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Construction of Multisubstituted Tetrahydropyrans by a Domino Oxa-Michael/Tsuji−Trost Reaction

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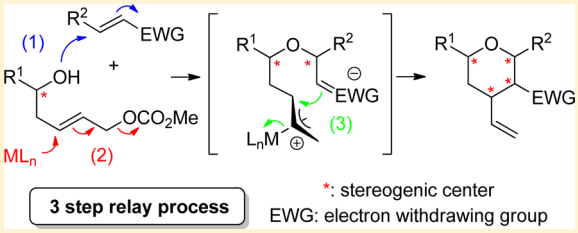
Supporting Information

ABSTRACT: Biologically significant tetrahydropyrans (THP) were synthesized by a Tandem oxa-Michael/Tsuji−Trost reaction. Different Michael acceptors were investigated, and optimal results in terms of diastereoselectivities and yields were obtained with nitro olefins. The influence of the reaction parameters, substrate patterns, and type of metal counterions on the yield and stereochemical outcome of this process is discussed, and an explanation for the observed stereoselectivities is proposed.



INTRODUCTION

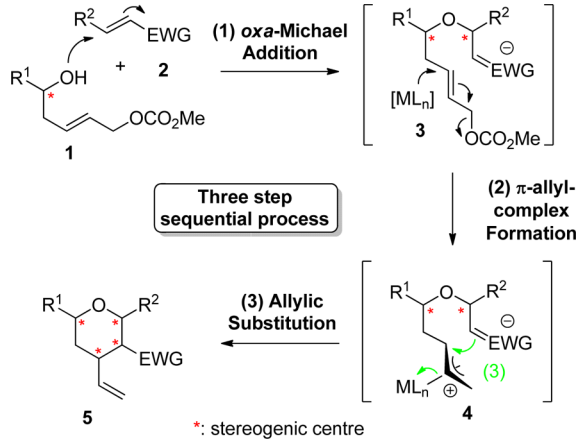
The development of efficient processes, that enable a rapid and easy access to optically active building blocks is of great importance, particularly for the synthesis of complex molecules. The metal-catalyzed asymmetric allylic substitution reaction, which involves the addition of a range of diverse nucleophiles, such as derivatives of malonate and tosyl amides, to an allyl metal intermediate, is one of the most studied processes.[1] In recent years, the notion of combining several metal-mediated processes in relay-type domino sequences has been attracting increasing attention.[2] Through the combination of several synthetic transformations in a one-pot fashion, domino reactions efficiently transform simple starting materials into products of structural complexity. The addition of nucleophilic carbons to Michael acceptors is a highly important C−C bond forming reaction in organic synthesis. In marked contrast, the conjugate addition of noncarbon nucleophiles such as alcohols[3] (oxa-Michael addition) has gained considerably less interest in the past decades. For a long time, this reaction has suffered from major drawbacks such as low reactivity and reversibility issues as well as a lack of stereoselectivity. Consequently, reports concerning the oxa-Michael reaction have remained quite scarce, and no general reaction protocols for this transformation have been reported until quite recently.[3e]

Tetrahydropyrans (THPs) are prevalent constitutional chemotypes and underlying structural moieties in a variety of biologically important natural products such as polyether antibiotics, marine toxins, pheromones, and pharmaceutical agents, etc.[4] As such, there have been extensive efforts made toward the synthesis of tetrahydropyrans and tetrahydropyran-containing compounds using various methods,[5,6] including cyclizations involving oxocarbenium ions[7] and epoxides,[8] hetero-Diels−Alder reactions,[9,10] Prins cyclizations,[11] intramolecular nucleophilic reactions,[12] Michael reactions,[13] reductions of cyclic hemiacetals,[14] cyclizations involving nonactivated double bonds,[15] and one-pot procedures based on alkene−alkyne couplings followed by ether formation.[16] Because of certain limitations of these existing methods, in particular with respect to convergence, brevity, and ready availability of the starting materials, we desired a more direct sequence for THP synthesis. Herein, we report in full detail[17] the design and development of a conceptually novel cascade reaction based on an oxa-Michael-addition and an allylic substitution and successfully implement this concept for the direct synthesis of polysubstituted tetrahydropyrans.

RESULTS AND DISCUSSION

Since deprotonated hydroxy groups may react with Michael acceptors to furnish carbon nucleophiles, we conceived a novel type of domino reaction based on an oxa-Michael reaction and palladium(0)-catalyzed asymmetric allylic alkylation (AAA) to construct multisubstituted THPs. As shown in Scheme 1, our

Scheme 1



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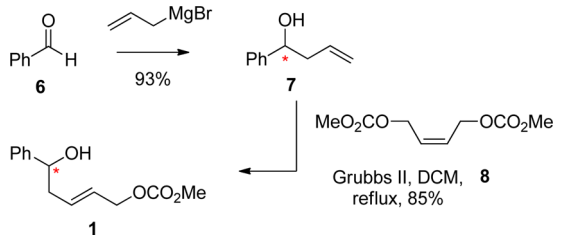
synthetic concept was based on a three-step sequential process involving an oxa-Michael and a Tsuji–Trost coupling. The deprotonated homoallylic alcohol can first add to an electrophilic olefin resulting in a nucleophilic carbon-enolate center (step 1)[3a,b,18] followed by palladium catalyzed π-allyl complex generation (step 2); afterward, the nucleophilic carbon will be captured in an intramolecular fashion through an allylic substitution reaction leading to the desired multisubstituted THPs in a highly direct and efficient fashion (step 3). In this process, three new stereogenic centers are generated. It should be noted that the synthetic design is highly convergent (two components are combined in one process) and flexible and may readily be adapted to various other substrates enabling direct access to a broad range of heterocycles.

With respect to linear allylic carbonates, allylic substitution reactions may result in problems of regioselectivtiy because of so-called memory effects.[19] One efficient solution to this problem is to use a combination of Feringa's phosphoramidite ligand and iridium(I),[20−22] and the groups of Hartwig,[20] Helmchen,[21] and Alexakis[22] contributed much to iridium-catalyzed asymmetric allylic alkylation. They employed achiral linear allylic carbonates to get chiral branched substitution products with the help of Feringa's phosphoramidite ligand and iridium(I). These reactions have led to excellent results using *C*-, *N*-, and *O*-nucleophiles with good enantioselectivity and regioselectivity. Although linear allylic carbonates and palladium catalysts are used in our reaction, it was conceived that no problems of regioselectivity would arise because a six-membered THP ring would be expected as the predominant product for sterical reasons. Subsequent to our initial report on this type of relay process,[17] related domino sequences have been reported by us[23] and others.[24]

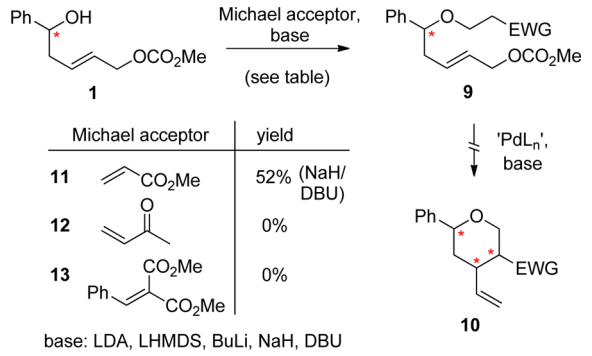
To initiate our study, the required homoallyl carbonate substrates (**1**) could be conveniently prepared stereoselectively with good yields (85%) by second-generation Grubbs catalyst mediated cross-metathesis of an homoallylic alcohol, itself readily available by allylation of the corresponding aldehyde and dicarbonate **8** (Scheme 2).

Scheme 2



With substrate **1** in hand, different Michael acceptors were then investigated in the presence of different bases and solvents. First, methyl acrylate (**11**) was evaluated, but no desired adduct product was obtained (Scheme 3). During this study, it was accidently found that a combination of DBU and NaH would result in the formation of desired adduct **9**, while neither DBU nor NaH alone could facilitate the reaction (Scheme 3). The Tsuji–Trost reaction was then investigated, but disappointedly no desired cyclized product could be obtained. In agreement with seminal reviews by Trost,[1c,d,f] it was conceived that carboxylate might not afford a carbon nucleophile that would be stabilized enough for the subsequent allylic substitution, and only few examples which use ketones as nucleophilic carbon sources have been reported.[18] With methyl vinyl ketone (**12**) as acceptor, the

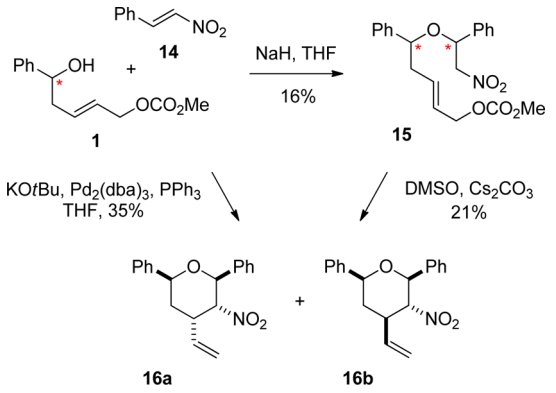
Scheme 3



step of conjugate addition was unsuccessful, not to mention the subsequent allylic substitution. Afterward, we studied derivatives of malonates as very classical substrates for Tsuji–Trost reactions. Accordingly, dimethyl 2-benzylidenemalonate **13** was prepared, but disappointingly again no oxa-Michael addition could be observed. In a similar fashion, these types of substrates were evaluated in the presence of both various bases and palladium catalysts. However, only traces of the desired tetrahydropyran products could be detected in some cases at best.

Subsequently, commercially available β-nitrostyrenes were evaluated as electrophilic alkenes, and the coupling of **1** and **14** was studied. At the beginning, the oxa-Michael and Tsuji–Trost reaction was studied as a stepwise process. We were pleased to see that both of these steps were indeed successful; i.e., the oxa-Michael addition to **15** and the ensuing allylic substitution to **16** proceeded. These two conversions were then combined to investigate the feasibility of a domino oxa-Michael/Tsuji–Trost reaction (Scheme 4). Gratifyingly, this relay process indeed

Scheme 4



worked, albeit initially in only low yields. However, the yield was slightly higher in comparison to the stepwise process. In detail, the coupling of **1** with **14** in the presence of KO^{t}Bu as base and $Pd_2(dba)_3$ as catalyst resulted in the formation of two major diastereomers, **16a** and **16b**, in a ratio of 1:1.5. The relative configurations of these two diastereomers was elucidated by analysis of the coupling constants, COSY and NOESY data (see Table 1).

Different conditions were then investigated to improve the diastereoselectivity. First, a variety of ligands, including bidentate ligands, such as DPPE, DPPB or DPPP, and chiral ligand like (*S*)-BINAP, were tried, but disappointingly, only lower yields or selectivities resulted (see Table 1, entries 4–7). When LHMDS was used, it was surprising to find that a third diastereomer **16c** was obtained. The orientation of the nitro group was now found

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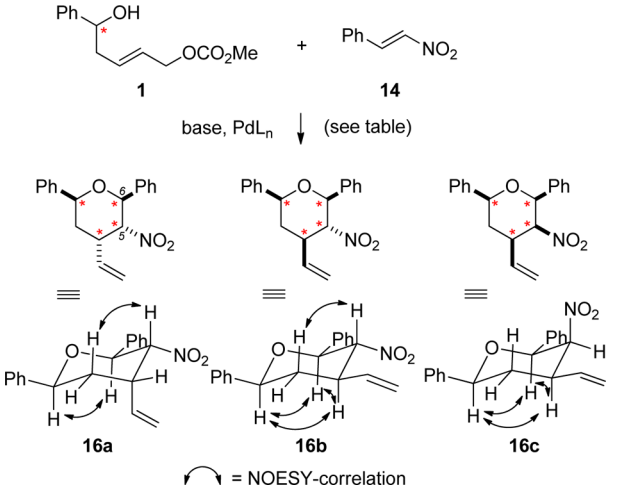
Table 1. Investigation of Different Ligands and Palladium Sources[a]



entry	Pd cat.	ligand	base[b]	yield[c] (%)	dr (**a**:**b**)[d]
1	$Pd_2(dba)_3$–$CHCl_3$	PPh_3	KO^{t}Bu	35	1:1.5 (trace of **c**)
2	$Pd(PPh_3)_4$	–/18-*c*-6	KO^{t}Bu	14	1:1.5
3	$[Pd(C_3H_5)Cl]_2$	PPh_3/18-*c*-6	KO^{t}Bu	14	**1:1.9**
4	$Pd_2(dba)_3$–$CHCl_3$	DPPE	KO^{t}Bu	35	1:1.1
5	$Pd_2(dba)_3$–$CHCl_3$	DPPB	KO^{t}Bu	53	1:1.1
6	$Pd_2(dba)_3$–$CHCl_3$	DPPP	KO^{t}Bu	53	1:1
7	$Pd_2(dba)_3$–$CHCl_3$	(*S*)-BINAP	KO^{t}Bu	22	1:1.1
8	$Pd_2(dba)_3$–$CHCl_3$	PPh_3	LiHMDS	27	1:2.2:2.6 (**a**/**b**/**c**)

[a]The reactions were carried out on a 0.2 mmol scale with 0.3 mmol of nitroolefin in 3 mL of THF. [b]Commercially available solutions of the bases in THF were used. [c]Yield of isolated product. [d]Ratio was determined by 1H NMR analysis of the crude product.

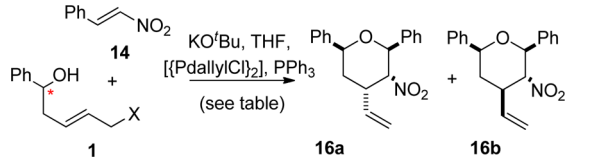
to be in an axial position (entry 8). This suggested that the lithium cation might play a certain role in this reaction. When $[Pd(C_3H_5)Cl]_2$ was used, the diastereoselectivity was found to be improved as compared to $Pd_2(dba)_3$ (entry 1, 3).

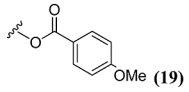
Motivated by previous reports on the influence of the leaving groups on the enantioselectivity of Tsuji–Trost reactions,[1c] a series of substrates (**17**–**19**) with different leaving groups were prepared and subjected to our procedure. However, the diasteroselectivities did not change significantly, and in contrast to previous results, 4-methoxybenzoate (**19**) gave the lowest selectivities. (Table 2, entry 3).

Other homoallylic alcohol analogues that were substituted with Boc carbonates were also investigated, but again poor diastereoselectivities and poor to moderate yields were observed. It was conceived that nitroolefins with aromatic substituents might generally only afford moderate stereoselectivities. Diastereomer **16a** was observed as the major product. The observed diastereoselectivity was opposite to the one observed above (Table 3, entries 1–4). No stereoselectivity was found for substrates with aliphatic substituents (entries 5 and 6).

Subsequently, we turned our attention to the investigation of nitroolefins with aliphatic substituents at the β-carbon atom, in a rational that this might have a beneficial effect on the stereochemical outcome of the process. First, alkene **20** was studied as a Michael acceptor. It could be readily prepared by base-catalyzed condensation of nitromethane with isobutyraldehyde and subsequent dehydration with trifluoroacetic anhydride.[17] Three diastereomers were observed (**21a**, **21b**, **21c**). However, in this case, promising diastereoselectivities resulted (**a**/**b**/**c** = 5.8:2.5:1),

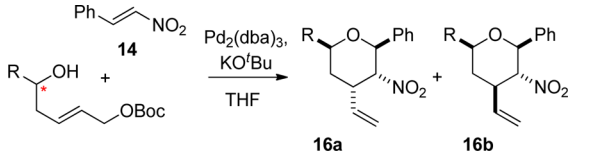
Table 2. Investigation of the Influence of Leaving Groups and Different Substrates on the Diastereoselectivity[a]



Entry	Substrate	Yield (%)[b]	d.r. (**16a**:**16b**)[c]
1	X = OBoc (**17**)	57	1: 1.4
2	X = OC(O)Me (**18**)	44	1: 1.4
3	X =  (**19**)	29	1: 1.2

[a]The reactions were carried out on a 0.2 mmol scale with 0.3 mmol of nitroolefin in 3 mL of THF. [b]Yield of isolated product. [c]Ratio was determined by 1H NMR analysis of the crude product.

Table 3. Investigation of Different Substrates[a]



entry	R	yield[b] (%)	dr (d1/d2)[c]
1	4-methylbenzyl	56	1:0.8
2	4-methoxybenzyl	51	1:1
3	2-methoxybenzyl	40	1:0.8
4	2-furyl	50	1:0.8
5	*c*-hexyl	40	five diastereomers
6	ethylbenzene	40	seven diastereomers

[a]The reactions were carried out on a 0.2 mmol scale with 0.3 mmol of nitroolefin in 3 mL of THF. [b]Yield of isolated product. [c]Ratio was determined by 1H NMR analysis of the crude product.

when $Pd_2(dba)_3$, PPh_3, LiHMDS and methyl carbonate were employed (Table 4). The relative configurations of these diastereomers **21a**–**c** were again elucidated by analysis of coupling constants and NOESY data.

An advantage of this transformation was that the major product, diastereomer **21a**, could be readily separated from the other two diastereomers by flash chromatography, which underlines the efficiency of the overall process. As shown in Table 4, various conditions and leaving groups were evaluated. It was found that the best result could be achieved when $Pd_2(dba)_3{\cdot}CHCl_3$, PPh_3, LiO^{t}Bu, and Boc-carbonate as leaving group were used (Table 4, entry 3).

In order to further analyze the influence of the β-substituent, the linear nitroolefin **22** was then investigated under these optimized conditions. Gratifyingly, good diastereoselectivities and yields were again observed (Scheme 5).

Subsequently, these optimized conditions were applied to other substrates, which resulted in good yields and diasteroselectivities, as shown in Figure 1. While this reaction was routinely carried out with 0.2 mmol of homoallylic alcohol, similar yields and selectivities were also obtained on larger scale reactions up to 2 mmol.

We then turned our attention to the synthesis of tetrahydropyrans bearing a tetrasubstituted carbon center by coupling with α-substituted nitroolefins. The reaction of **1** with **29** was studied

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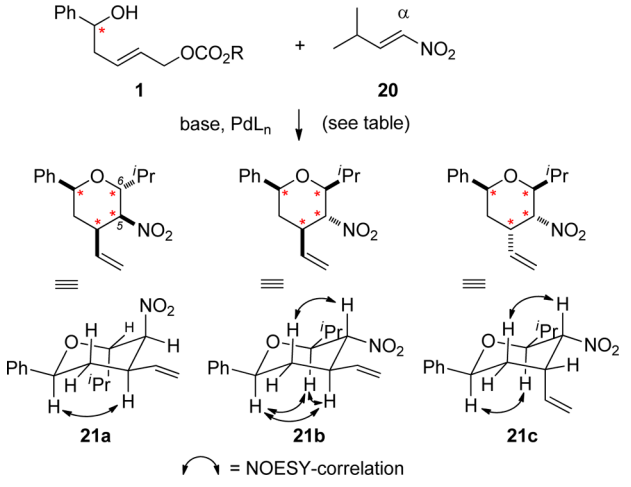
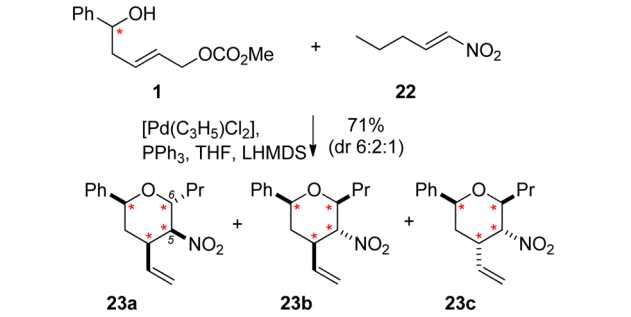
Table 4. Domino Process with Nitroolefin 16 as Michael Acceptor[a]



entry	substrate/PdL_n/base[b]	yield[c] (%)	dr **a**/**b**/**c**[d]
1	R = Me; $Pd_2(dba)_3$ (5%)/PPh_3 (20%)/ LiHMDS (1.5 equiv)	47	5.8:2.5:1
2	R = Me; $Pd_2(dba)_3$ (5%)/PPh_3 (20%)/KO^tBu (1.5 equiv)	63	4.4:1.4:1
3	**R = ^{t}Bu; $Pd_2(dba)_3$ (5%)/PPh_3 (20%)/ LiO^tBu (1.5 equiv)**	**78**	**5.2:1.4:1**

[a]The reactions were carried out on a 0.2 mmol scale with 0.3−0.4 mmol of nitroolefin in 3 mL of THF. [b]Commercially available solutions of the bases in THF were used. [c]Yield of isolated product. [d]Ratio was determined by ^{1}H NMR analysis of the crude product.

Scheme 5



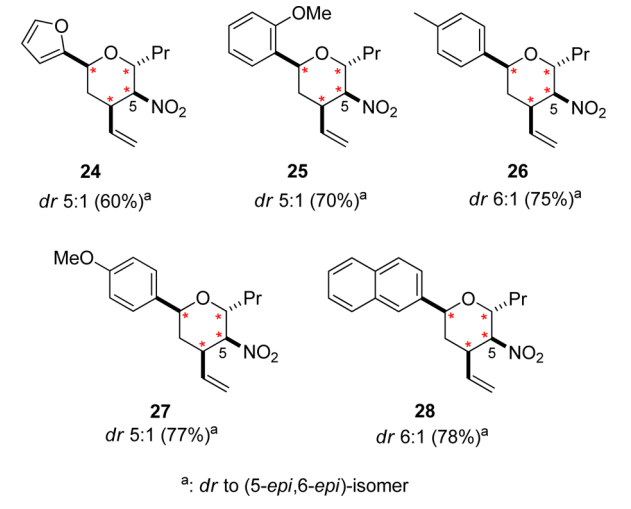
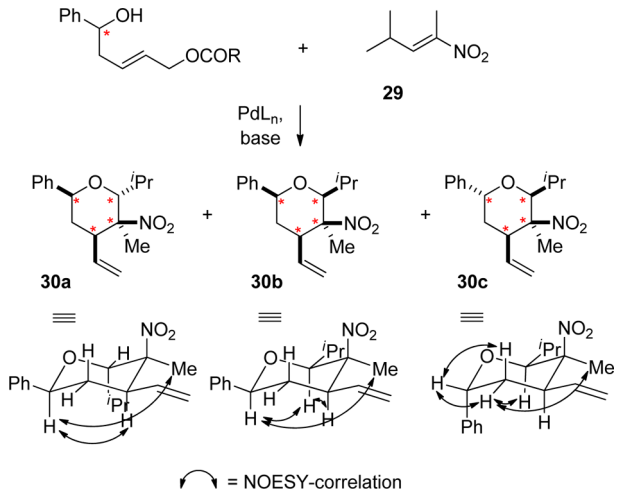


Figure 1. Selected tetrasubstituted THPs prepared by our method.

in detail. As shown in Table 5, three diastereomers were formed, i.e.m **30a−c**, which could not be separated by flash chromatography column. The relative configuration of **30a** and **30b** can be elucidated relatively easily, while it took some time to find out the correct relative configuration of **30c** because of considerable signal overlaps in the NMR spectra. It was surprising to find that the orientation of the phenyl group in **30c** was axial. Possibly, the phenyl group might be forced in an axial position to avoid strong 1,3-axial interaction between the isopropyl and the vinyl group, resulting in the depicted major conformer **30c**. In this reaction, various conditions, including leaving group, palladium catalysts and bases, were investigated. It was found that the best result could be achieved when a combination of allyl palladium chloride dimer, Boc-carbonate as leaving group and LiHMDS as base were used (Table 5, entry 8). Interestingly, the amount of diastereomer **30c** decreased drastically when the equivalents of nitroalkene were increased (entries 8 and 10).

To further evaluate nitroolefin **29** a substrate with a furyl group was evaluated, resulting, however, in only poor diastereoselectivities (Scheme 6).

Table 5. Domino Reaction with α-Substituted Nitroolefin 29[a]



entry	R	PdL_n/base[b]	yield[c] (%)	dr **a**/**b**/**c**[d]
1	OMe	$[Pd(C_3H_5)Cl]_2$/LiO^tBu	24	9.1:6.9:1
2	OMe	$Pd_2(dba)_3$/LiO^tBu	14	10.4:12.3:1
3	OMe	$Pd_2(dba)_3$/LiHMDS	17	12:11.7:1
4	OMe	$[Pd(C_3H_5)Cl]_2$/LiHMDS	39	4.8:3.4:1
5	OMe	$[Pd(C_3H_5)Cl]_2$/LiHMDS	71	10.3:8:1
6	PMB	$[Pd(C_3H_5)Cl]_2$/LiHMDS	43	14.4:10.2:1
7	^{t}Bu	$[Pd(C_3H_5)Cl]_2$/LiHMDS	44	1.4:1.3:1
8	**^{t}BuO**	**$[Pd(C_3H_5)Cl]_2$/LiHMDS**	**62**	**1.6:1:<0.05**
9	^{t}BuO	$[Pd(C_3H_5)Cl]_2$/LiHMDS (10%)	17	nd[e]
10	^{t}BuO	$[Pd(C_3H_5)Cl]_2$/PPh_3 (20%)/LiHMDS	44	1.4:1.3:1
11	^{t}BuO	$[Pd(C_3H_5)Cl]_2$/P(^{i}OPr)$_3$ (20%)/LiHMDS	44	1.4:1.3:1
12	^{t}BuO	$[Pd(C_3H_5)Cl]_2$/P(OEt)$_3$ (20%)/LiHMDS	44	1.4:1.3:1
13	^{t}BuO	$[Pd(C_3H_5)Cl]_2$/dppf (10%)/LiHMDS	44	1.4:1.3:1
14	^{t}BuO	$[Pd(C_3H_5)Cl]_2$/dppp (10%)/LiHMDS	44	1.4:1.3:1

[a]The reactions were carried out in 2.5 mL of THF with 0.2 mmol of homoallylic alcohol **6**, 2 mmol of nitroolefin, 0.3 mmol of base, and 0.01 mmol (5 mol %) of catalyst. [b]Commercially available solutions of the bases in THF were used as supplied. [c]Isolated yields. [d]Ratio was determined by ^{1}H NMR analysis of the crude product. [e]nd: not determined. PMB: *p*-methoxybenzyl.

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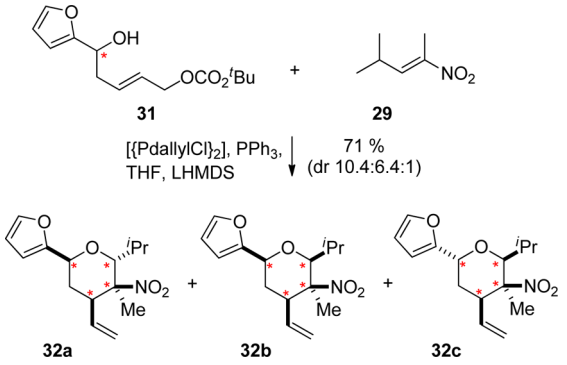
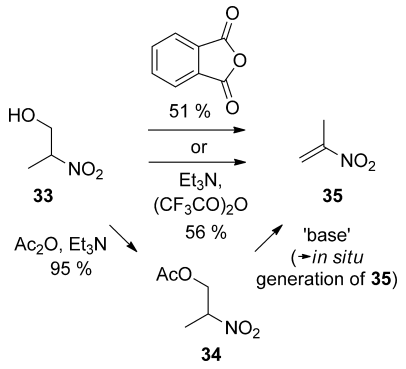
Scheme 6



Presumably, the energy difference between the diastereomers of the oxa-Michael adduct is too small to enable useful levels of asymmetric induction, despite the reversibility of the process (vide infra). In order to circumvent the inherent problem of the low selectivities of the oxa-Michael reaction, we then considered nitro olefins without a β-substituent. Consequently, nitroethylene **35** was chosen as the Michael acceptor. As shown in Scheme 7 it may be conveniently

Scheme 7



obtained directly from **33**. Alternatively, the precursor **34** can be synthesized, which may then be transformed into **35** in situ by base.

We were delighted to find that coupling of **1** with **35** obtained in situ in the presence of LiHMDS and $[Pd(C_3H_5)Cl]_2$ resulted in the formation of only one major diastereomer (**36a**) together with minor amounts of **36b** (Table 6). The relative configuration of these two diastereomers **36a** and **36b** was again elucidated by analysis of coupling constants and NOE data. Notably, the nitro group and the vinyl group were *syn* in both diastereomers. In this reaction, nitroolefin **35** could be prepared easily via dehydration with phthalic anhydride or trifluoroacetic anhydride. Different metal counterions were investigated in the domino coupling with methyl carbonate **1** as the substrate. When KO^{t}Bu was used as base, the lowest diastereoselectivity was observed (Table 6, entry 1), moderate diastereoselectivity could be obtained with NaHMDS (Table 6 entry 2), while LiHMDS gave the highest diastereoselectivity (Table 6, entry 3). A higher yield could be achieved with Boc carbonate **17** as substrate, and the observed stereoselectivity was still good (Table 6, entry 4).

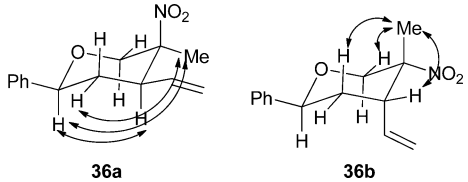
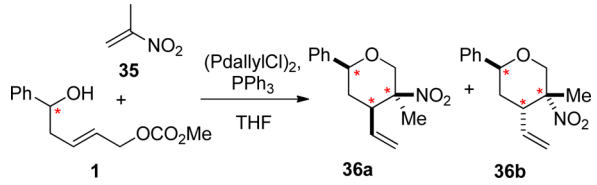


Table 6. Domino Reaction with Nitroolefin 31: Assembly of THPs with a Tetrasubstituted Carbon Center[a]



entry	R^1	PdL_n/base	yield[b] (%)	dr **38a**/**38b**[c]
1	OMe	$[Pd(C_3H_5)Cl]_2$/KO^{t}Bu	16	2.5:1
2	OMe	$[Pd(C_3H_5)Cl]_2$/NaHMDS	12	4.4:1
3	OMe	$[Pd(C_3H_5)Cl]_2$/LiHMDS	17	8.8:1
4	^{t}BuO	$[Pd(C_3H_5)Cl]_2$/LiHMDS	62	8.8:1

[a]The reactions were carried out on a 0.2 mmol scale with 0.4 mmol of nitroolefin in 2.5 mL of THF. [b]Yield of isolated product. [c]Ratio was determined by ^{1}H NMR analysis of the crude product.

In addition, the use of different equivalents of the nitroolefin was investigated. It was found that 2 equiv of nitroolefin **35** resulted in the highest yields, while more or less equivalents only led to lower conversion or no product formation at all. The selectivities increased in the order K, Na, Li, which corresponds to the chelative ability of these alkali metals, in agreement with our mechanistic proposal (vide infra).

As shown in Figure 2, the method was applicable to various aliphatic and aromatic substrates. Good diastereoselectivties (5:1 to 10:1) and moderate to good yields (25 −72%) were obtained.

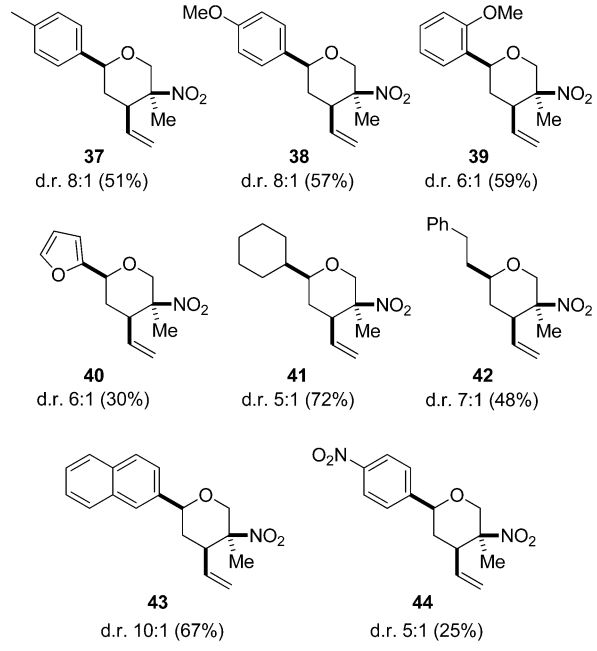


Figure 2. Investigation of the effectiveness of the methodology.

Similarly, a homologated α-substituted nitroethylene, i.e., the ethyl analogue **45**, was analyzed. It was prepared by base-mediated coupling of nitropropane with paraformaldehyde and subsequent dehydration, as described above. Coupling of **17** with **45** resulted in similar good selectivities but decreased yields (Scheme 8).

Mechanistically, the observed selectivities in these domino cyclizations may be explicable if these reactions proceed via Traxler−Zimmermann-type transition states. As shown in Scheme 9, the homoallylic alcoholate **50** may first attack an electrophilic nitro

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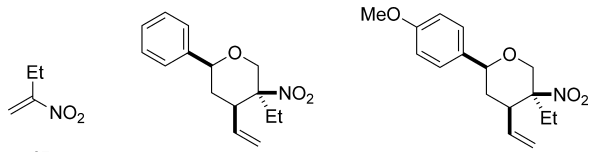
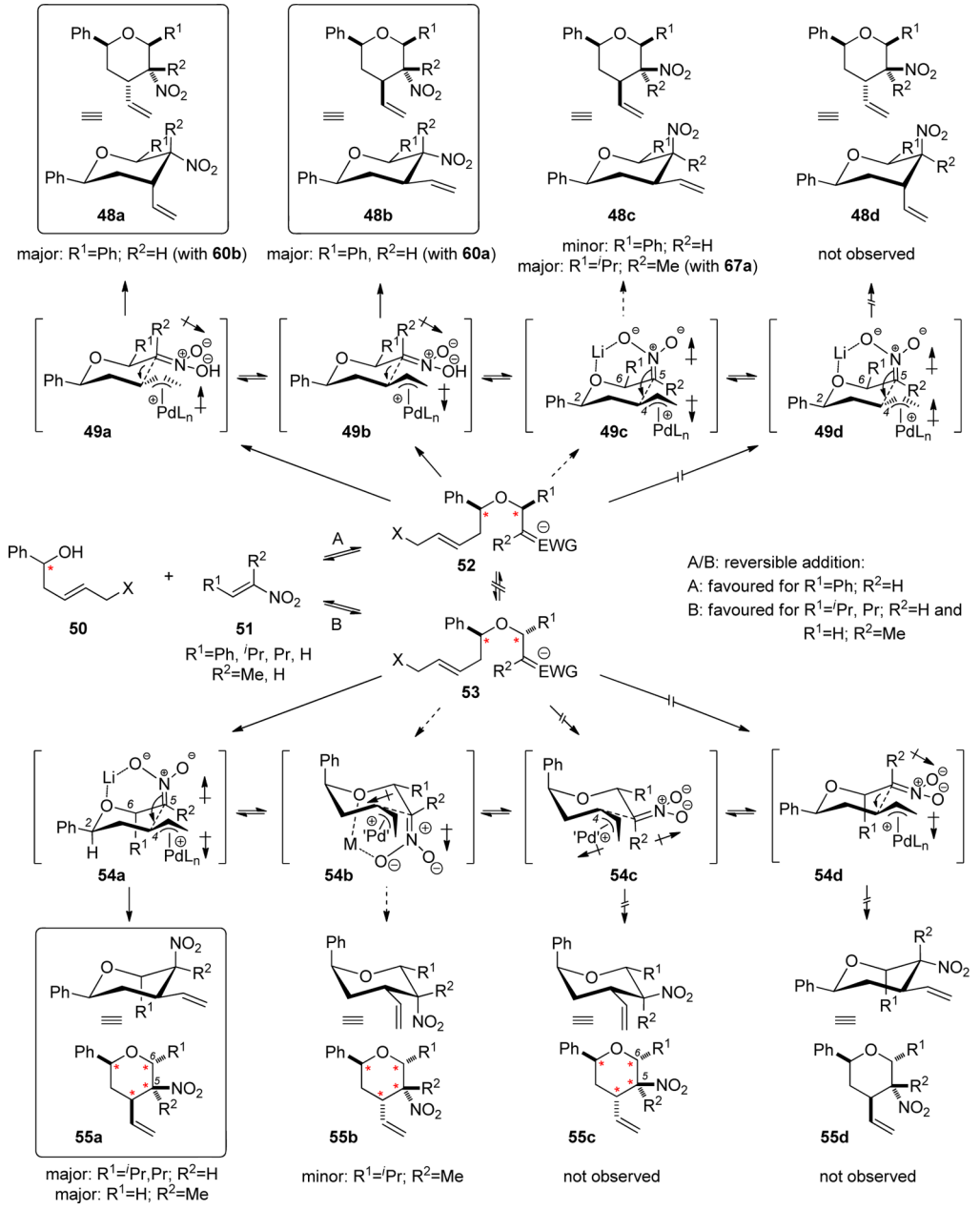
Scheme 8



olefin of general type **51** from either side, resulting in intermediates **52** or intermediate **53**, leading to transition states **49a–d** and **54a–d**, respectively. These transition states, i.e., **49a–d** and **54a–d**, would be expected to be in an equilibrium via η^3–η^1–η^3 (or π–δ–π) processes. The observed stereochemical outcome of these reactions, i.e., formation of the major products **48a**, **48b**, and **55a**, may arise from the corresponding transition states, viz. **49a**, **49b**, and **54a**. In transition states **49a** and **49b**, the substituents at C-2, C-5, and C-6 would be in equatorial positions (in contrast to **49c** and **49d** as well as **54b**, **54c** and **54d**) leading to a stabilization of these pathways. Generation of the axial configuration at C-5 in **55a**, in turn, may be explained by a chelation of the metal counterion to the ether oxygen and the nitro group, which would be more favorable with an axial nitro group, as shown in **54a**. Alternatively, also minimization of dipole–dipole interactions of the nitronate with the π-allyl complex would be more favorable for **54a** as compared to **49a** and **49b**. The intermediate chelate complex **54a** may also rationalize the observed selectivity at C-6, as this substituent would reside in a pseudo-equatorial position in this second 6-membered cycle. Depending on the substitution pattern of the nitro-olefin (i.e., R^1 and R^2), subtle difference in the relative stabilization of these pathways appear to be present, leading to either **48a**, **48b**, or **48c**. Presumably, a

Scheme 9



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sterically more demanding substituent R^1 at C-6 (here Ph) leads to formation of **48a** and **48b**, where both substituents at C-2 and C-6 are in equatorial positions, while a smaller substituent at this position (e.g., ^{i}Pr, Pr,H) favors formation of **55a**. This fine balance might also be influenced by chelative effects of the counterion. Importantly, the observed yields and selectivities of these reactions may only be explained if the initial oxa-Michael addition may not be stereodiscriminating. Intermediates **52** and **53** may be reversibly transformed into the more favorable diastereomers leading to the major products as observed.[25]

CONCLUSION

We have developed a new method to synthesize biologically significant multisubstituted THPs. This protocol combines an oxa-Michael with a metal-catalyzed reaction in an efficient way and generates up to three stereogenic centers resulting in a rapid increase of molecular complexity. The high degree of selectivity in this process is remarkable considering the stereochemical complexity of the process. Moreover, the heterocyclic products bear two functional handles (nitro and terminal olefin) which can be further elaborated. It is expected that this novel domino concept will be further explored and applied to the synthesis of functional molecules.

EXPERIMENTAL SECTION

General Information. NMR data were acquired on 300, 400, and 600 MHz NMR spectrometers and use the following abbreviations: s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet of doublets, ddd = doublet of doublets of doublets, brm = broad multiplet, brs = broad singlet. HRMS spectra were acquired using an MS spectrometer with a Q-TOF mass analyzer. Flash chromatography was carried out by column with silica gel Kieselgel S (grid size 32−62 μm). Solvents were dried and kept air-free in a solvent purification unit and were evaporated using a standard rotovapor and high vacuum. All reactions were carried out in oven-dried glassware under an Ar atmosphere.

General Procedure for Oxa-Michael/Tsuji−Trost Cascade. A solution of homoallylic alcohol and the nitroolefin in 1 mL of anhydrous THF was treated at −78 °C with a suspension of the palladium catalyst and phosphorus ligand in 1.5 mL of anhydrous THF and a solution of the base. The mixture was then warmed to room temperature and stirred until the alcohol was completely consumed (ca. 2 h). After being cooled to −78 °C, the reaction was stopped by addition of satd aq NH_4Cl solution. After being warmed to room temperature, the mixture was extracted three times with ethyl acetate. The combined organic phases were washed with brine, dried ($MgSO_4$), and filtered. Evaporation of the solvent in vacuo and purification of the residue by column chromatography on silica gel afforded the product.

*(E)-5-Hydroxy-5-phenylpent-2-enyl Methyl Carbonate (**1**).* 1-Phenylbut-3-en-1-ol (2.40 g, 16.2 mmol) and (Z)-but-2-ene-1,4-diyl dimethyl dicarbonate (6.61 g, 32.4 mmol) were dissolved in 40 mL of anhydrous CH_2Cl_2. A solution of second-generation Grubbs catalyst (0.275 g, 0.324 mmol) in 10 mL of anhydrous CH_2Cl_2 was added, and the mixture was refluxed overnight. The solvent was then removed in vacuo, and the residue was purified by flash chromatography and eluted with a gradient of petroleum ether and ethyl acetate, from 10:1 to 7:1 to 3:1, to give 3.88 g of pale brown oil (85%): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.25−7.38 (m, 5H), 5.65−5.92 (m, 2H), 4.74 (t, J = 6.2 Hz, 1H), 4.58 (d, J = 5.8 Hz, 2H), 3.77 (s, 3H), 2.52 (t, J = 6.2 Hz, 2H), 2.12 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 155.6, 143.7, 132.3, 128.4, 127.6, 127.6, 126.8, 125.7, 77.4, 76.6, 73.4, 68.1, 54.7, 42.1; HRMS (ESI+) calcd for $C_{13}H_{16}O_4Na$ $[M + Na]^+$ 259.0946, found 259.0942.

*(Z)-But-2-ene-1,4-diyl Dimethyl Dicarbonate (**8**).* Under argon, *cis*-2-butene-1,4-diol (5.29 g, 60.0 mmol) and pyridine (11.9 g, 150 mmol) were dissolved at room temperature in 120 mL of anhydrous THF, the solution was cooled to 0 °C, and methyl chloroformate (14.2 g, 150 mmol) was added to this solution. The mixture was then warmed to room temperature and stirred overnight. The reaction was diluted with water until the white precipitate disappeared. The mixture was then extracted with ethyl acetate three times, and the combined organic phases were washed with 1 N HCl, saturated aqueous $NaHCO_3$ solution, and brine and dried over anhydrous Na_2SO_4. After filtration, the solution was concentrated in vacuo, and the residue was purified by flash chromatography and eluted with a gradient of petroleum ether and ethyl acetate, from 12:1 to 6:1, to give 11.8 g of a colorless oil (96%): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.75 (t, J = 4.0 Hz, 2H), 4.70 (d, J = 4.6 Hz, 4H), 3.74 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 155.9, 128.3, 63.5, 55.2; HRMS (ESI+) calcd for $C_8H_{12}O_6Na$ $[M + Na]^+$ 227.0531, found 227.0527.

*3-Nitro-2,6-diphenyl-4-vinyltetrahydro-2H-pyran (**16**).* (*E*)-*tert*-Butyl 5-hydroxy-5-phenylpent-2-enyl carbonate (55.7 mg, 0.2 mmol) and *β-trans*-nitrostyrene (44.7 mg, 0.3 mmol) were dissolved in 1 mL of anhydrous THF, and the solution was cooled to −78 °C. The solution was then treated with a suspension of $Pd_2(dba)_3{\cdot}CHCl_3$ (10.4 mg, 0.0100 mmol) and PPh_3 (10.5 mg, 0.0400 mmol) in 1.5 mL of anhydrous THF and a solution of potassium *tert*-butoxide (1 M in THF, 0.300 mL, 1.5 equiv, as commercially supplied). The mixture was then warmed to room temperature and stirred until the alcohol was consumed. The reaction was then cooled to −78 °C again and quenched with saturated NH_4Cl solution. After being warmed to room temperature, the mixture was extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The solution was concentrated in vacuo, and the residue was purified with column of silica gel and eluted with the gradient of petroleum and ethyl acetate, from 60:1 to 30:1, to afford 35.0 mg of **16a** and 4-*epi*-**16b** as a pale-yellow viscous oil with a diastereomeric ratio of **16**:4-*epi*-**16** = 1.5:1 (combined yield: 57%). The two diastereomers could be isolated by preparative HPLC, eluted with isocratic eluent (hexane/EtOAc = 96:4).

16a: ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.28−7.50(m, 10H), 6.45 (ddd, J = 9.5, 10.2, 16.8 Hz, 1H), 5.36(d, J = 10.3 Hz, 1H), 5.30 (d, J = 16.8 Hz, 1H), 5.21 (d, J = 10.4 Hz, 1H), 4.96 (dd, J = 3.0, 10.5 Hz, 1H), 4.95 (dd, J = 5.2, 10.4 Hz, 1H), 3.41 (dddd, J = 4.4, 4.4, 4.4, 8.5 Hz, 1H), 2.23 (ddd, J = 4.5, 14.1, 14.1 Hz, 1H), 2.20 (ddd, J = 3.3, 14.1 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 140.8, 137.3, 132.6, 129.2, 129.0, 128.6, 128.5, 127.9, 127.8, 126.1, 126.1, 125.7, 120.2, 89.2, 77.2, 76.8, 75.9, 74.9, 42.6, 38.8; HRMS (ESI+) calcd for $C_{19}H_{19}NO_3Na$ $[M + Na]^+$ 332.1262, found 332.1258. 4-*epi*-**16b**: ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.27−7.39 (m, 10H), 5.67 (ddd, J = 8.3, 10.29, 17.5 Hz, 1H), 6.79−6.85 (d, J = 16.2 Hz, 1H), 5.14 (d, J = 10.3 Hz, 1H), 4.91 (d, J = 9.6 Hz, 1H), 4.79 (dd, J = 2.1, 11.6 Hz, 1H), 4.45 (d, J = 10.1 Hz, 1H), 3.25 (dddd, J = 4.1, 8.12, 11.8, 11,8 Hz, 1H), 2.22 (ddd, J = 2.4, 4.1, 14.1 Hz, 1H), 1.78 (ddd, J = 12.1, 12.1, 13.7 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ =140.6, 136.5, 135.2, 129.2, 128.7, 128.5, 128.0, 126.9, 125.7, 118.6, 92.7, 81.3, 79.4, 77.2, 76.8, 45.4, 38.1. 5-*epi*-**16c**: ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.28−7.50 (m, 10H), 5.93 (ddd, J = 6.7, 10.2, 17.1 Hz, 1H), 5.70 (d, J = 1.3, 1H), 5.38 (dd, J = 2.6, 4.3 Hz, 1H), 5.27 (d, J = 10.4 Hz, 1H), 5.28 (d, J = 17.2 Hz, 1H), 4.81 (dd, J = 3.3, 11.4 Hz, 1H), 3.41 (dddd, J = 3.9, 4.8, 6.7, 11.9 Hz, 1H), 2.61 (ddd, J = 11.9, 11.9, 13.2 Hz, 1H), 1.90 (ddd, J = 3.9, 3.9, 13.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ =136.1 (C7), 117.7 (C8), 85.6 (C5), 75.9 (C6), 72.6 (C2), 37.7 (C4), 32.1 (C3) (only chemical shifts of carbons in the THP ring are given).

*(E)-tert-Butyl 5-Hydroxy-5-phenylpent-2-enyl Carbonate (**17**).* 1-Phenylbut-3-en-1-ol (1.05 g, 7.1 mmol) and (*Z*)-but-2-ene-1,4-diyl *tert*-butyl dicarbonate (4.08 g, 14.2 mmol) were dissolved in 50 mL of anhydrous dichloromethane. A solution of second-generation Grubbs catalyst (0.301 g, 0.355 mmol) in 10 mL of anhydrous dichloromethane was then added, and the reaction mixture was refluxed overnight. The solvent was then removed in vacuo, and the residue was purified by column chromatography on silica gel and eluted with a gradient of petroleum ether and ethyl acetate, from 10:1 to 7:1 to 4:1, to afford 1.37 g of a viscous pale-brown oil (69%): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.21−7.35 (m, 5H), 4.62−5.81 (m, 2H), 4.69 (t, J = 6.2 Hz, 1H), 4.47 (d, J = 5.5 Hz, 2H), 3.53 (t, J = 6.6 Hz, 2H), 2.17 (s, br, 1H), 1.45 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 153.3, 143.7, 131.8, 128.4, 127.6, 127.2, 125.7, 82.1, 77.4, 77.0, 76.6, 73.4, 67.2, 42.1, 27.7; HRMS (ESI+) calcd for $C_{16}H_{22}O_4Na$ $[M + Na]^+$ 301.1415, found 301.1411.

*(E)-5-Hydroxy-5-phenylpent-2-enyl Acetate (**18**).* 1-Phenylbut-3-en-1-ol (1.40 g, 9.40 mmol) and (*Z*)-but-2-ene-1,4-diyl diacetate (3.25 g,

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18.9 mmol) were dissolved in 50 mL of anhydrous toluene. A solution of second-generation Grubbs catalyst (0.239 g, 0.15 mmol) in 10 mL of anhydrous toluene was then added, and the reaction mixture was then heated with stirring to 80 °C for 1.5 h. The solvent was then removed in vacuo, and the residue was purified by column chromatography on silica gel and eluted with a gradient of petroleum ether and ethyl acetate, from 8:1 to 4:1, to afford 1.27 g of a viscous pale-yellow oil (61%): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.25−7.38 (m, 5H), 5.63−5.82 (m, 2H), 4.74 (t, J = 6.2 Hz, 1H), 4.52 (d, J = 6.2 Hz, 2H), 2.52 (t, J = 6.2 Hz, 2H), 2.05 (s, 3H), 2.00 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.8, 143.7, 131.4, 128.4, 127.6, 127.4, 125.7, 77.4, 76.6, 73.4, 64.8, 42.1; HRMS (ESI+) calcd for $C_{13}H_{16}O_3Na$ $[M + Na]^+$ 243.0996, found 243.0994.

*(E)-5-Hydroxy-5-phenylpent-2-enyl 4-Methoxybenzoate (**19**).* 1-Phenylbut-3-en-1-ol (445 mg, 3 mmol) and (*Z*)-but-2-ene-1,4-diyl bis-(4-methoxybenzoate) (2.14 g, 6 mmol) were dissolved in 20 mL of anhydrous dichloromethane. A solution of second-generation Grubbs catalyst (127 mg, 0.15 mmol) in 10 mL of anhydrous dichloromethane was then added, and the reaction mixture was refluxed for 2 days. The solvent was then removed in vacuo, and the residue was purified by column chromatography on silica gel and eluted with a gradient of petroleum ether and ethyl acetate, from 6:1 to 3:1, to afford 489 mg of a viscous pale-yellow oil (52%): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.98−8.02 (m, 2H), 7.25−7.39 (m, 5H), 6.91−6.95 (m, 2H), 5.75−5.91 (m, 2H), 4.75−4.79 (m, 3H), 3.87 (s, 3H), 2.55 (t, J = 6.2 Hz, 2H), 2.16 (s, br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.5, 163.8, 144.2, 132.1, 131.5, 128.9, 128.3, 128.0, 126.2, 123.0, 114.0, 77.9, 77.0, 73.9, 65.4, 55.8, 42.7; HRMS (ESI+) calcd for $C_{38}H_{40}O_8Na$ $[2M + Na]^+$ 647.2621, found 647.2625.

*2-Isopropyl-3-nitro-6-phenyl-4-vinyltetrahydro-2H-pyran (**21**).* (*E*)-5-Hydroxy-5-phenylpent-2-enyl methyl carbonate (59.1 mg, 0.250 mmol) and (*E*)-3-methyl-1-nitrobut-1-ene (43.2 mg, 0.380 mmol) were dissolved in 1 mL of anhydrous THF, and the solution was cooled to −78 °C. A suspension $Pd_2(dba)_3{\cdot}CHCl_3$ (12.9 mg, 0.0125 mmol) and PPh_3 (13.1 mg, 0.05 mmol) in 1.5 mL of anhydrous THF was then added. Subsequently, a solution of potassium *tert*-butoxide (1 M in THF, 0.3 mL, 1.5 equiv) was added. The mixture was warmed to room temperature and stirred until the alcohol was consumed. The reaction was then cooled to −78 °C again and quenched with saturated NH_4Cl solution. After being warmed to room temperature, the mixture was extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The solution was then concentrated in vacuo, and the residue was purified by flash chromatography and eluted with a gradient of petroleum and ethyl acetate, from 60:1 to 30:1, to afford a mixture of diastereomers **21b** and **21c** and pure diastereomer **21a** with a diastereomeric ratio of **21a**:**b**:**c** = 5.2:1.4:1 as a viscous oil (combined yield: 43.0 mg; 78%).

21a: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.28−7.44 (m, 5H), 6.31 (ddd, J = 9.4, 10.2, 16.7 Hz, 1H), 5.27 (d, J = 10.2 Hz, 1H), 5.22 (d, J = 16.7 Hz, 1H), 4.75 (dd, J = 3.0, 8.0 Hz, 1H), 4.75 (dd, J = 5.1, 10.4 Hz, 1H), 4.09 (dd, J = 2.0, 10.1 Hz, 1H), 3.05 (dddd, J = 2.9, 5.3, 5.3, 9.4 Hz, 1H), 2.12 (ddd, J = 2.9, 2.9, 13.9 Hz, 1H), 1.94 (qd, J = 3.5, 6.9 Hz, 1H), 1.55 (ddd, J = 12.3, 12.3, 13.8 Hz, 1H), 1.08 (d, J = 6.7 Hz, 3H), 1.00 (d, J = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 133.2 (C7), 119.4 (C8), 81.9 (C6), 74.2 (C5), 73.7 (C2), 42.2 (C4), 29.2 (C3) (only chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{16}H_{21}NO_3Na$ $[M + Na]^+$ 298.1418, found 298.1414. **21b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.26−7.68 (m, 5H), 5.88 (ddd, J = 6.2, 10.2, 17.1 Hz, 1H), 5.22 (dd, J = 1.1, 16.1 Hz, 1H), 5.21 (dd, J = 1.0, 11.4 Hz, 1H), 4.79 (dd, J = 1.4, 4.2 Hz, 1H), 4.70 (dd, J = 3.3, 11.7 Hz, 1H), 3.98 (d, J = 10.3 Hz, 1H), 2.91 (dddd, J = 4.6, 4.6, 6.3, 12.2 Hz, 1H), 2.49 (ddd, J = 12.6, 12.6, 12.6 Hz, 1H), 2.29(dt, J = 17.6, 6.3 Hz, 1H)1.85 (ddd, J = 3.9, 3.9, 13.4 Hz, 1H), 1.07 (d, J = 6.5 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 141.7, 136.4, 128.5, 127.9, 126.1, 117.5, 84.6, 81.6, 77.3, 76.7, 71.8, 37.4, 31.8, 27.3, 19.4, 18.9. **21c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.28−7.44 (m, 5H), 5.63(ddd, J = 8.2, 10.3, 16.8 Hz, 1H), 5.18 (d, J = 16.8 Hz, 1H), 5.13 (dd, J = 10.3 Hz, 1H), 4.59 (dd, J = 2.3, 11.5 Hz, 1H), 4.42 (dd, J = 9.8, 10.7 Hz, 1H), 3.78 (dd, J = 2.1, 9.7 Hz, 1H), 3.05 (dddd, J = 4.0, 4.0, 7.6, 11.7 Hz, 1H), 2.13 (ddd, J = 2.4, 3.9, 13.8 Hz, 1H), 1.94 (qd, J = 3.5, 6.9 Hz, 1H), 1.55 (ddd, J = 12.3, 12.3, 13.8 Hz, 1H), 1.06 (d, J = 6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ =136.3 (C7), 118.2 (C8), 88.4 (C5), 85.6, 84.5, 81.9 (C6), 78.2 (C2), 45.2 (C4), 38.6 (C3) (only the chemical shifts of carbons in THP ring are reported);

*3-Nitro-6-phenyl-2-propyl-4-vinyltetrahydro-2H-pyran (**23**).* (*E*)-*tert*-Butyl 5-hydroxy-5-phenylpent-2-enyl carbonate (55.7 mg, 0.200 mmol) and (*E*)-1-nitropent-1-ene (34.5 mg, 0.300 mmol) were dissolved in 1 mL of anhydrous THF, and the solution was cooled to −78 °C. A suspension of $Pd_2(dba)_3{\cdot}CHCl_3$ (10.4 mg, 0.0100 mmol) and PPh_3 (10.5 mg, 0.0400 mmol) in 1.5 mL of anhydrous THF was then added. Subsequently, a solution of lithium *tert*-butoxide (1 M in hexane, 0.3 mL, 1.5 equiv) was added. The mixture was then warmed to room temperature and stirred until the alcohol was consumed. The reaction mixture was cooled to −78 °C and quenched with saturated NH_4Cl solution. After being warmed to room temperature, the mixture was extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The solution was then concentrated in vacuo, and the residue was purified by flash chromatography on silica gel and eluted with the gradient of petroleum and ethyl acetate, from 60:1 to 30:1, to afford pure diastereomer **23a** together with minor amounts of the 5-*epi*,6-*epi*-**23** (**23b**) and 4-*epi*,5-*epi*,6-*epi*-**23** (**23c**) with a diastereomeric ratio of 6.1:1:0.4 as a viscous oil (combined yield: 39.0 mg, 71%).

23a: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.26−7.43 (m,5H), 5.85 (ddd, J = 6.4, 10.5, 17.1 Hz, 1H), 5.22 (d, J = 17.4 Hz, 1H), 5.20 (d, J = 10.3 Hz, 1H), 4.72 (dd, J = 3.1, 11.3 Hz, 1H), 4.58 (d, J = 4.1 Hz, 1H), 4.50 (dd, J = 4.3, 9.6 Hz, 1H), 2.94 (dddd, J = 3.9, 4.5, 6.6, 12.7 Hz, 1H), 2.40 (ddd, J = 12.7, 12.7, 12.7 Hz,1H), 2.01 (ddt, J = 4.8, 9.1, 13.8 Hz, 1H), 1.80 (ddd, J = 3.9, 3.9, 13.7 Hz,1H), 1.61−1.39 (m, 3H), 0.96 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 141.7, 136.2, 128.5, 127.8, 126.1, 117.6, 86.4, 77.4, 76.6, 75.3, 71.2, 37.2, 32.2, 32.1, 18.9, 13.7. **23b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30−7.47 (m, 5H), 5.63 (ddd, J = 8.0, 10.2, 17.2 Hz, 1H), 5.15 (d, J = 17.2 Hz, 1H), 5.10 (d, J = 10.2 Hz, 1H), 4.56 (dd, J = 2.3, 10.3 Hz, 1H), 4.23 (dd, J = 9,5, 10.8 Hz, 1H), 3.88 (ddd, J = 3.0, 7.3, 9.9 Hz, 1H), 3.06 (dddd, J = 3.9, 7.9, 11.8, 11.8 Hz, 1H), 2.12 (ddd, J = 2.3, 4.3, 13.8 Hz,1H), 1.56 (ddd, J = 13.9, 13.9, 13.9 Hz, 1H), 1.64−1.42 (m, 4H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ =135.6 (C7), 118.3 (C8), 91.0 (C5), 78.1 (C6), 78.4 (C2), 45.2 (C4), 37.9 (C3) (only the chemical shifts of carbons in THP ring are reported). **23c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30−7.47 (m, 5H), 6.26 (ddd, J = 9.5, 10.2, 16.7 Hz, 1H), 5.24 (d, J = 10.2 Hz, 1H), 5.19 (d, J = 16.7 Hz, 1H), 4.70 (dd, J = 3.0, 10.7 Hz, 1H), 4.53 (dd, J = 6.0, 9.9 Hz, 1H), 4.20 (d, J = 10.8 Hz, 1H), 3.24 (dddd, J = 3.9, 4.5, 6.0, 8.5 Hz, 1H), 1.99 (ddd, J = 4.5, 10.7, 13.8 Hz,1H), 1.84 (ddd, J = 3.9, 3.9, 13.7 Hz, 1H), 11.64−1.42 (m, 4H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 133.0 (C7), 119.7 (C8), 88.0 (C5), 73.9 (C2), 72.8 (C6), 42.4 (C4), 38.5 (C3) (only the chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{32}H_{42}N_2O_6$ Na $[M + Na]^+$ 573.2939, found 573.2941.

*6-(Furan-2-yl)-3-nitro-2-propyl-4-vinyltetrahydro-2H-pyran (**24**).* (*E*)-*tert*-Butyl 5-(furan-2-yl)-5-hydroxypent-2-enyl carbonate (53.7 mg, 0.2 mmol) and (*E*)-1-nitropent-1-ene (46.0 mg, 0.4 mmol) were dissolved in 1 mL of anhydrous THF, and the solution was cooled to −78 °C. A suspension of $Pd_2(dba)_3{\cdot}CHCl_3$ (10.4 mg, 0.0100 mmol) and PPh_3 (10.5 mg, 0.0400 mmol) in 1.5 mL of anhydrous THF was then added. Subsequently, a solution of lithium *tert*-butoxide (1 M in THF, 0.3 mL, 1.5 equiv) was added. The mixture was then warmed to room temperature and stirred until the alcohol was consumed. The reaction mixture was cooled to −78 °C again and quenched with saturated NH_4Cl solution. After being warmed to room temperature, the mixture was extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The solution was concentrated in vacuo, and the residue was purified with column chromatography on silica gel and eluted with the gradient of petroleum and ethyl acetate, from 60:1 to 30:1, to afford pure diastereomer **24a** together with minor amounts of the 5-*epi*,6-*epi*-isomer (**24b**) and the 4-*epi*,5-*epi*,6-*epi*-isomer (**24c**) with a diastereomeric ratio of 5.2: 1: 0.8 as a viscous oil (combined yield: 50.7 mg, 78%). **24a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.42 (s, 1H), 6.38 (s, 2H), 5.83 (ddd, J = 6.8, 10.3, 17.2 Hz, 1H), 5.23 (d, J = 18.3 Hz, 1H), 5.22 (d, J = 8.0 Hz, 1H), 4.84 (dd, J = 3.9, 11.1 Hz, 1H), 4.56 (dd, J = 3.5, 4.6 Hz, 1H), 4.39 (dt, J = 3.7, 9.5 Hz, 1H), 2.85−3.00 (m, 1H), 2.64 (ddd, J = 11.3, 12.1,

13.4 Hz, 1H), 1.89−1.98 (m, 2H), 1.49−1.63 (m, 3H), 0.98 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 153.7, 142.5, 135.5, 118.0, 110.2, 107.2, 87.2, 77.4, 76.6, 74.2, 65.7, 37.4, 33.0, 28.0, 18.7, 13.6; HRMS (ESI+) calcd for $C_{14}H_{19}NO_4$ Na [M + Na]$^+$ 288.1211, found 288.1207. **24b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.40 (s, 1H), 6.36 (dt, J = 1.9, 3.4 Hz, 1H), 6.31 (dd, J = 3.5, 4.0 Hz, 1H), 5.68 (ddd, J = 8.1, 10.1, 17.2 Hz, 1H), 5.19 (d, J = 17.0 Hz, 1H), 5.15 (d, J = 10.2 Hz, 1H), 4.62 (dd, J = 2.1, 11.6 Hz, 1H), 4.23 (dd, J = 9.5, 10.8 Hz, 1H), 3.87 (ddd, J = 2.7, 8.0, 9.5 Hz, 1H), 3.03 (dddd, J = 4.2, 8.2, 12.0, 12.0 Hz, 1H), 2.13 (ddd, J = 2.4, 4.4, 13.9 Hz, 1H), 1.89 (ddd, J = 12.2, 12.2, 13.7 Hz, 1H), 1.27−1.61 (m, 4H), 0.90 (t, J = 8.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 135.4 (C7), 118.5 (C8), 78.2 (C6), 72.3 (C2), 68.1 (C5), 44.8 (C4), 33.8 (C3) (only the chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{14}H_{19}NO_4$ Na [M + Na]$^+$ 288.1211, found 288.1207. **24c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.40 (s, 1H), 6.36 (dt, J = 1.9, 3.4 Hz, 1H), 6.31 (dd, J = 3.5, 4.0 Hz, 1H), 6.20 (ddd, J = 9.4, 10.3, 16.6 Hz, 1H), 5.25 (d, J = 10.1 Hz, 1H), 5.21 (d, J = 16.6 Hz, 1H), 4.76 (dd, J = 2.4, 11.9 Hz, 1H), 4.53 (dd, J = 5.4, 10.2 Hz, 1H), 4.14 (ddd, J = 1.8, 8.2, 10.1 Hz, 1H), 3.25−3.33 (m, 1H), 2.31 (ddd, J = 4.8, 11.7, 13.7 Hz, 1H), 2.11 (ddd, J = 2.6, 2.6, 11.2 Hz, 1H), 1.27−1.61 (m, 4H), 0.90 (t, J = 8.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 132.6 (C7), 119.9 (C8), 87.9 (C5), 73.0 (C6), 68.1 (C2), 41.7 (C4), 34.7 (C3) (only the chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{14}H_{19}NO_4$ Na [M + Na]$^+$ 288.1211, found 288.1207.

*6-(2-Methoxyphenyl)-3-nitro-2-propyl-4-vinyltetrahydro-2H-pyran (**25**).* Under argon, (*E*)-*tert*-butyl-5-hydroxy-5-(2-methoxyphenyl)-pent-2-enyl carbonate (53.2 mg, 0.200 mmol) and (*E*)-1-nitropent-1-ene (46.0 mg, 0.400 mmol) were dissolved in 1 mL of anhydrous THF, and the solution was cooled to −78 °C. A suspension of $Pd_2(dba)_3$·$CHCl_3$ (10.4 mg, 0.0100 mmol) and PPh_3 (10.5 mg, 0.0400 mmol) in 1.5 mL of anhydrous THF was then added. Subsequently, a solution of lithium *tert*-butoxide (1 M in THF, 0.3 mL, 1.5 equiv) was added. The mixture was then warmed to room temperature and stirred until the alcohol was consumed. The reaction mixture was cooled to −78 °C again and quenched with saturated NH_4Cl solution. After being warmed to room temperature, the mixture was extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The solution was concentrated in vacuo, and the residue was purified by column chromatography on silica gel and eluted with the gradient of petroleum and ethyl acetate, from 40:1 to 20:1, to afford diastereomer **25a** together with minor amounts of the 5-*epi*,6-*epi*-compound (**25b**) and the 4-*epi*,5-*epi*,6-*epi*-isomer (**25c**) with a diastereomeric ratio of 5.2:1:0.6 as a viscous oil (combined yield: 42 mg, 70%). **25a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.57 (dd, J = 1.6, 8.5 Hz, 1H), 7.27 (d, J = 1.6, 15.6 Hz, 1H), 7.01 (ddd, J = 0.7, 7.5, 7.5 Hz, 1H), 6.87 (d, J = 8.2 Hz, 1H), 5.85 (ddd, J = 6.4, 10.4, 17.0 Hz, 1H), 5.20 (ddd, J = 1.2, 1.2, 17.2 Hz, 1H), 5.18 (ddd, J = 1.2, 1.2, 10.2 Hz, 1H), 5.12 (dd, J = 2.7, 11.6 Hz, 1H), 4.57 (d, J = 4.2 Hz, 1H), 4.47 (dd, J = 5.1, 9.5 Hz, 1H), 3.84 (s, 3H), 2.99 (dddd, J = 4.76.0, 6.0, 10.8 Hz, 1H), 2.27 (ddd, J = 12.0, 12.0, 12.9 Hz, 1H), 2.02−2.15 (m, 1H), 1.80 (ddd, J = 3.7, 3.7, 13.5 Hz, 1H), 1.52−1.62 (m, 2H), 1.41−1.49 (m, 1H), 0.99 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.1, 137.0, 130.7, 128.8, 127.2, 121.4, 117.7, 110.5, 86.9, 76.0, 65.5, 55.7, 37.7, 32.7, 31.3, 19.4, 14.1; HRMS (ESI+) calcd for $C_{34}H_{46}N_2O_8$Na [2M + Na]$^+$ 633.3151, found 633.3149. **25b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.45 (ddd, J = 2.1, 2.1, 7.5 Hz, 1H), 7.27 (ddd, J = 1.6, 1.6, 15.7 Hz, 1H), 6.99 (ddd, J = 0.7, 7.5, 7.5 Hz, 1H), 6.87 (dd, J = 3.3, 8.2 Hz, 1H), 5.64 (ddd, J = 8.1, 10.3, 17.2 Hz, 1H), 5.17 (ddd, J = 0.8, 0.8, 17.0 Hz, 1H), 5.11 (d, J = 11.3 Hz, 1H), 4.91 (dd, J = 1.8, 11.0 Hz, 1H), 4.26 (dd, J = 9.5, 10.8 Hz, 1H), 3.92 (ddd, J = 2.9, 8.1, 9.5 Hz, 1H), 3.84 (s, 3H), 3.12 (dddd, J = 4.2, 8.2, 11.9, 11.9 Hz, 1H), 2.22 (ddd, J = 2.0, 4.2, 13.7 Hz, 1H), 1.42 (ddd, J = 10.8, 13.2, 13.2 Hz, 1H), 1.27−1.62 (m, 4H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 135.9 (7), 117.9 (8), 91.3 (5), 78.1 (6), 73.3 (2), 45.2 (4), 36.6 (3), (only the chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{34}H_{46}N_2O_8$Na [2M + Na]$^+$ 633.3151, found 633.3149. **25c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.45 (ddd, J = 2.1, 2.1, 7.5 Hz, 1H), 7.27 (ddd, J = 1.6, 1.6, 15.7 Hz, 1H), 6.99 (ddd, J = 0.7, 7.5, 7.5 Hz, 1H), 6.87 (dd, J = 3.3, 8.2 Hz, 1H), 6.25 (ddd, J = 8.8, 11.0, 16.5 Hz, 1H), 5.28 (d, J = 10.3 Hz, 1H), 5.27 (d, J = 17.4 Hz, 1H), 5.06 (dd, J = 1.6, 11.3 Hz, 1H), 457 (dd, J = 5.3, 10.2 Hz, 1H), 4.16 (ddd, J = 2.0, 7.5, 9.9 Hz, 1H), 3.85 (s, 3H), 3.919−3.28 (m, 1H), 2.10 (ddd, J = 2.4, 2.4, 11.6 Hz, 1H), 1.79 (ddd, J = 4.8, 11.3, 13.9 Hz, 1H), 1.27- 1.62(m, 4H), 0.91 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 133.2 (7), 119.2 (8), 88.3 (5), 73.3 (6), 69.0 (2), 42.2 (4), 36.6 (3) (only the chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{34}H_{46}N_2O_8$Na [2M + Na]$^+$ 633.3151, found 633.3149.

*3-Nitro-2-propyl-6-p-tolyl-4-vinyltetrahydro-2H-pyran (**26**).* Under argon, (*E*)-*tert*-butyl-5-hydroxy-5-(4-methylphenyl)pent-2-enyl carbonate (50.1 mg, 0.200 mmol) and (*E*)-1-nitropent-1-ene (46.0 mg, 0.400 mmol) were dissolved in 1 mL of anhydrous THF, and the solution was cooled to −78 °C. A suspension of $Pd_2(dba)_3$·$CHCl_3$ (10.4 mg, 0.0100 mmol) and PPh_3 (10.5 mg, 0.0400 mmol) in 1.5 mL of anhydrous THF was then added. Subsequently, a solution of lithium *tert*-butoxide (1 M in THF, 0.3 mL, 1.5 equiv) was added. The mixture was then warmed to room temperature and stirred until the alcohol was consumed. The reaction mixture was cooled to −78 °C and quenched with saturated NH_4Cl solution. After being warmed to room temperature, the mixture was extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The solution was concentrated in vacuo, and the residue was purified by column chromatography on silica gel and eluted with the gradient of petroleum and ethyl acetate, from 40:1 to 20:1, to afford diastereomer **26a** together with minor amounts of the 5-*epi*,6-*epi*-isomer (**26b**) and the 4-*epi*,5-*epi*,6-*epi*-isomer (**26c**) with a diastereomeric ratio of 6.2:1:0.5 as a viscous oil (75%). **26a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.16−7.33 (m, 4H), 5.86 (ddd, J = 6.4, 10.4, 17.0 Hz, 1H), 5.21 (d, J = 17.0 Hz, 1H), 5.20 (d, J = 10.8 Hz, 1H), 4.69 (dd, J = 3.0, 11.6 Hz, 1H), 4.57 (dd, J = 1.3, 4.6 Hz, 1H), 4.18 (ddd, J = 1.6, 9.7, 12.1 Hz, 1H), 2.93−3.02 (m, 1H), 2.44 (ddd, J = 2.8, 12.8, 12.8 Hz, 1H), 2.30 (s, 3H), 1.82 (ddd, J = 3.8, 3.8, 13.5 Hz, 1H), 1.43−1.67 (m, 4H), 1.00 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 136.3 (C7), 117.5 (C8), 91.0 (C6), 86.5 (C5), 71.1 (C2), 37.3 (C4), 32.1 (C3) (only the chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{34}H_{46}N_2O_6$ Na [2M + Na]$^+$ 601.3253, found 601.3252. **26b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.16−7.33 (m, 4H), 5.66 (ddd, J = 8.0, 10.2, 17.2 Hz, 1H), 5.18 (d, J = 17.2 Hz, 1H), 5.13 (d, J = 10.8 Hz, 1H), 4.49(dd, J = 4.0, 9.7 Hz, 1H), 4.25 (dd, J = 9.3, 11.0 Hz, 1H), 3.91 (ddd, J = 2.7, 3.7, 9.8 Hz, 1H), 3.09 (dddd, J = 4.2, 8.2, 11.8, 11.8 Hz, 1H), 2.12 (ddd, J = 2.0, 2.0, 13.5 Hz, 1H), 2.30 (s, 3H), 1.61 (ddd, J = 11.9, 11.9, 13.7 Hz, 1H), 1.43−1.67 (m, 4H), 0.92 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz,$CDCl_3$) δ =135.7 (C7), 118.2 (C8), 78.4 (C6), 75.3 (C2), 68.1 (C5), 45.1 (C4), 37.8 (C3) (only the chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{34}H_{46}N_2O_6$ Na [2M + Na]$^+$ 601.3253, found 601.3252. **26c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.16−7.33 (m, 4H), 6.29 (ddd, J = 9.5, 10.1, 16.8 Hz, 1H), 5.25 (d, J = 17.6 Hz, 1H), 5.15 (d, J = 10.4 Hz, 1H), 5.12 (dd, J = 2.6, 11.6 Hz, 1H), 4.55 (dd, J = 4.0, 8.6 Hz, 1H), 4.18 (ddd, J = 2.2, 8.0, 9.7 Hz, 1H), 3.23−3.30 (m, 1H), 2.30(s, 3H), 1.97−2.12 (m, 2H), 1.43−1.67 (m, 4H), 0.90 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 133.1 (C7), 119.6 (C8), 88.1 (C5), 73.8 (C2), 72.8 (C6), 42.4 (C4), 38.5 (C3) (only the chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{34}H_{46}N_2O_6$ Na [2M + Na]$^+$ 601.3253, found 601.3252.

*6-(4-Methoxyphenyl)-3-nitro-2-propyl-4-vinyltetrahydro-2H-pyran (**27**).* (*E*)-*tert*-Butyl 5-hydroxy-5-(4-methoxyphenyl)pent-2-enyl carbonate (53.2 mg, 0.200 mmol) and (*E*)-1-nitropent-1-ene (46.0 mg, 0.400 mmol) were dissolved in 1 mL of anhydrous THF, and the solution was cooled to −78 °C. A suspension of $Pd_2(dba)_3$·$CHCl_3$ (10.4 mg, 0.0100 mmol) and PPh_3 (10.5 mg, 0.0400 mmol) in 1.5 mL of anhydrous THF were then added. Subsequently the solution of lithium *tert*-butoxide (1 M in THF, 0.3 mL, 1.5 equiv) was added. The mixture was then warmed to room temperature and stirred until the alcohol was consumed. The reaction mixture was cooled to −78 °C again and quenched with saturated NH_4Cl solution. After being warmed to room temperature, the mixture was extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The solution was then concentrated in vacuo, and the residue was purified by column chromatography on silica gel and eluted

with the gradient of petroleum and ethyl acetate, from 40:1 to 20:1, to afford diastereomer **27a** together with minor amounts of the 5-*epi*,6-*epi*-isomer (**27b**) and the 4-*epi*,5-*epi*,6-*epi*-isomer (**27c**) with a diastereomeric ratio of 5.4:1:0.8 as a viscous oil (combined yield: 47 mg, 77%). **27a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.34 (d, J = 8.5 Hz, 2H), 6.90 (d, J = 8.5 Hz, 2H), 5.66 (ddd, J = 8.2, 10.2, 17.2 Hz, 1H), 5.25 (d, J = 10.0 Hz, 1H), 5.21 (d, J = 16.8 Hz, 1H), 4.67 (dd, J = 2.9, 11.7 Hz, 1H), 4.56 (d, J = 4.1 Hz, 1H), 4.47 (dd, J = 4.7, 9.9 Hz, 1H), 3.82 (s, 3H), 2.96 (dddd, J = 3.8, 4.7, 9.3, 13.7 Hz, 1H), 2.45 (ddd, J = 12.6, 12.6, 12.6 Hz, 1H), 2.00−2.11 (m, 1H), 1.80 (ddd, J = 3.8, 3.8, 13.7 Hz, 1H), 1.52−1.62 (m, 2H), 1.41−1.49 (m, 1H), 1.00 (t, J = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ = 159.3, 136.3, 134.0, 127.5, 117.5, 113.9, 86.4, 77.3, 76.7, 75.3, 70.9, 55.3, 37.3, 32.3, 32.1, 18.9, 13.7; HRMS (ESI+) calcd for $C_{34}H_{46}N_2O_8Na$ [2M + Na]$^+$ 633.3151, found 633.3149. **27b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.34 (d, J = 8.5 Hz, 1H), 6.90 (d, J = 8.5 Hz, 1H), 5.85 (ddd, J = 6.3, 10.4, 17.0 Hz, 1H), 5.21 (d, J = 18.4 Hz, 1H), 5.20 (d, J = 9.3 Hz, 1H), 4.54 (dd, J = 2.1, 11.4 Hz, 1H), 4.24 (dd, J = 9.6, 10.7 Hz, 1H), 3.90 (ddd, J = 2.5, 8.0, 10.5 Hz, 1H), 3.81 (s, 3H), 3.08 (dddd, J = 4.1, 8.2, 11.6, 11.6 Hz, 1H), 2.10 (ddd, J = 2.2, 4.1, 13.7 Hz, 1H), 1.61 (ddd, J = 12.4, 12.4, 14.0 Hz, 1H), 1.27−1.62 (m, 4H), 0.91 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 135.7 (C7), 118.2 (C8), 91.0 (C7), 78.2 (C6), 73.6 (C2), 45.1 (C4), 37.7 (C3) (only the chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{34}H_{46}N_2O_8Na$ [2M + Na]$^+$ 633.3151, found 633.3149. **27c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.34 (d, J = 8.5 Hz, 2H), 6.90 (d, J = 8.5 Hz, 2H), 5.85 (ddd, J = 9.9, 9.9, 16.8 Hz, 1H), 5.25 (d, J = 10.0 Hz, 1H), 5.21 (d, J = 16.8 Hz, 1H), 4.68 (dd, J = 2.7, 10.7 Hz, 1H), 4.54 (dd, J = 2.1, 11.4 Hz, 1H), 4.47 (ddd, J = 1.6, 8.5, 10.0 Hz, 1H), 3.85 (s, 3H), 3.23−3.30 (m, 1H), 1.99 −2.07(m, 2H), 1.27−1.62 (m, 4H), 0.89 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 133.1 (C7), 119.6 (C8), 78.2 (C5), 73.6 (C2), 72.9 (C6), 42.4 (C4), 27.4 (C3) (only the chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{34}H_{46}N_2O_8Na$ [2M + Na]$^+$ 633.3151, found 633.3149.

*6-(Naphthalen-2-yl)-3-nitro-2-propyl-4-vinyltetrahydro-2H-pyran (**28**).* (*E*)-*tert*-Butyl 5-hydroxy-5-(naphthalen-2-yl)pent-2-enyl carbonate (65.7 mg, 0.2 mmol) and (*E*)-1-nitropent-1-ene (46.0 mg, 0.400 mmol) were dissolved in 1 mL of anhydrous THF, and the solution was cooled to −78 °C. A suspension of $Pd_2(dba)_3$·$CHCl_3$ (10.4 mg, 0.0100 mmol) and PPh_3 (10.5 mg, 0.0400 mmol) in 1.5 mL of anhydrous THF was then added. Subsequently, a solution of lithium *tert*-butoxide (1 M in THF, 0.3 mL, 1.5 equiv) was added. The mixture was then warmed to room temperature and stirred until the alcohol was consumed. The reaction mixture was cooled to −78 °C again and quenched with saturated NH_4Cl solution. After being warmed to room temperature, the mixture was extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The solution was concentrated in vacuo, and the residue was purified by column chromatography on silica gel and eluted with the gradient of petroleum and ethyl acetate, from 60:1 to 30:1, to afford pure diastereomer **28a** together with minor amounts of the 5-*epi*,6-*epi*-isomer (**28b**) and the 4-*epi*,5-*epi*,6-*epi*-isomer (**28c**) with a diastereomeric ratio of 6.3:1:0.7 as a viscous oil (combined yield: 50.7 mg, 78%). **28a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ =7.84−7.88 (m, 4H), 7.57 (d, J = 8.8 Hz, 1H), 7.47−7.52 (m, 2H), 5.88 (ddd, J = 6.4, 10.5, 17.1 Hz, 1H), 5.24 (d, J = 17.3 Hz, 1H), 5.24 (d, J = 10.5 Hz, 1H), 4.90 (dd, J = 2.7, 11.8 Hz, 1H), 4.61 (d, J = 3.6 Hz, 1H), 4.56 (dd, J = 4.5, 9.5 Hz, 1H), 3.02−3.05(m, 1H), 2.55 (ddd, J = 12.4, 12.4, 12.4 Hz, 1H), 1.88−1.97 (m, 1H), 1.93 (ddd, J = 3.6, 3.6, 13.4 Hz, 1H), 1.55−1.68 (m, 3H), 1.03 (t, J = 7.14 Hz, 3H); ^{13}C NMR (75 MHz, CDCl3) δ = 139.2, 136.2, 133.2, 133.1, 128.3, 128.0, 127.7, 126.1, 125.9, 124.8, 124.2, 117.6, 86.5, 77.3, 76.7, 75.4, 71.4, 37.3, 32.3, 32.2, 18.9, 13.7; HRMS (ESI+) calcd for $C_{40}H_{46}N_2O_6Na$ [M + Na]$^+$ 673.3253, found 673.3251. **28b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ =7.81−7.86 (m, 4H), 7.43−7.51 (m, 3H), 5.68 (ddd, J = 8.2, 10.2, 17.1 Hz, 1H), 5.24 (d, J = 17.2 Hz, 1H), 5.15 (d, J = 10.43 Hz, 1H), 4.75 (dd, J = 1.9, 11.4 Hz, 1H), 4.30 (dd, J = 9.5, 10.8 Hz, 1H), 3.98 (ddd, J = 2.9, 7.8, 9.5 Hz, 1H), 3.15 (dddd, J = 4.0, 8.0, 11.9, 11.9 Hz, 1H), 2.24 (ddd, J = 2.2, 4.2, 13.9 Hz, 1H), 1.70 (ddd, J = 12.1, 12.1, 13.7 Hz, 1H), 1.27−1.77 (m, 4H), 0.94 (t, J = 7.14 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 135.6 (C7), 118.3 (C8), 91.0 (C5), 78.6 (C2), 78.3 (C6), 45.2 (C4), 37.9 (C3) (only the chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{40}H_{46}N_2O_6Na$ [M + Na]$^+$ 673.3253, found 673.3251. **28c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.81−7.86 (m, 4H), 7.43−7.51 (m, 3H), 5.88 (ddd, J = 9.5, 10.1, 16.6 Hz, 1H), 5.30 (d, J = 9.9 Hz, 1H), 5.25 (d, J = 16.6 Hz, 1H), 4.90 (dd, J = 2.3, 11.6 Hz, 1H), 4.61 (dd, J = 5.3, 10.2 Hz, 1H), 4.24 (ddd, J = 3.8, 3.8, 9.5 Hz, 1H), 3.27−3.35 (m, 1H), 2.06−2.23 (m, 2H), 1.27−1.77 (m, 4H), 0.93 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 133.2 (C7), 119.8 (C8), 88.1 (C5), 74.1 (C2), 68.1 (C6), 42.4 (C4), 38.6 (C3) (only the chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{40}H_{46}N_2O_6Na$ [M + Na]$^+$ 673.3253, found 673.3251.

*2-Isopropyl-3-methyl-3-nitro-6-phenyl-4-vinyltetrahydro-2H-pyran (**30**).* (*E*)-*tert*-Butyl 5-hydroxy-5-*p*-tolylpent-2-enyl carbonate (55.7 mg, 0.2 mmol) and (*Z*)-4-methyl-2-nitropent-2-ene (0.2583 mg, 2 mmol) were dissolved in 1 mL of anhydrous THF, and the solution was cooled to −78 °C. A suspension of allylpalladium(II) chloride dimer (7.3 mg, 0.0200 mmol) and PPh_3 (15.7 mg, 0.0600 mmol) in 1.5 mL of anhydrous THF were added. Subsequently, a solution of LHMDS (1 M in THF, 0.3 mL, 1.5 equiv) was added. The mixture was then warmed to room temperature and stirred until the alcohol was consumed. The reaction mixture was cooled to −78 °C and quenched with saturated aqueous NH_4Cl solution. After being warmed to room temperature, the mixture was extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The solution was then concentrated in vacuo, and the residue was purified by column chromatography on silica gel and eluted with the gradient of petroleum and ethyl acetate, from 60:1 to 30:1, to afford 36.1 mg (0.124 μmol, 62%) of the three diastereomers **30a−c** with a diastereomeric ratio of 1.6:1:<0.05 as a viscous oil. **30a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30−7.50 (m, 5H), 5.60 (ddd, J = 7.4, 10.3, 17.3 Hz, 1H), 5.16 (d, J = 10.4 Hz, 1H), 5.09 (d, J = 17.2 Hz, 1H), 4.66 (dd, J = 2.6, 11.6 Hz, 1H), 3.90 (d, J = 6.9 Hz, 1H), 3.24 (ddd, J = 4.2, 7.4, 12.8 Hz, 1H), 2.05 (ddd, J = 3.6, 6.8, 13.9 Hz, 1H), 1.65 (ddd, J = 12.6, 12.6, 12.6 Hz, 1H), 1.57 (s, 3H), 1.75 (ttd, J = 6.6, 6.9, 8.4 Hz, 1H), 1.06 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ =134.1 (C7), 118.8 (C8), 110.6, 93.1, 92.1 (C5), 86.5 (C6), 79.1 (C2), 50.3 (C4), 35.5 (C3) (only the chemical shifts of carbons in THP ring are reported); HRMS (ESI+) calcd for $C_{17}H_{23}NO_3$ Na [M + Na]$^+$ 312.1575, found 312.1572. **30b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30−7.50 (m, 5H), 5.62 (ddd, J = 6.9, 10.0, 17.2 Hz, 1H), 5.26 (d, J = 11.7 Hz, 1H), 5.21 (d, J = 6.0 Hz, 1H), 5.09 (d, J = 17.2 Hz, 1H), 3.68 (d, J = 7.2 Hz, 1H), 3.14 (ddd, J = 4.0, 7.6, 12.9 Hz, 1H), 2.44 (dd, J = 3.9, 14.7 Hz, 1H), 2.09 (ddd, J = 6.2, 13.7, 13.7 Hz, 1H), 1.59 (s, 3H), 1.73 (dtt, J = 7.2, 7.2, 6.8 Hz, 1H), 1.07 (d, J = 6.8 Hz, 3H), 0.74 (d, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 134.3 (C7), 118.8 (C8), 93.1 (C5), 78.5 (C6), 72.7 (C2), 45.5 (C4), 27.8 (C3) (only the chemical shifts of carbons in THP ring are reported). **30c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30−7.50 (m, 5H), 5.61 (ddd, J = 7.7, 10.0, 17.1 Hz, 1H), 5.26 (d, J = 11.7 Hz, 1H), 5.09 (d, J = 17.2 Hz, 1H), 4.94 (dd, J = 6.3, 11.0 Hz, 1H), 4.08 (d, J = 9.7 Hz, 1H), 2.66 (ddd, J = 11.1, 13.2, 13.2 Hz, 1H), 2.51 (ddd, J = 2.3, 7.9, 12.8 Hz, 1H), 184 (dtt, J = 8.3, 6.5, 6.9 Hz, 1H), 2.00 (ddd, J = 2.4, 6.2, 13.4 Hz, 1H), 1.59 (s, 3H), 0.91 (d, J = 6.5 Hz, 3H), 0.86 (d, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 134.0 (C7), 118.8 (C8), 92.0 (C5), 79.9 (C6), 75.6 (C2), 48.1 (C4), 28.5 (C3) (only the chemical shifts of carbons in THP ring are reported).

*(E)-tert-Butyl 5-(Furan-2-yl)-5-hydroxypent-2-enyl carbonate (**31**).* 1-(Furan-2-yl)but-3-en-1-ol (1.38 g, 10 mmol) (1.38 g, 10 mmol) and (*Z*)-but-2-ene-1,4-diyl *tert*-butyl dicarbonate (2.88 g, 10 mmol) were dissolved in 40 mL of anhydrous dichloromethane. A solution of second-generation Grubbs catalyst (0.170 g, 0.2 mmol) in 10 mL of anhydrous dichloromethane was then added, and the reaction mixture was refluxed overnight. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel and eluted with the gradient of petroleum ether and ethyl acetate, from 12:1 to 8:1 to 4:1, to afford 1.78 g of a viscous pale-brown oil (66%): ^{1}H NMR 300 MHz, $CDCl_3$) δ = 7.40−7.41 (m, 1H), 6.35−6.37 (m, 1H), 6.27(d, J = 3.3 Hz, 1H), 5.70−5.88 (m, 2H), 4.77 (t, J = 6.4 Hz, 1H), 4.54 (d, J = 5.0 Hz, 2H), 2.66 (t, J = 5.4 Hz, 2H), 2.11 (s, br, 1H), 1.50(s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) = 155.8, 153.3, 142.0, 131.1, 127.5, 110.1, 106.2, 82.1,

77.4, 76.6, 67.2, 66.9, 38.5, 27.7; HRMS (ESI+) calcd for $C_{28}H_{40}O_{10}Na$ $[2M + Na]^+$ 559.2519, found 559.2518.

*6-(Furan-2-yl)-2-isopropyl-3-nitro-4-vinyltetrahydro-2H-pyran (**32**).* After an analogous procedure, workup, and purification as described above, the major diastereomer **a** together with **b** and **c** was a colorless oil with a ratio of 6.4:10.4:1 (combined yield: 43.5 mg, 78%). **32a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.41 (s, 1H), 6.36 (dd, J = 1.9, 3.3 Hz, 1H), 6.31 (d, J = 3.3 Hz, 2H), 5.62 (ddd, J = 7.5, 10.2, 17.5 Hz, 1H), 5.17 (d, J = 10.4 Hz, 1H), 5.10 (d, J = 17.0 Hz, 1H), 4.67 (dd, J = 2.5, 11.8 Hz, 1H), 3.84 (d, J = 7.4 Hz, 1H), 3.16 (ddd, J = 4.3, 7.5, 12.3 Hz, 1H), 2.03 (ddd, J = 2.7, 4.1, 13.7 1H), 1.92 (ddd, J = 12.3, 12.3, 13.7 Hz, 1H), 1.69−1.78 (m, 1H), 1.55 (s, 3H), 1.04 (d, J = 6.6 Hz, 3H), 0.82 (d, J = 6.9 Hz, 7H); ^{13}C NMR (126 MHz, $CDCl_3$) δ = 153.4, 142.3, 110.1, 106.8, 118.9; 119.0, 91.9, 86.6, 73.1, 50.1, 31.5, 30.2, 19.9, 18.6, 11.0; HRMS (ESI+) calcd for $C_{15}H_{21}NO_4$ Na $[M + Na]^+$ 302.1369, found 302.1366. **32b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.47 (s, 1H), 6.49 (d, J = 3.3 Hz, 1H), 6.39 (dd, J = 1.8, 3.2 Hz, 1H), 5.55 (ddd, J = 7.7, 10.0, 17.2 Hz, 1H), 5.24 (d, J = 17.0 Hz, 1H), 5.22 (d, J = 9.9 Hz, 1H), 4.96 (dd, J = 7.3, 11.1 Hz, 1H), 4.01 (d, J = 9.6 Hz, 1H), 2.66 (ddd, J = 11.2, 13.2, 13.2 Hz,1H), 2.48 (ddd, J = 2.8, 8.0, 12.8 Hz, 1H), 1.92 (ddd, J = 3.2, 7.1, 14.0 Hz, 1H), 1.61 (s, 3H), 1.66−1.77 (m, 1H), 0.75 (d, J = 6.3 Hz, 3H), 0.68 (d, J = 6.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ = 153.6, 142.9, 119.8; 119.8; 110.0, 107.8, 91.7, 78.9, 69.7, 47.8; 29.4, 26.0, 19.9, 17.8, 17.7; HRMS (ESI+) calcd for $C_{15}H_{21}NO_4$ Na $[M + Na]^+$ 302.1369, found 302.1366.

*5-Methyl-5-nitro-2-phenyl-4-vinyltetrahydro-2H-pyran (**36**).* (*E*)-*tert*-Butyl 5-hydroxy-5-phenylpent-2-enyl carbonate (55.7 mg, 0.2 mmol) and (*E*)-1-nitropent-1-ene (34.8 mg, 0.4 mmol) were dissolved in 1 mL of anhydrous THF, and the solution was cooled to −78 °C. A suspension of allylpalladium(II) chloride dimer (7.3 mg, 0.0200 mmol) and PPh_3 (15.7 mg, 0.0600 mmol) in 1.5 mL of anhydrous THF was added. Subsequently, a solution of LHMDS (1 M in THF, 0.3 mL, 1.5 equiv) was added. The mixture was then warmed to room temperature and stirred until the alcohol was consumed. The reaction was then cooled to −78 °C and quenched with saturated NH_4Cl solution. After being warmed to room temperature, the mixture was extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried (Na_2SO_4), and filtered. The solution was concentrated in vacuo, and the residue was purified with column of silica gel, eluted with the gradient of petroleum and ethyl acetate, from 60:1 to 30:1, to afford a mixture of diastereomers **36a** and the 4-*epi*,5-*epi*-isomer (**36b**) as a colorless oil with a diastereomeric ratio of 8.8:1 (combined yield: 31.0 mg; 62%). **36a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.31−7.41 (m, 5H), 5.67 (ddd, J = 7.3, 10.4, 17.4 Hz, 1H), 5.18 (dt, J = 1.0, 10.5 Hz, 1H), 5.13 (dt, J = 1.1, 17.1 Hz, 1H), 4.60 (dd, J = 2.6, 11.7 Hz, 1H), 4.12 (d, J = 10.8 Hz, 1H), 4.06 (d, J = 10.8 Hz, 1H), 3.39 (ddd, J = 4.4, 7.2, 12.2 Hz, 1H), 2.06 (ddd, J = 2.8, 4.3, 14.0 Hz, 1H), 1.74 (ddd, J = 12.3, 12.3, 13.9 Hz, 1H), 1.72 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 134.4, 128.6, 128.0, 125.7, 125.6, 118.7, 88.9, 79.9, 76.7, 75.1, 46.5, 35.7, 15.5; HRMS (FAB+) calcd for ($C_{14}H_{17}NO_3$) 247.1208, found 247.1203. **36b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ =7.31−7.41 (m, 5H), 6.13 (ddd, J = 9.0, 10.7, 16.6 Hz, 1H), 5.27 (d, J = 10.0 Hz, 1H), 5.26 (d, J = 17.4 Hz, 1H), 4.70 (dd, J = 2.9, 11.3 Hz, 1H), 4.01 (dd, J = 1.5, 11.9 Hz, 1H), 4.06 (d, J = 10.8 Hz, 1H), 3.39 (ddd, J = 3.0, 4.8, 9.0 Hz, 1H), 2.20 (ddd, J = 4.8, 11.4, 14.2 Hz, 1H), 2.01 (ddd, J = 3.0, 3.0, 14.3 Hz, 1H), 1.88 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 133.5 (C7), 120.1 (C8), 85.8 (C5) 74.9 (C2), 67.5 (C6), 46.4 (C4), 35.7 (C3), 23.6 (C9) (only the chemical shifts of carbons in THP ring are reported); HRMS (FAB+) calcd for ($C_{14}H_{17}NO_3$) 247.1208, found 247.1203.

*5-Methyl-5-nitro-2-p-tolyl-4-vinyltetrahydro-2H-pyran (**37**).* (*E*)-*tert*-Butyl 5-hydroxy-5-(4-methoxyphenyl)pent-2-enyl carbonate (58.5 mg, 0.2 mmol) and 2-nitroprop-1-ene (34.8 mg, 0.4 mmol,) were dissolved in 1 mL of anhydrous THF, and the solution was cooled to −78 °C. A solution of allylic palladium(II) chloride dimer (7.3 mg, 0.0200 mmol) and PPh_3 (15.7 mg, 0.0600 mmol) in 1.5 mL of anhydrous THF were then added. Subsequently, LiHMDS (1 M in THF, 0.3 mL) in THF was added. The mixture was then warmed to room temperature and stirred until the alcohol was consumed. The mixture was then cooled to −78 °C again and quenched with saturated NH_4Cl solution. After being warmed to room temperature, the mixture was extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and filtered. The solvent was removed in vacuo, and residue was purified by flash chromatography on silica gel and eluted with the gradient of petroleum ether and ethyl acetate, from 60:1, 30:1, to give 19.0 mg of a colorless viscous oil afford a mixture of the major diastereomer (**37a**) together with the 4-*epi*,5-*epi*-isomer (**37b**) as a colorless oil with a diastereomeric ratio of 8:1 (combined yield: 27.0 mg; 51%). **37a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.26 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 5.68 (ddd, J = 7.1, 10.4, 17.2 Hz, 1H), 5.18 (d, J = 10.4 Hz, 1H), 5.12 (d, J = 17.0 Hz, 1H) 4.56 (dd, J = 2.6, 11.7 Hz, 1H), 4.11 (d, J = 10.8 Hz, 1H), 4.04 (d, J = 10.6 Hz, 1H), 3.38 (ddd, J = 4.6, 7.1, 12.1 Hz, 1H), 2.38 (s, 3H), 2.04 (ddd, J = 2.7, 4.2, 13.9 Hz, 1H), 1.69 (s, 3H), 1.73 (ddd, J = 12.1, 12.1, 13.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 137.8, 134.5, 129.2, 125.6, 118.6, 89.0, 79.8, 75.2, 46.5, 35.7, 21.1, 15.5; HRMS (ESI+) calcd for $C_{15}H_{19}NO_3Na$ $[M + Na]^+$ 284.1262, found 284.1258.

*2-(4-Methoxyphenyl)-5-methyl-5-nitro-4-vinyltetrahydro-2H-pyran (**38**).* (*E*)-*tert*-Butyl 5-hydroxy-5-(4-methoxyphenyl)pent-2-enyl carbonate (61.7 mg, 0.2 mmol) and 2-nitroprop-1-ene (34.8 mg, 0.4 mmol,) were dissolved in 1 mL of anhydrous THF, and the solution was cooled to −78 °C. A solution of allyl palladium(II) chloride dimer (7.3 mg, 0.0200 mmol) and PPh_3 (15.7 mg, 0.0600 mmol) in 1.5 mL of anhydrous THF was then added. Subsequently, 0.3 mL of LiHMDS (1 M in THF, 0.3 mmol) in THF was added. The mixture was then warmed to room temperature and stirred until the alcohol was consumed. The mixture was cooled to −78 °C again and quenched with saturated NH_4Cl solution. After being warmed to room temperature, the mixture was extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and filtered. The solvent was removed in vacuo, and the residue was purified by flash chromatography on silica gel and eluted with the gradient of petroleum ether and ethyl acetate, from 40:1, 20:1, to afford a mixture of the major diastereomers (**38a**) and the 4-*epi*,5-*epi*-isomer (**38b**) as a colorless oil with a diastereomeric ratio of 8:1 (combined yield: 31.7 mg, 57%). **38a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.18−7.24 (m, 2H), 6.79−6.85 (m, 2H), 5.59 (ddd, J = 7.3, 10.4, 17.4 Hz, 1H), 5.01−5.19 (m, 2H), 4.47 (dd, J = 2.6, 11.5 Hz, 1H), 3.95(d, J = 10.8 Hz, 1H), 3.82 (s, 3H), 3.29 (ddd, J = 4.4, 7.1, 12.1 Hz, 1H), 1.94 (ddd, J = 2.6, 4.21, 13.9 Hz, 1H), 1.71 (s, 3H), 1.66 (ddd, J = 12.3, 12.3, 13.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ =15.9, 36.0, 47.0, 55.7, 75.6, 77.9, 80.1, 89.4, 114.3, 119.0, 127.4, 133.4, 134.9; HRMS (ESI+) calcd for $C_{15}H_{19}NO_4Na$ $[M + Na]^+$ 300.1211, found 300.1207.

*2-(2-Methoxyphenyl)-5-methyl-5-nitro-4-vinyltetrahydro-2H-pyran (**39**).* According to the procedure described above for compound **36**, (*E*)-*tert*-butyl 5-hydroxy-5-(2-methoxyphenyl)pent-2-enyl carbonate (61.7 mg, 0.2 mmol) was treated with 2-nitroprop-1-ene (34.8 mg, 0.4 mmol), allylpalladium(II) chloride dimer (7.3 mg, 0.02 mmol), PPh_3 (15.7 mg, 0.06 mmol), and 0.3 mL of LiHMDS (1 M in THF, 0.3 mmol) in anhydrous THF to give after an analogous workup and purification the major diastereomer **39a** together with the 4-*epi*,5-*epi*-isomer (**39b**) as a colorless oil with a diastereomeric ratio of 6:1 (combined yield: 32.8 mg, 59%). **39a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.45 (dd, J = 1.4, 7.6 Hz, 1H), 7.25−7.32 (m, 1H), 7.00 (t, J = 7.5 Hz, 1H), 6.89 (d, J = 8.4 Hz, 1H), 5.66 (ddd, J = 7.1, 10.4, 17.4 Hz, 1H), 5.11 (d, J = 10.6 Hz, 1H), 5.11 (td, J = 1.1, 17.2 Hz, 1H), 4.95 (dd, J = 2.5, 11.4 Hz, 1H), 4.13 (d, J = 10.6 Hz, 1H), 4.05 (d, J = 10.6 Hz, 1H), 3.85 (s, 3H), 3.40 (ddd, J = 4.4, 7.1, 11.9 Hz, 1H), 2.13 (ddd, J = 2.7, 4.2, 13.9 Hz, 1H), 1.72 (s, 3H), 1.58 (ddd, J = 11.7, 11.7, 14.3 Hz, 1H); ^{13}C NMR (75 MHz, $CHCl_3$) δ= 135.1, 129.1, 126.2, 121.2, 118.8, 110.7, 89.6, 77.8, 77.6, 75.7, 75.1, 55.7, 47.0, 34.6, 30.1, 15.9; HRMS (ESI+) calcd for $C_{15}H_{19}NO_4Na$ $[M + Na]^+$ 300.1211, found 300.1208.

*2-(Furan-2-yl)-5-methyl-5-nitro-4-vinyltetrahydro-2H-pyran (**40**).* According to the procedure described above for compound **36**, (*E*)-*tert*-butyl 5-(furan-2-yl)-5-hydroxypent-2-enyl carbonate (53.7 mg, 0.2 mmol) was treated with 2-nitroprop-1-ene (34.8 mg, 0.4 mmol), allylpalladium-(II) chloride dimer (7.3 mg, 0.02 mmol), PPh_3 (15.7 mg, 0.06 mmol), and 0.3 mL of LiHMDS (1 M in THF, 0.3 mmol) in anhydrous THF to give after an analogous workup and purification the major diastereomer **40a** together with the 4-*epi*,5-*epi*-isomer (**40b**) as a colorless oil with a diastereomeric ratio of 7:1 (combined yield: 14.2 mg, 30%). **40a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.43 (dd, J = 0.7, 1.8 Hz, 1H), 6.33−6.40

(m, 2H), 5.70 (ddd, J = 7.3, 10.6, 17.6 Hz, 1H), 5.21 (d, J = 0.8, 10.3 Hz, 1H), 5.16 (ddd, J = 1.2, 1.2, 17.2 Hz, 1H), 4.65 (dd, J = 3.8, 10.8 Hz, 1H), 4.10 (d, J = 10.6 Hz, 1H), 3.99 (d, J = 10.6 Hz, 1H), 3.33 (ddd, J = 6.2, 7.0, 11.3 Hz, 1H), 2.06 (ddd, J = 4.8, 4.8, 8.8 Hz, 1H), 1.69 (s, 3H), 2.00 (ddd, J = 11.7, 13.9, 13.9 Hz, 1H); ^{13}C NMR (75 MHz, $CHCl_3$) δ = 152.7, 142.7, 134.2, 118.9, 110.3, 107.4, 88.9, 74.9, 73.1, 46.1, 31.4, 15.4; HRMS (ESI+) calcd for $C_{12}H_{15}NO_4Na$ $[M + Na]^+$ 260.0899, found 260.0896.

*2-Cyclohexyl-5-methyl-5-nitro-4-vinyltetrahydro-2H-pyran (**41**).* According to the procedure described above for compound **36**, (*E*)-*tert*-butyl 5-cyclohexyl-5-hydroxypent-2-enyl carbonate (51.6 mg, 0.2 mmol) was treated with 2-nitroprop-1-ene (34.8 mg, 0.4 mmol), allylpalladium(II) chloride dimer (7.3 mg, 0.02 mmol), PPh_3 (15.7 mg, 0.06 mmol), and 0.3 mL of LiHMDS (1 M in THF, 0.3 mmol) in anhydrous THF to give after an analogous workup and purification the major diastereomer **41a** together with the 4-*epi*,5-*epi*-isomer (**41b**) as a colorless oil with a diastereomeric ratio of 5:1 (combined yield: 36.4 mg, 72%). **41a**: ^{1}H NMR (500 MHz, $CHCl_3$) δ = 5.64 (ddd, J = 7.4, 10.4, 17.3 Hz, 1H), 5.14 (d, J = 10.7 Hz, 1H), 5.09 (dt, J = 1.10, 17.0 Hz, 1H), 3.87 (s, 2H), 3.26 (ddd, J = 2.5, 6.3, 11.8 Hz, 1H), 3.15 (ddd, J = 4.7, 7.4, 12.1 Hz, 1H), 1.77 (ddd, J = 2.7, 4.4, 13.8 Hz, 1H), 1.58 (s, 3H), 1.43 (ddd, J = 12.6, 12.6, 12.6 Hz, 1H), 1.79−1.67 (m, 3H), 1.29−0.97 (m, 8H); ^{13}C NMR (125 MHz, $CHCl_3$) δ = 135.1, 118.3, 82.3, 76.8, 75.1, 46.4, 42.5, 30.6, 28.8, 28.6, 26.5, 26.1, 26.0, 15.3; HRMS (ESI+) calcd for $C_{14}H_{23}NO_3$ $[M + Na]^+$ 276.1575, found 276.1570.

*5-Methyl-5-nitro-2-phenethyl-4-vinyltetrahydro-2H-pyran (**42**).* According to the procedure described above for compound **36**, (*E*)-*tert*-butyl 5-hydroxy-7-phenylhept-2-enyl carbonate (55 mg, 0.2 mmol) was treated with 2-nitroprop-1-ene (34.8 mg, 0.4 mmol), allylpalladium(II) chloride dimer (7.3 mg, 0.02 mmol), PPh_3 (15.7 mg, 0.06 mmol), and 0.3 mL of LiHMDS (1 M in THF, 0.3 mmol) in anhydrous THF to give after an analogous workup and purification the major diastereomer **42a** together with the 4-*epi*,5-*epi*-isomer (**42b**) as a colorless oil with a diastereomeric ratio of 7:1 (combined yield: 26.4 mg, 48%). **42a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.19−7.32 (m, 5H), 5.63 (ddd, J = 7.4, 10.4, 17.6 Hz, 1H), 5.15 (d, J = 10.4 Hz, 1H), 5.08 (dt, J = 1.1, 17.0 Hz, 1H), 3.92 (d, J = 10.7 Hz, 1H), 3.89 (d, J = 11.0 Hz, 1H), 3.48 (dddd, J = 2.5, 4.1, 8.2, 11.4 Hz, 1H), 3.16 (ddd, J = 4.4, 7.1, 12.4 Hz, 1H), 2.64−2.83 (m, 2H), 1.73−1.94 (m, 2H), 1.76 (ddd, J = 2.5, 4.4, 13.7 Hz, 1H), 1.62 (s, 3H), 1.58 (ddd, J = 12.1, 12.3, 13.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 141.5, 134.7, 128.4, 126.0, 118.4, 89.3, 76.9, 76.8, 74.9, 46.2, 37.2, 33.7, 31.5; HRMS (ESI+) calcd for $C_{16}H_{21}NO_3Na$ $[M + Na]^+$ 298.1418, found 298.1418.

*5-Methyl-2-(naphthalen-2-yl)-5-nitro-4-vinyltetrahydro-2H-pyran (**43**).* According to the procedure described above for compound **36**, (*E*)-*tert*-butyl 5-hydroxy-5-(naphthalen-2-yl)pent-2-enyl carbonate (65.6 mg, 0.2 mmol) was treated with 2-nitroprop-1-ene (34.8 mg, 0.4 mmol), allylpalladium(II) chloride dimer (7.3 mg, 0.02 mmol), PPh_3 (15.7 mg, 0.06 mmol), and 0.3 mL of LiHMDS (1 M in THF, 0.3 mmol) in anhydrous THF to give after an analogous workup and purification the major diastereomer **43a** together with the 4-*epi*,5-*epi*-isomer (**43b**) as a colorless oil with a diastereomeric ratio of 10:1 (combined yield: 39.8 mg, 67%). **43a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.84−7.88 (m, 4H), 7.46−7.52 (m, 3H), 5.70 (ddd, J = 7.3, 10.6, 17.5 Hz, 1H), 5.20 (d, J = 10.4 Hz, 1H), 5.15 (d, J = 17.2 Hz, 1H), 4.77 (dd, J = 2.6, 11.7 Hz, 1H), 4.19 (d, J = 11.2 Hz, 1H), 4.12 (d, J = 10.8 Hz, 1H), 3.44 (ddd, J = 4.4, 7.1, 12.1 Hz, 1H), 2.15 (ddd, J = 2.7, 4.4, 14.1 Hz, 1H), 1.82 (ddd, J = 12.3, 12.3, 13.9 Hz, 1H), 1.77 (s, 3H); ^{13}C NMR (75 MHz, $CHCl_3$) δ = 138.2, 134.4, 133.2, 133.1, 128.4, 128.0, 127.7, 126.3, 126.1, 124.4, 123.6, 118.7, 89.0, 80.0, 75.2, 46.6, 35.8, 15.6; HRMS (FAB+) calcd for ($C_{18}H_{19}NO_3$) 297.1365, found 297.1356.

*(2S,4R,5R)-5-Methyl-5-nitro-2-(4-nitrophenyl)-4-vinyltetrahydro-2H-pyran (**44**).* According to the procedure described above for compound **36**, (*E*)-*tert*-butyl (5-hydroxy-5-(4-nitrophenyl)pent-2-en-1-yl) carbonate (64.6 mg, 0.2 mmol) was treated with 2-nitroprop-1-ene (34.8 mg, 0.4 mmol), allylpalladium(II) chloride dimer (7.3 mg, 0.02 mmol), PPh_3 (15.7 mg, 0.06 mmol), and 0.3 mL of LiHMDS (1 M in THF, 0.3 mmol) in anhydrous THF to give after an analogous workup and purification the major diastereomer **44a** together with the 4-*epi*,5-*epi*-isomer (**44b**) as a colorless oil with a diastereomeric ratio of 5:1 (combined yield: 39.1 mg, 67%). **44a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.24 (d, J = 8.8 Hz, 2H), 7.54 (d, J = 8.8 Hz, 2H), 5.67 (ddd, J = 7.3, 10.4, 17.4 Hz, 1H), 5.21 (td, J = 1.0, 10.4 Hz, 1H), 5.14 (td, J = 1.0, 10.2 Hz, 1H), 4.71 (dd, J = 2.6, 11.7 Hz, 1H), 4.14 (d, J = 11.3 Hz, 1H), 4.09(d, J = 10.8 Hz, 1H), 3.41 (ddd, J = 4.4, 7.3, 12.1 Hz, 1H), 2.11 (ddd, J = 2.7, 4.2, 13.9 Hz, 1H), 1.71 (S, 3H), 1.66 (ddd, J = 12.4, 12.4, 13.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 15.5, 35.8, 46.4, 75.0, 76.6, 77.4, 78.7, 88.5, 119.1, 123.8, 133.9, 147.9.

*5-Ethyl-5-nitro-2-phenyl-4-vinyltetrahydro-2H-pyran (**46**).* (*E*)-*tert*-Butyl 5-hydroxy-5-phenylpent-2-enyl carbonate (55.7 mg, 0.2 mmol) and 2-nitrobut-1-ene (40.4 mg, 0.4 mmol) were dissolved in 1 mL of anhydrous THF, and the solution was cooled to −78 °C. A solution of allylpalladium(II) chloride dimer (7.3 mg, 0.02 mmol) and PPh_3 (15.7 mg, 0.06 mmol) in 1.5 mL of anhydrous THF was added. Subsequently, LHMDS (1 M in THF, 0.3 mL) was added. The mixture was then warmed to room temperature and stirred until the alcohol was consumed. The mixture was then cooled to −78 °C and quenched with saturated NH_4Cl solution. After being warmed to room temperature, the mixture was extracted with ethyl acetate three times. The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and filtered. The solvent was removed in vacuo, and the residue was purified by flash chromatography on silica gel and eluted with the gradient of petroleum ether and ethyl acetate, from 60:1, 30:1, to give the major diastereomer **46a** together with the 4-*epi*,5-*epi*-isomer (**46b**) as a colorless oil with a diastereomeric ratio of 7:1 (combined yield: 13.1 mg, 25%). **46a**: ^{1}H NMR (500 MHz, $CHCl_3$) δ = 7.31−7.39 (m, 5H), 5.80 (ddd, J = 7.8, 10.4, 17.3 Hz, 1H), 5.17 (dt, J = 1.1, 10.4 Hz, 1H), 5.09 (dt, J = 1.1, 17.1 Hz, 1H), 4.60 (dd, J = 2.9, 11.6 Hz, 1H), 4.37 (d, J = 11.5 Hz, 1H), 4.11 (dd, J = 1.5, 11.6 Hz, 1H), 3.13 (ddd, J = 4.4, 7.5, 12.2 Hz, 1H), 2.27 (ddt, J = 1.2, 7.4, 14.7 Hz, 1H), 2.09 (dt, J = 7.3, 14.7 Hz, 1H), 2.04 (ddd, J = 3.1, 4.5, 14.0 Hz, 1H), 1.82 (ddd, J = 12.0, 12.0, 14.0 Hz, 1H), 1.04 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CHCl_3$) δ = 134.5, 130.9, 128.8, 128.5, 128.0, 125.7, 125.6, 118.4, 79.8, 69.7, 48.6, 36.2, 28.9, 20.7, 7.8; HRMS (ESI+) calcd for $C_{15}H_{19}NO_3Na$ $[M + Na]^+$ 284.1262, found 284.1259.

*5-Ethyl-2-(4-methoxyphenyl)-5-nitro-4-vinyltetrahydro-2H-pyran (**47**).* According to the procedure described above for compound **36**, (*E*)-*tert*-butyl (5-hydroxy-5-(4-methoxyphenyl)pent-2-en-1-yl) carbonate (61.7 mg, 0.2 mmol) was treated with 2-nitrobut-1-ene (40.4 mg, 0.4 mmol), allylpalladium(II) chloride dimer (7.3 mg, 0.02 mmol), PPh_3 (15.7 mg, 0.06 mmol), and 0.3 mL of LiHMDS (1 M in THF, 0.3 mmol) in anhydrous THF to give after an analogous workup and purification the major diastereomer **47a** together with the 4-*epi*,5-*epi*-isomer **b** as a colorless oil with a diastereomeric ratio of 6:1 (combined yield: 11.6 mg, 20%). **47a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.29 (d, J = 8.5 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 5.80 (ddd, J = 7.7, 10.4, 17.3 Hz, 1H), 5.17 (d, J = 10.4 Hz, 1H), 5.09 (d, J = 17.3 Hz, 1H), 4.54 (dd, J = 2.7, 11.5 Hz, 1H), 4.35 (d, J = 11.5 Hz, 1H), 4.10 (dd, J = 1.4, 11.5 Hz, 1H), 3.82 (s, 3H), 3.11 (ddd, J = 4.7, 7.7, 12.3 Hz, 1H), 2.26 (qd, J = 7.1, 14.6 Hz, 1H), 2.09 (qd, J = 7.1,14.6 Hz, 1H), 2.00 (ddd, J = 3.0, 4.4, 14.0 Hz, 1H), 1.82 (ddd, J = 12.1, 12.1, 14.0 Hz, 1H), 1.02 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.3, 134.5, 133.0, 127.0, 118.3, 113.9, 91.1, 79.5, 76.7, 69.7, 55.3, 48.6, 36.0, 20.6, 7.74; HRMS (ESI+) calcd for $C_{32}H_{41}N_2O_8Na$ $[2M + Na]^+$ 605.2839, found 605.2850.

■ ASSOCIATED CONTENT

Supporting Information

Copies of NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.

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