 176.0, 140.0, 128.8, 128.2, 125.9, 85.0, 79.8, 78.4, 41.7, 36.8 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{12}H_{13}O_3$: 205.0865, Found: 205.0858, $[M+Na]^+$ Calcd. for $C_{12}H_{12}NaO_3$: 227.0684, Found: 227.0678, $[M+K]^+$ Calcd. for $C_{12}H_{12}KO_3$: 243.0424, Found: 243.0417; **(±)-endo-20**: R_f = 0.20 (hexanes/EtOAc, 7:3); IR (ATR) ν_{max} 1775, 1194, 1029, 754, 581 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.41-7.27 (m, 5H, H_{Ar}), 5.14 (ddd, J = 7.0, 4.6, 2.4 Hz, 1H, H-1), 4.97 (dd, J = 8.3, 7.6 Hz, 1H, H-7), 4.69 (td, J = 4.6, 1.6 Hz, 1H, H-5), 2.93-2.82 (m, 2H, H-4), 2.82-2.74 (m, 1H, H-8_a), 2.26 (ddd, J = 14.5, 8.3, 2.4 Hz, 1H, H-8_b) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 175.4, 140.1, 128.8, 128.3, 126.2, 84.7, 81.8, 79.0, 41.1, 36.3 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{12}H_{13}O_3$: 205.0865, Found: 205.0859, $[M+Na]^+$ Calcd. for $C_{12}H_{12}NaO_3$: 227.0684, Found: 227.0679, $[M+K]^+$ Calcd. for $C_{12}H_{12}KO_3$: 243.0424, Found: 243.0419.

rac-(1R,5R,7R)-7-"Hexyl-2,6-dioxabicyclo[3.3.0]octane-3-one (**(±)-12**). The title compound was prepared according to general method 1 from diol **(±)-11** (354 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 80/20 then isocratic hexanes/EtOAc: 80/20) provided desired

lactone **(±)-12** (250 mg, 62%, pale yellow oil). All physical and spectral data were in good agreement with the literature.[18] R_f= 0.20 (hexanes/EtOAc, 4:1); IR (ATR) ν_{max} 2927, 1777, 1170, 1059, 831 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.11 (t, J = 4.8 Hz, 1H, H-1), 4.84-4.78 (m, 1H, H-5), 4.12-4.01 (m, 1H, H-7), 2.76 (dd, J = 18.8, 6.3 Hz, 1H, H-4_a), 2.64 (d, J = 18.8 Hz, 1H, H-4_b), 2.37 (ddd, J = 13.9, 4.8, 0.6 Hz, 1H, H-8_a), 1.66 (ddd, J = 13.9, 10.4, 5.0 Hz, 1H, H-8_b), 1.60-1.38 (m, 2 H, C$\underline{H}_2$(CH$_2$)$_4$CH$_3$), 1.38-1.19 (m, 8 H, CH$_2$(C$\underline{H}_2$)$_4$CH$_3$), 0.88 (t, J = 7.0 Hz, 3H, CH$_3$) ppm; ^{13}C NMR {^1H} (75 MHz, $CDCl_3$) δ_C 176.2, 85.1, 78.4, 77.5, 39.0, 36.8, 34.8, 31.9, 29.4, 26.1, 22.7, 14.2 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{12}H_{21}O_3$: 213.1491, Found: 213.1485, $[M+Na]^+$ Calcd. for $C_{12}H_{20}NaO_3$: 235.1310, Found: 235.1305.

rac-(1R,5R,7S)-7-^{n}Hexyl-2,6-dioxabicyclo[3.3.0]octane-3-one (**(±)-16**). The title compound was prepared according to general method 1 from diol **(±)-15** (354 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 80/20 then isocratic hexanes/EtOAc: 80/20) provided desired lactone **(±)-16** (157 mg, 39%, pale yellow oil). All physical and spectral data were in good agreement with the literature.[18] R_f = 0.20 (hexanes/EtOAc, 4:1); IR (ATR) ν_{max} 2928, 1775, 1152, 1066, 893 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.00 (ddd, J = 6.9, 4.5, 2.3 Hz, 1H, H-1), 4.53-4.43 (m, 1H, H-5), 3.97-3.86 (m, 1H, H-7), 2.73-2.66 (m, 2H, H-4), 2.41 (dt, J = 14.2, 6.9 Hz, 1H, H-8_a), 1.86 (ddd, J = 14.2, 7.9, 2.3 Hz, 1H, H-8_b), 1.73-1.43 (m, 2H, C$\underline{H}_2$(CH$_2$)$_4$CH$_3$), 1.43-1.12 (m, 8H, CH$_2$(C$\underline{H}_2$)$_4$CH$_3$), 0.86 (t, J = 7.0 Hz, 3H, CH$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 175.6, 84.8, 80.5, 78.3, 38.4, 36.5, 35.6, 31.8, 29.3, 26.1, 22.7, 14.2 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{12}H_{21}O_3$: 213.1491, Found: 213.1485, $[M+Na]^+$ Calcd. for $C_{12}H_{20}NaO_3$: 235.1310, Found: 235.1304, $[M+K]^+$ Calcd. for $C_{12}H_{20}KO_3$: 251.1050, Found: 251.1043.

rac-(1R,5R,7R)-7-^{n}Butyl-2,6-dioxabicyclo[3.3.0]octane-3-one (**(±)-14**). The title compound was prepared according to general method 1 from diol **(±)-13** (300 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 75/25 then isocratic hexanes/EtOAc: 75/25) provided desired lactone **(±)-14** (269 mg, 77%, pale yellow oil). All physical and spectral data were in good agreement with the literature.[18] R_f = 0.20 (hexanes/EtOAc, 4:1); IR (ATR) ν_{max} 2931, 1774, 1175, 1059, 832 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.11 (t, J = 4.9 Hz, 1H, H-1), 4.84-4.77 (m, 1H, H-5), 4.12-4.00 (m, 1H, H-7), 2.76 (dd, J = 18.8, 6.4 Hz, 1H, H-4_a), 2.63 (d, J = 18.8 Hz, 1H, H-4_b), 2.37 (dd, J = 13.9, 4.7 Hz, 1H, H-8_a), 1.66 (dd, J = 13.9, 10.4, 4.9 Hz, 1H, H-4_b), 1.60-1.43 (m, 2H, C$\underline{H}_2$(CH$_2$)$_2$CH$_3$), 1.43-1.17 (m, 4H, CH$_2$(C$\underline{H}_2$)$_2$CH$_3$), 0.90 (t, J = 7.0 Hz, 3H, CH$_3$) ppm; ^{13}C NMR {^1H} (75 MHz, $CDCl_3$) δ_C 176.2, 85.1, 78.4, 77.5, 39.0, 36.8, 34.5, 28.3, 22.8, 14.1 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{10}H_{17}O_3$: 185.1178, Found: 185.1172, $[M+Na]^+$ Calcd. for $C_{10}H_{16}NaO_3$: 207.0997, Found: 207.0992, $[M+K]^+$ Calcd. for $C_{10}H_{16}KO_3$: 223.0737, Found: 223.0730.

rac-(1R,5R,7S)-7-^{n}Butyl-2,6-dioxabicyclo[3.3.0]octane-3-one (**(±)-18**). The title compound was prepared according to general method 1 from diol **(±)-17** (300 mg, 1.90 mmol). The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 75/25 then isocratic hexanes/EtOAc: 75/25) provided desired lactone **(±)-18** (189 mg, 54%, pale yellow oil). All physical and spectral data were in good agreement with the literature.[18] R_f = 0.20 (hexanes/EtOAc, 4:1); IR (ATR) ν_{max} 2932, 1774, 1152, 1067, 898 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.01 (ddd, J = 6.9, 4.4, 2.2 Hz, 1H, H-1), 4.54-4.46 (m, 1H, H-5), 3.99-3.87 (m, 1H, H-7), 2.72 (d, J = 3.4 Hz, 2H, H-4), 2.48-2.36 (m, 1H, H-8_a), 1.87 (ddd, J = 14.3, 7.9, 2.2 Hz, 1H, H-8_b), 1.73-1.45 (m, 2H, C$\underline{H}_2$(CH$_2$)$_2$CH$_3$), 1.45-1.19 (m, 4H, CH$_2$(C$\underline{H}_2$)$_2$CH$_3$), 0.89 (t, J = 7.0 Hz, 3H, CH$_3$) ppm; ^{13}C NMR {^1H} (75 MHz, $CDCl_3$) δ_C 175.7, 84.8, 80.5, 78.4, 38.4, 36.5, 35.3, 28.3, 22.7, 14.1 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{10}H_{17}O_3$: 185.1178, Found: 185.1172, $[M+Na]^+$ Calcd. for $C_{10}H_{16}NaO_3$: 207.0997, Found: 207.0992.

(6-Methyltetrahydro-2H-pyran-2-yl) acetic acid (**(±)-24**). The title compounds were prepared according to general method 1 from alcohol **(±)-23** (217 mg, 1.90 mmol. After evaporation of acetic acid the residue was dissolved in EtOAc (50 mL) and solution of HCl was added (w = 0.12, 25 mL). The organic phase was separated, and the aqueous phase was extracted with EtOAc (9x50 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated in vacuo. The purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 50/50 then isocratic hexanes/EtOAc: 50/50) provided desired acids **(±)-*syn*-24** (198, 66%, white solid) and **(±)-*anti*-24** (66, 22%, colourless oil). According to general method 2 in 172 min. long run 1.52 g (53%) of **(±)-*syn*-24** and 0.79 g (30%) of **(±)-*anti*-24** were obtained. All physical and spectral data were in good agreement with the literature.[33] **(±)-*syn*-24**: R_f = 0.20 (hexanes/EtOAc, 1:1); mp 56.3-56.7 °C, lit.[34] mp 54-55 °C; IR (ATR) ν_{max} 2941, 1707, 1226, 1076, 937 cm^{-1} ^1H NMR (300 MHz, $CDCl_3$) δ_H 3.83-3.71 (m, 1H, H-6), 3.63-3.49 (m, 1H, H-2), 2.57 (dd, J = 16.0, 7.2 Hz, 1H, H_a from C$\underline{H}_2$CO), 2.51 (dd, J = 16.0, 5.3 Hz, 1H, H_b from C$\underline{H}_2$CO), 1.91-1.78 (m, 1H, H-3_a), 1.64 (tdd, J = 5.9, 4.5, 2.7 Hz, 2H, H-3_b and H-5_b), 1.59-1.46 (m, 1H, H-5_a), 1.37-1.23 (m, 2H, H-4), 1.21 (d, J = 6.2 Hz, 3H, CH$_3$) ppm; ^{13}C NMR {^1H} (75 MHz, $CDCl_3$) δ_C 175.3, 74.7, 74.1, 41.4, 32.9, 30.9, 23.3, 22.1 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_8H_{15}O_3$: 159.1021, Found: 159.1017, $[M+Na]^+$ Calcd. for $C_8H_{14}NaO_3$: 181.0841, Found: 181.0836, $[M+K]^+$ Calcd. for $C_8H_{14}KO_3$: 197.0580, Found: 197.0573; **(±)-*anti*-24**: R_f = 0.15 (hexanes/EtOAc, 1:1); IR (ATR) ν_{max} 2920, 1705, 1440, 1086, 902 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 4.24 (ddd, J = 12.3, 8.0, 4.7 Hz, 1H, H-2), 4.08-3.95 (m, 1H, H-6), 2.69 (dd, J = 15.3, 8.0 Hz, 1H, H_a from C$\underline{H}_2$CO), 2.46 (dd, J = 15.3, 4.7 Hz, 1H, H_b from C$\underline{H}_2$CO), 1.78-1.60 (m, 4H, H-5 and H-3), 1.44-1.28 (m, 2H, H-4), 1.21 (d, J = 6.5 Hz, 3H, C$\underline{H}_3$) ppm; ^{13}C NMR {^1H} (75 MHz, $CDCl_3$) δ_C 175.8, 68.2, 67.7, 39.0, 31.0, 29.8, 19.2, 18.1 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_8H_{15}O_3$: 159.1021, Found: 159.1019, $[M+Na]^+$ Calcd. for $C_8H_{14}NaO_3$: 181.0841, Found: 181.0837, $[M+K]^+$ Calcd. for $C_8H_{14}KO_3$: 197.0580, Found: 197.0576.

Synthesis of starting materials

(S)-1-((R)-Oxiran-2-yl)prop-2-en-1-ol (**26**). To a suspension of crushed molecular sieves (9.80 g, 4Å) in anhydrous CH_2Cl_2 (383 mL) was added dropwise the solution of L-(+)-DET (8.0 mL, 46.55 mmol, 0.24 equiv) in anhydrous CH_2Cl_2 (11.5 mL) at -25 °C followed by a solution of Ti(O^{i}Pr)$_4$ (11.5 mL, 38.79 mmol, 0.2 equiv) in anhydrous CH_2Cl_2 (11.5 mL). After 30 min. of stirring at same temperature the solution of ^{t}BuOOH (23.3 mL, 13.3 M in anhydrous CH_2Cl_2, 310.36 mmol, 1.6 equiv) was added dropwise and mixture was left to stir for another 15 min. Then the solution of divinylcarbinol **25** (16.32 g, 193.97 mmol, 1 equiv) in anhydrous CH_2Cl_2 (6 mL) was added and resulting mixture was stirred at -25 °C for 10 days. Subsequently, solution of tartaric acid (25 g, 168.76 mmol, 0.87 equiv) in water (63 mL) was added and the biphasic mixture was left to warm to room temperature under vigorous stirring. After

filtering of insoluble particles, the organic phase was separated, and aqueous one was extracted with CH_2Cl_2 (3x100 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. Distillation of the residue (23 mbar, 60-75 °C) provided desired epoxide **26** (9.90 g, colorless oil) in 51% yield. All physical and spectral data were in good agreement with the literature.[35] R_f = 0.30 (hexanes/EtOAc, 13:7); $[\alpha]_D^{20}$ +58.1 (*c* 1.70, $CHCl_3$); IR (ATR) ν_{max} 3406, 1251, 930, 885, 466 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.85 (ddd, *J* = 17.1, 10.5, 6.2 Hz, 1H, H-4), 5.39 (dt, *J* = 17.1, 1.3 Hz, 1H, H-5_a), 5.26 (dt, *J* = 10.5, 1.3 Hz, 1H, H-5_b), 4.38-4.29 (m, 1H, H-3), 3.09 (ddd, *J* = 6.0, 3.9, 2.9 Hz, 1H, H-2), 2.80 (dd, *J* = 5.0, 2.9 Hz, 1H, H-1_a), 2.75 (dd, *J* = 5.0, 3.9 Hz, 1H, H-1_b), 2.06 (s, 1H, OH) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 135.6, 117.8, 70.3, 54.0, 43.6 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_5H_9O_2$: 101.0603, Found: 101.0597, $[M+Na]^+$ Calcd. for $C_5H_8NaO_2$: 123.0422, Found: 123.0416.

(2R,3S)-Pent-4-ene-1,2,3-triol (**1**). Epoxide **26** (10.15 g, 101.38 mmol, 1 equiv) was dissolved in the solution of AcOH (2 mL, 35.48 mmol, 0.35 equiv) in water (338 mL). This mixture was stirred overnight at 60 °C and then concentrated in vacuo. The crude product (11.18 g, 93%, colorless oil) was used without further purification. All physical and spectral data were in good agreement with the literature.[35] R_f = 0.15 (CH_2Cl_2/MeOH, 17:3); $[\alpha]_D^{20}$ -25.8 (*c* 1.35, MeOH); IR (ATR) ν_{max} 3316, 1423, 1026, 992, 468 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ_H 6.01 (ddd, *J* =17.2, 10.5, 6.5 Hz, 1H, H-4), 5.32 (ddd, *J* = 17.2, 1.9, 1.4 Hz, 1H, H-5_a), 5.21 (ddd, *J* = 10.5, 1.9, 1.4 Hz, 1H, H-5_b), 4.07 (ddd, *J* = 6.5, 2.7, 1.4 Hz, 1H, H-3), 3.73-3.64 (m, 1H, H-2), 3.63-3.53 (m, 2H, H-1) ppm; ^{13}C NMR{^1H} (75 MHz, CD_3OD) δ_C 139.1, 116.4, 76.0, 74.9, 64.4 ppm; HRMS (ESI): *m/z* $[M+Na]^+$ Calcd. for $C_5H_{10}NaO_3$: 141.0528, Found: 141.0523.

(2R,3S)-1-Aminopent-4-ene-2,3-diol (**27**). A mixture of epoxide **26** (1.4 g, 13.98 mmol, 1 equiv) and ammonia (15 mL, 25% wt in water) was stirred overnight at room temperature and then concentrated in vacuo. The crude product (1.64 g, 82%, colorless oil) was used without further purification. All physical and spectral data were in good agreement with the literature.[36] R_f = 0.10 (CH_2Cl_2/MeOH, 17:3); $[\alpha]_D^{20}$ -36.0 (*c* 0.71, $CHCl_3$); IR (ATR) ν_{max} 3084, 1645, 1570, 991, 928 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ_H 5.97 (ddd, *J* =17.3, 10.5, 6.1 Hz, 1H, H-4), 5.30 (ddd, *J* = 17.3, 1.9, 1.5 Hz, 1H, H-5_a), 5.18 (ddd, *J* = 10.5, 1.9, 1.3 Hz, 1H, H-5_b), 3.97 (dddd, *J* = 6.1, 5.9, 1.5, 1.3 Hz, 1H, H-3), 3.44 (ddd, *J* = 7.9, 5.9, 3.5 Hz, 1H, H-2), 2.81 (dd, *J* = 13.2, 3.5 Hz, 1H, H-1_a), 2.64 (dd, *J* = 13.2, 7.9 Hz, 1H, H-1_b) ppm; ^{13}C NMR{^1H} (75 MHz, CD_3OD) δ_C 139.4, 116.4, 76.2, 76.0, 44.7 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_5H_{12}NO_2$: 118.0868, Found: 118.0865.

tert-Butyl (2R,3S)-2,3-dihydroxypent-4-enylcarbamate (**3a**). To a solution of amino alcohol **27** (1.33 g, 11.35 mmol, 1 equiv) in MeOH (26.4 mL) was added Et_3N (8.9 mL, 63.58 mmol, 5.6 equiv) and the mixture was left to stir for 10 min. Subsequently, Boc_2O (3.15 g, 14.42 mmol, 1.27 equiv) was added portion wise and the resulting mixture was stirred at room temperature overnight. After concentration in vacuo, the residue was purified by MPLC (hexanes/EtOAc: 100/0 to 50/50 then isocratic hexanes/EtOAc: 50/50) providing desired product **3a** (1.76 g, white solid) in 71% yield. All physical and spectral data were in good agreement with the literature.[15d] R_f = 0.20 (hexanes/EtOAc, 1:1); mp 71.2-71.7 °C; $[\alpha]_D^{20}$ -14.9 (*c* 2.20, MeOH); IR (ATR) ν_{max} 3296, 1677, 1549, 1073, 669 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.92 (ddd, *J* = 17.1, 10.5, 6.0 Hz, 1H, H-4), 5.37 (dt, *J* = 17.1, 1.4 Hz, 2H, H-5_a), 5.32-5.21 (m, 1H, H-5_b), 5.12 (s, 1H, NH), 4.05 (tt, *J* = 6.0, 1.4 Hz, 2H, H-3), 3.61 (td, *J* = 6.0, 3.4 Hz, 1H, H-2), 3.39 (dd, *J* = 14.7, 6.0 Hz, 2H, H-1_a), 3.27 (dd, *J* = 14.7, 3.4 Hz, 1H, H-1_b), 3.06 (s, 2H, OH), 1.44 (s, 9H, $CH(C\underline{H}_3)_3$) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 157.8, 136.8, 117.5, 80.3, 74.0, 73.9, 42.4, 28.5 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{10}H_{20}NO_4$: 218.1392, Found: 218.1387, $[M+Na]^+$ Calcd. for $C_{10}H_{19}NNaO_4$: 240.1212, Found: 240.1206, $[M+K]^+$ Calcd. for $C_{10}H_{19}KNO_4$: 256.0951, Found: 256.0945.

Benzyl (2R,3S)-2,3-dihydroxypent-4-enylcarbamate (**3b**). To a solution of amino alcohol **27** (1.24 g, 9.48 mmol, 1 equiv) and $NaHCO_3$ (1.83 g, 21.81 mmol, 2.3 equiv) in H_2O (20 mL) was added dropwise CbzCl (2.3 mL, 14.23 mmol, 1.5 equiv) at 0 °C. The resulting mixture was stirred at same temperature for 5h. Reaction mixture was then extracted with $CHCl_3$ (2x15 mL), the combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. Crystallization of the crude material from the mixture hexanes/EtOAc = 1/2 provided protected aminodiol **3b** (1.17 g, white solid) in 62% yield. All physical and spectral data were in good agreement with the literature.[37] R_f = 0.15 (hexanes/EtOAc, 1:1); mp 93.8-94.0 °C, lit.[37] mp 93 °C; $[\alpha]_D^{20}$ +1.1 (*c* 1.52, MeOH); IR (ATR) ν_{max} 3318, 1688, 1541, 1003, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.43-7.27 (m, 5H, H_{Ar}), 5.91 (ddd, *J* = 17.2, 10.5, 6.4 Hz, 1H, H-4), 5.36 (dt, *J* = 17.2, 1.4 Hz, 1H, H-5_a), 5.31-5.25 (m, 1H, H-5_b), 5.24 (s, 1H, NH), 5.12 (s, 2H, $PhC\underline{H}_2$), 4.11-4.02 (m, 1H, H-3), 3.65 (dd, *J* = 9.5, 5.0 Hz, 1H, H-2), 3.50-3.31 (m, 2H, H-1), 2.95 (s, 1H, OH), 2.65 (s, 1H, OH) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 158.0, 136.6, 136.3, 128.7, 128.4, 128.3, 117.9, 74.1, 73.5, 67.3, 42.7 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{13}H_{18}NO_4$: 252.1236, Found: 252.1230, $[M+Na]^+$ Calcd. for $C_{13}H_{17}NNaO_4$: 274.1055, Found: 274.1049, $[M+K]^+$ Calcd. for $C_{13}H_{17}KNO_4$: 290.0795, Found: 290.0788.

N-((2R,3S)-2,3-Dihydroxypent-4-enyl)-4-methylbenzenesulfonamide (**3c**). To a solution of amino alcohol **27** (3.66 g, 31.2 mmol, 1 equiv) in pyridine (18.3 mL) was added TsCl (5.96 g, 31.24 mmol, 1 equiv) at 0 °C. The mixture was left to warm to room temperature and stirred for next 18 h. Pyridine was concentrated in vacuo; the residue was suspended in EtOAc (20 mL) and filtered through short pad of silica gel. Pad was then washed using EtOAc (100 mL) and filtrate was concentrated in vacuo. The crude product was purified by MPLC (hexanes/EtOAc: 100/0 to 30/70 then isocratic hexanes/EtOAc: 30/70) providing desired product **3c** (5.92 g, 70%, white solid). All physical and spectral data were in good agreement with the literature.[26] R_f = 0.20 (hexanes/EtOAc, 3:7); mp 93.0-93.4 °C, lit.[26] mp 67-70 °C; $[\alpha]_D^{20}$ +8,8 (*c* 0.80; $CHCl_3$); IR (ATR) ν_{max} 3430, 3127, 1305, 1153, 544 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.77-7.69 (m, 2H, H_{Ar}), 7.30 (dd, *J* = 8.5, 0.6 Hz, 2H, H_{Ar}), 5.82 (ddd, *J* = 17.2, 10.5, 6.1 Hz, 1H, H-4), 5.50-5.37 (m, 1H, NH), 5.32 (dt, *J* = 17.2, 1.4 Hz, 1H, H-5_a), 5.22 (dt, *J* = 10.5, 1.4 Hz, 1H, H-5_b), 4.21 (ddt, *J* = 6.1, 4.9, 1.4 Hz, 1H, H-3), 3.70 (ddd, *J* = 7.0, 4.9, 3.5 Hz, 1H, H-2), 3.12 (ddd, *J* = 13.3, 7.0, 3.5 Hz, 1H, H-1_a), 3.07-2.95 (m, 1H, H-1_b), 2.83 (s, 2H, OH), 2.42 (s, 3H, CH_3) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 143.8, 136.6, 136.1, 129.9, 127.2, 117.9, 74.3, 72.4, 44.5, 21.7 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{12}H_{18}NO_4S$: 272.0957, Found: 272.0951, $[M+Na]^+$ Calcd. for $C_{12}H_{17}NNaO_4S$: 294.0776, Found: 294.0770, $[M+K]^+$ Calcd. for $C_{12}H_{17}KNO_4S$: 310.0515, Found: 310.0509.

Ethyl 3-hydroxypent-4-enoate (**28**). To a solution of LiHMDS (41.78 g, 249.70 mmol, 1.1 equiv) in anhydrous THF (400 mL) was added dropwise anhydrous EtOAc (22.3 mL, 227.00 mmol, 1 equiv) at -78 °C. The reaction mixture was stirred for 20 min at same temperature. Subsequently, a solution of freshly distilled acrolein (22.8 mL, 340.50 mmol, 1.5 equiv) in anhydrous THF (100 mL) was added dropwise over period of 30 min. The resulting mixture was stirred for 1 h at -78 °C, then it was left to warm to 0 °C and quenched by addition of saturated aqueous solution of NH_4Cl (300 mL). After concentration under vacuum to the 1/5 of previous volume Et_2O (400 mL) was added. Organic phase was separated, and aqueous phase was extracted with Et_2O (3x200 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. Distillation of a residue (4 mbar, 75-76 °C) provided desired hydroxyketone **28** (26.01 g, 79%, colorless oil). All physical and spectral data were in good agreement with the literature.[38] R_f = 0.30 (hexanes/EtOAc, 7:3); IR (ATR) ν_{max} 3292, 1446, 962, 634, 546 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.88 (ddd, *J* = 17.2, 10.5, 5.5 Hz, 1H, H-4), 5.31 (dt, *J* = 17.2, 1.3 Hz, 1H, H-5_a), 5.15 (dt, *J* = 10.5, 1.3 Hz, 1H, H-5_b), 4.58-4.48 (m, 1H, H-3), 4.17 (q, *J* = 7.1 Hz, 2H, $C\underline{H}_2CH_3$), 2.99 (s, 1H, OH), 2.58 (dd, *J* = 16.2, 4.4 Hz, 1H, H-2_a), 2.50 (dd, *J* = 16.2, 8.0 Hz, 1H, H-2_b), 1.27 (t, *J* = 7.1 Hz, 3H, $CH_2C\underline{H}_3$) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 172.4, 138.9, 115.5, 69.1, 60.9, 41.3, 14.3 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_7H_{13}O_3$: 145.0865, Found: 220.1331, $[M+Na]^+$ Calcd. for $C_7H_{12}NaO_3$: 167.0684, Found: 167.0678.

Pent-4-ene-1,3-diol (**(±)-5**). To a solution of ethyl ester **28** (3.42 g, 23.69 mmol, 1 equiv) in anhydrous CH_2Cl_2 (40 mL) was added imidazole (3.23 g, 47.38 mmol, 2 equiv) and TBSCl (4.46 g, 29.61 mmol, 1.25 equiv) at 0 °C. The mixture was left to stir at room temperature for 15h. Subsequently, the resulting suspension was washed with deionized water (3x15 mL). Organic phase was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was dissolved in anhydrous THF (93 mL) and a solution of DiBAl-H (53.4 mL, 1 M in CH_2Cl_2, 53.40 mmol, 2.3 equiv) was added dropwise at 0 °C. Resulting mixture was left to warm to 15 °C over a period of 1 hour and then cooled to 0 °C again. Subsequently, saturated solution of Rochelle salt (20 mL) was added and this emulsion was stirred for 5 h at room temperature. Organic phase was separated, and aqueous phase was extracted with Et_2O (3x90 mL). Combined organic phases were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product (3-(*tert*-butyldimethylsilyloxy)pent-4-en-1-ol) (**31**) was dissolved in MeOH (75 mL) and DOWEX marathon H^+ form (13.5 g) was added. This suspension was left to stir at room temperature until full conversion was observed (overnight). Filtration of DOWEX residues was followed by concentration in vacuo. The crude product was purified by MPLC using gradient (hexanes/EtOAc: 100/0 to 35/65 then isocratic hexanes/EtOAc: 35/65) providing desired product **(±)-5** (1.45 g, 60% over 3 steps, colorless oil). All physical and spectral data were in good agreement with the literature.[39] R_f = 0.20 (hexanes/EtOAc, 3:7); IR (ATR) ν_{max} 3317, 1422, 1049, 922, 663 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 6.00-5.83 (m, 1H, H-4), 5.28 (d, *J* = 17.2 Hz, 1H, H-5_a), 5.14 (d, *J* = 10.4 Hz, 1H, H-5_b), 4.41 (dt, *J* = 11.5, 5.7 Hz, 1H, H-3), 3.95-3.75 (m, 2H, H-1), 2.50 (s, 2H, OH), 1.91-1.66 (m, 2H, H-2) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 140.7, 114.8, 72.9, 61.2, 38.3 ppm; HRMS (ESI): *m/z* $[M+Na]^+$ Calcd. for:$C_5H_{10}NaO_2$: 125.0579, Found: 125.0573.

2-Methylhex-5-ene-2,4-diol (**(±)-7**). To a solution of ethyl ester **28** (17.75 g, 123.12 mmol, 1 equiv) in anhydrous CH_2Cl_2 (205 mL) was added imidazole (16.76 g, 246.24 mmol, 2 equiv) and TBSCl (23.20 g, 153.90 mmol, 1.25 equiv) at 0 °C. The mixture was left to warm to room temperature and stirred until full conversion was observed (overnight)., After washing with deionized water (3x80 mL), organic phase was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product (quantitative yield) was used without further purification. To the solution of crude ethyl 3-*tert*-butyldimethylsilyloxy)pent-4-enoate (**29**) (14.31 g, 55.37 mmol, 1 equiv) in anhydrous THF (222 mL) was added dropwise solution of MeMgBr (46.2 mL, 3 $_M$ in Et_2O, 138.43 mmol, 2.5 equiv) at -78 °C. The resulting mixture was stirred for 30 min at this temperature and then left to warm to room temperature (90 min). The reaction was quenched with saturated solution of NH_4Cl (150 ml) and diluted with Et_2O (240 mL). Organic phase was separated, and aqueous phase was extracted with Et_2O (3x240 mL). Combined organic phases were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product (4-(*tert*-butyldimethylsilyloxy)-2-methylhex-5-en-2-ol (**30**), quantitative yield) was dissolved in MeOH (300 mL) and DOWEX marathon H^+ form (30.60 g) was added. This suspension was left to stir at room temperature until full conversion was observed (overnight). Filtration of DOWEX residues was followed by concentration in vacuo. The crude product was purified by MPLC using gradient (hexanes/EtOAc: 100/0 to 65/35 then isocratic hexanes/EtOAc: 65/35) providing desired product **(±)-7** (6.16 g, 87% over 3 steps, colorless oil). All physical and spectral data were in good agreement with the literature.[40] R_f = 0.20 (hexanes/EtOAc, 7:3); IR (ATR) ν_{max} 3330, 1381, 1150, 910, 526 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.84 (ddd, *J* = 17.2, 10.4, 5.9 Hz, 1H, H-5), 5.23 (dt, *J* = 17.2, 1.4 Hz, 1H, H-6_a), 5.07 (dt, *J* = 10.4, 1.5 Hz, 1H, H-6_b), 4.49 (dddt, *J* = 10.8, 5.9, 2.6, 1.4 Hz, 1H, H-4), 3.42 (s, 2H, OH), 1.71 (dd, *J* = 14.6, 10.8 Hz, 1H, H-3_a), 1.55 (dd, *J* = 14.6, 2.6 Hz, 1H, H-3_b), 1.32 (s, 3H, H-1), 1.25 (s, 3H, $C\underline{H}_3$) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 141.1, 114.3, 71.7, 71.0, 47.7, 31.9, 27.8 ppm; HRMS (ESI): *m/z* $[M+Na]^+$ Calcd. for $C_7H_{14}NaO_2$: 153.0892, Found: 153.0887.

3-Hydroxypent-4-enenitrile (**32**). To a solution of $^iPr_2NH$ (23.48 mL, 214.36 mmol, 1.6 equiv) in anhydrous THF (268 mL) was added dropwise solution of ^nBuLi (126 mL, 1.6 M in hexanes, 201.0 mmol, 1.6 equiv) at -78 °C. The mixture was left to stir for 30 min and then solution of acetonitrile (7 mL, 133.98 mmol, 1 equiv) in anhydrous THF (67 mL) was added dropwise at the same temperature. After stirring over period 1 hour at -78 °C, solution of acrolein (10.8 mL, 160.77 mmol, 1.2 equiv) in anhydrous THF (54 mL) was added dropwise and resulting mixture was stirred for 2.5 h. The reaction mixture was quenched with saturated solution of NH_4Cl (150 mL) and diluted with Et_2O (200 mL). Subsequently, organic phase was separated, and aqueous phase was extracted with Et_2O (3x300 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. Distillation of a residue (6-7 mbar, 80-83 °C) provided desired nitrile **32** (9.7 g, 74%, pale yellow oil). All physical and spectral data were in good agreement with the literature.[41] R_f = 0.60 (hexanes/EtOAc, 1:1); IR (ATR) ν_{max} 3417, 1415, 1053, 932, 491 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.92 (ddd, *J* = 17.1, 10.4, 5.9 Hz, 1H, H-4), 5.47-5.36 (m, 1H, H-5_a), 5.33-5.27 (m, 1H, H-5_b), 4.52-4.41 (m, 1H, H-3), 2.64 (dd, *J* = 15.8, 4.8 Hz, 1H, H-2_a), 2.57 (dd, *J* = 15.8, 5.4 Hz, 1H, H-2_b), 2.30 (s, 1H, OH) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 137.4, 117.6, 117.4, 68.6, 26.1 ppm;

HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:C_5H_8NO: 98.0606, Found: 98.0599, $[M+Na]^+$ Calcd. for C_5H_7NNaO: 120.0425, Found: 120.0418.

5-Aminopent-1-en-3-ol (**33**). To a solution of nitrile **32** (9 g, 92.67 mmol, 1 equiv) in anhydrous THF (185 mL) was portion-wise added LAH (5.56 g, 146.42 mmol, 1.58 equiv) at 0 °C. The reaction was left to warm to room temperature and stirred until full conversion was observed (overnight). Subsequently $Na_2SO_4 \cdot 10\ H_2O$ (179 g, 556.04 mmol, 6 equiv) and celite (60 g) were added and this suspension was diluted with CH_2Cl_2 (200 mL). After next 2 h of stirring, solids were filtered and washed with CH_2Cl_2 (200 mL). The filtrate was dried over Na_2SO_4, filtered and concentrated in vacuo. Distillation of crude product (13 mbar, 90 °C) provided desired amino alcohol **33** (2.53 g, 27%, yellow oil). All physical and spectral data were in good agreement with the literature.[42] R_f = 0.10 (EtOAc). IR (ATR) ν_{max} 3358, 2933, 1425, 917, 671 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.87 (ddd, *J* = 17.1, 10.4, 5.2 Hz, 1H, H-2), 5.27 (dt, *J* = 17.1, 1.6 Hz, 1H, H-1_a), 5.08 (dt, *J* = 10.4, 1.6 Hz, 1H, H-1_b), 4.35 (dddd, *J* = 7.0, 5.2, 3.7, 1.6 Hz, 1H, H-3), 3.09 (ddd, *J* = 12.2, 6.1, 4.0 Hz, 1H, H-5_a), 2.95-2.83 (m, 1H, H-5_b), 2.57 (s, 3H, NH_2 and OH), 1.70 (ddt, *J* = 13.9, 6.1, 4.0 Hz, 1H, H-4_a), 1.62-1.47 (m, 1H, H-4_b) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 141.3, 113.9, 73.8, 40.3, 37.7 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_5H_{12}NO$: 102.0919, Found: 102.0913, $[M+Na]^+$ Calcd. for $C_5H_{11}NNaO$: 124.0738, Found: 124.0734.

tert-Butyl 3-hydroxypent-4-enylcarbamate (**(±)-9a**). To a solution of amino alcohol **33** (0.80 g, 7.91 mmol, 1 equiv) in CH_2Cl_2 (40 mL) was added dropwise solution of Boc_2O (2.21 g, 10.12 mmol, 1.28 equiv) and Et_3N (1.32 mL, 9.49 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL) at 0 °C. After stirring for 15h at room temperature was resulting mixture concentrated in vacuo. Residue was purified by MPLC (hexanes/EtOAc: 100/0 to 65/35 then isocratic hexanes/EtOAc: 65/35) providing desired product **(±)-9a** (1.37 g, 86%, colorless oil). All physical and spectral data were in good agreement with the literature.[43] R_f = 0.20 (hexanes/EtOAc, 13:7); IR (ATR) ν_{max} 3367, 2978, 1681, 1166, 990 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.89 (ddd, *J* = 17.2, 10.5, 5.5 Hz, 1H, H-4), 5.26 (dt, *J* = 17.2, 1.5 Hz, 1H, H-5_a), 5.10 (dt, *J* = 10.5, 1.5 Hz, 1H, H-5_b), 4.86 (s, 1H, NH), 4.18 (ddd, *J* = 10.0, 5.5, 1.5 Hz, 1H, H-3), 3.52-3.31 (m, 1H, H-1_a), 3.22-3.08 (m, 1H, H-1_b), 2.93 (s, 1H, OH), 1.79-1.53 (m, 2H, H-2), 1.44 (s, 9H, $C(C\underline{H}_3)_3$) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 157.0, 140.6, 114.5, 79.7, 70.3, 37.5, 37.3, 28.5 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{10}H_{20}NO_3$: 202.1443, Found: 202.1439, $[M+Na]^+$ Calcd. for $C_{10}H_{19}NNaO_3$: 224.1263, Found: 224.1258, $[M+K]^+$ Calcd. for $C_{10}H_{19}KNO_3$: 240.1002, Found: 240.0997.

Benzyl 3-hydroxypent-4-enylcarbamate (**(±)-9b**). To a solution of amino alcohol **33** (0.81 g, 8.03 mmol, 1 equiv) and Et_3N (1.4 mL, 10.04 mmol, 1.25 equiv) in anhydrous THF (50 mL) was added dropwise CbzCl (1.38 g, 9.61 mmol, 1.2 equiv) at -15 °C. The reaction mixture was left to stir at room temperature for 15h. Subsequently, the saturated solution of NaCl was added (50 mL), organic phase was separated, and aqueous phase was extracted with Et_2O (3x50 mL). Combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of residuum by MPLC (hexanes/EtOAc: 100/0 to 50/50 then isocratic hexanes/EtOAc: 50/50) provided desired product **(±)-9b** (0.94 g, 50%, colorless oil). All physical and spectral data were in good agreement with the literature.[44] R_f = 0.20 (hexanes/EtOAc, 1:1); IR (ATR) ν_{max} 3325, 1692, 1518, 1257, 695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.39-7.28 (m, 5H, H_{Ar}), 5.88 (ddd, *J* = 17.1, 10.5, 5.8 Hz, 1H, H-4), 5.25 (dt, *J* = 17.1, 1.4 Hz, 1H, H-5_a), 5.12 (dt, *J* = 10.5, 1.4 Hz, 1H, H-5_b), 5.12-5.07 (m, 3H, NH and Ph-C$\underline{H}_2$), 4.21 (dddd, *J* = 8.7, 5.8, 2.9, 1.4 Hz, 1H, H-3), 3.59-3.40 (m, 1H, H-1_a), 3.33-3.19 (m, 1H, H-1_b), 2.13 (s, 1H, OH), 1.83-1.57 (m, 2H, H-2) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 157.1, 140.5, 136.6, 128.7, 128.3, 128.2, 114.8, 70.8, 66.9, 37.9, 37.0 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{13}H_{18}NO_3$: 236.1287, Found: 236.1281, $[M+Na]^+$ Calcd. for $C_{13}H_{17}NNaO_3$: 258.1106, Found: 258.1100, $[M+K]^+$ Calcd. for $C_{13}H_{17}KNO_3$: 274.0846, Found: 274.0840.

N-(3-Hydroxypent-4-enyl)-4-methylbenzenesulfonamide (**(±)-9c**). To a solution of amino alcohol **33** (0.81 g, 8.01 mmol, 1 equiv) in pyridine (16 mL) was added TsCl (1.53 g, 8.01 mmol, 1 equiv) at 0 °C. The mixture was stirred at room temperature for 3h and pyridine was removed in vacuo. Obtained residue was purified by MPLC (isocratic CH_2Cl_2/MeOH: 99/1) providing desired product **(±)-9c** (1.14 g, 56%, white solid). All physical and spectral data were in good agreement with the literature.[43] R_f = 0.20 (hexanes/EtOAc, 4:6); mp 70.2-70.8 °C, lit.[43] mp 70.0-71.5 °C; IR (ATR) ν_{max} 3274, 1425, 1319, 1154, 549 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.74 (d, *J* = 8.2 Hz, 2H, H_{Ar}), 7.30 (d, *J* = 8.2 Hz, 2H, H_{Ar}), 5.79 (ddd, *J* = 17.1, 10.6, 5.8 Hz, 1H, H-4), 5.24 (s, 1H, NH), 5.18 (dt, *J* = 17.1, 1.2 Hz, 1H, H-5_a), 5.08 (dt, *J* = 10.6, 1.2 Hz, 1H, H-5_b), 4.27-4.20 (m, 1H, H-3), 3.18-3.10 (m, 1H, H-1_a), 3.03 (td, *J* = 12.3, 5.2 Hz, 1H, H-1_b), 2.42 (s, 3H, C$\underline{H}_3$), 2.07 (s, 1H, OH), 1.73 (dddd, *J* = 16.9, 8.0, 5.2, 4.1 Hz, 1H, H-2_a), 1.66-1.58 (m, 1H, H-2_b) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 143.5, 140.1, 137.1, 129.8, 127.3, 115.3, 71.9, 40.7, 35.6, 21.7 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{12}H_{18}NO_3S$: 256.1007, Found: 256.1001, $[M+Na]^+$ Calcd. for $C_{12}H_{17}NNaO_3S$: 278.0827, Found: 278.0822, $[M+K]^+$ Calcd. for $C_{12}H_{17}KNO_3S$: 294.0566, Found: 294.0560.

3-Hydroxyundec-1-en-5-one (**34**). To a solution of $^iPr_2NH$ (4.9 mL, 44.77 mmol, 1.4 equiv) in anhydrous THF (65 mL) was added dropwise solution of ^nBuLi (26 mL, 1.6 M in hexanes, 41.57 mmol, 1.3 equiv) at -78 °C. The mixture was left to stir for 30 min and then solution of octan-2-one (5 mL, 31.98 mmol, 1 equiv) in anhydrous THF (16 mL) was added dropwise at the same temperature. After stirring over period of 1 h at -78 °C, solution of acrolein (2.4 mL, 35.18 mmol, 1.1 equiv) in anhydrous THF (12 mL) was added dropwise and resulting mixture was stirred for 2.5 h. The reaction was quenched with saturated solution of NH_4Cl (50 mL) and diluted with Et_2O (50 mL). Subsequently, organic phase was separated, and aqueous phase was extracted with Et_2O (3x100 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of crude product by MPLC (isocratic hexanes/EtOAc: 90/10) provided hydroxyketone **34** (2.78 g, 49%, colorless oil). All physical and spectral data were in good agreement with the literature.[18] R_f = 0.25 (hexanes/EtOAc, 4:1); IR (ATR) ν_{max} 2928, 1705, 1376, 990, 525 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.86 (ddd, *J* = 17.1, 10.5, 5.5 Hz, 1H, H-2), 5.29 (dt, *J* = 17.1, 1.4 Hz, 1H, H-1_a), 5.13 (dt, *J* = 10.5, 1.4 Hz, 1H, H-1_b), 4.59-4.55 (m, 1H, H-3), 2.66 (dd, *J* = 17.4, 3.9 Hz, 1H, H-4_a), 2.62 (dd, *J* = 17.4, 8.2 Hz, 1H, H-4_b), 2.43 (t, *J* = 7.4 Hz, 2H, H-6), 1.62-1.52 (m, 2H, H-7), 1.36-1.22 (m, 6H, H-8, H-9 and H-10) 0.88 (t, *J* = 7.0 Hz, 3H, CH_3) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 211.7, 139.2, 115.1, 68.8, 48.7, 43.9, 31.7, 29.0, 23.7, 22.6, 14.2 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{11}H_{21}O_2$: 185.1542,

Found: 185.1535, $[M+Na]^+$ Calcd. for $C_{11}H_{20}NaO_2$: 207.1361, Found: 207.1355.

3-Hydroxynon-1-en-5-one (**35**). To a solution of $^iPr_2NH$ (4.9 mL, 44.77 mmol, 1.4 equiv) in anhydrous THF (65 mL) was added dropwise solution of ^nBuLi (26 mL, 1.6 $_M$ in hexanes, 41.57 mmol, 1.3 equiv) at -78 °C. The mixture was left to stir for 30 min and then solution of hexan-2-one (3.9 mL, 31.98 mmol, 1 equiv) in anhydrous THF (16 mL) was added dropwise at the same temperature. After stirring over period of 1 h at -78 °C, solution of acrolein (2.4 mL, 35.18 mmol, 1.1 equiv) in anhydrous THF (12 mL) was added dropwise and resulting mixture was stirred for 1h. The reaction was quenched with saturated solution of NH_4Cl (50 mL) and diluted with Et_2O (50 mL). Subsequently, organic phase was separated, and aqueous phase was extracted with Et_2O (3x100 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of crude product by MPLC (isocratic hexanes/EtOAc: 90/10) provided hydroxyketone **35** (2.06 g, 41%, colorless oil). All physical and spectral data were in good agreement with the literature.[18] R_f = 0.25 (hexanes/EtOAc, 4:1); IR (ATR) ν_{max} 3421, 2933, 1704, 1379, 991 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.86 (ddd, J = 17.2, 10.5, 5.4 Hz, 1H, H-2), 5.29 (dt, J = 17.2, 1.4 Hz, 1H, H-1_a), 5.13 (dt, J = 10.5, 1.4 Hz, 1H, H-1_b), 4.61-4.53 (m, 1H, H-3), 2.66 (dd, J = 17.4, 3.9 Hz, 1H, H-4_a), 2.62 (dd, J = 17.4, 8.2 Hz, 1H, H-4_b), 2.44 (t, J = 7.5 Hz, 2H, H-6), 1.60-1.52 (m, 2H, H-7), 1.37-1.26 (m, 2H, H-8), 0.91 (t, J = 7.4 Hz, 3H, CH_3) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 211.7, 139.2, 115.1, 68.8, 48.7, 43.6, 25.8, 22.4, 14.0 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_9H_{17}O_2$: 157.1229, Found: 157.1222, $[M+Na]^+$ Calcd. for $C_9H_{16}NaO_2$: 179.1048, Found: 179.1044, $[M+K]^+$ Calcd. for $C_9H_{16}KO_2$: 195.0787, Found: 195.0783.

rac-syn-Undec-1-ene-3,5-diol (**(±)-11**) and *rac-anti-Undec-1-ene-3,5-diol* (**(±)-15**). Procedure A: To a suspension of $NaBH_4$ (0.57 g, 14.92 mmol, 2.5 equiv) in benzene (36 mL) was added dropwise solution of hydroxyketone **34** (1.10 g, 5.97 mmol, 1 equiv) in benzene (36 mL) at room temperature. After 21 h of stirring a solution of HCl (2 M, 130 mL) and EtOAc (100 mL) were added. Organic phase was separated, and aqueous phase was extracted with EtOAc (5x100 mL). Combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by MPLC (isocratic hexanes/EtOAc: 80/20) providing diols **(±)-11** (0.29 g, 26%, colorless oil) and **(±)-15** (0.43g, 39%, colorless oil). All physical and spectral data were in good agreement with the literature.[18] Procedure B: To a suspension of $NaBH(OAc)_3$ (6.33 g, 29.85 mmol, 5 equiv) in benzene (36 mL) was added dropwise solution of hydroxyketone **34** (1.10 g, 5.97 mmol, 1 equiv) in benzene (36 mL) at room temperature. After 18h of stirring a solution of HCl (2 M, 30 mL) and EtOAc (100 mL) were added. Organic phase was separated, and aqueous phase was extracted with EtOAc (3x100 mL). Combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by MPLC (isocratic hexanes/EtOAc: 80/20) providing diols **(±)-11** (0.19 g, 17%, colorless oil) and **(±)-15** (0,58 g, 52%, colorless oil). All physical and spectral data were in good agreement with the literature.[18] **(±)-11**: R_f = 0.15 (hexanes/EtOAc, 4:1); IR (ATR) ν_{max} 3346, 2927, 1712, 1457, 989 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.89 (ddd, J = 17.2, 10.4, 5.9 Hz, 1H, H-2), 5.26 (dt, J = 17.2, 1.4 Hz, 1H, H-1_a), 5.10 (dt, J = 10.4, 1.4 Hz, 1H, H-1_b), 4.43-4.33 (m, 1H, H-3), 3.95-3.82 (m, 1H, H-5), 2.44 (s, 2H, OH), 1.72-1.19 (m, 12 H, H-4, H-6, H-7, H-8, H-9 and H-10), 0.88 (t, J = 6.8 Hz, 3H, CH_3) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 140.9, 114.6, 74.0, 72.7, 42.2, 38.3, 32.0, 29.4, 25.5, 22.7, 14.2 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{11}H_{23}O_2$: 187.1698, Found: 187.1691, $[M+Na]^+$ Calcd. for $C_{11}H_{22}NaO_2$: 209.1518, Found: 209.1513; **(±)-15**: R_f = 0.15 (hexanes/EtOAc, 4:1); IR (ATR) ν_{max} 3392, 2928, 1712, 1176, 1055 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.94 (ddd, J = 17.2, 10.5, 5.4 Hz, 1H, H-2), 5.30 (dt, J = 17.2, 1.5 Hz, 1H, H-1_a), 5.15 (dt, J = 10.5, 1.5 Hz, 1H, H-1_b), 4.52-4.43 (m, 1H, H-3), 4.00-3.88 (m, 1H, H-5), 2.07 (s, 2H, OH), 1.81-1.61 (m, 12H, H-4, H-6, H-7, H-8, H-9 and H-10), 0.88 (t, J = 6.8 Hz, 3H, CH_3) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 140.9, 114.5, 70.9, 69.5, 42.3, 37.8, 32.0, 29.4, 25.7, 22.8, 14.2 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{11}H_{23}O_2$: 187.1698, Found: 187.1692, $[M+Na]^+$ Calcd. for $C_{11}H_{22}NaO_2$: 209.1518, Found: 209.1511.

rac-syn-Non-1-ene-3,5-diol (**(±)-13**) and *rac-anti-Non-1-ene-3,5-diol* (**(±)-17**). Procedure A: To a suspension of $NaBH_4$ (0.42 g, 11.20 mmol, 2.5 equiv) in benzene (27 mL) was added dropwise solution of hydroxyketone **35** (0.70 g, 4.48 mmol, 1 equiv) in benzene (27 mL) at room temperature. After stirring for 21h a solution of HCl (2 M, 80 mL) and EtOAc (80 mL) were added. Organic phase was separated, and aqueous phase was extracted with EtOAc (3x80 mL). Combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by MPLC (isocratic hexanes/EtOAc: 80/20) providing diols **(±)-13** (0.18 g, 25%, pale yellow oil) and **(±)-17** (0.26 g, 37%, pale yellow oil). All physical and spectral data were in good agreement with the literature.[18] Procedure B: To a suspension of $NaBH(OAc)_3$ (4.75 g, 22.40 mmol, 5 equiv) in benzene (27 mL) was added dropwise solution of hydroxyketone **35** (0.70 g, 4.48 mmol, 1 equiv) in benzene (27 mL) at room temperature. After 18h of stirring a solution of HCl (2 M, 23 mL) and EtOAc (80 mL) were added. Organic phase was separated, and aqueous phase was extracted with EtOAc (3x80 mL). Combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by MPLC (isocratic hexanes/EtOAc: 80/20) providing diols **(±)-13** (0.13 g, 18%, pale yellow oil) and **(±)-17** (0.38 g, 54%, pale yellow oil). All physical and spectral data were in good agreement with the literature.[18] **(±)-13**: R_f = 0.15 (hexanes/EtOAc, 4:1); IR (ATR) ν_{max} 3346, 2931, 1711, 1422, 990 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.89 (ddd, J = 17.2, 10.4, 5.9 Hz, 1H, H-2), 5.26 (dt, J = 17.2, 1.4 Hz, 1H, H-1_a), 5.10 (dt, J = 10.4, 1.4 Hz, 1H, H-1_b), 4.43-4.33 (m, 1H, H-3), 3.95-3.83 (m, 1H, H-5), 2.60 (s, 2H, OH), 1.75-1.20 (m, 8H, H-4, H-6, H-7 and H-8), 0.91 (t, J = 7.0, 3H, CH_3) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 140.9, 114.6, 74.0, 72.7, 43.2, 38.0, 27.7, 22.8, 14.2 ppm; HRMS (ESI): *m/z* $[M+Na]^+$ Calcd. for $C_9H_{18}NaO_2$: 181.1205, Found: 181.1200; **(±)-17**: R_f = 0.15 (hexanes/EtOAc, 4:1); IR (ATR) ν_{max} 3347, 2931, 1421, 1042, 921 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.94 (ddd, J = 17.2, 10.5, 5.4 Hz, 1H, H-2), 5.30 (dt, J = 17.2, 1.5 Hz, 1H, H-1_a), 5.15 (dt, J = 10.5, 1.5 Hz, 1H, H-1_b), 4.54-4.43 (m, 1H, H-3), 3.99-3.89 (m, 1H, H-5), 2.36 (s, 2H, OH), 1.80-1.62 (m, 2H, H-4) 1.61-1.17 (m, 6H, H-6, H-7 and H-8), 5.15 (t, J = 7.0 Hz, 3H, CH_3) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 140.9, 114.5, 70.9, 69.5, 42.3, 37.5, 28.0, 22.8, 14.2 ppm; HRMS (ESI): *m/z* $[M+Na]^+$ Calcd. for $C_9H_{18}NaO_2$: 181.1205, Found: 181.1200.

3-Hydroxy-1-phenylpent-4-en-1-one (**36**). To a solution of $^iPr_2NH$ (7.3 mL, 66.58 mmol, 1.6 equiv) in anhydrous THF (83 mL) was added dropwise solution of ^nBuLi (39 mL, 1.6 $_M$ in hexanes, 62.42 mmol, 1.5 equiv) at -78 °C. The mixture was left

to stir for 30 min and then solution of acetophenone (4.9 mL, 41.62 mol, 1 equiv) in anhydrous THF (21 mL) was added dropwise at the same temperature. After stirring over period of 1 h at -78 °C, solution of acrolein (3.3 mL, 49.94 mmol, 1.2 equiv) in anhydrous THF (17 mL) was added dropwise and resulting mixture was stirred for 1 h. The reaction was quenched with saturated solution of NH_4Cl (50 mL) and diluted with Et_2O (50 mL). Subsequently, organic phase was separated, and aqueous phase was extracted with Et_2O (3x100 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of crude product by MPLC (isocratic hexanes/EtOAc: 85/15) provided hydroxyketone **36** (3.54 g, 48%, pale yellow oil). R_f = 0.15 (hexanes/EtOAc, 17:3); IR (ATR) ν_{max} 3433, 1675, 1211, 753, 687 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.97 (ddd, J = 7.1, 3.1, 1.7 Hz, 2H, H_{Ar}), 7.64-7.56 (m, 1H, H_{Ar}), 7.52-7.44 (m, 2H, H_{Ar}), 5.98 (ddd, J = 17.2, 10.5, 5.6 Hz, 1H, H-4), 5.37 (dt, J = 17.2, 1.5 Hz, 1H, H-5_a), 5.19 (dt, J = 10.5, 1.5 Hz, 1H, H-5_b), 4.47 (dddt, J = 7.8, 5.6, 3.8, 1.5 Hz, 1H, H-3), 3.24 (dd, J = 16.5, 3.8 Hz, 1H, H-2_a), 3.17 (dd, J = 16.5, 7.8 Hz, 1H, H-2_b) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 200.2, 139.2, 136.8, 133.7, 128.8, 128.3, 115.3, 68.9, 45.0 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_{11}H_{13}O_2$: 177.0916, Found: 177.0910, $[M+Na]^+$ Calcd. for $C_{11}H_{12}NaO_2$: 199.0735, Found: 199.0729, $[M+K]^+$ Calcd. for $C_{11}H_{12}KO_2$: 215.0474, Found: 215.0468.

1-Phenylpent-4-ene-1,3-diol (**(±)-19**). To a solution of hydroxyketone **36** (1.04 g, 5.87 mmol, 1 equiv) in anhydrous EtOH (29 mL) was added in small portions $NaBH_4$ (0.66 g, 17.33 mmol, 2.95 equiv) at 0 °C and the mixture was left to stir at this temperature for 1 h. Subsequently, solution of HCl (2 M, 45 mL) was added, resulting mixture was stirred 5 min at room temperature and then EtOH was removed in vacuo. The residue was dissolved in EtOAc (50 mL), organic phase was separated, and the aqueous phase was extracted with EtOAc (2x50 mL). Combined organic phases were dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of crude product by MPLC (hexanes/EtOAc: 100/0 to 70/30 then isocratic hexanes/EtOAc: 70/30) provided inseparable mixture of diols **(±)-19** (0.85 g, 83%, colorless oil, syn/anti = 53/47 based on ^1H NMR). All physical and spectral data were in good agreement with the literature.[45] **(±)-*syn*-19**: R_f = 0.20 (hexanes/EtOAc, 7:3); ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.40-7.25 (m, 5H, H_{Ar}), 5.93-5.82 (m, 1H, H-4), 5.28 (dt, J = 17.2, 1.4 Hz, 1H, H-5_a), 5.12 (dt, J = 10.4, 1.4 Hz, 1H, H-5_b), 4.97 (dd, J = 9.6, 3.3 Hz, 1H, H-1), 4.44-4.37 (m, 1H, H-3), 2.63 (s, 2H, OH), 2.04-1.93 (m, 1H, H-2_a), 1.87-1.80 (m, 1H, H-2_b) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 144.4, 140.5, 128.6, 127.6, 125.7, 114.8, 73.5, 70.6, 44.4 ppm; **(±)-*anti*-19**: R_f = 0.20 (hexanes/EtOAc, 7:3); ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.40-7.25 (m, 5H, H_{Ar}), 6.02-5.90 (m, 1H, H-4), 5.30 (dt, J = 17.2, 1.5 Hz, 1H, H-5_a), 5.17 (dt, J = 10.5, 1.5 Hz, 1H, H-5_b), 5.04 (dd, J = 8.7, 3.2 Hz, 1H, H-1), 4.52-4.44 (m, 1H, H-3), 2.63 (s, 2H, OH), 2.11-2.03 (m, 1H, H-2_a), 1.94-1.87 (m, 1H, H-2_b) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 144.4, 140.5, 128.6, 127.8, 125.8, 114.8, 74.9, 71.7, 45.4 ppm; **(±)-19**: IR (ATR) ν_{max} 3381, 1393, 1056, 756, 698 cm^{-1}; HRMS (ESI): *m/z* $[M+Na]^+$ Calcd. for $C_{11}H_{14}NaO_2$: 201.0892, Found: 201.0886, $[M+K]^+$ Calcd. for $C_{11}H_{14}KO_2$: 217.0631, Found: 217.0624.

Hept-6-en-2-ol (**(±)-23**). To a suspension of Mg (12.6 g, 518.50 mmol, 1.4 equiv) in anhydrous THF (296 mL) were added dropwise 1,2-dibromoethane (6.96 g, 37.04 mmol, 0.1 equiv) and then 4-bromobut-1-ene (37.6 mL, 370.36 mmol, 1 equiv). The resulting mixture was left to stir for 2 h and then it was added dropwise at -78 °C to the suspension of propylene oxide (20.7 mL, 296.29 mmol, 0.8 equiv) and CuI (5.64 g, 29.6 mmol, 0.08 equiv) in anhydrous THF (158 mL). After stirring over a period of 1.5 h at -78 °C, the reaction mixture was left to warm to room temperature and stirred at this temperature for 1 h. Subsequently, the reaction was quenched with NH_4Cl (400 mL), the organic phase was separated, and the aqueous phase was extracted with Et_2O (3x400 mL). Combined organic phases were dried over Na_2SO_4, filtered and concentrated in vacuo. Distillation of a crude product (17-20 mbar, 65-70 °C) afforded alcohol **(±)-23** (24.33 g, 72%, colorless oil). All physical and spectral data were in good agreement with the literature.[46] R_f = 0.20 (hexanes/EtOAc, 4:1); IR (ATR) ν_{max} 3332, 2930, 1120, 908, 639 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 5.80 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H, H-6), 5.06-4.91 (m, 2H, H-7), 3.86-3.73 (m, 1H, H-2), 2.16-1.98 (m, 2H, H-5), 1.65-1.34 (m, 4H, H-3 and H-4), 1.18 (d, J = 6.2 Hz, 3H, CH_3) ppm; ^{13}C NMR{^1H} (75 MHz, $CDCl_3$) δ_C 138.8, 114.7, 68.2, 38.9, 33.8, 25.2, 23.7 ppm; HRMS (ESI): *m/z* $[M+H]^+$ Calcd. for:$C_7H_{15}O$: 115.1123, Found: 115.1117.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Optimization of reaction conditions; ^1H, ^{13}C, and NMR spectra of all compounds (PDF)

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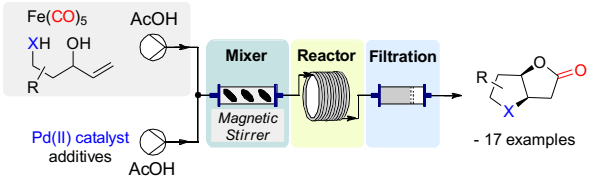

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