Second Generation Synthesis of Northern Fragment of Mandelalide A: Role of Pi-Stacking on Sharpless Dihydroxylation of *cis*-Enynes

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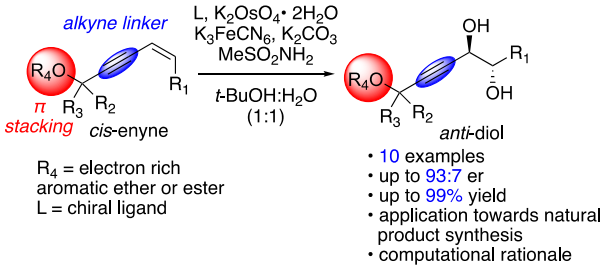
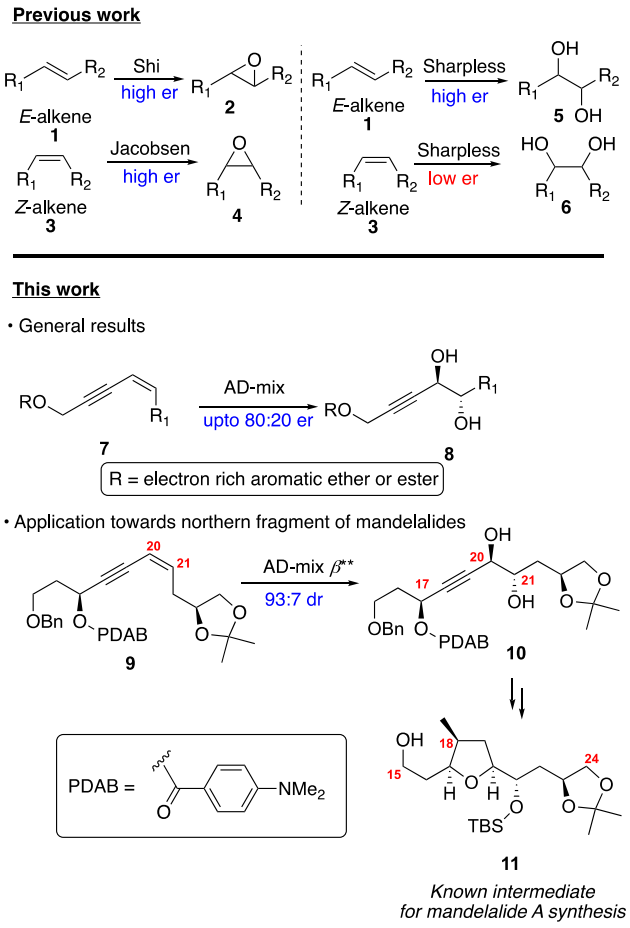


Abstract. The development of a pi-stacking-based approach for increased stereoselectivity in Sharpless asymmetric and diastereomeric dihydroxylation of *cis*-enynes is disclosed. The use of neighboring, electron-rich benzoate esters proved key to the success of this process. DFT study reveals the substrate benzoate ester groups rigidify the dihydroxylation transition states by forming a favorable pi-stacking interaction in both the **Major-TS** and **Minor-TS**. The energetic preference for the **Major-TS** was found in part due to the favorable eclipsing conformation of the alkene substituent as opposed to the disfavored bisecting conformation found in the **Minor-TS**. The application to a second-generation synthesis of the C15-C24 northern portion of mandelalide A is demonstrated.

Introduction.

Asymmetric epoxidation and dihydroxylation of alkenes has proven transformational for the efficient introduction of chirality into achiral substrates.[1,2] For epoxidations, *trans*-alkenes **1** tend to prove the most amenable substrates for directed Sharpless-type[1b, 3] epoxidations as well as organocatalytic methods (e.g. Shi epoxidations[4]) whereas *cis*-alkenes **3** have been shown to be superior with Jacobsen-type epoxidations[5] and recently developed Shi-type epoxidations[6] (Scheme 1). For 1,1-disubstituted and mono-substituted alkenes, indirect methods for their net asymmetric epoxidation have been widely demonstrated through kinetic resolution approaches.[7] In contrast, asymmetric methods of direct dihydroxylation of an alkene are more limited in scope. While ample substrate scope has been demonstrated for *trans*-alkenes **1** using the Sharpless' asymmetric dihydroxylation,[8] the direct asymmetric dihydroxylation of *cis*-alkenes **3** to the corresponding *anti*-diols **6** remains a problem that has not yet been fully resolved.[9] Sharpless and co-workers did develop some specific ligands for the dihydroxylation of *cis*-alkenes;[10] however, these ligands have proven only modestly effective and have seen limited use.[11] Currently, the synthetic community is primarily limited to multi-step solutions involving the use of *trans*-alkenes **1** to access *anti*-diols **6**. For example, Shi epoxidation of a *trans*-alkene **1** followed by the opening of the epoxide with an oxygen-based nucleophile does deliver the target *anti*-diol **6**.[12] Alternatively, the *trans*-alkene **1** can be dihydroxylated followed by an inversion through activation as a cyclic sulfate and displaced with an oxygen nucleophile.[13] In this Article, we disclose the notable increase in enantioselectivity of the Sharpless-type dihydroxylation of *cis*-1,2-disubstituted alkenes **7** containing a neighboring, electron-rich propargylic benzoate moiety. The computational rationale for these findings as well as the application of this discovery to

a second-generation synthesis of the C15-C24 portion of mandelalide A **16** is demonstrated.

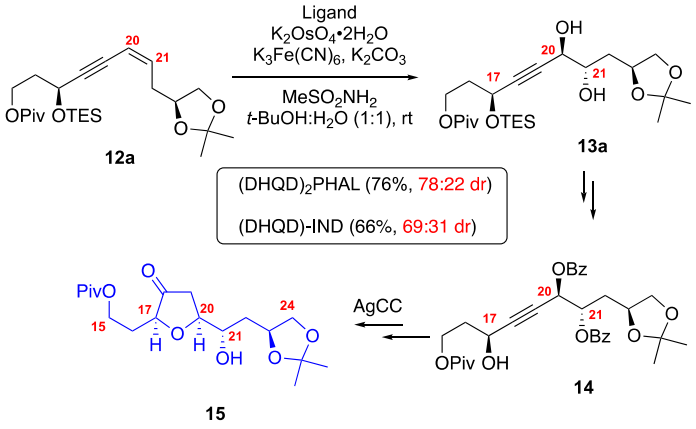


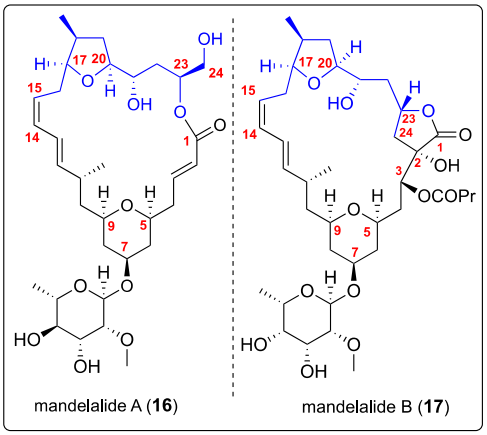
Scheme 1. Asymmetric Oxidation of Alkenes and Application to Mandelalide A

Results and Discussion.

During our total synthesis of mandelalide A,[14] we required the construction of a 1,2-*anti* propargylic diol **13a** for use in a subsequent Ag-catalyzed cyclization (AgCC) (Scheme 2). Given the complexity of functional groups in this portion of the carbon backbone, the most expedient route to access this *anti*-diol was through the use of a diastereoselective

dihydroxylation of *cis*-enyne **12a**. We had hoped that Sharpless' *cis*-alkene ligand system (DHQD)-IND[10] would prove effective in our case; however, the diastereoselectivity was actually lower than with the standard $(DHQD)_2PHAL$ system – given approximately 78:22 dr with $(DHQD)_2PHAL$ as compared to 69:31 dr with (DHQD)-IND. It should be noted that the surrounding chiral environment of the *cis* alkene **12**a appears to have minimal impact on the diastereoselectivity of the process (22:78 dr with $(DHQ)_2PHAL$). For our first-generation synthesis of this natural product **16**, we took advantage of the fact that these diastereomers proved separable on silica gel chromatography. While effective, this process wasted approximately 20-30% of the valuable starting enyne that had to be discarded.



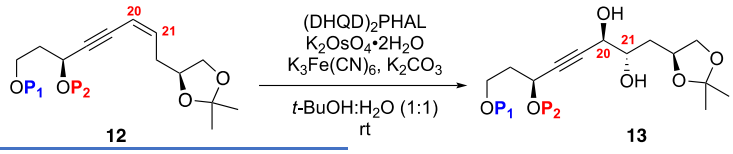


Scheme 2. Asymmetric Dihydroxylation of *cis*-Enyne and First-Generation Synthesis of Mandelalide A.

Our continued efforts for accessing other members of the mandelalide family [e.g. mandelalide B (**17**)] have required production of larger quantities of the desired diastereomeric diol **13a**. Consequently, we set out to explore in depth the potential controlling elements of dihydroxylations of 1,2-disubstituted *cis*-enynes (Table 1). Prior researchers have shown that tri-substituted *cis*-alkenes proved to be the most effective substrates for providing moderate to high enantioselectivity.[15] Brimble and co-workers have shown that 1,2-disubstituted *cis*-olefins are generally poor substrates for Sharpless-type dihydroxylation reactions.[16] Additionally, Lera,[15a] Tietze,[15b] Mayer[15c] and Bruckner[15d] demonstrated that the presence of an aromatic allylic ether or ester moiety in trisubstituted enynes and alkenes might help in achieving higher stereoselectivity in the asymmetric dihydroxylation.

We hypothesized that the tactical use of pi-stacking[17,18] could lead to improvements in our diastereoselectivity through better controlling the spatial positioning of the substrate within the extended pi-systems of the $(DHQD)_2PHAL$-Os catalyst. This approach showed initial promise as substitution of the P_1 and P_2 moieties with substituents that are capable of pi-stacking did lead to a marked improvement in the diastereoselectivity in this sequence (88:12 dr, 67%, **13d**, Entry 4, Table 1).

TABLE 1. Impact of Neighboring Ether/Ester Substitution on Selectivity in Sharpless Dihydroxylation.



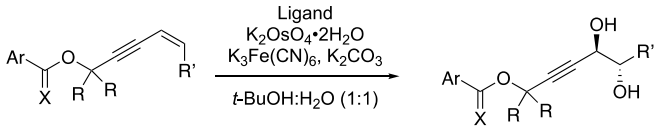
Entry	Substrate	P_1	P_2	Yield	dr
1	12a	Piv	TES	76% (**13a**)	78:22
2	12b	Bn	TES	73% (**13b**)	79:21
3	12c	TES	Bn	48% (**13c**)	82:18
4	12d	Bn	PMB	67% (**13d**)	88:12

Intrigued by the initial positive benefits of pi-stacking with *cis*-enyne systems, we set out to explore the enantioselectivity of this concept on an achiral substrate **18** (Table 2). Starting from the simplified PMBO-protected propargylic ether **18a**, we found only a modest level of enantioselectivity using the pseudoenantiomeric ligand pair $(DHQD)_2PHAL$ and $(DHQ)_2PHAL$ (Entries 1 and 2). Inspired by Corey and co-workers' pioneering work with Sharpless dihydroxylations on allylic benzoates,[17a] we decided to explore the impact of propargylic benzoates on our enyne system. The parent benzoate **18b** showed no change in enantioselectivity, but an improvement in chemical yield was noted. We are not certain of the exact rationale for this yield improvement at this time. One possible explanation for the similar enantioselectivities observed between these two substrates (**18a** and **18b**) could be the competing effects of the comparatively less electron rich nature of benzoate **18b** [that might negatively impact its donor acceptor pi-stacking ability[19] with $(DHQD)_2PHAL$)] versus the gains in transition preorganization

introduced through restricted rotation and dipoles from the incorporation of the sp^2-hybridized ester moiety in **18b**.[20] Similar selectivity was observed for the biphenylic benzoate **18c** (Entry 4). The absolute configuration of **19c** was confirmed by Mosher ester analysis.[21] *Cis*-alkenes are known to be challenging substrates for Sharpless dihydroxylations, most likely due to poorer fit within the cavity created by the ligand-OsO_4 complex.[10a] We therefore believed it was critical to maximize the pi-stacking interactions in our system to compensate. Subsequent use of more electron-rich systems appeared to support this hypothesis. Entries 5-7 containing additional oxygenation on the benzoate moiety did lead to modest increases in enantioselectivity (up to 54% ee with **18e** in entry 6). The use of a *N*,*N*-dimethyl amino group was potentially more attractive on the benzoate moiety as it both increased the electron-rich nature of the aromatic ring and also opened the door for subsequent selective removal in the presence of other ester moieties (through pre-activation by quaternization of the amino moiety). Wang and co-workers recently reported high levels of enantioselectivity in the dihydroxylation of a series of 1,1-disubstituted alkenes.[17b] Indeed, the *p-N,N*-dimethylamino benzoate (PDAB) **18g** did give comparable to slightly improved enantioselectivity (Entry 8). As expected, with electron poor benzoate substrate (**18h**), a drop in enantioselectivity was observed (Entry 9). Changing the ligand system to $(DHQD)_2PYR$ (Entry 10) showed similar selectivity as $(DHQD)_2PHAL$ (Entry 8). Use of the more bulkier propyl ligand [$(Pr\text{-}DHQD)_2PHAL$] led to slight reduction in enantioselectivity (Entry 11). A reversal in enantioselectivity was observed for both the $(DHQD)_2AQN$ and the Sharpless ligand designed for *cis* alkenes [(DHQD)-IND] (Entries 12-13). We also explored the impact of substitution at the R and R' positions (Entries

14-15); however, limited augmentation in the enantioselectivity was observed with variants **18i** and **18j**.

TABLE 2. Exploration of Enantioselectivity in Sharpless Dihydroxylation of *cis*-Enynes.



18 **19**

18a: X = H, H; R = H; R' = Pent; Ar = 4-OMe-C_6H_4
18b: X = O; R = H; R' = Pent; Ar = -C_6H_5
18c: X = O; R = H; R' = Pent; Ar = 4-Ph-C_6H_4
18d: X = O; R = H; R' = Pent; Ar = 4-OMe-C_6H_4
18e: X = O; R = H; R' = Pent; Ar = 2,4,6-$(OMe)_3$-C_6H_2
18f: X = O; R = H; R' = Pent; Ar = 2-OBn-4-OMe-C_6H_3
18g: X = O; R = H; R' = Pent; Ar = 4-(*N,N*-Me_2)-C_6H_4
18h: X = O; R = H; R' = Pent; Ar = 4-F-C_6H_4
18i: X = O; R = H; R' = Cyhex; Ar = 4-(*N,N*-Me_2)-C_6H_4
18j: X = O; R = Me; R' = Pent; Ar = 4-(*N,N*-Me_2)-C_6H_4

Entry	Substrate	Time (h)	Ligand	% Yield	er
1	**18a**	22	$(DHQD)_2PHAL$	40 (**19a**)	67:33
2	**18a**	20	$(DHQ)_2PHAL$	42 (**19a**)	36:64
3	**18b**	21	$(DHQD)_2PHAL$	75 (**19b**)	67.6:32.4
4	**18c**	48	$(DHQD)_2PHAL$	72 (**19c**)	68.2:31.8
5	**18d**	24	$(DHQD)_2PHAL$	67 (**19d**)	71.4:28.6
6	**18e**	18	$(DHQD)_2PHAL$	90 (**19e**)	77:23
7	**18f**	14	$(DHQD)_2PHAL$	42[a] (**19f**)	72.5:27.5
8	**18g**	23	$(DHQD)_2PHAL$	84 (**19g**)	76:24
9	**18h**	5	$(DHQD)_2PHAL$	99[b] (**19h**)	66.4:33.6
10	**18g**	24	$(DHQD)_2PYR$	80[b] (**19g**)	78:22
11	**18g**	15	$(Pr\text{-}DHQD)_2PHAL$	81 (**19g**)	67.5:32.5

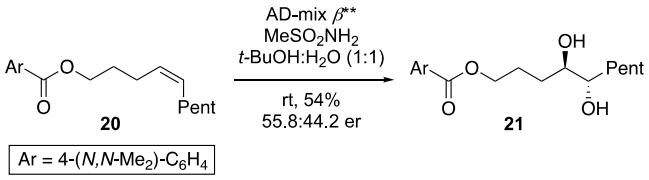
12	**18g**	23	$(DHQD)_2AQN$	84[b] (**19g**)	31.7:68.3
13	**18g**	19	DHQD-IND	45 (**19g**)	46.7:53.3
14	**18i**	18	$(DHQD)_2PHAL$	79 (**19i**)	79.5:20.5
15	**18j**	12	$(DHQD)_2PHAL$	74[b] (**19j**)	79:21

[a] yield over two steps; [b] based on recovery of starting material.

In order to confirm that the propargylic benzoate was key to the increased enantioselectivity observed, we synthesized the precursors lacking the alkyne (compound **20**) and lacking the pi-stacking moiety on the propargylic alcohol (compound **22**) (Scheme 3). Asymmetric dihydroxylation using our optimum conditions on the non-alkyne-containing substrate **20** gave low enantioselectivity (55.8:44:2 er) (Eq. 1, Note that the absolute stereochemical assignment of **21** is based on analogy). Interestingly, use of the propargylic alcohol enyne **22** led to a reversal in selectivity – favoring the opposite enantiomer (Eq. 2). This stereochemical assignment was confirmed by derivatization of triol **23** to ester **19c**.

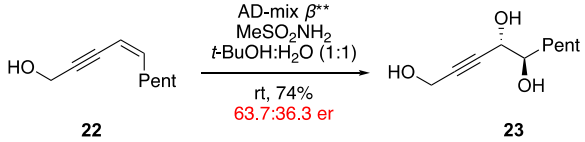
• Asymmetric dihydroxylation without alkyne linker

(Eq. 1)



• Asymmetric dihydroxylation without PDAB ester

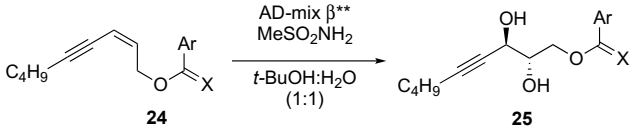
(Eq. 2)



Scheme 3. Control Experiments to Verify Controlling Elements in Asymmetric Dihydroxylation.

While not useful for our mandelalide work, we also became intrigued about the potential for placing the benzoate more proximal to the *cis*-alkene (Table 3). Use of the PMB ether (**24a**) gave essentially no enantioselectivity (53:47 er, Entry 1). In contrast, benzoates **24b** and **24c** gave improved levels of enantioselectivity (Entries 2 and 3) – albeit slightly below the levels observed for the propargylic series (Entries 4 and 5; Table 2). Interestingly, the PDAB substrate **24d** gave no selectivity – possibly pointing to a competing directing effect between the alkyne and the PDAB moiety (Entry 4).

TABLE 3. Exploration of Enantioselectivity in Sharpless Dihydroxylation of *cis*-Allyl Ether and Esters.



24 **25**

24a: X = H, H; Ar = 4-OMe-C_6H_4
24b: X = O; Ar = 4-OMe-C_6H_4
24c: X = O; Ar = 4-Ph-C_6H_4
24d: X = O; Ar = 4-(*N*,*N*-Me_2)C_6H_4

Entry	Substrate	Time (h)	% Yield	er
1	**24a**	4.5	65 (**25a**)	53:47
2	**24b**	5.5	63 (**25b**)	69:31
3	**24c**	24	70 (**25c**)	66:34
4	**24d**	20	73 (**25d**)	52.4:47.5

Density functional theory (DFT) was employed to explore the origins of selectivity for the dihydroxylation of *cis*-enynes. Substrate **18g**, $(DHQD)_2PHAL$ ligand, and osmium tetroxide were used in all computations. Geometry optimizations and vibrational frequencies were computed using B3LYP[22] with the LanL2DZ[23] basis set and effective core potential for osmium and 6-31G(d)[24] for all other atoms. Grimme's D3BJ[25] dispersion corrections were calculated for the optimized structures using the DFT-D3 software.[26] Solvation corrections were computed for 2-methyl-2-propanol using PCM[27] and B3LYP with LanL2DZ for osmium and 6-31+G(d,p) for all other atoms. Single point energy refinements were computed using B3LYP with the SDD[28] basis set for osmium and the 6-311++G(2df,p)[29] basis set for all other atoms. All quantum mechanical computations used the Gaussian 09 computational package.[30]

The computed major and minor dihydroxylation transition structures are shown in Figure 1, top. The **Major-TS** leading to the experimentally favored product is 0.9 kcal/mol more stable than the **Minor-TS**, in good agreement with experiments ($\Delta G^{\ddagger}_{(exp)}$ = 0.7 kcal/mol). The reaction is concerted asynchronous; vibrational analyses show that both bonds in the transition structures are being formed at the same time but to varying degrees. The forming C-O bond proximal to the alkyne was consistently longer by ~0.2 Å compared to the C-O bond proximal to the alkyl chain. Importantly, both the **Major-TS** and **Minor-TS** feature pi-stacking between the substrate *p*-*N*,*N*-dimethylaminobenzoate group and catalyst quinoline ring.

Distortion/interaction model[31] was used to understand the origin of selectivity (Figure 1, bottom left; see SI). The catalyst and enyne in the **Minor-TS** are more distorted than in the **Major-TS** ($\Delta\Delta G_d^{\ddagger}$ = +1.5 kcal/mol). The interactions between the catalyst and enyne

in the **Minor-TS** are slightly more stabilizing than in the **Major-TS** ($\Delta\Delta G_i^{\ddagger}$ = –0.5 kcal/mol) but do not make up for the greater distortion energy. The bulk of the distortion in the minor transition state arises from the substrate ($\Delta G_d^{\ddagger}$ = +0.9 kcal/mol in substrate vs +0.6 kcal/mol in catalyst), rather than ligand or catalyst distortion. Upon inspection, it is clear that the substrate in the **Minor-TS** features a disfavored bisected conformation between the alkyl substituent and the reacting alkene (Figure 1, bottom right, C_1-C_2-C_3-C_4 = ~180°; see SI). In contrast, the alkyl substituent in the **Major-TS** substrate is in a more favorable eclipsing conformation with the reacting alkene. We computed a model substrate system in which we varied this torsion systematically. The torsional angle corresponding to the **Major-TS** was found to be ~1.2 kcal/mol more stable than the one corresponding to the **Minor-TS**. This suggests that the alkyl group orientation relative to the reacting alkene may indeed be responsible for the bulk of the distortion, and therefore the bulk of the selectivity.

We hypothesize that the substrate benzoate ester groups rigidify the dihydroxylation transition states by forming a favorable pi-stacking interaction in both the **Major-TS** and **Minor-TS**. With this anchoring interaction in place, the substrate has limited conformational freedom, thereby leading to the enhanced selectivity observed by experiments and computations. The omission of groups capable of pi-stacking removes this rigidification, thereby leading to poorer transition state preorganization, explaining the observed drop in selectivity in experiments.

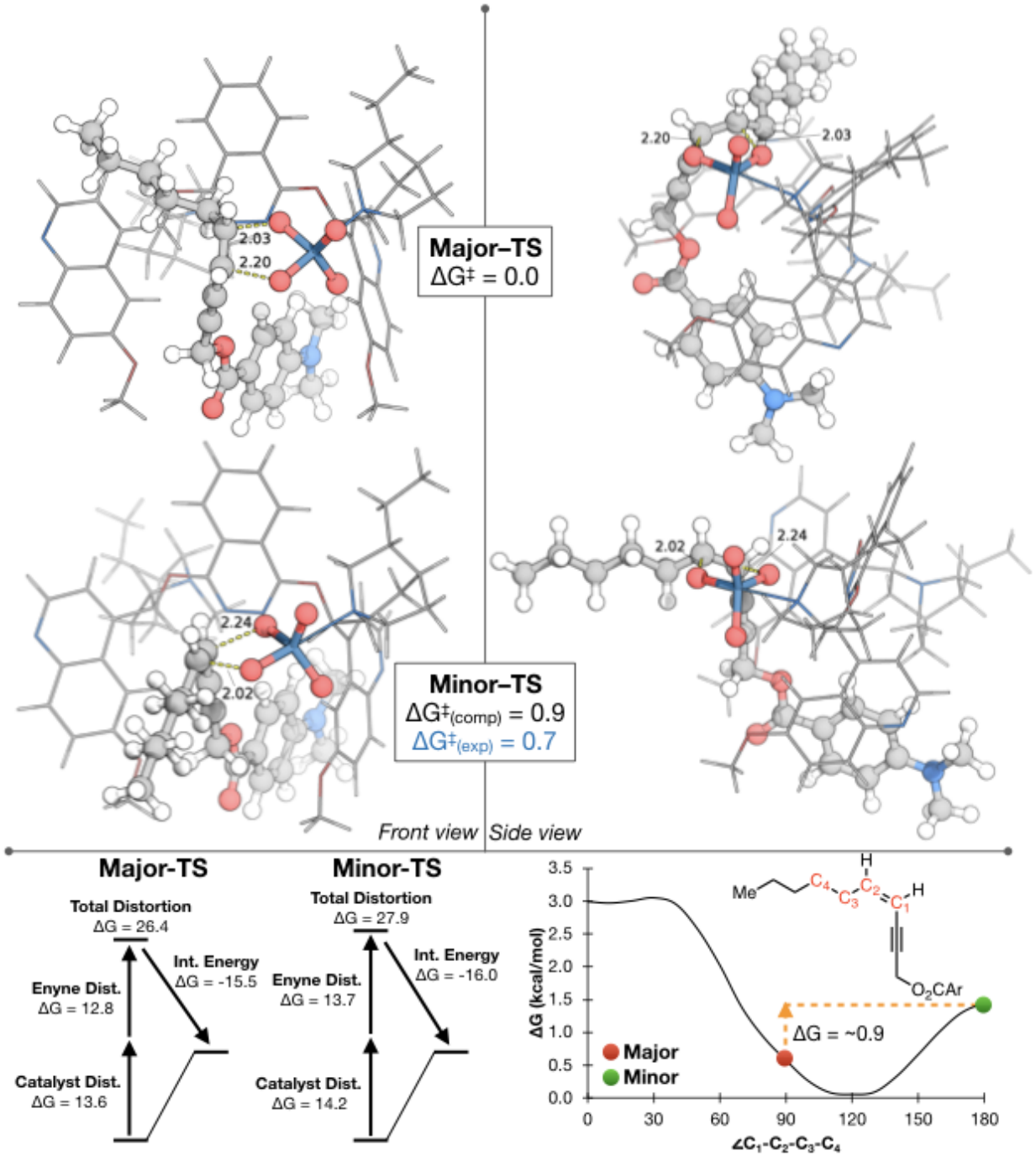
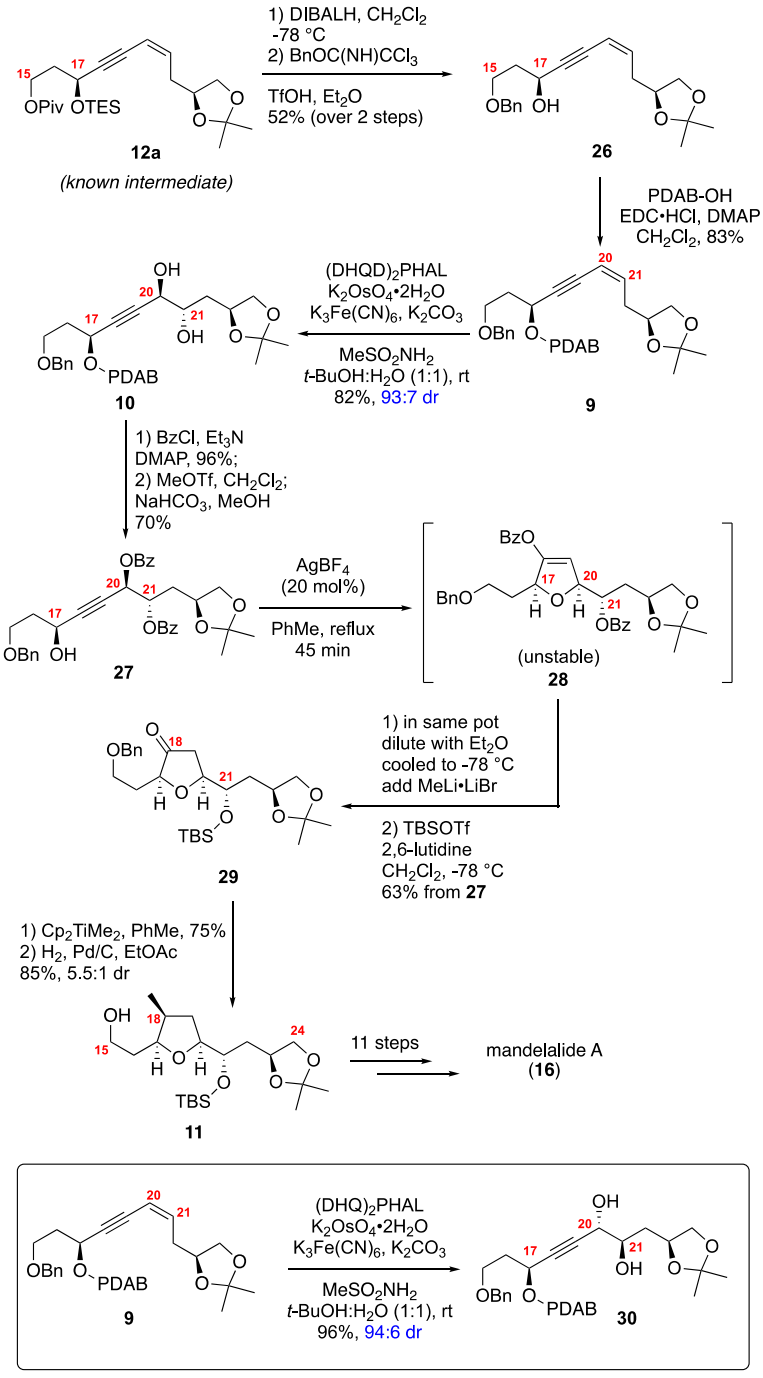


Figure 1. (Top) Computed stereodetermining dihydroxylation transition structures. $(DHQD)_2PHAL$ is shown as tubes; osmium tetroxide and **18g** are shown as balls and sticks. Yellow dotted lines are the two forming C–O bonds. Distances are in Ångströms,

energies in kcal/mol (Bottom Left). Distortion/interaction model for the two transition states (Bottom Right). Model substrate torsion plotted against energy (see SI).

The application of this technology to a second-generation synthesis of the C15-C24 northern portion of mandelalide A is shown in Scheme 4. Starting from the previously prepared pivaloate **12a**,[14] DIBAL-H reduction followed by benzyl ether formation in acidic medium gave secondary alcohol **26**. Next, PDAB moiety was installed smoothly into the dihydroxylation precursor **9**. To our delight, the key dihydroxylation using $(DHQD)_2PHAL$ gave outstanding levels of diastereoselectivity (93:7 dr) and excellent chemical yield. It is important to mention here that dihydroxylation reaction of enyne **9** with pseudo-enantiomeric ligand $(DHQ)_2PHAL$ provided a similar level selectivity favoring now the opposite diastereomer **30** (96:4 dr). This pair of results would appear to indicate that there is not a matched/mismatched relationship between the chiral Sharpless ligands and the inherent facial selectivity of the enantioenriched system. Next, benzoylation at C20 and C21 provided the triester. Subsequent selective removal of the PDAB in the presence of two benzoate esters was smoothly accomplished by quaternarization of the dimethylamino moiety followed by *in situ* saponification to provide alcohol **27**. We are unaware of a prior application of this approach for the selective removal of an amino-benzoate in the presence of other esters. Next, silver-catalyzed cyclization (AgCC) proceeded smoothly to yield the dihydropyran **28** which was processed in situ to the ketone **29** due to its inherent instability. Finally, methylenation with Petasis reagent followed by hydrogenation incorporated the required

methyl stereochemistry at C18 along with removal of the Bn group at the same step - linking this route with our previously published total synthesis of mandelalide A.[14]



Scheme 4. Application to Northern Fragment of Mandelalide A.

In conclusion, we have identified possible generalized controlling elements for the enantioselective dihydroxylations of *cis*-enyne moieties. The importance of electron-rich pi-stacking moieties in this process should pave the way for further improvements for asymmetric dihydroxylation of the most challenging class of olefins (*cis* alkenes). Through an extensive DFT study, we propose the benzoate ester groups rigidify the dihydroxylation transition states, and the origin of selectivity is due to a favorable eclipsing alkyl group conformation in the **Major-TS** as opposed to a disfavored bisecting conformation in the **Minor-TS**. The subsequent application of this technology to the formal synthesis of mandelalide A has been demonstrated. In this application, the enantioselectivity of the key diastereoselective dihydroxylation reaction has been amplified from 69:31 to 93:7 through the careful selection of nearby pi-stacking substituents.

Experimental Section

General Information. Infrared spectra were recorded neat unless otherwise indicated and are reported in cm^{-1}. ^{1}H NMR spectra were recorded in deuterated solvents and are reported in ppm relative to tetramethylsilane and referenced internally to the residually protonated solvent. $^{13}C\{^{1}H\}$ NMR spectra were recorded in deuterated solvents and are reported in ppm relative to tetramethylsilane and referenced internally to the carbon resonance of the solvent. HRMS data were acquired on a TOF-MS instrument with an EI or ES source unless otherwise mentioned.

Routine monitoring of reactions was performed using EM Science DC-Alufolien silica gel, aluminum-backed TLC plates. Flash chromatography was performed with the indicated eluents on EM Science Gedurian 230-400 mesh silica gel.

Air and/or moisture sensitive reactions were performed under usual inert atmosphere conditions. Reactions requiring anhydrous conditions were performed under a blanket of argon, in glassware dried in an oven at 120°C or by flame, then cooled under argon. Dry THF and DCM were obtained via a solvent purification system. All other solvents and commercially available reagents were either purified via literature procedures or used without further purification.

A. General procedure for esterification (DCC or EDC coupling).

To a stirred solution of alcohol (1 eq.) in CH_2Cl_2 (0.06 molar in SM) was added sequentially carboxylic acid (2 or 3 eq.), DCC or EDC•HCl (2 or 3 eq.), DMAP (2 or 3 eq.) at rt. After the alcohol was consumed (typically overnight), the reaction was quenched by sat. aq. NH_4Cl and extracted with CH_2Cl_2. The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with EtOAc / hexanes.

B. General procedure for asymmetric dihydroxylation.

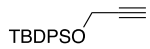
To a stirred solution of *cis*-enyne (1 eq.) in *t*-BuOH : H_2O (1:1) (0.18 molar in SM) (at 0 °C or rt) were added sequentially AD mix L**[32] (generally 2.6 g for 1.0 mmol of alkene, unless otherwise mentioned), $MeSO_2NH_2$ (1 eq.). After completion of the reaction, it was quenched by addition of solid Na_2SO_3 and stirred for another 5 min and extracted with EtOAc. The dried (Na_2SO_4) extract was concentrated *in vacuo* purified by chromatography over silica gel (for compounds containing *p-N,N*-dimethyl benzoate moiety: the column was neutralized with 10% Et_3N in hexanes), eluting with EtOAc / hexanes.

C. General procedure for racemic dihydroxylation .

To a stirred solution of *cis*-enyne (1 eq.) in *t*-BuOH : H_2O (1:1) (0.02 molar in SM) at rt was added NMO (4.0 eq., 4.8 M in H_2O) followed by $K_2OsO_4 \cdot 2H_2O$ (0.01 eq.). After consumption of the alkene, the reaction was quenched by sat. aq. thiosulfate and extracted with EtOAc. The dried (Na_2SO_4) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with EtOAc / hexanes.

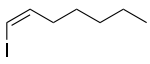
D. General procedure for Mosher ester synthesis (for determination of *ee*).

To a stirred solution of diol (1 eq.) in CH_2Cl_2 (0.05 molar in SM) was added sequentially Mosher acid (4 eq.), DCC (4 eq.), DMAP (4 eq.) at rt. After the diol was consumed, the reaction was quenched by sat. aq. NH_4Cl and extracted with CH_2Cl_2. With the crude mass ^{19}F and ^1H NMR analysis were done to determine the ee.



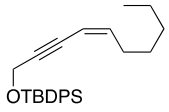
SI-2

*tert-butyldiphenyl(prop-2-yn-1-yloxy)silane (**SI-2**).* To a stirred solution of propargyl alcohol alcohol **SI-1** (3.0 g, 53.51mmol) in CH_2Cl_2 (107 mL) at 0°C was added imidazole (4.0 g, 58.87 mmol) followed by TBDPSCl (16.18 g, 15.3 mL, 58.87 mmol). After 5 min, the reaction was warmed to rt. After overnight stirring, the reaction was quenched by H_2O (80 mL) and extracted with CH_2Cl_2 (3 X 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 2-5% EtOAc / hexanes, to give the known compound **SI-2**[33] (15.63 g, 53.1 mmol, 99%) as a colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 8.0, 1.7 Hz, 4H), 7.41-7.47 (m, 6 H), 4.34 (d, *J* = 2.4 Hz, 2H), 2.41 (t, *J* = 2.4 Hz, 1H), 1.10 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 135.6, 132.9, 129.8, 127.7, 82.0, 73.0, 52.5, 26.7, 19.1 ppm.



SI-4

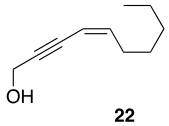
*(Z)-1-iodohept-1-ene (**SI-4**).* To a stirred solution of the Wittig salt [made from CH_2I_2 and PPh_3] (6.35 g, 11.98 mmol) in THF (40 mL) at rt was drop wise added NaHMDS (6.0 mL, 11.98 mmol, 2 M in THF). After 5 min, the reaction was cooled down to -78 °C and DMPU (5.12 g, 4.81 mL, 39.92 mmol) was added and stirred for another 5 min before addition of the hexanal **SI-3** (1.0 g, 9.98 mmol) in THF (5 mL + 5 mL rinse). After 2.5 h, the reaction was quenched by sat. aq. NH_4Cl (50 mL) and extracted with EtOAc (3 X 40 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 2-2.2% EtOAc / hexanes, to give the known commercially available compound **SI-4** (1.6 g, 7.1 mmol, 72%, *Z*:*E* > 11:1) as a colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 6.18-6.21 (m, 2H), 2.13-2.18 (m, 2H), 1.45 (quint, *J* = 7.12 Hz, 2H), 1.32-1.36 (m, 4 H), 0.92 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 141.5, 82.1, 34.7, 31.3, 27.6, 22.5, 14.0 ppm.



SI-5

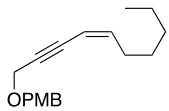
*(Z)-tert-butyl(dec-4-en-2-yn-1-yloxy)diphenylsilane (**SI-5**).* To a stirred suspension of $Pd(PPh_3)_4$ (379.0 mg, 0.328 mmol) and CuI (125.0 mg, 0.656 mmol) in *i*-Pr_2NH (15 mL) at 0 °C was drop wise added a solution of alkyne **SI-2** (1.93 g, 6.56 mmol) and iodide **SI-4** (1.47 g, 6.56 mmol) in *i*-Pr_2NH (15 mL) and the reaction was allowed to warm up to rt. After overnight stirring, the reaction was quenched by sat. aq. NH_4Cl (20 mL) and extracted with EtOAc (3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 1.6-2.5% Et_2O / hexanes, to give the compound **SI-5** (2.3 g, 5.90 mmol, 90%, *Z*:*E* > 11:1) as a yellow liquid. IR (neat) 2931, 2858, 1472, 1113, 823, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* =

7.4 Hz, 4H), 7.39-7.46 (m, 6H), 5.91 (dt, *J* = 10.8, 7.4 Hz, 1H), 5.47 (d, *J* = 10.8 Hz, 1H), 4.50 (d, *J* = 1.8 Hz, 2H), 2.29 (q, *J* = 7.3 Hz, 2H), 1.42 (quint, *J* = 6.8 Hz, 2H), 1.31-1.33 (m, 4H), 1.10 (s, 9H), 0.92 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 144.3, 135.6, 133.3, 129.7, 127.7, 108.6, 91.5, 82.0, 53.3, 31.4, 30.2, 28.5, 26.7, 22.5, 19.2, 14.0 ppm; HRMS (ES+) calcd. for $C_{26}H_{35}OSi$ (M+H) 391.2457, found 391.2463.



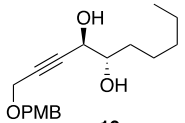
22

*(Z)-dec-4-en-2-yn-1-ol (**22**).* To a stirred solution of silyl ether **SI-5** (1.67 g, 4.27 mmol, *Z*:*E* > 11:1) in THF (64 mL) at 0 °C was added TBAF (6.41 mL, 6.41 mmol, 1 M in THF) and the reaction mixture was allowed to warm up to rt immediately. After overnight stirring the reaction was quenched with H_2O (50 mL). The organic solvent (THF) was removed in *vacuo* and the resulting aqueous layer was extracted with EtOAc (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 5-9% Et_2O/ hexanes, to give the compound **22** (347.0 mg, 2.28 mmol, 53% only for *Z* -isomer) as a yellow liquid. IR (neat) 3338, 2957, 2928, 2858, 1016 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 5.91 (dt, *J* = 10.9, 7.4 Hz, 1H), 5.48-5.50 (m, 1H), 4.43 (s, 2H), 2.29-2.32 (m, 2H), 1.77 (br s, 1H), 1.42 (quint, *J* = 6.8 Hz, 2H), 1.30-1.36 (m, 4H), 0.91 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 144.9, 108.2, 91.2, 82.6, 51.7, 31.4, 30.2, 28.5, 22.5, 14.0 ppm; HRMS (ES+) calcd. for $C_{10}H_{17}O$ (M+H) 153.1297, found 153.1287.



18a

*(Z)-1-((dec-4-en-2-yn-1-yloxy)methyl)-4-methoxybenzene (**18a**)*. To a stirred solution of alcohol **22** (129.0 mg, 0.847 mmol) and PMB-imidate (718.0 mg, 0.53 mL, 2.54 mmol) in Et_2O (11 mL) at 0 °C was added TfOH (63 µL, 0.063 mmol, 1 M in Et_2O). After 20 min, the reaction was warmed up to rt. After 2 h, the reaction was quenched by sat. aq. $NaHCO_3$ (10 mL) and extracted with Et_2O (3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 2-3% Et_2O / hexanes, to give the compound **18a** (173.0 mg, 0.635 mmol, 75%) as a yellow liquid. ^1H NMR (700 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.5 Hz, 2 H), 6.91 (d, *J* = 8.5 Hz, 2H), 5.97 (dt, *J* = 10.7, 7.5 Hz, 1H), 5.53 (d, *J* = 10.8 Hz, 1H), 4.58 (s, 2H), 4.32 (d, *J* = 1.4 Hz, 2H), 3.83 (s, 3H), 2.36 (q, *J* = 7.4 Hz, 2H), 1.43-1.47 (m, 2H), 1.34-1.47 (m, m, 4H), 0.92 (t, J = 6.9 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 159.4, 144.8, 129.8, 129.7, 113.8, 108.4, 89.2, 83.4, 70.9, 57.6, 55.3, 31.4, 30.3, 28.5, 22.5, 14.1 ppm; HRMS (EI^+) calcd. for $C_{18}H_{24}O_2$ (M+) 272.1776, found 272.1770.

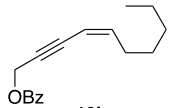


19a

*(4R,5S)-1-((4-methoxybenzyl)oxy)dec-2-yne-4,5-diol (**19a**).* The diol **19a** (25.5 mg, 0.083 mmol, 40% yield, 35% ee determined by Mosher ester analysis) was prepared by "**General procedure B**" from enyne **18a** (56.8 mg, 0.208 mmol) using AD mix β** at rt for 22 h. $[\alpha]_D^{20}$ = -0.48° (*c* = 0.84, $CHCl_3$); IR (neat) 3389, 2932, 1613, 1514, 1250, 1075 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.5 Hz, 2 H), 6.90 (d, *J* = 8.5 Hz, 2H), 4.54 (s, 2H), 4.39 (s, 1H), 4.21 (s, 2H), 3.82 (s, 3H), 3.69-3.71 (m, 1H), 2.73 (bs, 1H), 2.20 (bs), 1.51-1.60 (m, 3H), 1.31-1.37 (m, 5H), 0.91 (t, *J* = 6.6 Hz) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 159.5, 129.8, 129.3, 113.9, 83.9, 82.9, 74.1, 71.4, 66.4, 57.0, 55.3,

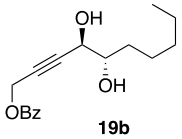
32.8, 31.7, 25.3, 22.5, 14.0 ppm; HRMS (ES+) calcd. for $C_{18}H_{26}O_4Na$ (M+Na) 329.1729, found 329.1714. (AG-VII-26)

The diol *ent*-**19a** (19.4 mg, 0.091 mmol, 42% yield, 27.5% ee determined by Mosher ester analysis) was prepared by "**General procedure B**" from enyne **18a** (58.8 mg, 0.216 mmol) using AD mix α**at rt for 20 h. $[\alpha]_D^{20}$ = -1.0° (*c* = 0.90, $CHCl_3$).



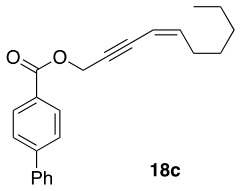
18b

*(Z)-dec-4-en-2-yn-1-yl benzoate (**18b**).* To a stirred solution of alcohol **22** (30.5 mg, 0.20 mmol) in CH_2Cl_2: Et_3N (2 mL, 1:1) at 0 °C was added sequentially BzCl (42.3 mg, 0.30 mmol, 35 *μ*L), DMAP (5.0 mg, 0.04 mmol). After 2.5 h, the reaction was quenched by sat. aq. $NaHCO_3$ (2 mL) solution and extracted with CH_2Cl_2 (3 X 5 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 10-30% EtOAc / hexanes, to give **18b** (53.0 mg, 0.2 mmol, 100%) as a colorless liquid. IR (neat) 2955, 2928, 1727, 1267, 1108 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.09-8.11 (m, 2H), 7.58-7.61 (m, 1H), 7.46-7.48 (m, 2H), 6.00 (dt, *J* = 10.8, 7.5 Hz, 1H), 5.50-5.53 (m, 1H), 5.11 (d, *J* = 2.0 Hz, 2H), 2.34 (dq, *J* = 7.5, 1.4 Hz, 2H), 1.41-1.45 (m, 2H), 1.30-1.35 (m, 4H), 0.89 (t, *J* = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 165.9, 145.8, 132.2 129.8, 129.7, 128.4, 108.1, 86.9, 83.7, 53.5, 31.3, 30.3, 28.4, 22.5, 14.0 ppm; HRMS (ES+) calcd. for $C_{17}H_{21}O_2$ (M+H) 257.1542, found 257.1548.



19b

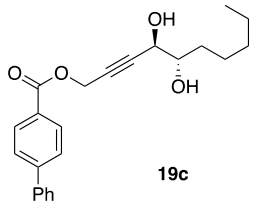
*(4R,5S)-4,5-dihydroxydec-2-yn-1-yl benzoate (**19b**).* The diol **19b** (17.0 mg, 0.058 mmol, 75% yield, 35% ee) was prepared by "**General procedure B**" from enyne **18b** (20.0 mg, 0.078 mmol) using AD mix β** at 0 °C-rt for 21 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-1 column, 99:1 to 70:30 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 22.3 min (minor) and 25.5 min (major)]; $[\alpha]_D^{20}$ = -2.23° (*c* = 0.85, $CHCl_3$); IR (neat) 3265, 2952, 1722, 1269, 1112 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.07-8.09 (m, 2H), 7.59-7.62 (m, 1H), 7.46-7.49 (m, 2H), 4.99 (d, *J* = 1.7 Hz, 2H), 4.41 (s, 1H), 3.73 (s, 1H), 2.65 (d, *J* = 3.8 Hz, 1H), 2.06 (d, *J* = 5.0 Hz, 1H), 1.56-1.59 (m, 2H), 1.49-1.55 (m, 1H), 1.35-1.40 (m, 1H), 1.27-1.34 (m, 4H), 0.89 (t, *J* = 7.0 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 165.9, 133.4, 129.8, 129.4, 128.5, 84.3, 81.0, 74.1, 66.4, 52.8, 32.8, 31.7, 25.2, 22.5, 14.0 ppm; HRMS (ES+) calcd. for $C_{17}H_{22}O_4Na$ (M+Na) 313.1416, found 313.1414.



18c

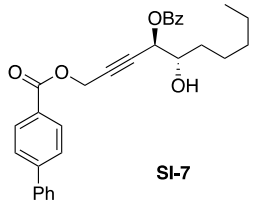
*(Z)-dec-4-en-2-yn-1-yl [1,1'-biphenyl]-4-carboxylate (**18c**).* The propargylic ester **18c** (69.0 mg, 0.207 mmol, 97% yield) was prepared by "**General procedure A**" from alcohol **22** (32.6 mg, 0.214 mmol) and [1,1'-biphenyl]-4-carboxylic acid **SI-6** (85.0, 0.428 mmol) using EDC•HCl. IR (neat) 2931, 1724, 1609, 1267, 1099, 747 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.3 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 1H), 6.01 (dt, *J* = 10.8, 7.5 Hz, 1H), 5.53 (dt, *J* = 10.8, 1.3 Hz, 1H), 5.13 (d, *J* = 1.9 Hz, 2H), 2.35 (q, *J* = 7.6 Hz, 2H), 1.44 (quin, *J* = 7.3 Hz, 2H), 1.32-1.34 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR

(175 MHz, $CDCl_3$) δ 165.8, 145.9, 145.8, 139.9, 130.3, 128.9, 128.4, 128.2, 127.3, 127.1, 108.1, 86.9, 83.7, 53.5, 31.3, 30.3, 28.4, 22.4, 14.0 ppm; HRMS (AP+) calcd. for $C_{23}H_{24}O_2$ (M) 332.1874, found 332.1877.



19c

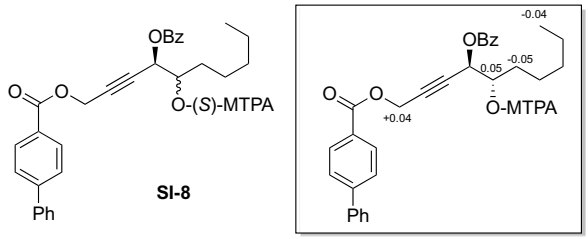
*(4R,5S)-4,5-dihydroxydec-2-yn-1-yl [1,1'-biphenyl]-4-carboxylate (**19c**).* The diol **19c** (20.8 mg, 0.056 mmol, 72% yield, 36.3% ee) was prepared by "**General procedure B**" from enyne **18c** (26.3 mg, 0.079 mmol) using AD mix β** at rt for 48 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-3 column, 99:1 to 60:40 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 24.2 min (minor) and 25.0 min (major)]; $[\alpha]_D^{20}$ = -0.65° (*c* = 1.08, $CHCl_3$); IR (neat) 3271, 2953, 1723, 1609, 1267, 1099, 744 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.14 (dt, *J* = 8.6, 1.9 Hz, 2H), 7.69 (dt, *J* = 8.6, 1.9 Hz, 2H), 7.64-7.65 (m, 2H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.42 (tt, *J* = 7.4, 1.3 Hz, 1H), 5.01 (d, *J* = 1.8 Hz, 2H), 4.41-4.43 (m, 1H), 3.72-3.75 (m, 1H), 2.69 (d, *J* = 7.1 Hz, 1H), 2.09 (d, *J* = 7.1 Hz, 1H), 1.57-1.61 (m, 2H), 1.51-1.56 (m, 1H), 1.36-1.41 (m, 1H), 1.30-1.35 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 165.8, 146.1, 139.8, 130.3, 128.9, 128.2, 128.1, 127.3, 127.1, 84.4, 81.0, 74.1, 66.4, 52.7, 32.8, 31.7, 25.2, 22.5, 14.0 ppm; HRMS (ES+) calcd. for $C_{23}H_{26}O_4Na$ (M+Na) 389.1729, found 389.1747.



SI-7

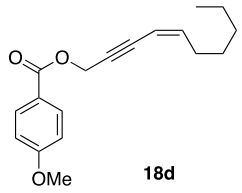
*(4R,5S)-4-(benzoyloxy)-5-hydroxydec-2-yn-1-yl [1,1'-biphenyl]-4-carboxylate (**SI-7**).* To a stirred solution of diol **19c** (19.6 mg, 53.0 *μ*mol) in CH_2Cl_2 (0.5 mL) at rt was added Imidazole (7.2 mg, 106.0 *μ*mol) followed by benzoyl chloride (7.5 mg, 6.2 *μ*L, 53.0 *μ*mol). After 6 h, the reaction mixture was quenched with H_2O (1 mL) and extracted with CH_2Cl_2 (3 x 4 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by column chromatography over silica gel, eluting with 10-20% EtOAc/Hexanes to obtain **SI-7** (6.5 mg, 13.8 *μ*mol, 26%, 77% BRSM) as an oil. $[\alpha]_D^{20}$ = -5.5° (*c* = 0.2, $CHCl_3$); IR (neat) 3347, 2919, 2850, 1724, 1262 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.3 Hz, 2H), 8.11 (d, *J* = 7.0 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 7.3 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.49 (q, *J* = 7.3 Hz, 4H), 7.42-7.44 (m, 1H), 5.70 (dt, *J* = 3.7, 1.6 Hz, 1H), 5.03 (d, *J* = 1.6 Hz, 2H), 3.97-3.99 (m, 1H), 2.12 (d, *J* = 5.7 Hz, 1H), 1.71-1.76 (m, 1H), 1.64-1.69 (m, 1H), 1.41-1.48 (m, 1H), 1.31-1.38 (m, 5H), 0.91 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 165.7, 165.4, 146.1, 139.9, 133.5, 130.4, 129.9, 129.4, 128.9, 128.5, 128.3, 128.1, 127.3, 127.1, 81.8, 81.3, 72.8, 68.5, 52.7, 32.8, 31.7, 25.2, 22.5, 14.0 ppm; HRMS (ES+) calcd. for $C_{30}H_{31}O_5$ (M+H) 471.2171, found 471.2161.

Determination of absolute stereochemistry by Mosher ester analysis:



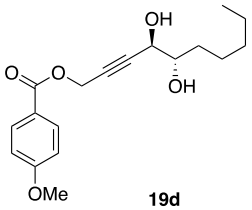
(S)-MTPA ester (***SI-8***)**.** To a stirred solution of alcohol **SI-7** (6.5 mg, 13.8 *μ*mol) in CH_2Cl_2 (0.2 mL) at rt was sequentially added (*R*)-(−)-*α*-Methoxy-*α*-(trifluoromethyl)phenylacetyl chloride (14.0 mg, 10.0 *μ*L, 55.3 *μ*mol), DMAP (7.7 mg,

63.0 μmol). After 2.5 h, the reaction mixture was quenched with H_2O (0.5 mL) and extracted with CH_2Cl_2 (3 x 2 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by column chromatography over silica gel, eluting with 10-25% EtOAc/Hexanes to obtain **SI-8** (9.5 mg, 13.8 μmol, 100%, 2.2:1 dr) as an oil.



18d

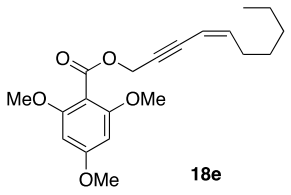
*(Z)-dec-4-en-2-yn-1-yl 4-methoxybenzoate (**18d**).* The propargylic ester **18d** (36.7 mg, 0.128 mmol, 72% yield) was prepared by "**General procedure A**" from alcohol **22** (27.0 mg, 0.177 mmol) and 4-methoxybenzoic acid **SI-9** (81.0 mg, 0.532 mmol) using DCC. IR (neat) 2932, 2119, 1720, 1607, 1256, 1095, 769 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.9 Hz, 2H), 6.94 (d, *J* = 8.9 Hz, 2H), 5.99 (dt, *J* = 10.8, 7.4 Hz, 1H), 5.51 (d, *J* = 10.8 Hz, 1H), 5.07 (d, *J* = 1.9 Hz, 2H), 3.88 (s, 3H), 2.33 (q, *J* = 7.4 Hz, 2H), 1.43 (quint, *J* = 7.4 Hz, 2H), 1.30-1.33 (m, 4H), 0.89 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 165.7, 163.5, 145.6, 131.8, 122.1, 113.6, 108.1, 87.1, 83.4, 55.4, 53.2, 31.3, 30.3, 28.4, 22.4, 14.0 ppm; HRMS (EI+) calcd. for $C_{18}H_{22}O_3$ (M+H) 286.1569, found 286.1574.



19d

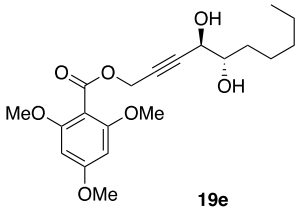
*(4R,5S)-4,5-dihydroxydec-2-yn-1-yl 4-methoxybenzoate (**19d**).* The diol **19d** (15.0 mg, 0.047 mmol, 67% yield, 42.8% ee by Mosher ester analysis) was prepared by "**General procedure B**" from enyne **18d** (20.0 mg, 0.070 mmol) using AD mix β** at rt. $[\alpha]_D^{20}$ = -

0.91° (*c* = 0.55, $CHCl_3$); IR (neat) 3318, 2928, 1715, 1608, 1259, 1168 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 4.94 (d, *J* = 1.6 Hz, 2H), 4.40 (s, 1H), 3.88 (s, 3H), 3.72 (s, 1H), 2.98 (d, *J* = 5.3 Hz, 1H), 2.31 (s, 1H), 1.56 (q, *J* = 8.0 Hz, 2H), 1.49-1.54 (m, 1H), 1.26-1.37 (m, 5H), 0.89 (t, *J* = 7.0 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 165.8, 163.7, 131.9, 121.7, 113.7, 84.2, 81.1, 74.1, 66.4, 55.5, 52.5, 32.7, 31.7, 25.3, 22.5, 14.0 ppm; HRMS (ES+) calcd. for $C_{18}H_{25}O_5$ (M+H) 321.1702, found 321.1718.



18e

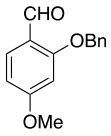
*(Z)-dec-4-en-2-yn-1-yl 2,4,6-trimethoxybenzoate (**18e**).* The propargylic ester **18e** (131.0 mg, 0.378 mmol, 90% yield) was prepared by "**General procedure A**" from alcohol **22** (64.0 mg, 0.420 mmol) and 2,4,6-trimethoxybenzoic acid **SI-10** (178.0 mg, 0.840 mmol) using EDC•HCl. ^1H NMR (400 MHz, $CDCl_3$) δ 6.10 (s, 2H), 5.96 (dt, *J* = 10.8, 7.4 Hz, 1H), 5.49 (d, *J* = 10.8 Hz, 1H), 5.05 (d, *J* = 1.8 Hz, 2H), 3.82 (s, 3H), 3.81 (s, 6H), 2.33 (q, *J* = 7.2 Hz, 2H), 1.37-1.45 (m, 2H), 1.27-1.35 (m, 4H), 0.89 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.8, 162.7, 158.9, 145.4, 108.3, 105.4, 90.6, 87.1, 83.4, 55.9, 55.4, 53.6, 31.3, 30.2, 28.5, 22.5, 14.0 ppm.



19e

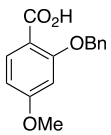
*(4R,5S)-4,5-dihydroxydec-2-yn-1-yl 2,4,6-trimethoxybenzoate (**19e**).* The diol **19e** (59.7 mg, 0.156 mmol, 90% yield, 54% ee by Mosher ester analysis) was prepared by

"**General procedure B**" from enyne **18e** (60.2 mg, 0.174 mmol) using AD mix β** at rt for 18 h. $[\alpha]_D^{20}$ = +1.2° (*c* = 0.92, $CHCl_3$); IR (neat) 3390, 2934, 1725, 1609, 1159, 1132 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.11 (s, 2H), 4.90-4.91 (m, 2H), 3.83 (s, 3H), 3.81 (s, 6H), 3.67-3.71 (m, 1H), 3.00 (br s, 1H), 2.32 (br s, 1H), 1.47-1.59 (m, 3H), 1.25-1.38 (m, 5H), 0.89 (t, *J* = 6.7 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.9, 162.9, 158.9, 104.9, 90.7, 84.2, 81.1, 74.3, 66.5, 56.0, 55.5, 52.9, 32.8, 31.7, 25.3, 22.6, 14.0 ppm; HRMS (ES+) calcd. for $C_{20}H_{28}O_7Na$ (M+ Na) 403.1733, found 403.1737.



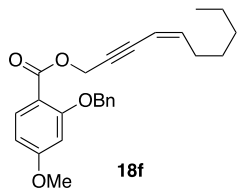
SI-12

*2-(benzyloxy)-4-methoxybenzaldehyde (**SI-12**).* To a stirred solution of 2-hydroxy-4-methoxybenzaldehyde **SI-11** (5.00 g, 32.86 mmol) in acetone (60 mL) was added K_2CO_3 (9.08 g, 65.72 mmol) followed by benzyl bromide (8.73 g, 6.06 mL, 49.29 mmol). After 3 days of stirring, the reaction mixture was filtered and the dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 10-50% EtOAc / hexanes, to give the known commercially available compound **SI-12** (6.00 g, 24.07 mmol, 73%,). ^1H NMR (700 MHz, $CDCl_3$) δ 10.41 (d, *J* = 0.5 Hz, 1H), 7.86 (d, *J* = 8.7 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 6.58 (dd, *J* = 8.6, 2.0 Hz, 1H), 6.53 (d, *J* = 2.2 Hz, 1H), 5.17 (s, 2H), 3.86 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 188.2, 166.1, 162.8, 135.9, 130.5, 128.7, 128.3, 127.3, 119.3, 106.2, 99.2, 70.4, 55.6 ppm.



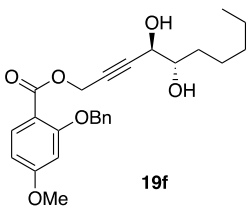
SI-13

*2-(benzyloxy)-4-methoxybenzoic acid (**SI-13**).* To a stirred solution of aldehyde **SI-12** (316.0 mg, 1.31 mmol) in *t*-BuOH:H_2O:THF (7 mL : 7 mL: 2 mL) at rt was added $NaClO_2$ (369.0 mg, 3.26 mmol), NaH_2PO_4 (271.0 mg, 1.97 mmol) and 2-Me-2-butene (919.0 mg, 1.4 mL, 13.1 mmol) sequentially. After 32 h, added H_2O (10 mL) and extracted with EtOAc (3X10 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 20-100% EtOAc / hexanes, to give the known commercially available compound **SI-13** (234.0 mg, 0.907 mmol, 69%,). ^{1}H NMR (700 MHz, $CDCl_3$) δ 10.68 (bs, 1H), 8.14 (d, *J* = 8.7 Hz, 1H), 7.39-7.46 (m, 5H), 6.65 (dd, *J* = 8.8, 2.2 Hz, 1H), 6.61 (d, *J* = 2.2 Hz, 1H), 5.25 (s, 2H), 3.86 (s, 3H) ppm; ^{13}C{^{1}H} NMR (175 MHz, $CDCl_3$) δ 165.4, 165.0, 158.9, 135.5, 134.4, 129.1, 129.1, 127.9, 110.8, 106.9, 99.9, 72.1, 55.7 ppm.



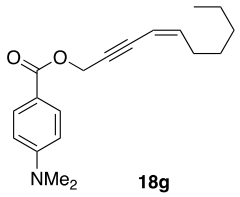
18f

*(Z)-dec-4-en-2-yn-1-yl 2-(benzyloxy)-4-methoxybenzoate (**18f**).* The propargylic ester **18f** was prepared by "**General procedure A**" from alcohol **22 (40.0 mg, 0.263 mmol)** and carboxylic acid **SI-13** (135.6 mg, 0.526 mmol) using EDC•HCl. After normal work up, the dried ($MgSO_4$) extract was concentrated *in vacuo* and passed through a small plug of silica to give the crude ester **18f** which was used in the next dihydroxylation step without further purification.



19f

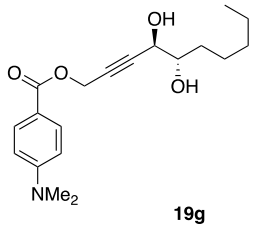
*(4R,5S)-4,5-dihydroxydec-2-yn-1-yl 2-(benzyloxy)-4-methoxybenzoate (**19f**).* The diol **19f** (46.9 mg, 0.110 mmol, 42% yield over two steps, 45% ee) was prepared by "**General procedure B**" from crude enyne **18f** using AD mix β** at rt for 14 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-2 column, 99:1 to 60:40 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 35.7 min (minor) and 48.8 min (major)]; $[\alpha]_D^{20}$ = -0.4° (*c* = 1.0, $CHCl_3$); IR (neat) 3307, 2931, 1725, 1610, 1246, 1076 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.6 Hz, 1H), 7.54 (d, *J* = 7.4 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 6.52-6.54 (m, 2H), 5.18 (s, 2H), 4.94 (d, *J* = 1.6 Hz, 2H), 4.36 (s, 1H), 3.84 (s, 3H), 3.67-3.70 (m, 1H), 2.68 (d, *J* = 7.0 Hz, 1H), 2.09 (d, *J* = 7.0 Hz, 1H), 1.46-1.58 (m, 3H), 1.23-1.37 (m, 5H), 0.88 (t, *J* = 7.0 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 164.8, 164.5, 160.6, 136.5, 134.2, 128.6, 127.8, 126.8, 111.9, 105.2, 100.6, 84.0, 81.4, 74.1, 70.5, 66.4, 55.5, 52.2, 32.7, 31.7, 25.2, 22.5, 14.0 ppm; HRMS (ES+) calcd. for $C_{25}H_{30}O_6Na$ (M+Na) 449.1940, found 449.1923.



18g

*(Z)-dec-4-en-2-yn-1-yl 4-(dimethylamino)benzoate (**18g**).* The propargylic ester **18g** (63.2 mg, 0.211 mmol, 64% yield) was prepared by "**General procedure A**" from alcohol **22** (50.0 mg, 0.328 mmol) and 4-(dimethylamino)benzoic acid **SI-14** (109.0 mg, 0.657 mmol) using EDC•HCl. IR (neat) 2922, 1709, 1608, 1368, 1273, 1183 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.96 (d, *J* = 9.0 Hz, 2H), 6.66 (d, *J* = 9.0 Hz, 2H), 5.97 (dt, *J* = 10.8, 7.6 Hz, 1H), 5.51 (d, *J* = 10.8 Hz, 1H), 5.04 (d, *J* = 1.5 Hz, 2H), 3.06 (s, 6H), 2.33

(q, *J* = 7.5 Hz, 2H), 1.43 (quint, *J* = 7.3 Hz, 2H), 1.31-1.35 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 166.2, 153.4, 145.4, 131.5, 116.3, 110.6, 108.2, 87.7, 83.1, 52.7, 40.0, 31.3, 30.2, 28.4, 22.4, 14.0 ppm; HRMS (EI+) calcd. for $C_{19}H_{26}NO_2$ (M+H) 300.1964, found 300.1959.



19g

*(4R,5S)-4,5-dihydroxydec-2-yn-1-yl 4-(dimethylamino)benzoate (**19g**).* The diol **19g** (20.4 mg, 0.061 mmol, 84%, 52% ee) was prepared by "**General procedure B**" from enyne **18g** (22.0 mg, 0.073 mmol) using AD mix β** at rt for 23 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-2 column, 99:1 to 50:50 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 30.1 min (minor) and 48.0 min (major)]; $[\alpha]_D^{20}$ = -1.08° (*c* = 1.75, $CHCl_3$); IR (neat) 3274, 2926, 1702, 1611, 1277, 1185, 1094 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.93 (d, *J* = 9.1 Hz, 2H), 6.65 (d, *J* = 9.1 Hz, 2H), 4.92 (d, *J* = 1.7 Hz, 2H), 4.39 (s, 1H), 3.71 (s, 1H), 3.06 (s, 6H), 2.81 (s, 1H), 2.19 (d, *J* = 3.5 Hz, 1H), 1.48-1.60 (m, 3H), 1.25-1.39 (m, 5H), 0.89 (t, *J* = 7.0 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 166.3, 153.5, 131.6, 115.9, 110.6, 83.8, 81.7, 74.2, 66.5, 52.0, 40.0, 32.7, 31.7, 25.3, 2.5, 14.0 ppm; HRMS (ES+) calcd. for $C_{19}H_{28}NO_4$ (M+H) 334.2018, found 334.2033.

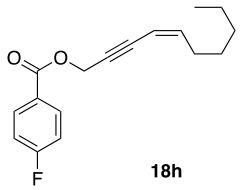
The diol **19g** (7.0 mg, 0.021 mmol, 49% yield (80% brsm), 56% ee) was prepared by "**General procedure B**" from enyne **18g** (13.0 mg, 0.043 mmol) using AD mix L** [L** = $(DHQD)_2PYR$] at rt for 24 h. Enantiomeric ratio was determined by chiral HPLC

[250 x 4.6 mm Phenomenex Lux 5u Cellulose-2 column, 99:1 to 50:50 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 30.0 min (minor) and 48.0 min (major)].

The diol **19g** (16.4 mg, 0.049 mmol, 81% yield, 35% ee) was prepared by "**General procedure B**" from enyne **18g** (18.1 mg, 0.060 mmol) using AD mix L** [L** = (Pr-DHQD)$_2$PHAL] at rt for 15 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-2 column, 99:1 to 50:50 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 30.1 min (minor) and 48.5 min (major)].

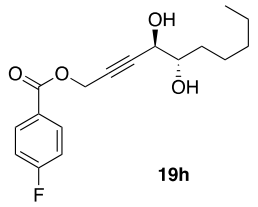
The diol ***ent*-19g** (8.3 mg, 0.025 mmol, 64% yield (84% brsm), 36.6% ee) was prepared by "**General procedure B**" from enyne **18g** (11.8 mg, 0.039 mmol) using AD mix L** [L** = (DHQD)$_2$AQN] at rt for 23 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-2 column, 99:1 to 50:50 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 30.0 min (major) and 48.1 min (minor)]; $[\alpha]_D^{20}$ = -0.63° (*c* = 0.48, $CHCl_3$).

The diol ***ent*-19g** (5.7 mg, 0.017 mmol, 45%, 6.6% ee) was prepared by "**General procedure B**" from enyne **18g** (11.3 mg, 0.038 mmol) using AD mix L** [L** = DHQD-IND] at rt for 19 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-2 column, 99:1 to 50:50 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 30.1 min (major) and 48.5 min (minor)]; $[\alpha]_D^{20}$ = +3.14° (*c* = 0.51, $CHCl_3$).



18h

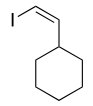
*(Z)-dec-4-en-2-yn-1-yl 4-fluorobenzoate (**18h**).* The propargylic ester **18h** (49.3 mg, 0.180 mmol, 91% yield) was prepared by "**General procedure A**" from alcohol **22** (30.1 mg, 0.198 mmol) and carboxylic acid **SI-19** (55.4 mg, 0.395 mmol) using EDC•HCl. IR (neat) 2957, 2929, 1729, 1265, 1088 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.11-8.13 (m, 2H), 7.14 (t, *J* = 8.6 Hz, 2H), 6.01 (dt, *J* = 10.8, 7.5 Hz, 1H), 5.51 (dt, *J* = 10.8, 1.5 Hz, 1H), 5.09 (d, *J* = 2.0 Hz, 2H), 2.33 (qd, *J* = 7.4, 1.1 Hz, 2H), 1.41-1.45 (m, 2H), 1.30-1.34 (m, 4H), 0.89 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 165.9 (d, *J* = 254.3 Hz), 164.9, 145.9, 132.4 (d, *J* = 9.4 Hz), 125.9 (d, *J* = 2.9 Hz), 115.6 (d, *J* = 22.0 Hz), 108.0, 86.7, 83.8, 53.6, 31.3, 30.3, 28.4, 22.5, 14.0 ppm; HRMS (AP+) calcd. for $C_{17}H_{19}O_2F$ (M) 274.1369, found 274.1373.



19h

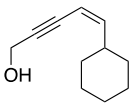
*(4R,5S)-4,5-dihydroxydec-2-yn-1-yl 4-fluorobenzoate (**19h**).* The diol **19h** (17.6 mg, 0.057 mmol, 61% (99% BRSM) yield, 33% ee) was prepared by "**General procedure B**" from enyne **18h** (25.7 mg, 0.094 mmol) using AD mix β** at rt for 5 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-1 column, 90:10 to 70:30 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 13.4 min (minor) and 16.3 min (major)]; $[\alpha]_D^{20}$ = -1.69° (*c* = 0.83, $CHCl_3$); IR (neat) 3260, 2928, 1728, 1604, 1268 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.09-8.11 (m, 2H), 7.13-7.17 (m, 2H), 4.98 (d, *J* = 1.7 Hz, 2H), 4.44 (br s, 1H), 3.73 (br s, 1H), 2.52 (d, *J* = 6.5 Hz, 1H), 1.96 (d, *J* = 4.6 Hz, 1H), 1.56-1.60 (m, 2H), 1.49-1.55 (m, 1H), 1.36-1.39 (m, 1H), 1.29-1.35 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 166.0 (d, *J*

= 254.7 Hz), 164.9, 132.4 (d, *J* = 9.4 Hz), 125.6 (d, *J* = 3.0 Hz), 115.7 (d, *J* = 22.0 Hz), 84.4, 80.9, 74.1, 66.4, 52.8, 32.8, 31.7, 25.2, 22.5, 14.0 ppm; HRMS (ES+) calcd. for $C_{17}H_{21}O_4FNa$ (M+Na) 331.1322, found 331.1328.



SI-17

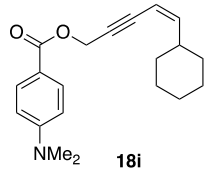
*(Z)-(2-iodovinyl)cyclohexane (**SI-17**).* To a stirred solution of the Wittig salt [made from CH_2I_2 and PPh_3] **SI-16** (9.1 g, 17.16 mmol) in THF (60 mL) at rt was added drop wise NaHMDS (8.58 mL, 17.16 mmol, 2 M in THF). After 5 min, the reaction was cooled down to -78 °C and DMPU (8.8 g, 8.3 mL, 68.642 mmol) was added and stirred for another 5 min before addition of the cyclohexanecarbaldehyde **SI-15** (1.6 g, 1.73 mL, 14.3 mmol) in THF (8 mL + 2 mL rinse). After 8 h, the reaction was quenched by sat. aq. NH_4Cl (50 mL) and extracted with EtOAc (3 X 40 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with pentane, to give the known compound **SI-17**[34] (2.55 g, 10.80 mmol, 76%, *Z*:*E* = 11:1) as a colorless liquid. ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.08 (d, *J* = 7.3 Hz, 1H), 5.99-6.02 (m, 1H), 2.31-2.36 (m, 1H), 1.73-1.75 (m, 4H), 1.33-1.38 (m, 2H), 1.13-1.24 (m, 4H) ppm; ^{13}C{^{1}H} NMR (175 MHz, $CDCl_3$) δ 146.3, 79.5, 43.6, 31.3, 25.9, 25.5 ppm.



SI-18

*(Z)-5-cyclohexylpent-4-en-2-yn-1-ol (**SI-18**).* To a stirred suspension of iodide **SI-17** (2.55 g, 10.8 mmol) in THF (60 mL) at 0 °C was added sequentially propagyl alcohol **SI-1** (1.45 g, 25.9 mmol, 1.54 mL), *i*-Pr_2NH (3.28 g, 32.4 mmol, 4.6 mL), $Pd(PPh_3)_4$ (250.0

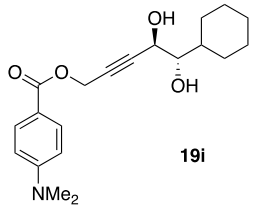
mg, 0.216 mmol) and CuI (83.0 mg, 0.432 mmol) and the reaction was allowed to warm up to rt. After overnight stirring, the reaction was quenched by sat. aq. NH_4Cl (50 mL). After evaporating the organic solvent (THF), the resulting aqueous solution was extracted with EtOAc (3 X 40 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 0-16% Et_2O / hexanes, to give the compound **SI-18** (910.0 mg, 5.54 mmol, 51%, pure *Z* isomer) as a yellow liquid. IR (neat) 3367, 2921, 2850, 1155, 1113 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.77-5.79 (m, 1H), 5.40 (dtd, *J* = 10.8, 2.1, 0.6 Hz, 1H), 4.45 (dd, *J* = 6.1, 2.1 Hz, 2H), 2.56-2.61 (m, 1H), 1.67-1.75 (m, 5H), 1.58 (t, *J* = 6.2 Hz, 1H), 1.32-1.37 (m, 2H), 1.17-1.23 (m, 1H), 1.09-1.15 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 150.3, 106.1, 90.7, 82.7, 51.8, 39.3, 32.3, 25.9, 25.6 ppm; HRMS (AP+) calcd. for $C_{11}H_{16}O$ (M) 164.1201, found 164.1199.



18i

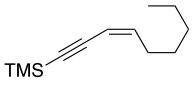
*(Z)-5-cyclohexylpent-4-en-2-yn-1-yl 4-(dimethylamino)benzoate (**18i**).* The propargylic ester **18i** (292.0 mg, 0.937 mmol, 99% yield) was prepared by "**General procedure A**" from alcohol **SI-18** (155.8 mg, 0.948 mmol) and 4-(dimethylamino)benzoic acid **SI-14** (313.0 mg, 1.90 mmol) using EDC•HCl. IR (neat) 2920, 1709, 1608, 1182, 1095 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.97 (d, *J* = 9.1 Hz, 2H), 6.67 (d, J = 9.0 Hz, 2H), 5.79-5.82 (m, 1H), 5.41 (dt, *J* = 10.8, 1.9 Hz, 1H), 5.05 (d, *J* = 2.0 Hz, 2H), 3.07 (s, 6H), 1.71-1.73 (m, 4H), 1.66-1.68 (m, 1H), 1.31-1.37 (m, 2H), 1.16-1.23 (m, 1H), 1.09-1.14 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 166.3, 153.5, 150.7, 131.5, 116.3, 110.7,

106.3, 87.3, 83.2, 52.8, 40.1, 39.3, 32.3, 25.9, 25.6 ppm; HRMS (ES+) calcd. for $C_{20}H_{26}NO_2$ (M+H) 312.1964, found 312.1970.



19i

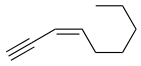
*(4R,5S)-5-cyclohexyl-4,5-dihydroxypent-2-yn-1-yl 4-(dimethylamino)benzoate (**19i**).* The diol **19i** (20.2 mg, 0.058 mmol, 79% yield, 59% ee) was prepared by "**General procedure B**" from enyne **18i** (23.1 mg, 0.074 mmol) using AD mix β** at rt for 18 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-3 column, 99:1 to 50:50 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 29.3 min (minor) and 30.7 min (major)]; $[\alpha]_D^{20}$ = -2.95° (*c* = 0.61, $CHCl_3$); IR (neat) 3421, 2924, 2852, 1705, 1608, 1183 cm^{-1}; ^{1}H NMR (700 MHz, C_6D_6) δ 8.22 (d, *J* = 9.1 Hz, 2H), 6.30 (d, J = 9.1 Hz, 2H), 4.77 (d, *J* = 1.7 Hz, 2H), 4.38-4.39 (m, 1H), 3.31 (dd, *J* = 7.9, 4.1 Hz, 1H), 2.26 (s, 6H), 2.09-2.11 (m, 1H), 1.64-1.67 (m, 2H), 1.48-1.58 (m, 3H), 1.13-1.20 (m, 2H), 0.97-1.06 (m, 2H), 0.80-0.86 (m, 1H) ppm; ^{13}C{^{1}H} NMR (175 MHz, C_6D_6) δ 165.9, 153.2, 131.6, 116.7, 110.8, 85.0, 81.3, 78.2, 64.4, 51.7, 40.4, 38.9, 28.74, 28.70, 26.4, 25.9, 25.8 ppm; HRMS (ES+) calcd. for $C_{20}H_{28}NO_4$ (M+H) 346.2018, found 346.2022.



SI-21

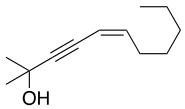
*(Z)-trimethyl(non-3-en-1-yn-1-yl)silane (**SI-21**).* To a stirred suspension of iodide **SI-4** (625.0 mg, 2.79 mmol) in THF:*i*-Pr_2NH (16 mL, 1:1) at 0 °C was added sequentially TMS acetylene **SI-20** (493.0 mg, 5.02 mmol, 0.7 mL), $Pd(PPh_3)_4$ (162.0 mg, 0.139

mmol) and CuI (53.0 mg, 0.279 mmol) and the reaction was allowed to warm up to rt. After overnight stirring, the reaction was quenched by sat. aq. NH_4Cl (20 mL). After evaporating the organic solvent (THF), the resulting aqueous solution was extracted with EtOAc (3 X 10 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give crude **SI-21** which was used in the next step without further purification.



SI-22

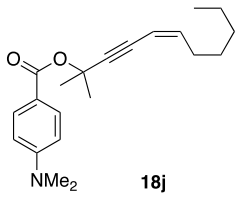
*(Z)-non-3-en-1-yne (**SI-22**).* To a stirred solution of crude **SI-21** in Et_2O:THF (20 ml, 3:1) at rt was added TBAF (3.4 mL, 3.4 mmol, 1 M in THF). After overnight stirring the reaction was quenched with H_2O (10 mL) and extracted with Et_2O (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* at low temperature and the volatile enyne **SI-22** was used in the next step without further purification. An analytical sample was prepared for spectroscopic determination. ^1H NMR (700 MHz, $CDCl_3$) δ 6.03 (dt, *J* = 10.8, 7.5 Hz, 1H), 5.45-5.48 (m, 1H), 3.09 (d, *J* = 2.2 Hz, 1H), 2.35 (qd, *J* = 7.5, 1.4 Hz, 2H), 1.42-1.46 (m, 2H), 1.32-1.36 (m, 4H), 0.92 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 146.3, 107.9, 81.1, 80.6, 31.4, 30.2, 28.4, 22.5, 14.0 ppm; HRMS (AP+) calcd. for C_9H_{15} (M+H) 123.1174, found 123.1173.



SI-23

*(Z)-2-methylundec-5-en-3-yn-2-ol (**SI-23**).* To a stirred solution of crude enyne **SI-22** in THF (25 ml) at -78 °C was added *n*-BuLi (1.7 mL, 3.07 mmol, 1.76 M in hexane). After 1 h, acetone (243.0 mg, 4.18 mmol, 0.31 mL) was added dropwise over 2 min. After 1 h, the reaction was allowed to warm up to rt over 2 h. After 4 h stirring the reaction was

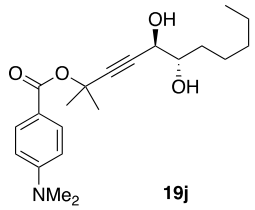
quenched with H_2O (10 mL) and extracted with Et_2O (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 5-50% Et_2O / pentane, to give **SI-23** (190.0 mg, 1.05 mmol, 38% over 3 steps) as a white solid. IR (neat) 3355, 2980, 2929, 1457, 1363, 1164 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.93 (dt, *J* = 10.7, 7.4 Hz, 1H), 5.48 (d, *J* = 10.8 Hz, 1H), 2.30 (q, *J* = 7.4 Hz, 2H), 1.94 (s, 1H), 1.58 (s, 6H), 1.41-1.45 (m, 2H), 1.31-1.37 (m, 4H), 0.92 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 108.4, 97.8, 79.0, 65.7, 31.5, 31.4, 30.1, 28.4, 22.5, 14.1 ppm; HRMS (AP+) calcd. for $C_{12}H_{21}O$ (M+H) 181.1592, found 181.1599.



18j

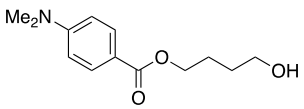
*(Z)-2-methylundec-5-en-3-yn-2-yl 4-(dimethylamino)benzoate (**18j**).* To a stirred solution of alcohol **SI-23** (47.0 mg, 0.26 mmol.) in 1,2-DCB (0.8 mL) was added sequentially 4-(dimethylamino)benzoic acid **SI-14** (172.3 mg, 1.04 mmol), EDC•HCl (200.0 mg, 1.04 mmol), DMAP (128.0 mg, 1.04 mmol) and the reaction was heated to 150 °C. After 10 h, the reaction was quenched by H_2O (1 mL) and extracted with CH_2Cl_2. The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel (neutralized with 10% Et_3N in hexanes), eluting with 10-20% EtOAc / hexanes, to give the tertiary benzoate **18j** (33.8 mg, 0.103 mmol, 40%) as a clear liquid. IR (neat) 2923, 2855, 1708, 1608, 1098 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.91 (d, *J* = 4.9 Hz, 2H), 6.66 (d, *J* = 9.0 Hz, 2H), 5.92 (dt, *J* = 10.7, 7.5 Hz, 1H), 5.50 (dt, *J* = 10.7, 1.3 Hz, 1H), 3.05 (s, 6H), 2.31 (qd, *J* = 7.4, 1.3 Hz, 2H), 1.84 (s, 6H), 1.39-1.43 (m, 2H), 1.29-1.31

(m, 4H), 0.89 (t, *J* = 7.0 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 165.2, 153.2, 144.5, 131.3, 118.0, 110.6, 108.7, 94.9, 80.8, 72.2, 40.1, 31.4, 30.1, 29.4, 28.4, 22.4, 14.1 ppm; HRMS (ES+) calcd. for $C_{21}H_{30}NO_2$ (M+H) 328.2277, found 328.2285.



19j

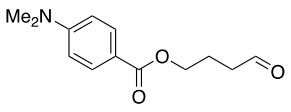
*(5R,6S)-5,6-dihydroxy-2-methylundec-3-yn-2-yl 4-(dimethylamino)benzoate (**19j**).* The diol **19j** (3.2 mg, 8.85 *μ*mol, 74% yield, 58% ee) was prepared by "**General procedure B**" from enyne **18j** (4.0 mg, 12.0 *μ*mol) using AD mix β** at rt for 12 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-3 column, 90:10 to 70:30 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 16.8 min (minor) and 17.5 min (major)]; $[\alpha]_D^{20}$ = -10.0° (*c* = 0.17, $CHCl_3$); IR (neat) 3404, 2920, 2852, 1690, 1606, 1290 cm^{-1}; ^{1}H NMR (700 MHz, C_6D_6) δ 8.17 (d, *J* = 4.9 Hz, 2H), 6.32 (d, *J* = 9.1 Hz, 2H), 4.18 (br s, 1H), 3.64 (br s, 1H), 2.95 (d, *J* = 6.6 Hz, 1H), 2.37 (s, 1H), 2.27 (s, 6H), 1.69 (s, 3H), 1.67 (s, 3H), 1.59-1.64 (m, 1H), 1.53-1.58 (m, 1H), 1.48-1.53 (m, 1H), 1.17-1.24 (m, 3H), 1.11-1.16 (m, 1H), 0.83 (t, *J* = 7.2 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, C_6D_6) δ 165.9, 153.2, 131.5, 117.9, 110.7, 87.7, 83.8, 75.2, 71.5, 67.1, 38.9, 33.5, 31.9, 28.74, 28.70, 25.5, 22.6, 13.9 ppm; HRMS (ES+) calcd. for $C_{21}H_{32}NO_4$ (M+H) 362.2331, found 362.2334.



SI-25

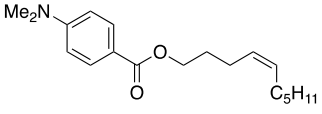
*4-hydroxybutyl 4-(dimethylamino)benzoate (**SI-25**).* To a stirred solution of butane-1,4-diol **SI-24** (3.49 g, 38.76 mmol) in CH_2Cl_2 (73 mL) at rt was added sequentially 4-

(dimethylamino)benzoic acid SI-14 (6.04 g, 36.56 mmol), EDC•HCl (7.0 g, 36.56 mmol), DMAP (4.5 g, 36.56 mmol). After 21 h, the reaction was quenched by H_2O (50 mL) and extracted with CH_2Cl_2 (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by recrystallization with toluene, to give **SI-25** (6.0 g, 25.29 mmol, 69%) as a white solid. IR (neat) 3418, 2944, 1699, 1609, 1184 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.93 (d, *J* = 9.1 Hz, 2H), 6.67 (d, *J* = 9.0 Hz, 2H), 4.33 (t, *J* = 6.5 Hz, 2H), 3.75 (t, *J* = 6.5 Hz, 2H), 3.06 (s, 6H), 1.85-1.89 (m, 2H), 1.73-1.78 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 166.9, 153.3, 131.2, 117.3, 110.7, 63.9, 62.5, 40.0, 29.4, 25.4 ppm; HRMS (ES+) calcd. for $C_{13}H_{20}NO_3$ (M+H) 238.1443, found 238.1435.



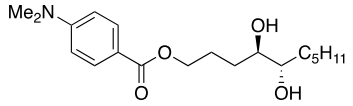
SI-26

*4-oxobutyl 4-(dimethylamino)benzoate (**SI-26**).* To a stirred solution of alcohol **SI-25** (710.0 mg, 2.99 mmol) in CH_2Cl_2 (30 mL) at rt was added DMP (3.20 g, 7.48 mmol). After 2 h, the reaction was quenched by sat. aq. $NaHCO_3$ (15 mL) and sat. aq. $Na_2S_2O_3$•$5H_2O$ (15 mL) and extracted with CH_2Cl_2 (3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel (neutralized with 2% Et_3N in hexanes), eluting with 20-50% EtOAc / hexanes, to give **SI-26** (492.0 mg, 2.09 mmol, 70%). ^1H NMR (400 MHz, $CDCl_3$) δ 9.85 (t, *J* = 1.4 Hz, 1H), 7.90 (d, *J* = 9.2 Hz, 2H), 6.67 (d, *J* = 9.1 Hz, 2H), 4.33 (t, *J* = 6.3 Hz, 2H), 3.0 (s, 6H), 2.64 (td, J = 7.2, 1.4 Hz, 2H), 2.08-2.15 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 201.5, 166.8, 153.4, 131.3, 116.8, 110.7, 63.1, 40.7, 40.1, 21.7 ppm.



20

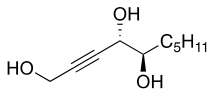
*(Z)-dec-4-en-1-yl 4-(dimethylamino)benzoate (**20**).* To a stirred solution of the Wittig salt hexyltriphenylphosphonium bromide **SI-27** (716.0 mg, 1.67 mmol) in THF (11 mL) at -78 °C was drop wise added NaHMDS (0.84 mL, 1.67 mmol, 2 M in THF). After 5 min, the reaction was warmed up to -40 °C and stirred for 5 min before recooling down to -78 °C and aldehyde **SI-26** (246.0 mg, 1.05 mmol) in THF (5 mL + 5 mL rinse) was added. After 1 h, the reaction was warmed up to -40 °C and after overnight stirring, the reaction was warmed up to rt and stirred for 15 min before quenching by H_2O (20 mL) and extracted with EtOAc (3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 10-25% EtOAc / hexanes, to give **20** (251.8 mg, 0.83 mmol, 79%) as a colorless liquid. IR (neat) 2955, 2923, 1705, 1609, 1277 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.94 (d, *J* = 9.0 Hz, 2H), 6.67 (d, *J* = 9.0 Hz, 2H), 5.39-5.47 (m, 2H), 4.29 (t, *J* = 6.5 Hz, 2H), 3.06 (s, 6H), 2.22 (q, *J* = 7.2 Hz, 2H), 2.06 (q, *J* = 7.2 Hz, 2H), 1.81-1.85 (m, 2H), 1.34-1.40 (m, 2H), 1.26-1.33 (m, 4H), 0.89 (t, *J* = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 167.0, 153.3, 131.2, 131.1, 128.3, 117.4, 110.7, 63.6, 40.0, 31.5, 29.4, 28.9, 27.2, 23.7, 22.5, 14.0 ppm; HRMS (ES+) calcd. for $C_{19}H_{30}NO_2$ (typically M+ or M+H) 304.2277, found 304.2277.



21

*(4R,5S)-4,5-dihydroxydecyl 4-(dimethylamino)benzoate (**21**).* The diol **21** (33.0 mg, 0.098 mmol, 54% yield, 11.6% ee) was prepared by "**General procedure B**" from enyne **20** (55.0 mg, 0.181 mmol) using AD mix β** at rt for 2.5 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-3 column,

99:1 to 70:30 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 20.5 min (major) and 21.5 min (minor)]; $[\alpha]_D^{20}$ = +0.24° (*c* = 3.30, $CHCl_3$); IR (neat) 3344, 2929, 1698, 1611, 1184 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.92 (d, *J* = 9.1 Hz, 2H), 6.66 (d, *J* = 9.1 Hz, 2H), 4.33 (t, *J* = 6.5 Hz, 2H), 3.68 (d, *J* = 8.7 Hz, 1H), 3.65 (s, 1H), 3.05 (s, 6H), 2.37 (s, 1H), 2.15 (s, 1H), 1.98-2.04 (m, 1H), 1.80-1.86 (m, 1H), 1.56-1.65 (m, 2H), 1.50-1.55 (m, 1H), 1.44-1.47 (m, 2H), 1.27-1.34 (m, 5H), 0.90 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 167.2, 153.3, 131.3, 116.9, 110.7, 74.7, 74.2, 64.1, 40.1, 31.9, 31.4, 27.6, 25.7, 25.6, 22.6, 14.1 ppm; HRMS (ES+) calcd. for $C_{19}H_{32}NO_4$ (M+H) 338.2331, found 338.2329.

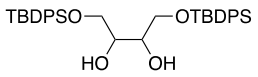


23

*(4S,5R)-dec-2-yne-1,4,5-triol (**23**).* The triol **23** (41.4 mg, 0.22 mmol, 74%, 27.4% ee) was prepared by "**General procedure B**" from enyne **22 (46.0 mg, 0.30 mmol)** using AD mix β** at rt for 40 h. Enantiomeric ratio was determined (by synthesizing the known biphenyl-ester diol ***ent*-19c**) by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-3 column, 99:1 to 60:40 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 23.9 min (major) and 24.7 min (minor)]; $[\alpha]_D^{20}$ = -23.5° (*c* = 0.2, $CHCl_3$); IR (neat) 3347, 2955, 2859, 1110, 1021 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 4.35 (s, 1H), 4.32 (s, 2H), 3.98-4.03 (m, 1H), 3.86-3.90 (m, 1H), 3.74 (br s, 1H), 3.51-3.58 (m, 1H), 1.48-1.60 (m, 3H), 1.30-1.35 (m, 5H), 0.92 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 85.2, 83.2, 74.4, 66.4, 50.7, 32.8, 31.7, 25.4, 22.6, 14.0 ppm; HRMS (ES+) calcd. for $C_{10}H_{18}O_3Na$ (M+H) 209.1154, found 209.1156.

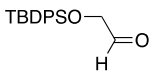
SI-29

*(Z)-2,2,11,11-tetramethyl-3,3,10,10-tetraphenyl-4,9-dioxa-3,10-disiladodec-6-ene (**SI-29**).* To a stirred solution of (*Z*)-but-2-ene-1,4-diol **SI-28** (3.0 g, 34.04 mmol) in CH_2Cl_2 (68 mL) at 0°C was added imidazole (7.0 g, 102.2 mmol) followed by TBDPSCl (28.0 g, 26.6 mL, 102.2 mmol). After 5 min, the reaction was warmed to rt. After 2h 45 min, the reaction was quenched by H_2O (60 mL) and extracted with CH_2Cl_2 (3 X 40 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 2.5-5% EtOAc / hexanes, to give the known compound **SI-29**[35] (19.0 g, 33.7 mmol, 99%) as a colorless liquid. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 7.9, 1.3 Hz, 8H), 7.42-7.44 (m, 4H), 7.36-7.38 (m, 8H), 5.66 (t, *J* = 3.4 Hz, 2H), 4.15 (d, *J* = 4.2 Hz, 4H), 1.05 (s, 18H) ppm; ^{13}C{^{1}H} NMR (175 MHz, $CDCl_3$) δ 135.56, 133.67, 129.94, 129.60, 127.65, 60.51, 26.79, 19.12 ppm.



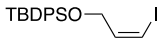
SI-30

*2,2,11,11-tetramethyl-3,3,10,10-tetraphenyl-4,9-dioxa-3,10-disiladodecane-6,7-diol (**SI-30**).* To a stirred solution of alkene **SI-29** (2.17 g, 3.84 mmol) in acetone : H_2O (7 mL : 7 mL) at rt was sequentially added NMO (2.4 mL, 11.52 mmol, 4.8 M in H_2O) and K_2OsO_4•$2H_2O$ (7.1 mg, 19.2 *μ*mol). After overnight stirring, the reaction was quenched by addition of solid $NaHSO_3$ (500 mg) and extracted with EtOAc (3 X 20 mL). The dried ($NaSO_4$) extract was concentrated *in vacuo* and the crude diol **SI-30** was used in the next step without further purification.



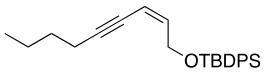
SI-31

*2-((tert-butyldiphenylsilyl)oxy)acetaldehyde (**SI-31**).*To the stirred crude diol **SI-30** in CH_2Cl_2 (20 mL) was added to the silica supported $NaIO_4$ (made by mixing 1.23 g $NaIO_4$ and 5.0 g silica gel in 2.4 mL H_2O). After a week, the reaction mixture was filtered and the dried ($MgSO_4$) filtrate was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 5-9% EtOAc / hexanes, to give the known compound **SI-31**[35] (1.4 g, 4.7 mmol, 61% over two steps) as a colorless liquid. ^{1}H NMR (700 MHz, $CDCl_3$) δ 9.75 (s, 1H), 7.69 (d, *J* = 7.5 Hz, 4H), 7.47-7.49 (m, 2H), 7.42-7.44 (m, 4H), 4.24 (s, 2H), 1.13 (s, 9H) ppm; ^{13}C{^{1}H} NMR (175 MHz, $CDCl_3$) δ 201.7, 135.5, 132.5, 130.1, 127.9, 70.0, 26.7, 19.3 ppm.



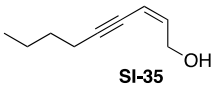
SI-32

*(Z)-tert-butyl((3-iodoallyl)oxy)diphenylsilane (**SI-32**).* To a stirred solution of the Wittig salt **SI-16** (2.84 g, 5.35 mmol) in THF (18 mL) at rt was drop wise added NaHMDS (2.7 mL, 5.35 mmol, 2 M in THF). After 5 min, the reaction was cooled down to -78 °C and DMPU (2.74 g, 2.6 mL, 21.4 mmol) was added and stirred for another 5 min before addition of the aldehyde **SI-31** (1.33 g, 4.46 mmol) in THF (2 mL + 2 mL rinse). After 2.5 h, the reaction was quenched by sat. aq. NH_4Cl (25 mL) and extracted with EtOAc (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 2-2.5% Et_2O / hexanes, to give the known compound **SI-32**[36] (1.35 g, 3.2 mmol, 72%, *Z*:*E* > 42:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.9, 1.8 Hz, 4H), 7.41-7.47 (m, 6H), 6.54 (dt, *J* = 7.7, 5.2 Hz, 1H), 6.25 (dt, *J* = 7.7, 1.8 Hz, 1H), 4.33 (dd, *J* = 5.3, 1.8 Hz, 2H), 1.09 (s, 9H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 140.9, 135.6, 133.4, 129.8, 127.8, 80.3, 67.5, 26.8, 19.2 ppm.



SI-34

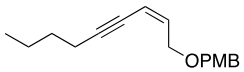
*(Z)-tert-butyl(non-2-en-4-yn-1-yloxy)diphenylsilane (**SI-34**).* To a stirred suspension of $Pd(PPh_3)_4$ (185.0 mg, 0.16 mmol) and CuI (61.0 mg, 0.32 mmol) in *i*-Pr_2NH (15 mL) at 0 °C was drop wise added a solution of hex-1-yne **SI-33** (263.0 mg, 3.2 mmol) and iodide **SI-32** (1.35 g, 3.2 mmol) in *i*-Pr_2NH (8 mL) and the reaction was allowed to warm up to rt. After overnight stirring, the reaction was quenched by sat. aq. NH_4Cl (15 mL) and extracted with EtOAc (3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 2-3.3% Et_2O / hexanes, to give the compound **SI-34** (1.08 g, 2.87 mmol, 90%) as a colorless liquid. IR (neat) 3072, 2932, 1472, 1114, 701 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.9, 1.3 Hz, 4H), 7.44-7.46 (m, 2H), 7.39-7.42 (m, 4H), 6.03 (dt, *J* = 10.9, 6.1 Hz, 1H), 5.49 (dquin, *J* = 10.9, 1.9 Hz, 1H), 4.50 (dd, *J* = 6.1, 1.5 Hz, 2H), 2.24 (td, *J* = 7.0, 2.1 Hz, 2H), 1.39-1.44 (m, 2H), 1.31-1.37 (m, 2H), 1.09 (s, 9H), 0.88 (t, *J* = 7.3 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 140.8, 135.6, 133.8, 129.6, 127.6, 109.7, 96.2, 62.5, 30.7, 26.8, 21.9, 19.2, 19.1, 13.6 ppm; HRMS (ES+) calcd. for $C_{25}H_{33}OSi$ (M+H) 377.2301, found 377.2302.



SI-35

*(Z)-non-2-en-4-yn-1-ol (**SI-35**).* To a stirred solution of silyl ether **SI-34** (1.06 g, 2.82 mmol) in THF (37 mL) at 0 °C was added TBAF (3.1 mL, 3.1 mmol, 1 M in THF) and the reaction mixture was allowed to warm up to rt immediately. After overnight stirring the reaction was quenched with H_2O (20 mL). The organic solvent (THF) was removed in *vacuo* and the resulting aqueous layer was extracted with EtOAc (3 X 30 mL). The dried

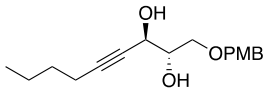
($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 10-33% EtOAc / hexanes, to give the known compound **SI-35**[37] (274.0 mg, 1.99 mmol, 70%) as a colorless oil. ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.00 (dt, *J* = 10.9, 6.3 Hz, 1H), 5.58 (dquin, *J* = 10.9, 1.5 Hz, 1H), 4.39 (t, *J* = 5.6 Hz, 2H), 2.34 (td, *J* = 7.1, 2.1 Hz, 2H), 1.90 (t, *J* = 5.8 Hz, 1H), 1.51-1.55 (m, 2H), 1.41-1.46 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (175 MHz, $CDCl_3$) δ 139.8, 111.2, 96.7, 60.9, 30.7, 21.9, 19.2, 13.5 ppm.



24a

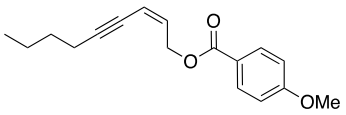
*(Z)-1-methoxy-4-((non-2-en-4-yn-1-yloxy)methyl)benzene (**24a**).* To a stirred solution of NaH (23.0 mg, 0.563 mmol, 60%) in THF (0.5 mL) at 0 °C was added allyl alcohol **SI-35** (51.8 mg, 0.375 mmol) and stirred at the same temperature for 10 min and at rt for 20 min. Then the reaction mixture was recooled to 0 °C and to it was added PMBCl (71.0 mg, 61.3 □L, 0.45 mmol) followed by TBAI (14.0 mg, 0.038 mmol). After 5 min, the reaction was warmed up to rt and stirred for 20 h before refluxing for another 4h. The reaction was cooled down to 0 °C and was quenched by sat. aq. NH_4Cl (1 mL) and extracted with EtOAc (3 X 5 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 4-7% EtOAc / hexanes, to give the compound **24a** (57.0 mg, 0.221 mmol, 59%, (74% brsm)) as a yellow liquid. IR (neat) 2958, 2873, 1717, 1613, 1514, 1249, 821 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.1 Hz, 2H), 6.90 (d, J = 7.9 Hz, 2H), 5.99 (dt, *J* = 10.8, 6.4 Hz, 1H), 5.64 (dd, *J* = 10.8, 0.8 Hz, 1H), 4.48 (s, 2H), 4.28 (d, *J* = 6.4 Hz, 2H), 3.82 (s, 3H), 2.34 (t, *J* = 6.9 Hz, 2H), 1.50-1.54 (m, 2H), 1.44 (sextet, *J* = 7.4 Hz, 2H), 0.94 (t, *J* = 7.3 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (175 MHz, $CDCl_3$) δ 159.2, 137.9, 130.4, 129.5, 113.7, 112.2, 96.5, 76.4,

71.9, 67.6, 55.3, 30.7, 21.9, 19.2, 13.6 ppm; HRMS (ES+) calcd. for $C_{17}H_{23}O_2$ (M+H) 259.1698, found 259.1687.



25a

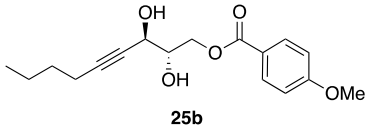
*(2S,3R)-1-((4-methoxybenzyl)oxy)non-4-yne-2,3-diol (**25a**).* The diol **25a** (19.9 mg, 0.068 mmol, 65% yield, 6.5% ee determined by Mosher ester analysis) was prepared by "**General procedure B**" from enyne **24a** (27.0 mg, 0.105 mmol) using AD mix β** at 0 °C for 4.5 h. $[\alpha]_D^{20}$ = +1.37° (*c* = 0.95, $CHCl_3$); IR (neat) 3403, 2932, 1613, 1514, 1248, 1035 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.28-7.27 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 4.52 (s, 2H), 4.49-4.51 (m, 1H), 3.80-3.84 (m, 5H), 3.67 (dd, *J* = 9.4, 3.5 Hz, 1H), 2.78 (d, J = 7.5 Hz, 1H), 2.68 (d, *J* = 6.3 Hz, 1H), 2.23 (td, J = 7.1, 1.9 Hz, 2H), 1.47-1.52 (m, 2H), 1.38-1.43 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H)ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ ppm; HRMS (ES+) calcd. for $C_{17}H_{25}O_4$ (M+H) 293.1753, found 293.1745.



24b

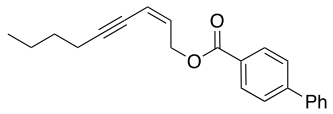
*(Z)-non-2-en-4-yn-1-yl 4-methoxybenzoate (**24b**).* The allylic ester **24b** (48.0 mg, o.176 mmol, 99% yield) was prepared by "**General procedure A**" from alcohol **SI-35** (24.6 mg, 0.178 mmol) and 4-methoxybenzoic acid **SI-9** (81.3 mg, 0.535 mmol) using DCC. IR (neat) 2958, 2118, 1716, 1607, 1257, 1101, 770 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 6.05 (dt, *J* = 10.7, 6.5 Hz, 1H), 5.72 (d, *J* = 10.7 Hz, 1H), 5.05 (d, *J* = 6.5 Hz, 2H), 3.88 (s, 3H), 2.37 (td, *J* = 7.0, 1.8 Hz, 2H), 1.55 (quint, *J* = 7.2 Hz, 2H), 1.45 (sex, *J* = 7.4 Hz, 2H), 0.94 (t, *J* = 7.4 Hz, 3H) ppm;

$^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 166.2, 163.3, 134.9, 131.7, 122.5, 113.6, 113.4, 97.6, 75.9, 62.7, 55.4, 30.7, 22.0,19.2, 13.6 ppm; HRMS (ES+) calcd. for $C_{17}H_{21}O_3$ (M+H) 273.1491, found 273.1495.



25b

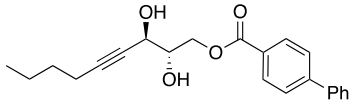
*(2S,3R)-2,3-dihydroxynon-4-yn-1-yl 4-methoxybenzoate (**25b**).* The diol **25b** (15.4 mg, 0.050 mmol, 63% yield, 38% ee) was prepared by "**General procedure B**" from enyne **24b** (21.6 mg, 0.079 mmol) using AD mix β** at rt for 5.5 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-2 column, 99:1 to 70:30 hexanes:^{i}PrOH, 0.5 mL/min, 254 nm, retention times 104.4 min (minor) and 111.2 min (major)]; $[\alpha]_D^{20}$ = +3.43° (*c* = 1.4, $CHCl_3$); IR (neat) 3405, 2958, 1714, 1607, 1259, 770 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.9 Hz, 2H), 6.94 (d, *J* = 8.9 Hz, 2H), 4.53-4.56 (m, 2H), 4.50 (dd, *J* = 11.7, 4.0 Hz, 1H), 4.04 (quint, *J* = 4.3 Hz, 1H), 3.88 (s, 3H), 2.71 (d, *J* = 5.9 Hz, 1H), 2.55 (d, *J* = 6.4 Hz, 1H), 2.22 (td, *J* = 7.1, 1.9 Hz, 2H), 1.50 (quint, *J* = 7.2 Hz, 2H), 1.41 (sext, J = 7.3 Hz, 2H), 0.92 (t, *J* = 7.3 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 166.8, 166.6, 131.8, 122.0, 113.7, 88.6, 76.7, 72.8, 65.4, 64.1, 55.5, 30.5, 21.9, 18.4, 13.5 ppm; HRMS (ES+) calcd. for $C_{17}H_{23}O_5$ (M+H) 307.1545, found 307.1536.



24c

*(Z)-non-2-en-4-yn-1-yl [1,1'-biphenyl]-4-carboxylate (**24c**).* The allylic ester **24c** (74.6 mg, 0.234 mmol, 85% yield) was prepared by "**General procedure A**" from alcohol **SI-35** (38.0 mg, 0.275 mmol) and (1,1'-biphenyl)-4-carboxylic acid **SI-6** (110.0 mg, 0.551

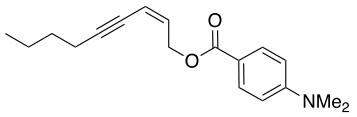
mmol) using EDC•HCl. IR (neat) 2926, 1722, 1609, 1269, 1113, 747 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.15 (dt, *J* = 8.6, 1.8 Hz, 2H), 7.68 (d, *J* = 8.6 Hz, 2H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.42 (tt, *J* = 7.2, 1.1 Hz, 1H), 6.08 (dt, *J* = 10.7, 6.5 Hz, 1H), 5.75 (dquint, *J* = 10.7, 1.4 Hz, 1H), 5.11 (dd, J = 6.5, 1.3 Hz, 2H), 2.38 (td, *J* = 7.2, 2.0 Hz, 2H), 1.54-1.57 (m, 2H), 1.46 (sext, J = 7.4 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 166.3, 145.7, 140.0, 134.6, 130.2, 128.9, 128.1, 127.3, 127.0, 113.7, 97.7, 75.9, 62.9, 30.7, 22.0, 19.2, 13.6 ppm; HRMS (ES+) calcd. for $C_{22}H_{23}O_2$ (M+H) 319.1698, found 319.1709.



25c

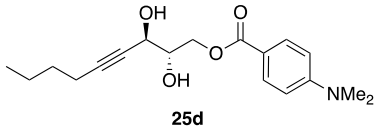
*(2S,3R)-2,3-dihydroxynon-4-yn-1-yl [1,1'-biphenyl]-4-carboxylate (**25c**).* The diol **25c** (18.50 mg, 0.052 mmol, 70% yield, 32% ee) was prepared by "**General procedure B**" from enyne **24c** (23.90 mg, 0.075 mmol) using AD mix β** at rt for 18 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-2 column, 99:1 to 70:30 hexanes:*i*-PrOH, 0.5 mL/min, 254 nm, retention times 79.3 min (minor) and 87.1 min (major)]; $[\alpha]_D^{20}$ = +7.53° (*c* = 0.73, $CHCl_3$); IR (neat) 3367, 2958, 1717, 1609, 1277, 1125 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.64 (d, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 1H), 4.55-4.61 (m, 3H), 4.09 (quint, J = 5.7 Hz, 1H), 2.70 (d, *J* = 6.0 Hz, 1H), 2.54 (d, *J* = 6.4 Hz, 1H), 2.24 (td, *J* = 7.1, 1.6 Hz, 2H), 1.51 (quint, *J* = 7.4 Hz, 2H), 1.42 (sext, *J* = 7.4 Hz, 2H), 0.92 (t, *J* = 7.4 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 166.9, 146.0, 139.9, 130.3, 128.9, 128.4, 128.2, 127.3, 127.1, 88.7, 76.6, 72.7, 65.6,

64.1, 30.5, 21.9, 18.4, 13.5 ppm; HRMS (ES+) calcd. for $C_{22}H_{25}O_4$ (M+H) 353.1753, found 353.1747.



24d

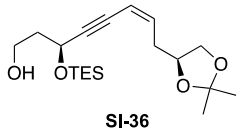
*(Z)-non-2-en-4-yn-1-yl 4-(dimethylamino)benzoate (**24d**).* The allylic ester **24d** (35.6 mg, 0.125 mmol, 81% yield) was prepared by "**General procedure A**" from alcohol **SI-35** (21.4 mg, 0.155 mmol) and 4-(dimethylamino)benzoic acid **SI-14** (52.0 mg, 0.31 mmol) using EDC•HCl. IR (neat) 2922, 1708, 1608, 1365, 1270 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 9.47 (d, *J* = 9.0 Hz, 2H), 6.66 (d, *J* = 9.0 Hz, 2H), 6.06 (dt, *J* = 10.8, 6.4 Hz, 1H), 5.69-5.71 (m, 1H), 5.04 (dd, *J* = 6.5, 1.4 Hz, 2H), 3.06 (s, 6H), 2.37 (td, *J* = 7.1, 2.1 Hz, 2H), 1.53-1.58 (m, 2H), 1.43-1.48 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 166.8, 153.3, 135.6, 131.4, 116.9, 112.9, 110.7, 97.4, 76.0, 62.3, 40.1, 30.7, 22.0, 19.3, 13.6 ppm; HRMS (ES+) calcd. for $C_{18}H_{24}NO_2$ (M+H) 286.1807, found 286.1810.



25d

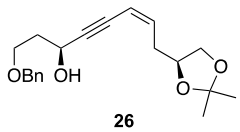
*(2S,3R)-2,3-dihydroxynon-4-yn-1-yl 4-(dimethylamino)benzoate (**25d**).* The diol **25d** (14.0 mg, 0.044 mmol, 73% yield, 4.9% ee) was prepared by "**General procedure B**" from enyne **24d** (18.4 mg, 0.060 mmol) using AD mix β** at rt for 20 h. Enantiomeric ratio was determined by chiral HPLC [250 x 4.6 mm Phenomenex Lux 5u Cellulose-3 column, 90:10 to 50:50 hexanes:*i*-PrOH, 0.5 mL/min, 254 nm, retention times 28.3 min (minor) and 30.0 min (major)]; $[\alpha]_D^{20}$ = +0.8° (*c* = 0.5, $CHCl_3$); IR (neat) 3404, 2926, 1702, 1608, 1279, 1185 cm^{-1}; ^1H NMR (700 MHz, C_6D_6) δ 8.21 (d, *J* = 9.0 Hz, 2H), 6.32

(d, *J* = 9.0 Hz, 2H), 4.65 (dd, *J* = 6.6, 6.5 Hz, 1H), 4.58 (dd, J = 11.7, 4.1 Hz, 1H), 4.47 (quint, *J* = 2.1 Hz, 1H), 3.97 (dt, J = 6.5, 4.2 Hz, 1H), 2.29 (s, 6H), 1.92 (td, *J* = 6.9, 2.0 Hz, 2H), 1.20-1.28 (m, 4H), 0.75 (t, *J* = 7.2 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, C_6D_6) δ 167.3, 153.2, 131.6, 117.1, 110.7, 87.1, 77.9, 73.2, 65.3, 64.3, 38.9, 30.5, 21.8, 18.2, 13.3 ppm; HRMS (ES+) calcd. for $C_{18}H_{26}NO_4$ (M+H) 320.1862, found 320.1866.



SI-36

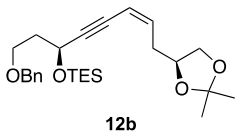
*(S,Z)-8-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-3-((triethylsilyl)oxy)oct-6-en-4-yn-1-ol (**SI-36**).* To a stirred solution of known (*S*,*Z*)-8-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)-3-((triethylsilyl)oxy)oct-6-en-4-yn-1-yl pivalate **12a**[14] (255.0 mg, 0.58 mmol) in CH_2Cl_2 (6 mL) at -78°C was added DIBAL-H (1.16 mL, 1.16 mmol, 1.0 M in hexane). After 15 min, the reaction was quenched by MeOH (1 mL) and sat. aq. Rochelle's salt (5 mL) and stirred until two layers got separated, extracted with CH_2Cl_2 (3 X 5 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give the crude alcohol **SI-36** which was used in the next step without further purification.



26

*(S,Z)-1-(benzyloxy)-8-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)oct-6-en-4-yn-3-ol (**26**).* To a stirred solution of crude alcohol **SI-36** in Et_2O (6 mL) at 0 °C, was added sequentially benzyl acetimidate (176.0 mg, 0.69 mmol, 129.0 *μ*L) and TfOH (0.23 mmol, 136.0 *μ*L, 1M in Et_2O). The reaction was allowed to warm up to rt. After overnight (8 h), the reaction was quenched by sat. aq. $NaHCO_3$ (6 mL) and extracted with Et_2O (3 X 5 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over

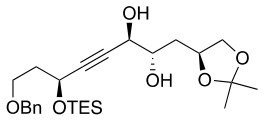
silica gel, eluting with 10-30% EtOAc / hexanes, to give **26** (100.0 mg, 0.30 mmol, 52% over 2 steps) as a yellow liquid. $[\alpha]_D^{20}$ = -10.23° (*c* = 1.3, $CHCl_3$); IR (neat) 3426, 2930, 2870, 1454, 1370, 1103 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.35-7.38 (m, 4H), 7.30-7.32 (m, 1H), 5.97 (dt, *J* = 10.8, 7.4 Hz, 1H), 5.64 (dd, *J* = 10.8, 1.5 Hz, 1H), 4.78-4.79 (m, 1H), 4.57 (d, *J* = 11.9 Hz, 1H), 4.54 (d, *J* = 11.9 Hz, 1H), 4.19 (quint, *J* = 6.3 Hz, 1H), 4.03 (d, *J* = 4.8, 6.0 Hz, 1H), 3.88 (ddd, *J* = 9.4, 8.5, 4.1 Hz, 1H), 3.71 (ddd, *J* = 10.0, 6.0, 4.6 Hz, 1H), 3.63 (dd, *J* = 8.0, 6.8 Hz, 1H), 3.15 (d, *J* = 5.5 Hz, 1H), 2.59-2.61 (m, 2H), 2.11-2.16 (m, 1H), 1.98-2.03 (m, 1H), 1.45 (s, 3H), 1.37 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 138.3, 137.8, 128.5, 127.8, 127.7, 111.4, 109.1, 94.6, 81.3, 74.9, 73.4, 68.7, 67.7, 61.9, 36.9, 34.3, 26.9, 25.6 ppm; HRMS (ES+) calcd. for $C_{20}H_{26}O_4Na$ (M+Na) 353.1729, found 353.1723.



12b

*(((S,Z)-1-(benzyloxy)-8-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)oct-6-en-4-yn-3-yl)oxy)triethylsilane (**12b**).* To a stirred solution of alcohol **26** (27.7 mg, 0.08 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C was sequentially added 2,6-lutidine (43.0 mg, 0.40 mmol, 46.0 *μ*L) and TESOTf (66.0 mg, o.25 mmol, 57.o *μ*L). After 10 min, the reaction was quenched by sat. aq. $NaHCO_3$ (2 mL) and extracted with CH_2Cl_2 (3 X 4 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 4-12% EtOAc / hexanes, to give **12b** (33.0 mg, 0.07 mmol, 93%) as a yellow liquid. $[\alpha]_D^{20}$ = -3.18° (*c* = 1.1, $CHCl_3$); IR (neat) 2954, 2876, 1455, 1097, 744 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.35-7.38 (m, 4H), 7.29-7.31 (m, 1H), 5.94 (dt, *J* = 10.8, 7.4 Hz, 1H), 5.62 (dd, *J* = 10.8, 1.5 Hz, 1H), 4.76 (td, *J* = 7.3, 1.4 Hz, 1H), 4.55 (d, *J* =

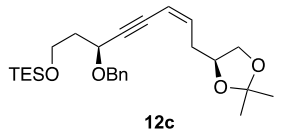
11.9 Hz, 1H), 4.50 (d, *J* = 11.9 Hz, 1H), 4.19 (quint, *J* = 6.5 Hz, 1H), 4.03 (dd, *J* = 8.0, 6.0 Hz, 1H), 3.65-3.68 (m, 1H), 3.61-3.64 (m, 1H), 3.59 (dd, *J* = 7.9, 7.1 Hz, 1H), 2.59-2.60 (m, 2H), 1.99-2.07 (m, 2H), 1.44 (s, 3H), 1,37 (s, 3H), 0.99 (t, *J* = 7.9 Hz, 9H), 0.63-0.72 (m, 6H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 138.4, 137.8, 128.4, 127.6, 127.5, 111.4, 109.0, 95.7, 80.5, 74.9, 73.1, 68.8, 66.4, 60.2, 39.0, 34.2, 26.8, 25.6, 6.8, 4.7 ppm.



13b

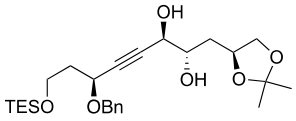
*(2S,3R,6S)-8-(benzyloxy)-1-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-6-((triethylsilyl)oxy)oct-4-yne-2,3-diol (**13b**).* To a stirred solution of *cis*-enyne **12b** (32.0 mg, 0.07 mmol) in *t*-BuOH : H_2O (0.3 mL, 1:1 mixture) at 0 °C were added sequentially AD mix β** (161.0 mg), $MeSO_2NH_2$ (14.0 mg, 0.14 mmol). After 17 h, the reaction was quenched by sat. aq. $Na_2S_2O_3•5H_2O$ (0.5 mL), stirred for another 5 min and extracted with EtOAc. The dried (Na_2SO_4) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with Et_2O:hexanes:CH_2Cl_2 (1:4:1→1:3:1→1:2:1→1:1:1→4:2:1→3:1:1→4:1:1) to give **13b** (24.5 mg, 0.05 mmol, 73%, 79:21 dr) as a yellow liquid. Major diastereomer: $[\alpha]_D^{20}$ = -12.5° (*c* = 0.32, $CHCl_3$); IR (neat) 3395, 2919, 1667, 1455, 1097 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.34-7.38 (m, 4H), 7.31 (t, *J* = 7.0 Hz, 1H), 4.66 (t, *J* = 6.6 Hz, 1H), 4.53 (d, *J* = 11.6 Hz, 1H), 4.49 (d, *J* = 11.6 Hz, 1H), 4.39 (t, *J* = 4.2 Hz, 1H), 4.35-4.37 (m, 1H), 4.10 (dd, *J* = 8.0, 6.2 Hz, 1H), 3.88-3.92 (m, 1H), 3.58-3.63 (m, 3H), 2.54 (d, *J* = 5.2 Hz, 1H), 2.37 (d, *J* = 3.8 Hz, 1H), 1.96-2.04 (m, 2H), 1.79-1.86 (m, 2H), 1.44 (s, 3H), 1.38 (s, 3H), 0.99 (t, *J* = 7.9 Hz, 9H), 0.62-0.71 (m, 6H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 138.3, 128.4, 127.7,

127.6, 108.9, 88.6, 81.2, 73.3, 73.0, 71.5, 69.4, 66.5, 66.1, 59.7, 38.8, 35.8, 26.9, 25.7, 6.8, 4.7 ppm; HRMS (ES+) calcd. for $C_{26}H_{43}O_6Si$ (M+H) 479.2829, found 479.2822.



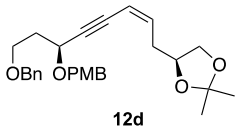
12c

*(((S,Z)-3-(benzyloxy)-8-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)oct-6-en-4-yn-1-yl)oxy)triethylsilane (**12c**).* To a stirred suspension of NaH (3.6 mg, 0.09 mmol, 60% in mineral oil) in THF (1.2 mL) at 0 °C, was added sequentially BnBr (31.0 mg, 22.0 *μ*L, 0.18 mmol), crude alcohol **SI-36** (made from 0.06 mmol of **12a**, in a similar procedure discussed earlier) in THF (0.3 mL), TBAI (4.4 mg, 0.01 mmol). After 15 min, the reaction was warmed to rt. After overnight, the reaction was quenched by H_2O (2 mL) at 0 °C and extracted with EtOAc (3 X 5 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to give **12c** (16.3 mg, 0.036 mmol, 61%) as a clear liquid. IR (neat) 2954, 2875, 1455, 1092, 744 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.34-7.38 (m, 4H), 7.29-7.30 (m, 1H), 5.98-6.01 (m, 1H), 5.68 (d, *J* = 10.8 Hz, 1H), 4.82 (d, *J* = 11.5 Hz, 1H), 4.53 (d, *J* = 11.6 Hz, 1H), 4.49 (t, *J* = 6.5 Hz, 1H), 4.22 (quint, *J* = 6.3 Hz, 1H), 4.04-4.06 (m, 1H), 3.81-3.84 (m, 1H), 3.76-3.79 (m, 1H), 3.63 (t, *J* = 7.4 Hz, 1H), 2.63-2.65 (m, 2H), 2.06-2.09 (m, 1H), 1.96-2.00 (m, 1H), 1.44 (s, 3H), 1.38 (s, 3H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.60 (q, J = 7.9 Hz, 6H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 138.0, 137.9, 128.1, 127.7, 127.4, 111.2, 108.9, 93.2, 82.1, 74.7, 70.5, 68.6, 66.2, 58.6, 38.9, 34.2, 26.6, 25.4, 6.5, 4.2 ppm.



13c

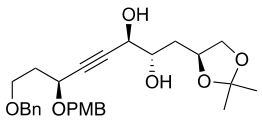
*(2S,3R,6S)-6-(benzyloxy)-1-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-8-((triethylsilyl)oxy)oct-4-yne-2,3-diol (**13c**).* To a stirred solution of *cis*-enyne **12c** (14.8 mg, 0.033 mmol) in *t*-BuOH : H_2O (0.2 mL, 1:1 mixture) at 0 °C were added sequentially AD mix β** (73.0 mg), $MeSO_2NH_2$ (6.4 mg, 0.06 mmol). After 36 h, the reaction was quenched by sat. aq. $Na_2S_2O_3$•$5H_2O$ (0.5 mL), stirred for another 5 min and extracted with EtOAc. The dried (Na_2SO_4) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 20-80% Et_2O:hexanes to give **13c** (10.4 mg, 0.022 mmol, 67%, 82:18 dr) as a yellow liquid. Major diastereomer: IR (neat) 3395, 2912, 1658, 1097 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.35-7.37 (m, 4H), 7.31-7.32 (m, 1H), 4.79 (d, *J* = 11.7 Hz, 1H), 4.54 (d, *J* = 11.7 Hz, 1H), 4.46 (d, *J* = 2.3 Hz, 1H), 4.39-4.41 (m, 2H), 4.12 (dd, *J* = 8.1, 6.0 Hz, 1H), 3.95 (br s, 1H), 3.79-3.82 (m, 1H), 3.74-3.78 (m, 1H), 3.60-3.62 (m, 1H), 2.53 (br s, 1H), 2.43 (br s, 1H), 2.03-2.07 (m, 1H), 1.94-1.98 (m, 1H), 1.84-1.88 (m, 2H), 1.44 (s, 3H), 1.39 (s, 3H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.60 (q, *J* = 8.0 Hz, 6H) ppm; HRMS (ES+) calcd. for $C_{26}H_{43}O_6Si$ (M+H) 479.2829, found 479.2822.



12d

*(S)-4-((S,Z)-8-(benzyloxy)-6-((4-methoxybenzyl)oxy)oct-2-en-4-yn-1-yl)-2,2-dimethyl-1,3-dioxolane (**12d**).* To a stirred solution of alcohol **26** (404.3 mg, 1.22 mmol) in THF (6 mL) at 0 °C was added NaH (98.0 mg, 2.44 mmol, 60% dispersion in mineral oil). After 5 min, the reaction was warmed to rt and after 40 min, it was recooled to 0°C. Next, sequentially added PMBCl (267.5 mg, 1.71 mmol, 0.23 mL) and TBAI (90.0 mg, 0.24 mmol). After 22 h, the reaction was quenched by H_2O (5 mL) and the organic solvent (THF) was removed in *vacuo* and the aqueous phase was extracted with EtOAc (3 X 5

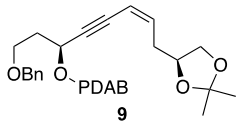
mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 3-14% EtOAc / hexanes, to give **12d** (470 mg, 1.04 mmol, 85%) as a colorless oil. $[\alpha]_D^{20}$ = -48.07° (*c* = 0.57, $CHCl_3$); IR (neat) 2986, 2868, 1612, 1514, 1249, 826 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.34-7.36 (m, 2H), 7.29-7.31 (5H), 6.88 (d, *J* = 8.5 Hz, 2H), 5.99 (dt, *J* = 10.8, 7.4 Hz, 1H), 5.68 (dd, *J* = 10.8, 1.3 Hz, 1H), 4.74 (d, *J* = 11.2 Hz, 1H), 4.44-4.51 (m, 4H), 4.22 (quint, *J* = 6.2 Hz, 1H), 4.04 (dd, *J* = 8.0, 5.9 Hz, 1H), 3.81 (s, 3H), 3.62-3.69 (m, 3H), 2.59-2.67 (m, 2H), 2.11-2.15 (m, 1H), 2.03-2.08 (m, 1H), 1.44 (s, 3H), 1.37 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 159.2, 138.4, 138.2, 130.0, 129.6, 128.3, 127.6, 127.5, 113.8, 111.4, 109.1, 93.2, 82.2, 74.8, 73.0, 70.4, 68.8, 66.4, 66.0, 55.2, 36.2, 34.4, 26.9, 25.6 ppm; HRMS (ES+) calcd. for $C_{28}H_{35}O_5$ (M+H) 451.2484, found 451.2480.



13d

*(2S,3R,6S)-8-(benzyloxy)-1-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-6-((4-methoxybenzyl)oxy)oct-4-yne-2,3-diol (**13d**).* To a stirred solution of enyne **12d** (750 mg, 1.66 mmol) in a 1:1 mixture (6.6 mL) of *t*-BuOH and H_2O was added AD mix β** (2.2 g) followed by $MeSO_2NH_2$ (158 mg, 95.1 mmol) at rt. After 36 h, added another portion of AD mix *β*** (540 mg) and after 7 h, the reaction was quenched with Na_2SO_3 (2.0 g) and extracted with EtOAc (5 x 10 mL). The dried (Na_2SO_4) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 1:1:1 EtOAc/hexanes/CH_2Cl_2 to give **13d** (539.0 mg, 1.11 mmol, 67%, 88:12 dr) as colorless oil. Major diastereomer: $[\alpha]_D^{20}$ = -49.86° (*c* = 0.74, $CHCl_3$); IR (neat) 3408, 2918, 2868, 1612, 1514, 1249, 1074 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.34-7.36 (m, 2H), 7.29-7.30

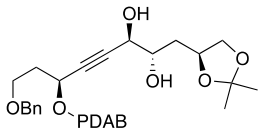
(m, 3H), 7.27 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 4.71 (d, *J* = 11.3 Hz, 1H), 4.59 (d, *J* = 12.2 Hz, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 4.43-4.45 (m, 2H), 4.35-4.38 (m, 2H), 4.10 (dd, J = 8.1, 6.0 Hz, 1H), 3.91-3.94 (m, 1H), 3.81 (s, 3H, 3.62-3.64 (m, 2H), 3.60 (dd, *J* = 7.7 Hz, 1H), 2.58 (d, *J* = 5.5 Hz, 1H), 2.45 (d, *J* = 6.0 Hz, 1H), 2.06-2.12 (m, 1H), 2.00-2.05 (m, 1H), 1.80-1.88 (m, 2H), 1.43 (s, 3H), 1.38 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 159.3, 138.3, 129.8, 129.6, 128.3, 127.7, 127.6, 113.8, 119.0, 86.1, 83.2, 73.3, 73.0, 71.5, 70.5, 69.4, 66.5, 66.1, 65.6, 55.2, 36.1, 35.9, 26.9, 25.6 ppm; HRMS (ES+) calcd. for $C_{28}H_{36}O_7Na$ (M+Na) 507.2359, found 507.2350.



9

*(S,Z)-1-(benzyloxy)-8-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)oct-6-en-4-yn-3-yl 4-(dimethylamino)benzoate (**9**).* To a stirred solution of alcohol **26** (62.0 mg, 0.187 mmol.) in CH_2Cl_2 (4 mL) was added sequentially 4-(dimethylamino)benzoic acid **SI-14** (62.0 mg, 0.375 mmol), EDC•HCl (72.0 mg, 0.375 mmol), DMAP (46.0 mg, 0.375 mmol). After 40 h, the reaction was quenched by sat. aq. NH_4Cl (4 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel (neutralized with 2% Et_3N in hexanes), eluting with 10-33% EtOAc / hexanes, to give the benzoate **9** (74.2 mg, 0.155 mmol, 83%) as a clear liquid. $[\alpha]_D^{20}$ = +40.3° (*c* = 1.03, $CHCl_3$); IR (neat) 2918, 1705, 1607, 1528, 1093 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.93 (d, *J* = 9.1 Hz, 2H), 7.32-7.36 (m, 4H), 7.26-7.28 (m, 1H), 6.66 (d, *J* = 9.1 Hz, 2H), 6.00 (dt, *J* = 10.8, 7.4 Hz, 1H), 5.91-5.93 (m, 1H), 5.62 (dq, *J* = 10.7, 1.5 Hz, 1H), 4.54 (s, 2H), 4.18 (quint, *J* = 6.3 Hz, 1H), 4.01 (dd, *J* = 8.1, 6.0 Hz, 1H), 3.68-3.74 (m, 2H), 3.59 (dd, *J* = 8.1, 7.0 Hz, 1H), 3.07 (s, 6H), 2.58-2.60

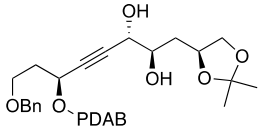
(m, 2H), 2.29-2.33 (m, 1H), 2.21-2.25 (m, 1H), 1.43 (s, 3H), 1.36 (s, 3H), ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 165.7, 153.4, 139.0, 138.2, 131.5, 128.4, 127.6, 127.5, 116.5, 111.2, 110.7, 109.0, 91.9, 81.6, 74.9, 73.1, 68.8, 66.1, 61.6, 40.1, 35.4, 34.2, 26.8, 25.7 ppm; HRMS (ES+) calcd. for $C_{29}H_{36}NO_5$ (M+H) 478.2593, found 478.2585.



10

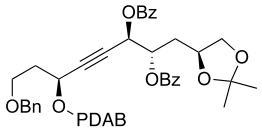
*(3S,6R,7S)-1-(benzyloxy)-8-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-6,7-dihydroxyoct-4-yn-3-yl 4-(dimethylamino)benzoate (**10**)*. To a stirred solution of enyne **9** (62.0 mg, 0.13 mmol) in a 1:1 mixture (1.4 mL) of *t*-BuOH and H_2O was added AD mix β** (360.0 mg) followed by $MeSO_2NH_2$ (13.0 mg, 0.13 mmol) at rt. After 29 h, the reaction was quenched with sat. aq. $Na_2S_2O_5$•$5H_2O$ (2 mL) and extracted with EtOAc (5 x 4 mL). The dried (Na_2SO_4) extract was concentrated *in vacuo* and purified by chromatography over silica gel (neutralized with 2% Et_3N in hexanes), eluting with 25-90% EtOAc/hexane to give **10** (54.7 mg, 0.107 mmol, 82%) as colorless oil. The diastereomeric ratio was determined from ^{1}H NMR analysis of the crude reaction mixture to be 93:7 dr (**10**:**30**). $[\alpha]_D^{20}$ = +5.22 ° (*c* = 0.44, $CHCl_3$); IR (neat) 3386, 2918, 1704, 1607, 1371 cm^{-1}; ^{1}H NMR (700 MHz, C_6D_6) δ 8.22 (d, *J* = 8.8 Hz, 2H), 7.27 (d, *J* = 7.5 Hz, 2H), 7.15-7.17 (m, 2H), 7.06-7.08 (m, 1H), 6.33 (d, *J* = 8.7 Hz, 2H), 6.09 (t, *J* = 6.8 Hz, 1H), 4.29 (s, 2H), 4.18-4.22 (m, 2H), 3.83-3.87 (m, 2H), 3.54-3.57 (m, 1H), 3.48-3.51 (m, 1H), 3.43 (t, *J* = 7.7 Hz, 1H), 2.27 (s, 6H), 2.23-2.26 (m, 1H), 2.16 (dd, *J* = 12.4, 5.6 Hz, 1H), 1.80 (ddd, *J* = 14.1, 7.9, 2.9 Hz, 1H), 1.69 (ddd, *J* = 13.8, 9.6, 4.5 Hz, 1H), 1.38 (s, 3H), 1.29 (s, 3H) pppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, C_6D_6) δ 165.8, 153.2, 138.6, 131.6, 128.2, 127.9, 127.3, 116.9, 110.8, 108.4, 84.7, 84.2, 73.4, 72.7, 71.7, 69.6, 66.5, 65.8, 61.7, 38.9,

36.5, 35.3, 26.9, 25.7 ppm; HRMS (ES+) calcd. for $C_{29}H_{37}NO_7$ (M+H) 512.2648, found 512.2640.



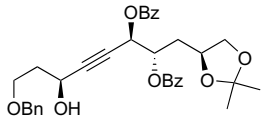
30

*(3S,6S,7R)-1-(benzyloxy)-8-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-6,7-dihydroxyoct-4-yn-3-yl 4-(dimethylamino)benzoate (**30**).* To a stirred solution of enyne **9** (12.6 mg, 0.026 mmol) in a 1:1 mixture (0.4 mL) of *t*-BuOH and H_2O was added AD mix α** (114.0 mg) followed by $MeSO_2NH_2$ (3.0 mg, 0.026 mmol) at rt. After 20 h, the reaction was quenched with sat. aq. $Na_2S_2O_5$•$5H_2O$ (1 mL) and extracted with EtOAc (5 x 3 mL). The dried (Na_2SO_4) extract was concentrated *in vacuo* and purified by chromatography over silica gel (neutralized with 2% Et_3N in hexanes), eluting with 50-100% EtOAc/hexane to give **30** (12.8 mg, 0.025 mmol, 96%) as colorless oil. The diastereomeric ratio was determined from ^1H NMR analysis of the crude reaction mixture to be 94:6 dr (**30**:**10**). $[\alpha]_D^{20}$ = +14.24 ° (*c* = 1.32, $CHCl_3$); IR (neat) 3333, 2918, 1700, 1606, 1371 cm^{-1}; ^1H NMR (700 MHz, C_6D_6) δ 8.24 (d, *J* = 8.9 Hz, 2H), 7.27 (d, J = 7.5 Hz, 2H), 7.15-7.16 (m, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.32 (d, *J* = 9.0 Hz, 2H), 6.18-6.19 (m, 1H), 4.36 (dd, *J* = 3.9, 1.4 Hz, 1H), 4.28 (s, 2H), 3.96-4.00 (m, 1H), 3.78 (dt, *J* = 8.6, 3.7 Hz, 1H), 3.74 (br s, 1H), 3.68 (dd, *J* = 8.0, 6.1 Hz, 1H), 3.56-3.59 (m, 1H), 3.49-3.52 (m, 1H), 3.28 (t, *J* = 7.7 Hz, 1H), 2.26-2.29 (m, 8H), 2.16-2.21 (m, 1H), 1.88 (dt, *J* = 14.1, 8.7 Hz, 1H), 1.63 (dt, *J* = 14.1, 3.7 Hz, 1H), 1.29 (s, 3H), 1.19 (s, 3H), ppm; $^{13}C\{^1H\}$ NMR (175 MHz, C_6D_6) δ 165.7, 153.2, 138.7, 131.6, 128.2, 128.0, 127.3, 117.0, 110.7, 108.9, 84.4, 84.2, 74.3, 72.8, 72.7, 69.4, 65.9, 65.8, 61.6, 38.9, 35.5, 35.4, 26.6, 25.6 ppm.



SI-37

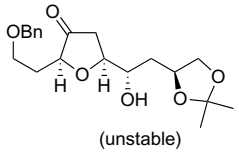
*(2S,3R,6S)-8-(benzyloxy)-1-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-6-((4-(dimethylamino)benzoyl)oxy)oct-4-yne-2,3-diyl dibenzoate (**SI-37**).* To a stirred solution of diol **10** (320.0 mg, 0.63 mmol) in CH_2Cl_2 (7.5 mL) and Et_3N (7.5 mL) at 0 °C was added DMAP (15.0 mg, 0.12 mmol) followed by benzoyl chloride (354.2 mg, 0.29 mL, 2.52 mmol). After 5 min, the reaction mixture was warmed to rt. After 28 h, the brown reaction mixture was quenched with sat. aq. $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by column chromatography over silica gel, eluting with 5-25% EtOAc/Hexanes to obtain **SI-37** (435.3 mg, 0.60 mmol, 96%) as a sticky yellow oil. $[\alpha]_D^{20}$ = -52.8° (*c* = 0.66, $CHCl_3$); IR (neat) 2930, 2868, 1725, 1607, 1270 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.00 (t, *J* = 7.9 Hz, 4H), 7.93 (d, *J* = 9.0 Hz, 2H), 7.55-7.58 (m, 1H), 7.52-7.54 (m, 1H), 7.30-7.36 (m, 6H), 7.25-7.27 (m, 1H), 6.65 (d, *J* = 8.9 Hz, 2H), 6.07-6.08 (m, 1H), 5.88 (t, *J* = 6.8 Hz, 1H), 5.66 (dt, *J* = 9.5, 3.0 Hz, 1H), 4.48-4.52 (m, 2H), 4.21-4.25 (m, 1H), 4.04 (dd, *J* = 8.1, 6.1 Hz, 1H), 3.66-3.72 (m, 2H), 3.63 (d, *J* = 7.3 Hz, 1H), 3.07 (s, 6H), 2.26-2.32 (m, 2H), 2.17-2.24 (m, 2H), 1.43 (s, 3H), 1.33 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 165.6, 165.5, 165.0, 153.5, 138.2, 133.3, 133.1, 131.6, 129.9, 129.8, 129.7, 129.4, 128.4, 128.3, 127.6, 127.5, 116.4, 110.7, 109.1, 85.7, 78.9, 73.1, 72.7, 71.8, 69.6, 65.9, 65.8, 60.8, 40.1, 35.1, 34.6, 27.0, 25.7 ppm; HRMS (ES+) calcd. for $C_{43}H_{46}NO_9$ (M+H) 720.3173, found 720.3171.



27

*(2S,3R,6S)-8-(benzyloxy)-1-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-6-hydroxyoct-4-yne-2,3-diyl dibenzoate (**27**).* To a stirred solution of tribenzoate **SI-37** (14.4 mg, 20.0 □mol) in CH_2Cl_2 (0.3 mL) at 0 °C were added sequentially $NaHCO_3$ (3.0 mg, 36.0 □mol), MeOTf (3.9 mg, 2.6 □L, 24.0 □mol). After 15 minutes, the reaction was warmed up to rt. After 12 h, the solvent (CH_2Cl_2) was evaporated with Ar flush and MeOH (0.2 mL) was added. After an additional 1 h, another portion of $NaHCO_3$ (2.1 mg, 25.0 □mol) was added. After 4 h, the reaction was diluted with EtOAc (1 mL) and quenched with sat. aq. NH_4Cl (1 mL) and extracted with EtOAc (3 x 3 mL).The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by column chromatography over silica gel, eluting with 5-25% EtOAc/Hexanes to obtain **27** (8.0 mg, 13.97 □mol, 70%) as a sticky yellow oil. $[\alpha]_D^{20}$ = -50.37° (*c* = 0.81, $CHCl_3$); IR (neat) 3428, 3064, 2985, 2871, 1726, 1274, 1095, 1026 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.03 (ddd, *J* = 18.5, 8.0, 1.0 Hz, 4H), 7.56-7.59 (m, 2H), 7.43 (td, *J* = 7.8, 3.5 Hz, 4H), 7.32-7.34 (m, 2H), 7.28-7.29 (m, 2H), 6.06 (dd, *J* = 3.3, 1.5 Hz, 1H), 5.64 (dt, *J* = 9.7, 3.3 Hz, 1H), 4.68-4.71 (m, 1H), 4.51 (d, *J* = 11.8 Hz, 1H), 4.48 (d, *J* = 11.8 Hz, 1H), 4.23-4.27 (m, 1H), 4.05 (dd, *J* = 8.0, 5.9 Hz, 1H), 3.86 (td, *J* = 9.1, 4.0 Hz, 1H), 3.68 (ddd, *J* = 9.9, 5.4, 4.6 Hz, 1H), 3.64 (dd, *J* = 8.0, 6.7 Hz, 1H), 3.12 (d, *J* = 6.6 Hz, 1H), 2.33 (ddd, *J* = 14.4, 8.1, 3.4 Hz, 1H), 2.19 (ddd, *J* = 14.6, 9.7, 5.0 Hz, 1H), 2.12 (ddt, *J* = 14.5 , 8.7, 4.4 Hz, 1H), 1.96 (dtd, *J* = 14.5, 5.9, 4.0 Hz, 1H), 1.44 (s, 3H), 1.33 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 165.6, 165.1, 137.7, 133.4, 133.3, 129.9, 129.8, 129.7, 129.4, 128.4, 127.8, 127.6, 109.0, 88.1,

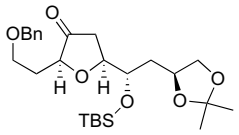
78.6, 73.4, 72.7, 71.9, 69.5, 67.6, 65.6, 61.4, 36.4, 34.4, 27.0, 25.6 ppm; HRMS (ES+) calcd. for $C_{34}H_{36}O_8Na$ (M+Na) 595.2308, found 595.2286.



(unstable)

28a

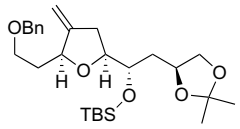
*(2S,5S)-2-(2-(benzyloxy)ethyl)-5-((S)-2-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-1-hydroxyethyl)dihydrofuran-3(2H)-one (**28a**).* To a stirred solution of alcohol **27** (226.0 mg, 0.395 mmol) in toluene (4 mL) was added $AgBF_4$ (7.0 mg, 0.04 mmol). The reaction mixture was refluxed in dark. After 40 min, the reaction was cooled down to -78 °C and diluted with Et_2O (4 mL). After 5 min, MeLi•LiBr (1.44 mL, 3.16 mmol, 2.2 M in Et_2O) was added. After 2 h, the reaction was quenched with aq. sat. NH_4Cl (4 mL) and extracted with EtOAc (3 x 10 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to obtain the crude alcohol **28a** as colorless oil which was used in the next step without further purification.



29

*(2S,5S)-2-(2-(benzyloxy)ethyl)-5-((S)-1-((tert-butyldimethylsilyl)oxy)-2-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)dihydrofuran-3(2H)-one (**29**).* To a stirred solution of crude alcohol **28a** in CH_2Cl_2 (5.6 mL) at -78 °C was added 2,6-lutidine (254.0 mg, 0.28 mL, 2.37 mmol) followed by TBSOTf (418.0 mg, 0.36 mL, 1.58 mmol). After 2 h, the reaction was quenched with aq. sat. $NaHCO_3$ (5 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5-17% EtOAc/hexanes to obtain **29** (119.0 mg, 0.248 mmol, 63%

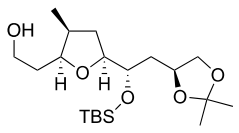
over 3 steps) as a colorless oil. $[\alpha]_D^{20}$ = -13.33° (*c* = 0.51, $CHCl_3$); IR (neat) 2927, 2857, 1761, 1472, 1251, 1104 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.29-7.36 (m, 5H), 4.52 (d, *J* = 12.1 Hz, 1H), 4.46 (d, *J* = 12.0 Hz, 1H), 4.25-4.29 (m, 1H), 4.09-4.12 (m, 1H), 4.04-4.08 (m, 2H), 3.93 (dd, *J* = 5.9, 5.3 Hz, 1H), 3.70 (dt, *J* = 9.2, 6.6 Hz, 1H), 3.59 (dt, *J* = 9.4, 6.2 Hz, 1H), 3.5 (t, *J* = 7.5 Hz, 1H), 2.37 (dd, *J* = 17.9, 6.2 Hz, 1H), 2.31 (dd, *J* = 17.9, 10.6 Hz, 1H), 2.05-2.10 (m, 1H), 1.94-1.99 (m, 1H), 1.68 (ddd, *J* = 12.9, 9.2, 2.2 Hz, 1H), 1.55-1.57 (m, 1H), 1.42 (s, 3H), 1.36 (s, 3H), 0.90 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 215.1, 138.2, 128.3, 127.6, 127.5, 108.8, 78.9,78.4, 72.7, 72.2, 71.2, 69.8, 65.8, 38.8, 36.8, 30.9, 27.1, 25.9, 25.7, 18.2, -4.1, -4.6 ppm; HRMS (ES+) calcd. for $C_{26}H_{43}O_6Si$ (M+H) 479.2829, found 479.2846.



SI-38

*((S)-1-((2S,5S)-5-(2-(benzyloxy)ethyl)-4-methylenetetrahydrofuran-2-yl)-2-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)(tert-butyl)dimethylsilane (**SI-38**).* To a stirred solution of ketone **29** (119.0 mg, 0.248 mmol) in toluene (2.6 mL) was added Cp_2TiMe_2[38] (2.8 mL, 1.244 mmol, 0.46 M in THF) and the reaction mixture was heated to 78 °C in the dark. After 16.5 h, added another portion of Cp_2TiMe_2 (2.8 mL, 1.244 mmol, 0.46 M in THF). After another 4 h, the reaction mixture was passed through a small silica plug and the organic solvent (toluene) was removed *in vacuo* and purified by chromatography over silica gel, eluting with 5-8% EtOAc/hexanes to obtain the alkene **SI-38** (89.1 mg, 0.187 mmol, 75%) as colorless oil. $[\alpha]_D^{20}$ = -28.37° (*c* = 0.49, $CHCl_3$); IR (neat) 2926, 2854, 1463, 1369, 1100, 837 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.36 (d, *J* = 4.5 Hz, 4H), 7.29-7.31 (m, 1H), 4.97 (d, *J* = 1.8 Hz, 1H), 4.85 (d, *J* = 1.9 Hz, 1H), 4.56 (d, *J* =

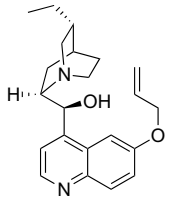
11.8 Hz, 1H), 4.51 (d, *J* = 11.9 Hz, 1H), 4.39 (d, J = 8.6 Hz, 1H), 4.26-4.29 (m, 1H), 4.06 (dd, *J* = 5.9, 7.8 Hz, 1H), 3.96 (ddd, *J* = 9.7, 6.2, 2.4 Hz, 1H), 3.80 (dt, *J* = 10.0, 6.1 Hz, 1H), 3.66 (dd, *J* = 7.5, 6.2 Hz, 2H), 3.51 (t, *J* = 7.6 Hz, 1H), 2.49 (dd, *J* = 15.7, 5.9 Hz, 1H), 2.32-2.36 (m, 1H), 2.03 (dtd, *J* = 15.2, 7.6, 3.4 Hz, 1H), 1.82 (ddt, *J* = 14.5, 8.7, 5.9 Hz, 1H), 1.67 (ddd, *J* = 13.6, 8.8, 2.4 Hz, 1H), 1.54 (ddd, *J* = 13.8, 10.0, 3.8 Hz, 1H), 1.42 (s, 3H), 1.36 (s, 3H), 0.91 (s, 9H), 0.11 (s, 3H), 0.11 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 151.1, 138.5, 128.3, 127.7, 127.5, 108.6, 104.4, 81.4, 78.0, 73.1, 72.5, 71.5, 69.9, 67.3, 36.8, 35.5, 34.7, 27.1, 26.0, 25.8, 18.2, -4.1, -4.7 ppm; HRMS (ES+) calcd. for $C_{27}H_{44}O_5NaSi$ (M+Na) 499.2856, found 499.2867..



11

*2-((2S,3S,5S)-5-((S)-1-((tert-butyldimethylsilyl)oxy)-2-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-3-methyltetrahydrofuran-2-yl)ethan-1-ol (**11**).* To a stirred solution of alkene **SI-38** (42.0 mg, 88.10 *μ*mol) in EtOAc (1.4 mL) under argon atmosphere at rt was added 10 % Pd/C (13.2 mg, 30% by wt). The argon was then removed by flushing with H_2 gas. After 5 min, the reaction was sealed under 1 atm of H_2 (balloon). After 30 h, the hydrogen was removed by flushing with argon, and the reaction mixture was filtered through Celite-® washing with EtOAc (10 mL). The filtered extract was concentrated in vacuo and purified by chromatography over silica gel, eluting with 17-50% EtOAc/hexanes to obtain the known compound[Error! Bookmark not defined.] **11** (29.0 mg, 74.62 *μ*mol, 85%, 5.5:1 dr) as colorless oil. ^{1}H NMR (700 MHz, $CDCl_3$) δ 4.23-4.27 (m, 1H), 4.06 (dd, *J* = 7.6, 6.0 Hz, 1H), 4.01 (ddd, *J* = 10.3, 7.2, 2.6 Hz, 1H), 3.95 (ddd, *J* = 8.6, 5.5, 2.8 Hz, 1H), 3.78-3.82 (m, 3H), 3.50 (t, *J* = 7.7 Hz, 1H), 2.55 (br s, 1H), 2.33-2.37

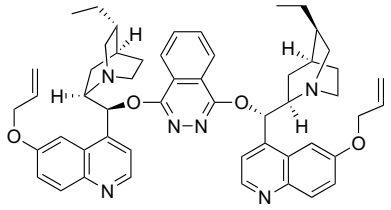
(m, 1H), 1,97 (dt, *J* = 12.4, 6.9 Hz, 1H), 1.66-1.75 (m, 3H), 1.57-1.60 (m, 2H), 1.41 (s, 3H), 1.36 (s, 3H), 0.96 (d, *J* = 7.1 Hz, 3H), 0.92 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (175 MHz, $CDCl_3$) δ 108.7, 82.1, 81.3, 72.5, 70.8, 69.9, 61.9, 37.2, 35.7, 34.9, 33.1, 27.1, 25.9, 25.8, 18.2, 15.3, -4.1, -4.6 ppm.



SI-40

*(S)-(6-(allyloxy)quinolin-4-yl)((1S,2R,4S,5R)-5-ethylquinuclidin-2-yl)methanol (**SI-40**).* To a stirred solution of known 4-((*S*)-((1*S*,2*R*,4*S*,5*R*)-5-ethylquinuclidin-2-yl)(hydroxy)methyl)quinolin-6-ol (**SI-39**)[39] (670.0 mg, 2.145 mmol) in acetone (214 mL) at rt was added Cs_2CO_3 (1.75 g, 5.362 mmol). After 30 min, allyl bromide (285.0 mg, 2.36 mmol, 0.2 mL) was added. After 24 h, the reaction was quenched by sat. aq. NH_4Cl C (15 mL) and evaporated the organic solvent (acetone) before extracting with 10% MeOH in CH_2Cl_2 (3 X 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel (neutralized with 2% Et_3N in CH_2Cl_2), eluting with 5-7% MeOH/ CH_2Cl_2, to give **SI-40** (527.6 mg, 1.497 mmol, 70%). $[\alpha]_D^{20}$ = +28.0° (*c* = 1.05, $CHCl_3$); IR (neat) 3252, 2961, 1619, 1508, 1241 cm^{-1}; ^{1}H NMR (700 MHz, CD_3OD) δ 8.74 (d, *J* = 4.6 Hz, 1H), 8.01 (d, *J* = 9.2 Hz, 1H), 7.80 (d, *J* = 4.5 Hz, 1H), 7.51 (dd, *J* = 9.2, 2.6 Hz, 1H), 7.47 (d, *J* = 2.6 Hz, 1H), 6.16-6.22 (m, 2H), 5.52 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.32 (dq, *J* = 10.7, 1.4 Hz, 1H), 4.86-4.87 (m, 1H), 4.82-4.85 (m, 1H), 3.98 (ddd, *J* = 11.8, 8.6, 2.1 Hz, 1H), 3.59 (t, *J* = 9.3 Hz, 1H), 3.46-3.49 (m, 2H), 3.27-3.31 (m, 1H), 2.43-2.47 (m, 1H), 2.00 (s, 1H), 1.83-1.95 (m, 3H), 1.61-1.73 (m, 2H), 1.23 (ddd, *J* = 13.6, 9.7, 4.3 Hz, 1H), 0.99 (t, *J* = 7.4 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR

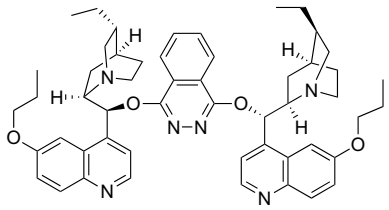
(175 MHz, CD_3OD) δ 157.6, 146.9, 145.8, 143.4, 133.1, 130.3, 126.1, 122.5, 118.9, 116.3, 101.9, 69.2, 67.4, 59.9, 50.1, 49.2, 34.9, 25.1, 24.0, 23.3, 17.5, 10.4 ppm; HRMS (ES+) calcd. for $C_{22}H_{29}N_2O_2$ (M+H) 353.2229, found 353.2222.



SI-42

*1,4-bis((S)-(6-(allyloxy)quinolin-4-yl)((1S,2R,4S,5R)-5-ethylquinuclidin-2-yl)methoxy)phthalazine (**SI-42**).* To a stirred solution of alcohol **SI-40** (91.4 mg, 0.259 mmol) in THF (1.5 mL) at 0 °C was added NaH (12.0 mg, 0.287 mmol, 60% dispersion in mineral oil). After 5 min, the reaction was refluxed for 50 min and then cooled to rt and 1,4-dichlorophthalazine **SI-41** (26.0 mg, 0.130 mmol) was added and refluxed. After an additional 5 h, another portion of NaH (12.0 mg, 0.287 mmol, 60% dispersion in mineral oil) was added at rt and reflux was continued. After 18 h, the reaction was cooled to 0 °C and quenched by H_2O (2 mL) and extracted with EtOAc (3 X 5 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel (neutralized with 2% Et_3N in CH_2Cl_2), eluting with 10-20% MeOH/EtOAc, to give [(Allyl-DHQD)$_2$PHAL] **SI-42** (56.6 mg, 0.068 mmol, 52%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.67 (d, *J* = 4.5 Hz, 2H), 8.33 (dd, *J* = 6.1, 3.2 Hz, 2H), 8.01 (d, *J* = 9.2 Hz, 2H), 7.94 (dd, *J* = 6.0, 3.4 Hz, 2H), 7.61 (d, *J* = 2.5 Hz, 2H), 7.45 (d, *J* = 4.5 Hz, 2H), 7.40 (dd, *J* = 9.1, 2.6 Hz, 2H), 6.97 (d, *J* = 6.0 Hz, 2H), 6.09-6.15 (m, 2H), 5.48 (dq, *J* = 17.3, 1.5 Hz, 2H), 5.31 (dq, *J* = 10.6, 1.3 Hz, 2H), 4.64-4.71 (m, 4H), 3.41-3.44 (m, 2H), 2.76-2.83 (m, 4H), 2.65-2.74 (m, 4H), 1.95-1.98 (m, 2H), 1.71 (br s, 2H), 1.52-1.59 (m, 4H), 1.44-1.48 (m, 2H), 1.39-1.43 (m, 6H), 0.82 (t, *J* = 7.1 Hz, 6H) ppm; ^{13}C{^{1}H} NMR (175 MHz,

$CDCl_3$) δ 156.5, 156.4, 147.5, 144.9, 144.8, 132.9, 132.1, 131.6, 127.3, 122.8, 122.5, 122.0, 118.8, 117.9, 103.4, 76.5, 69.1, 60.2, 50.9, 50.0, 37.5, 27.3, 26.3, 25.3, 23.5, 11.9 ppm.



SI-43

*1,4-bis((S)-((1S,2R,4S,5R)-5-ethylquinuclidin-2-yl)(6-propoxyquinolin-4-yl)methoxy)phthalazine (**SI-43**).* To a stirred solution of alkene **SI-42** (74.0 mg, 90.0 *μ*mol) in EtOAc (2 mL) under argon atmosphere at rt was added 10 % Pd/C (10.0 mg, 10% by wt). The argon was then removed by flushing with H_2 gas. After 5 min, the reaction was sealed under 1 atm of H_2 (balloon). After 24 h, the hydrogen was removed by flushing with argon, and the reaction mixture was filtered through Celite-® washing with EtOAc (10 mL). The filtered extract was concentrated in vacuo and purified by chromatography over silica gel (neutralized with 1% Et_3N in hexanes), eluting with 16-25% MeOH/ EtOAc to obtain [(Pr-DHQD)$_2$PHAL] **SI-43** (70.0 mg, 83.7 *μ*mol, 93%). $[\alpha]_D^{20}$ = -125.0° (*c* = 0.16, $CHCl_3$); IR (neat) 2923, 2871, 1620, 1461 cm^{-1}; ^1H NMR (700 MHz, CD_3OD at 60 °C) δ 8.56 (d, *J* = 4.7 Hz, 1H), 8.48 (dd, *J* = 6.2, 3.2 Hz, 1H), 8.12 (dd, *J* = 6.0, 3.3 Hz, 1H), 7.95 (d, *J* = 9.2 Hz, 1H), 7.58-7.59 (m, 2H), 7.44 (dd, *J* = 9.2, 2.6 Hz, 1H), 7.13 (d, *J* = 4.9 Hz, 1H), 4.05-4.11 (m, 2H), 3.48 (td, *J* = 9.1, 5.0 Hz, 1H), 2.87-2.95 (m, 3H), 2.75-2.79 (m, 1H), 2.26-2.29 (m, 1H), 1.83-1.88 (m, 2H), 1.79 (br s, 1H), 1.65-1.69 (m, 1H), 1.55-1.58 (m, 5H), 1.29 (t, *J* = 7.4 Hz, 1H), 1.05 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (175 MHz, CD_3OD) δ 157.9, 156.3,

146.4, 144.4, 143.5, 133.1, 129.9, 127.0, 122.8, 122.7, 122.1, 118.0, 101.7, 75.1, 69.7, 59.3, 50.4, 49.4, 36.4, 26.1, 25.6, 24.9, 22.2, 21.2, 10.6, 9.5 ppm; HRMS (ES+) calcd. for $C_{52}H_{63}N_6O_4$ (M+H) 835.4911, found 835.4924.

Acknowledgement. Prof. Claudia Maier (OSU) and Jeff Morré (OSU) are acknowledged for mass spectra data.

Funding Sources. Financial support provided by the National Science Foundation (CHE-1665246) and Oregon State University (Milton Harris fellowship for A.G.). No competing financial interests have been declared.

Supporting Information. The supporting information including ^{1}H, $^{13}C\{1H\}$ NMR spectra and HPLC chromatogram are available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Jørgensen, K. A. Transition-metal-catalyzed epoxidations. *Chem. Rev.* **1989**, *89*, 431-458. (b) Katsuki, T; Martin, V. Asymmetric Epoxidation of Allylic Alcohols: the Katsuki–Sharpless Epoxidation Reaction. *Org. React.* **1995**, *48*, 1. (c) Davis, R. L.; Stiller, J.; Naicker, T.; Jiang, H.; Jørgensen, K. A. Asymmetric Organocatalytic Epoxidations: Reactions, Scope, Mechanisms, and Applications. *Angew. Chem. Int. Ed*. **2014**, *53*, 7406-7426. (d) Zhu, Y.; Wang, Q.; Cornwall, R. G.; Shi, Y. Organocatalytic Asymmetric Epoxidation and Aziridination of Olefins and Their Synthetic Applications. *Chem. Rev. 2014*, **114**, 8199-8256. (e) Shi, Y. Organocatalytic Asymmetric Epoxidation of Olefins by Chiral Ketones. *Acc. Chem. Res*. **2004**, *37*, 488−496.

(2) Sawano, T; Yamamoto, H.; Substrate-Directed Catalytic Selective Chemical Reactions. *J. Org. Chem.* **2018**, *83*, 4889-4904.

(3) Johnson, R. A.; Sharpless, K. B. Catalytic Asymmetric Epoxidation of allylic alcohols. Ojima, I. Ed. *Catalytic Asymmetric Synthesis (2nd Edition)* **2000**, 231-280.

(4) Tu, Y.; Wang, Z.-X.; Shi, Y. An Efficient Asymmetric Epoxidation Method for trans-Olefins Mediated by a Fructose-Derived Ketone. *J. Am. Chem. Soc.* **1996**, *118*, 9806-9807.

(5) (a) E. N. Jacobsen, W. Zhang, A. R. Muci, J. R. Ecker, L. Deng. Highly enantioselective epoxidation catalysts derived from 1,2-diaminocyclohexane. *J. Am. Chem. Soc.*, **1991**, *113*, 7063-7064. (b) Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. An Efficient Catalytic Asymmetric Epoxidation Method. *J. Am. Chem. Soc.* **1997**, *119*, 11224−11235.

(6) (a) Tian, H.; She, X.; Shu, L.; Yu, H.; Shi, Y. Highly Enantioselective Epoxidation of cis-Olefins by Chiral Dioxirane. *J. Am. Chem. Soc.* **2000**, *122*, 11551-11552. (c) Tian, H.; She, X.; Yu, H.; Shu, L.; Shi, Y. Designing New Chiral Ketone Catalysts. Asymmetric Epoxidation of cis-Olefins and Terminal Olefins. *J. Org. Chem.* **2002**, *67*, 2435-2446.

(7) (a) Martinez, L. E.; Leighton, J. L.; Carsten, D. H.; Jacobsen, E. N. Highly Enantioselective Ring Opening of Epoxides Catalyzed by (salen)Cr(III) Complexes. *J. Am. Chem. Soc.* **1995**, *117*, 5897−5898. (b) Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. Asymmetric catalysis with water: efficient kinetic resolution of terminal epoxides by means of catalytic hydrolysis. *Science* **1997**, *277*, 936−938. (c) Jacobsen,

E. N. Asymmetric Catalysis of Epoxide Ring-Opening Reactions. *Acc. Chem. Res.* **2000**, *33*, 421-431.

(8) Kolb, H. C.; VanNieuwehze, M. S.; Sharpless, K. B. Catalytic Asymmetric Dihydroxylation. *Chem. Rev.* 1994, 94, 2483-2547.

(9) Dornan; P. K.; Zachary K Wickens; Z. K.; Grubbs, R. H. Tandem Z-selective cross metathesis – dihydroxylation for the synthesis of anti-1,2-diols. *Angew. Chem. Int. Ed*. **2015**, *54*, 7134-7138.

(10) Wang, L.; Sharpless, K. B. Catalytic asymmetric dihydroxylation of cis-disubstituted olefins. *J. Am. Chem. Soc*. **1992**, *114*, 7568-7570. (b) VanNieuwenhze, M. S.; Sharpless, K. B. The asymmetric dihydroxylation of cis-allylic and homoallylic alcohols. *Tetrahedron Lett.* **1994**, *35*, 843.

(11) (a) Dong, S.; Paquette, L. A. Stereoselective Synthesis of Conformationally Constrained 2‘-Deoxy-4‘-thia β-Anomeric Spirocyclic Nucleosides Featuring Either Hydroxyl Configuration at C5’. *J. Org. Chem.* **2005**, *70*, 1580-1596. (b) Halim, R.; Brimble, M. A.; Merten, J. Synthesis of the ABC Fragment of the Pectenotoxins. *Org. Lett.* **2005**, *7*, 2659-2662. (c) Hicks, J. D.; Flamme, E. M.; Roush, W. R. Synthesis of the C(43)−C(67) Fragment of Amphidinol 3. *Org. Lett.* **2005**, *7*, 5509-5512. (d) Ermolenko, L.; Sasaki, N. A. Diastereoselective Synthesis of All Eight L-Hexoses from L-Ascorbic Acid. *J. Org. Chem.* **2006**, *71*, 693-703. (e) Yuen, T.Y.; Brimble, M. A. Total Synthesis of 7′,8′-Dihydroaigialospirol. *Org. Lett.* **2012**, *14*, 5154-5157.

(12) (a) Araki, S.; Butsugan, Y. Electrophilic substitution reaction of meso-ionic sesquifulvalene. *Tetrahedron Lett.* **1984,** *25*, 441-445. (b) Palazon, J. M.; Anorbe, B.; Martin, V. S. General method to transform chiral 2,3-epoxyalcohols into erythro or threo

1,2-epoxyalcohols with total stereochemical control. *Tetrahedron Lett.* **1986,** *27*, 4987-4990. (c) Prestwich, G. D.; Graham, S. McG.; Kuo, J.-W.; Vogt, R. G. Tritium-labeled enantiomers of disparlure. Synthesis and in vitro metabolism. *J. Am. Chem. Soc.* **1989**, *111*, 636–642.

(13) (a) Lohray, B. B. Cyclic Sulfites and Cyclic Sulfates: Epoxide like Synthons. *Synthesis* **1992**, 1035-1052. (b) Megia-Fernandez, A.; Morales-Sanfrutos, J.; Hernandez-Mateo, F.; Santoyo- Gonzalez, F. Synthetic Applications of Cyclic Sulfites, Sulfates and Sulfamidates in Carbohydrate Chemistry. *Curr. Org. Chem.* **2011**, *15,* 401-432.

(14) Veerasamy, N.; Ghosh, A.; Li, J.; Watanabe, K.; Serrill, J. D.; Ishmael, J. E.; McPhail, K. L.; Carter, R. G. Enantioselective Total Synthesis of Mandelalide A and Isomandelalide A: Discovery of a Cytotoxic Ring-Expanded Isomer. *J. Am. Chem. Soc.* **2016**, *138*, 770-773.

(15) (a) Tietze, L. F.; Gorlitzer, J. Efficient Enantioselective Synthesis of Chiral Precursors for the Preparation of Vitamin E. *LiebigsAnn. Recueil.* **1997***,* 2221-2225. (b) Alvarez, S.; Alvarez, R.; de Lera, A. R. Enantioselective synthesis of all of the stereoisomers of (E)-13,14-dihydroxyretinol (DHR).*Tetrahedron: Asymmetry.* **2004**, *15*, 839–846. (c) Ji, N.; O'Dowd, H.; Rosen, B. M.; Myers, A. G. Enantioselective Synthesis of N1999A2. *J. Am. Chem. Soc.* **2006**, *128*, 14825-14827. (d) Burghart-Stoll, H.; Kapferer, T.; Bruckner, R. Asymmetric Dihydroxylations of Enynes with a Trisubstituted C═C Bond. An Unprecedented Route to γ-Lactone Building Blocks with a Quaternary Stereocenter. *Org. Lett.* **2011**, *13,* 1016-1019.

(16) Naysmith, B. J.; Furkert, D.; Brimble, M. A. Synthesis of highly substituted pyranonaphthalene spiroketals related to the griseusins using a HausereKraus annulation strategy. *Tetrahedron*. **2014**, *70*, 1199-1206.

(17) (a) Corey, E. J.; Guzman-Perez, A.; Noe, M. C. The application of a mechanistic model leads to the extension of the Sharpless asymmetric dihydroxylation to allylic 4-methoxybenzoates and conformationally related amine and homoallylic alcohol derivatives. *J. Am. Chem. Soc.* **1995**, *117*, 10805-10816. (b) Zhao, Y.; Xing, X.; Zhang, S.; Wang, D. Z. N,N-Dimethylaminobenzoates enable highly enantioselective Sharpless dihydroxylations of 1,1-disubstituted alkenes. *Org. Biomol. Chem*. **2014**, *12*, 4314-4317.

(18) Carter, R. G.; Weldon, D. J. Studies Directed toward the Total Synthesis of Azaspiracid: Stereoselective Construction of C1−C12, C13−C19, and C21−C25 Fragments. *Org. Lett.* **2000**, *2,* 3913-3916.

(19) Krenske, E. H.; Houk, K. N. Aromatic Interactions as Control Elements in Stereoselective Organic Reactions. *Acc. Chem. Res.* **2013**, *46*, 979-989.

(20) Corey, E. J.; Noe, M. C. A Critical Analysis of the Mechanistic Basis of Enantioselectivity in the Bis-Cinchona Alkaloid Catalyzed Dihydroxylation of Olefins. *J. Am. Chem. Soc.* **1996**, *118*, 11038-1105.

(21) (a) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. High-field FT NMR application of Mosher's method. The absolute configurations of marine terpenoids. *J. Am. Chem. Soc*. **1991**, *113*, 4092-4096. (b) Dale, J. A.; Mosher, H. S. Nuclear magnetic resonance enantiomer regents. Configurational correlations via nuclear magnetic resonance chemical shifts of diastereomeric mandelate, O-methylmandelate, and

.alpha.-methoxy-.alpha.-trifluoromethylphenylacetate (MTPA) esters. *J. Am. Chem. Soc.* **1973**, *95*, 512-519. (c) Sullivan, G. R.; Dale, J. A.; Mosher, H. S. Correlation of configuration and fluorine-19 chemical shifts of .alpha.-methoxy-.alpha.-trifluoromethylphenyl acetate derivatives. *J. Org. Chem*. **1973**, *38*, 2143-2149.

(22) Becke, A. D. Density-functional thermochemistry. III. The role of exact exchange. *J. Chem. Phys.*, **1993**, *98*, 5648-5652.

(23) (a) Dunning Jr., T. H.; Hay, P. J. in *Modern Theoretical Chemistry*, Ed. H. F. Schaefer III, Vol. 3 (Plenum, New York, 1977) 1-28; (b) Hay, P. J.; Wadt, W. R. Ab initio effective core potentials for molecular calculations. Potentials for the transition metal atoms Sc to Hg. *J. Chem. Phys.* **1985**, *82*, 270-283; (c) Wadt, W. R.; Hay, P. Ab initio effective core potentials for molecular calculations. Potentials for main group elements Na to Bi. J. *J. Chem. Phys.* **1985**, *82*, 284-298; (d) Hay, P. J.; Wadt, W. R. Ab initio effective core potentials for molecular calculations. Potentials for K to Au including the outermost core orbitals. *J. Chem. Phys.* **1985**, *82*, 299-310.

(24) Hehre, W. J.; Ditchfield, R.; Pople, Self—Consistent Molecular Orbital Methods. XII. Further Extensions of Gaussian—Type Basis Sets for Use in Molecular Orbital Studies of Organic Molecules. *J. A. J. Chem. Phys.* **1972**, *56*, 2257-2261.

(25) Grimme, S.; Ehrlich, S.; Goerigk, L. Effect of the damping function in dispersion corrected density functional theory. *J. Comput. Chem.* **2011**, *32*, 1456-1465.

(26) Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. A consistent and accurate ab initio parametrization of density functional dispersion correction (DFT-D) for the 94 elements H-Pu. *J. Chem. Phys.* **2010**, *132*, 154104.

(27) Miertuš, S.; Scrocco, E.; Tomasi, J. Electrostatic interaction of a solute with a continuum. A direct utilizaion of AB initio molecular potentials for the prevision of solvent effects. *Chem. Phys.* **1981**, *55*, 117−129.

(28) Martin, J. M. L.; Sundermann, A. Correlation consistent valence basis sets for use with the Stuttgart–Dresden–Bonn relativistic effective core potentials: The atoms Ga–Kr and In–Xe. *J. Chem. Phys.* **2001**, *114*, 3408-3420.

(29) Hariharan, P. C.; Pople, J. A. The influence of polarization functions on molecular orbital hydrogenation energies. *Theor. Ceim. Acc.* **1973**, *28*, 213−222.

(30) (For complete author list, see SI). Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; et al. *Gaussian 09*; Gaussian Inc.: Wallingford, CT, 2009.

(31) Bickelhaupt, F. M.; Houk, K. N. Analyzing Reaction Rates with the Distortion/Interaction-Activation Strain Model. *Angew. Chem. Int. Ed.* **2017**, *56*, 10070-10086.

(32) AD mix L** are prepared in mol:mol ratios of 3:1:95:92 [Ligand:K_2OsO_4•H_2O:K_2CO_3:$K_3Fe(CN)_6$] where the ligand for AD mix α** is $(DHQ)_2PHAL$ and AD mix β** is $(DHQD)_2PHAL$.

(33) De La Cruz, L. K. C., Benoit, S. L., Pan, Z., Yu, B., Maier, R. J., Ji, X., Wang, B. Click, Release, and Fluoresce: A Chemical Strategy for a Cascade Prodrug System for Codelivery of Carbon Monoxide, a Drug Payload, and a Fluorescent Reporter. *Org. Lett.* **2018**, *20*, 897-900.

(34) Rao, S. A.; Knochel, P. Stereospecific preparation of polyfunctional olefins by the carbometalation of alkynes with polyfunctional zinc-copper organometallics.

Stereospecific preparation of five-membered carbocycles by intramolecular carbocupration. *J. Am. Chem. Soc.* **1991**, *113*, 5735-5741.

(35) Francesch, A.; A´ lvarez, R.; Lo´pez, S.; de Lera, A. R. Synthesis of Retinals Fluorinated at Odd-Numbered Side-Chain Positions and of the Corresponding Fluorobacteriorhodopsins. *J. Org. Chem.* **1997**, *62*, 310–319.

(36) Kojima, A.; Honzawa, S.; Boden, C. D. J.; Shibasaki, M. Tandem Suzuki cross-coupling-Heck reactions. *Tetrahedron Lett*. **1997***, 38*, 3455-3458.

(37) Gabriele, B.; Salerno, G.; Lauria, E. A General and Facile Synthesis of Substituted Furans by Palladium-Catalyzed Cycloisomerization of (*Z*)-2-En-4-yn-1-ols. *J. Org. Chem.* **1999**, *64*, 7687−7692.

(38) Payack, J. F.; Hughes, D. L.; Cai, D.; Cottrell, I. F.; Verhoeven, T. R. Dimethyltitanocene. *Org. Synth.* **2002**, *79*, 19–27.

(39) Nakano, A.; Kawahara, S.; Akamatsu, S.; Morokuma, K.; Nakatani, M.; Iwabuchi, Y.; Takahashi, K.; Ishihara, J.; Hatakeyama, S. β-Isocupreidine–hexafluoroisopropyl acrylate method for asymmetric Baylis–Hillman reactions. *Tetrahedron.* **2006**, *62*, 381-389.