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Diastereoselective Flexible Synthesis of Carbocyclic C-nucleosides†

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†Dedicated to Prof. Jaroslav Jonas of Masaryk University on the occasion of his 80th birthday

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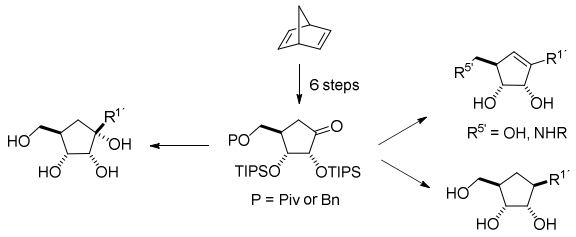


Abstract

Carbocyclic C-nucleosides are quite rare. Our route enables flexible preparation of three classes of these nucleoside analogs from common precursors – properly substituted cyclopentanones, which can be prepared racemic (in six steps) or optically pure (in ten steps) from inexpensive norbornadiene. The methodology allows flexible manipulation of individual positions around the cyclopentane ring, namely highly diastereoselective installation of carbo- and heterocyclic substituents at position 1′, orthogonal functionalization of position 5′, and efficient inversion of stereochemistry at position 2′. Newly prepared carbocyclic C-analog of tubercidine, profiled in MCF7 (breast cancer) and HFF1 (human foreskin fibroblasts) cell cultures, is less potent than tubercidine itself, but more selectively toxic towards the tumorigenic cells.

Introduction

For several decades, nucleoside analogs have been of high interest to medicinal chemists. Numerous biologically active nucleosides have been identified and more than 30 of them are now

clinically used.[1] Classical nucleosides (structure **A** in Figure 1) possess the hemiaminal motif; their chemical and metabolic stability is therefore often limited and the resulting metabolites can be a source of undesired side effects.[1a,2] Significant effort has thus been invested into identification of more stable analogs while preserving the biological activity. Two main strategies involve replacement of the C-N bond between sugar and base by the more stable C-C bond (C-nucleosides, structure **B** in Figure 1)[3] and replacement of the tetrahydrofuran motif by a carbocyclic ring (e. g., cyclopentane), which leads to carbocyclic N-nucleosides (structure **C** in Figure 1).[4]

Structure **D** in Figure 1 combines the stabilizing elements of structures **B** and **C** (i. e. C-C connection between the (heterocyclic) base and the carbocyclic scaffold) and represents carbocyclic C-nucleosides, which are only sporadically documented in the literature. It is conceivable that, at least in some cases, those compounds might be more robust versions of nucleoside analogs **B** and **C**. Furthemore, installation of certain substituents (e. g. X= OH) is meaningful only in this series, as this would lead to chemically unstable ketals and aminals in the other analog series. Compounds with general structure **D** where X = H are quite rare and we are aware of only one analog of type **D** containing X = OH with ribose-like substitution pattern – moderately active inhibitor of human glycosylase NEIL1 (compound **1a** in Figure 1) which we reported recently.[5] This scarcity could be caused by the lack of sufficiently efficient and versatile synthetic routes to these compounds that would allow flexible variation of the substituents on the cyclopentane core. To our best knowledge, the reported syntheses are focused on the production of single target carbocylic C-nucleosides[6] and do not allow easy manipulation of the substituents, which would enable the SAR mapping and facile identification of direct analogs of nucleosides **A**-**C** with attractive biological activity.

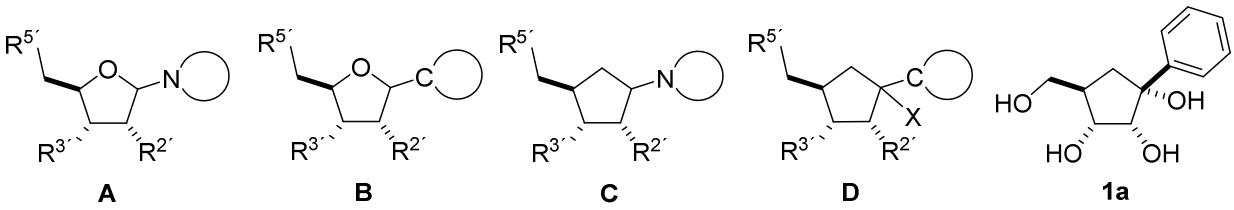
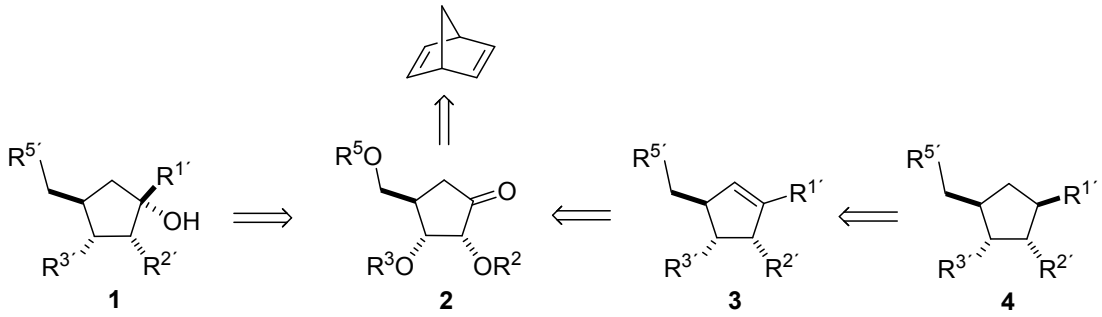


Figure 1. Generic structures of natural nucleosides (**A**) and their analogs **B**, **C** and **D**. For the sake of consistency, the numbering of substituents in **D** is the same as in nucleosides **A**, **B** and **C**.

We envisioned that a properly protected cyclopentanone **2** could be a suitable flexible precursor for three sub-series of target carbocyclic C-nucleosides (Scheme 1). Specifically, stereoselective additions of organometallic reagents[5] were to produce compounds in series **1** and transition metal-catalyzed couplings utilizing (heretofore unknown) enol triflate of **2** were to afford unsaturated analogs **3**. Stereoselective hydrogenation of **3** was envisioned to yield sub-series **4**. Similarly to **1**,

unsaturated compounds **3** are also meaningful in the class of carbocyclic C-nucleosides, but not for **A**, **B** or **C**, where the presence of double bond would lead to unstable oxonium salts and/or enamines. Precursor **2** with the desired stereochemistry was to be prepared from inexpensive norbornadiene.[7]

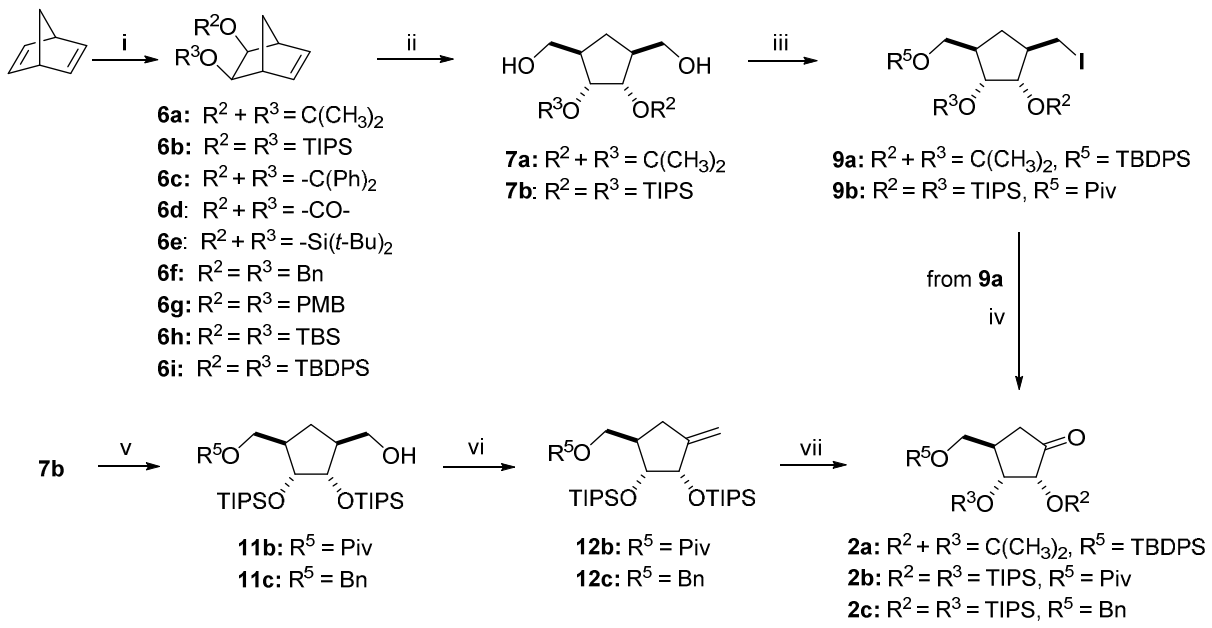
Scheme 1. Retrosynthetic Analysis of Carbocyclic C-nucleosides 1, 3 and 4



Results and Discussion

In order to prepare analogs represented by generic structure **1** (Scheme 1), we first focused on improvement of preparation of the acetonide-protected cyclopentanone **2a**, which we had previously used to prepare compound **1a**.[5] We modified the route reported for a closely related analog of **2a**.[7] Briefly, diastereoselective cis dihydroxylation of norbornadiene followed by reaction with 2,2-dimethoxypropane provided acetonide-protected diol **6a**, subsequent ozonolytical cleavage and reduction afforded intermediate **7a**, which was then monosilylated and converted into iodide **9a** (Scheme 2). Finally, elimination followed by oxidative cleavage yielded the desired cyclopentanone **2a**.

Scheme 2. Preparation of Racemic Key Cyclopentanone Intermediates[a]



[a] Reagents and conditions: i) a) $K_2OsO_4.2H_2O$, NMO acetone:H_2O 4:1, 40 °C then $Na_2S_2O_5$, (55%); b) 2,2-dimethoxypropane, TsOH, acetone, rt, (95%, **6a**); TIPSOTf, imidazole, DMAP, DMF, 65 °C, (88%, **6b**); dimethoxydiphenylmethane, TsOH, CH_2Cl_2, rt, (85%, **6c**); 1,1´-carbonyldiimidazole, $PhCH_3$, 55 °C, (80%, **6d**); di-*tert*-butylsilyl bis(trifluoromethanesulfonate), imidazole, CH_2Cl_2, 0 °C to rt, (78%, **6e**); BnBr, NaH, TBAI, DMF, rt, (77%, **6f**); PMBCl, NaH, TBAI, DMF, rt, (93%, **6g**); TBSCl, imidazole, CH_2Cl_2, rt, (76%, **6h**); TBDPSCl, imidazole, CH_2Cl_2, rt, (25%, **6i**); ii) a) O_3, CH_2Cl_2/MeOH, -78 °C then $NaBH_4$, -78 °C to rt, (50-65%, **7a**, 70-80%, **7b**); iii) NaH, TBDPSCl, THF, rt, (76%, **8a**) then Ph_3P, I_2, imidazole, CH_2Cl_2, 0 °C to rt, (85%, **9a**) PivCl, DIPEA, DMAP, CH_2Cl_2, rt (70%, **9b**) then Ph_3P, I_2, imidazole, CH_2Cl_2, 0 °C to rt, 87%, **9b**; iv) a) DBU, $PhCH_3$, 110 °C, (75%, **10a**); b) O_3, CH_2Cl_2/MeOH, -78 °C, then thiourea, -78 °C to rt, (92%, **2a**); v) PivCl, DIPEA, DMAP, CH_2Cl_2, rt (70%, **11b**); NaH, BnBr, THF, rt, (65-75%, **11c**); vi) Bu_3P, 3-NO_2PhSeCN, THF, rt, then H_2O_2, 0 °C to rt (80%, over 2 steps, **12b**, 75% over 2 steps, **12c**); vii) O_3, CH_2Cl_2, -78 °C then thiourea, rt, (90%, **2b**, 86%, **2c**).

Unfortunately, we soon realized that the utility of acetonide-protected cyclopentanone **2a** was quite limited. While it did undergo highly diastereoselective additions[5] with a variety of nucleophiles (the other diastereomers could not be detected by TLC or NMR), the final deprotection of acetonide in many cases proved to be extremely difficult. For instance, we were not able to convert the adduct which we prepared by reaction of cyclopentanone **2a** with (2,4-bis(benzyloxy)pyrimidin-5-yl)lithium into the desired target compound, i. e. uracil-containing analog of compound **1a**. Under a variety of standard conditions[8] (e. g., aqueous HCl in MeOH, CH_3COOH, CF_3COOH, camphorsulfonic acid, PPTS, I_2 in MeOH, $FeCl_3.6H_2O$, BCl_3, Dowex® 50WX8 100-200 mesh, $In(OTf)_3$[9]) at different temperatures as well as in the presence of additives (e.g. ethylene glycol or propan-1,3-dithiol in order to promote transketalization), we observed either low conversion or decomposition. This failure can be rationalized by facile carbocation formation at position 1´ under

acidic conditions. Indeed, in some cases we were able to isolate the products of elimination (i. e. with a double bond between the carbon atoms at positions 1′ and 6′) in low yields.

We thus needed to identify suitable alternative protecting group(s) for the hydroxyls at 2′ and 3′ positions, which i) would be compatible with the conditions of the synthetic sequence in Scheme 2, ii) would be easily cleaved (preferably under non-acidic conditions) and iii) ideally would be orthogonal to the group protecting the hydroxyl at position 5′.

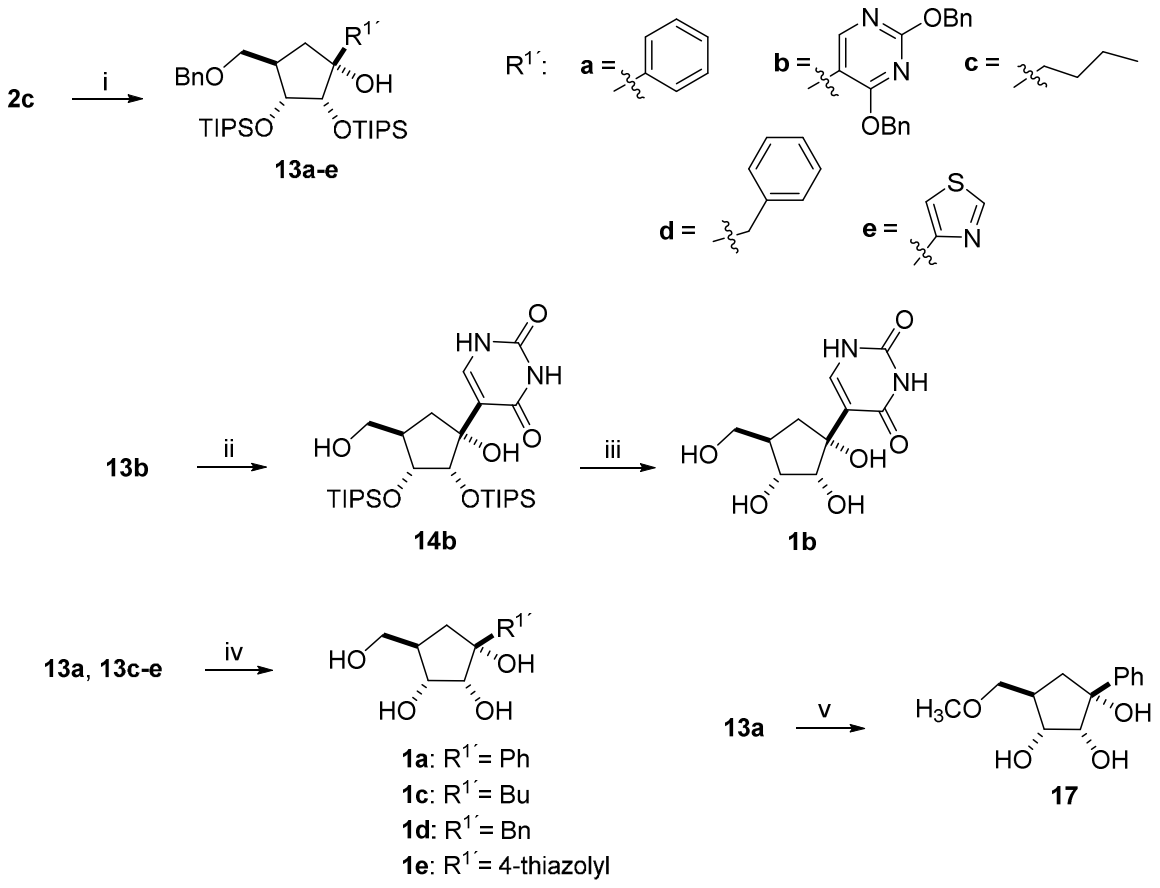
First, we utilized intermediate **6c** and prepared the analog of cyclopentanone **2a** with diphenyl ketal in place of acetonide, which we hoped to remove hydrogenolytically[10]. Unfortunately, the deprotection failed under different conditions (H_2, $HCOONH_4$, different metal catalysts, e. g., PtO_2, Pd/C, $Pd(OH)_2$/C), in different solvents at various temperatures with or without additives (AcOH, TFA). We mainly observed only the starting material and no traces of the desired product. Then, we tried a variety of several cyclic and non-cyclic protecting groups; e. g., carbonate, bis(*t*-butyl)silyl, Bn, PMB, TBS, and TBDPS. Rather surprisingly, even very early intermediates, i. e. protected diols **6b**-**6i** (Scheme 2) were not known, except for recently reported but poorly described carbonate **6d**.[11] TBDPS-protected intermediate **6i** was obtained in low yield and thus was not elaborated further. Carbonate **6d** and TBS-protected intermediate **6h** underwent undesired transformations during the ozonolytical cleavage followed by reduction with $NaBH_4$. The stability of the intermediates derived from **6e** bearing cyclic silicon-based protecting group was limited and purification by flash chromatography of the corresponding alkene and ketone provided only low yields of the compounds. On the other hand, we were able to convert intermediates protected with Bn, PMB and TIPS groups (compounds **6f**, **6g** and **6b**, respectively) into the desired cyclopentanones efficiently on multigram scale. However, the stability of some of the cyclopentanones proved to be limited. For instance, the analogs of compound **2a** with benzyls or PMB in place of acetonide underwent elimination even during the purification on neutral alumina and epimerization at position 2′ in the presence of triethylamine in dichloromethane.

Gratifyingly, we realized that the stability of TIPS-protected cyclopentanones **2b** and **2c** was much better – we could purify the compounds by chromatography and store them at 25 °C for months without noticeable decomposition. However, we had to modify the route used for **2a** as the elimination of HI from iodide **9b** was extremely sluggish. Fortunately, one-pot selenation of intermediates **11b** and **11c** and subsequent oxidation followed by intramolecular elimination[12] proceeded smoothly and provided the desired exocyclic alkenes **12b** and **12c**, respectively, which enabled preparation of cyclopentanones **2b** and **2c** on relatively large (> 5 g) scale (Scheme 2). It is likely that while the steric hindrance caused by the TIPS group at 2′-hydroxyl makes abstraction of

proton at position 1′ in **9b** difficult during the elimination, analogous shielding provided by the TIPS group in cyclopentanones **2b** and **2c** positively contributes to their stability by protecting the otherwise easily enolizable position 2′.[13]

The TIPS-protected cyclopentanone **2c** underwent highly diastereoselective addition with lithiated bis(benzyloxy)pyrimidine (Scheme 3) and the resulting adduct was successfully converted into the desired target compound **1b**. By the same methodology, we resynthesized the tetraol **1a** (in 8 steps from norbornadiene, 10% overal yield; previously[5] in 13 steps with 4% overall yield) and prepared additional target compounds **1c-e** bearing alkyl and (hetero)aryl moieties via sequential deprotection of the adducts **13c-13e** (Scheme 3).

Scheme 3. **Synthesis of Racemic Pseudouridine Analog 1b and Related Compounds 1a and 1c-e**[b]

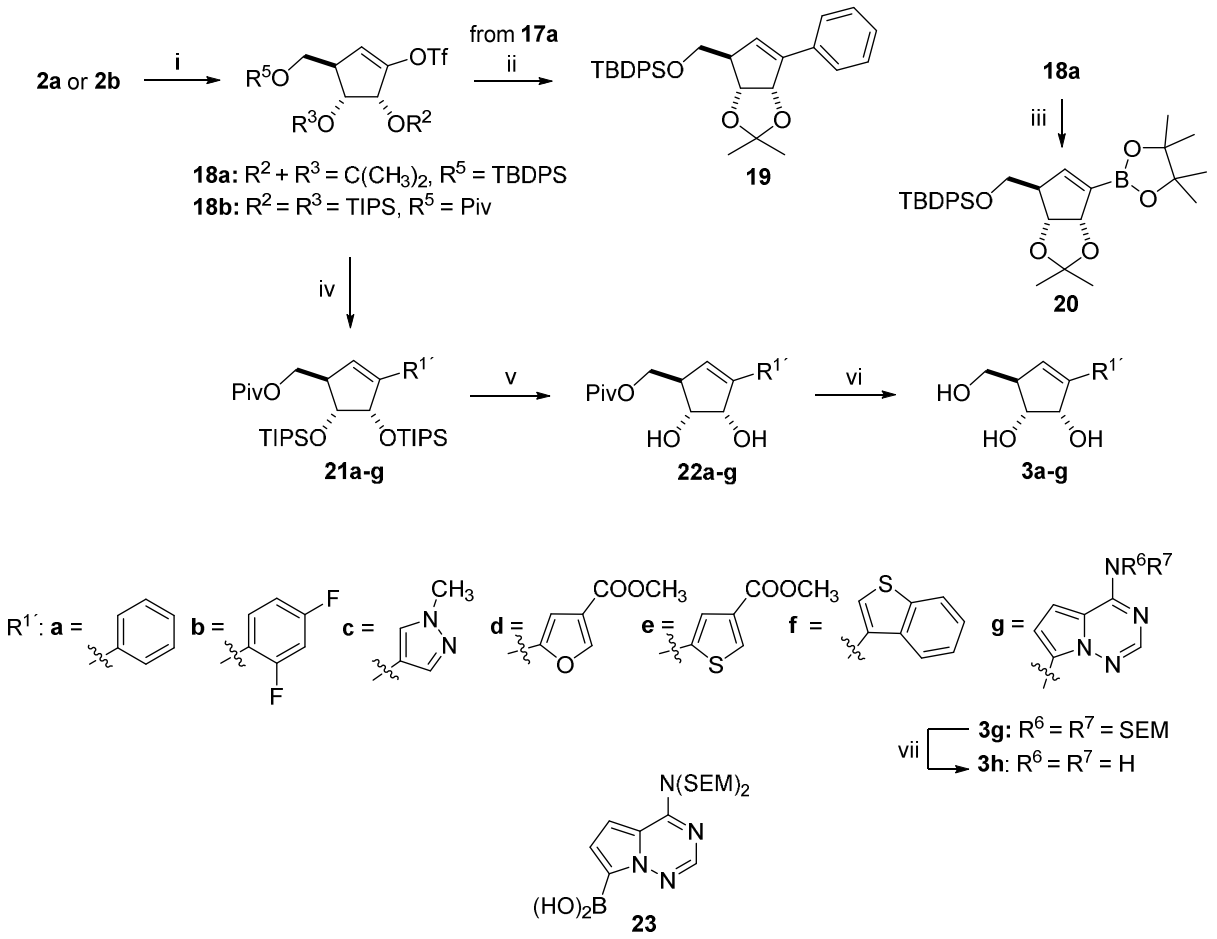


[b] Reagents and conditions: i) PhLi, THF, 0°C (55%, **13a**); 2,4-bis(benzyloxy)-5-bromopyrimidine, *n*-BuLi, THF, -78 °C then **2c**, -78 °C to rt, (45%, **13b**); *n*-BuMgCl, THF, 0 °C to rt (38%, **13c**); BnMgCl, THF, 0 °C to rt, (79%, **13d**); 4-bromothiazole, $(CH_3)_2MgCl{\cdot}LiCl$ (90 %, **13e**); ii) Pd/C, H_2, EtOH, 80 °C, (93%, **14b**); iii) TBAF, THF, rt, (85%, **1b**); iv) a) TBAF, THF, rt, (96%, **14a**, 82%, **14c**, 90%, **14d**); Li, naphthalene, THF, rt, then TBAF, THF, rt (53%, **1e** over 2 steps) b) $Pd(OH)_2/C$, H_2 (50 bar), THF, 70 °C, (92%, **1a**, 93%, **1c**, 92%, **1d**~~)e)~~; v) a) Pd/C, H_2, EtOH, 80 °C, (75%, **15**); b) NaH, MeI, THF, 0 °C to rt, (67%, **16**); c) TBAF, THF, rt, (42%).

In addition, orthogonal deprotection of the benzyl group allowed us to selectively modify the hydroxyl at position 5′: debenzylation of compound **13a** followed by methylation and cleavage of the TIPS groups provided target compound **17** (Scheme 3).

Next, we addressed the sub-series **3** depicted in Scheme 1. Treatment of acetonide-protected cyclopentanone **2a** with LDA at -78 °C followed by addition of *N*-phenyl-bis(trifluoromethansulfonimide) provided stable enol triflate **18a** in good yield (Scheme 4). In contrast, in order to get a clean and complete conversion of TIPS-protected **2b** into enol triflate **18b**, we had to optimize the conditions (KHMDS added to a mixture of **2b** and Comins' reagent). The Suzuki coupling of both **18a** and **18b** with phenylboronic acid proceeded smoothly and afforded compounds **19** and **21a**, respectively, in good yields (Scheme 4). We also explored the possibility to carry out the coupling in the reversed fashion. Along this line, we were able to convert enol triflate **18a** into the corresponding boronate **20** by Pd-catalyzed borylation;[14] but, in contrast, we were not able to perform analogous transformation on enol triflate **18b** under a variety of conditions.

Scheme 4. **Formation of Enol Triflates and Their Conversion into Racemic Target Compounds 3a-h**[c]

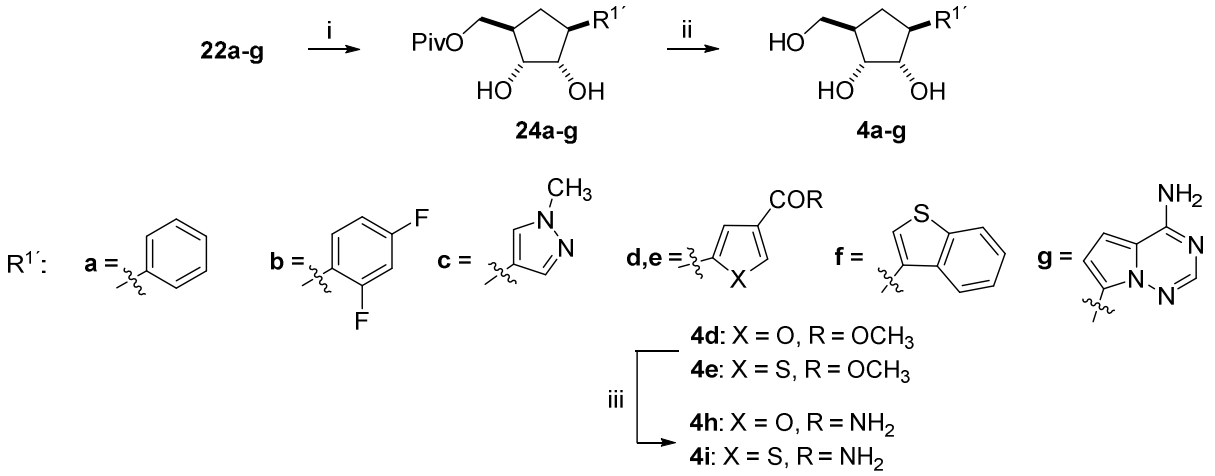


[c]Reagents and conditions: i) LDA, THF, -78 °C then $PhNTf_2$, -78 °C to rt, (80%, **18a**); KHMDS, Comins' reagent, THF, -78 °C to rt, (97%, **18b**; ii) $PhB(OH)_2$, $Pd(dppf)Cl_2$, K_3PO_4, DME, H_2O, 80 °C, (70-80%, **19**); iii) pin_2B_2, $Pd(Ph_3P)_2Cl_2$, Ph_3P, KBr, KOPh, $PhCH_3$, 50 °C (70 %, **20**); iv) $PhB(OH)_2$, $Pd(dppf)Cl_2$, K_3PO_4, DME, H_2O, 80 °C, (92%, **21a**); 2,4-difluorophenylboronic acid, $Pd(PPh_3)_4$, LiCl, Na_2CO_3, DME, H_2O, 80 °C, (76%, **21b**); 1-methylpyrazole-4-boronic acid pinacol ester, $Pd(dppf)Cl_2$, K_3PO_4, DME, H_2O, 80 °C, (87%, **21c**); 4-(methoxycarbonyl)furan-2-boronic acid pinacol ester, $Pd(dppf)Cl_2$, K_3PO_4, DME, H_2O, 80 °C, (81%, **21d**); 4-(methoxycarbonyl)thienyl-2-boronic acid pinacol ester, $Pd(dppf)Cl_2$, K_3PO_4, DME, H_2O, 80 °C, (99%, **21e**); 3-benzothienylboronic acid, $Pd(dppf)Cl_2$, K_3PO_4, DME, H_2O, 80°C, (75%, **21f**); boronic acid **23**, $Pd(dppf)Cl_2$, K_3PO_4, DME, H_2O, 80 °C, (87%, **21g**); v) TBAF, THF, rt, (89%, **22a**, 90%, **22b**, 91%, **22c**, 86%, **22d**, 74%, **22e**, 83%, **22f**, 88%, **22g**); vi) MeONa, MeOH, 65 °C, (89%, **3a**, 87%, **3b**, 91%, **3c**, 63%, **3d**, 50%, **3e**, 91%, **3f**, 88%, **3g**); vii) PPTS, MeOH, H_2O, 55 °C, (75%, **3h**).

Once again, acetonide cleavage turned out to be problematic. We obtained best results (38% yield) when we used PPTS to deprotect intermediate **19** to afford **3a**. More forcing conditions (aq. HCl, CH_3COOH, CF_3COOH) were incompatible with the presence of the double bond and (partial) cleavage of the TBDPS group was also observed. On the other hand, selective TIPS deprotection on **21a** was successful and yielded the desired intermediate **22a** in high yield (89%). Final cleavage of the pivaloate with DIBAL or sodium methoxide proceeded uneventfully and provided the target compound **3a**. Using different boronic acids/boronates, we prepared additional target compounds **3b-f** with diverse substituents at position 1′. In order to prepare the new unsaturated carbocyclic analog of tubercidine **3h** (with the isosteric base that allowed linkage by the C-C bond), we utilized heretofore unknown boronic acid **23**, whose preparation from commercially available 7-bromopyrrolo[1,2-*f*][1,2,4]triazin-4-amine as well as the coupling were in our hands more reliable than with the (known) unprotected analog.[15] The SEM groups were removed from intermediate **3g** under mild conditions (Scheme 5).

Finally, we focused on preparation of saturated analogs represented by generic structure **4** in Scheme 1.

Scheme 5. **Diastereoselective Hydrogenation of Cyclopentene Intermediates**[d]



[d]Reagents and conditions: i) Crabtree's catalyst, H_2, CH_2Cl_2, rt, (94%, **24a**, 92%, **24b**, 95%, **24d**, 99%, **24e**, 86%, **24f**); $Pd(OH)_2$/C, H_2, THF, rt, (44%, **24c**); $Pd(OH)_2$/C, H_2, THF, rt, then PPTS, MeOH, H_2O, 55 °C, (44 %, **24g**); ii) MeONa, MeOH, 65 °C, (89%, **4a**, 90%, **4b**, 53%, **4c**, 74%, **4d**, 61%, **4e**, 88%, **4f**, 84%, **4g**); iii) 7 M NH_3, MeOH, 100 °C, (22%, 75% brsm, **4h**, 43%, **4i**).

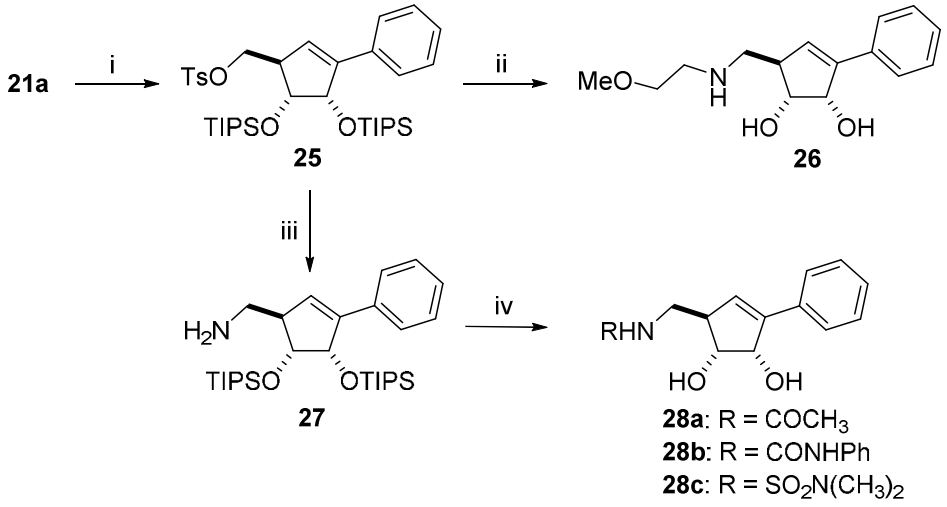
Expectedly, hydrogenation of the TIPS-protected intermediate **21a** proceeded exclusively from the less hindered top face of the cyclopentene scaffold and yielded only the undesired diastereomer with the opposite configuration at the newly created stereogenic center. On the other hand, we were able to perform hydrogenation of diol **22a** with practically perfect desired diastereoselectivity in the presence of Crabtree's catalyst[16] to yield pivaloate **24a**. Final deprotection afforded triol **4a** in high overall yield (66 % over 5 steps from **2b**). The relative configurations of the triols **4a** and **4c** were unambiguously confirmed by X-ray crystallography (see the Supporting Information). We then investigated the scope of the highly diastereoselective hydrogenation in preparation of target compounds possessing various substituents at position 1.

The hydrogenation of intermediates possessing aromatic and O and S heteroaromatic moieties (**22b**, **22d**, **22e** and **22f**) also proceeded with excellent diastereoselectivity (we could not detect the undesired diastereomer in the crude reaction mixture by NMR). On the other hand, the rate and diastereoselectivity of the hydrogenation of the substrates with N-containing substituents (compounds **22c** and **22g**) were significantly worse, which is likely caused by preferential coordination of the catalyst to the nitrogen atoms. We tried a variety of conditions, varying pressure (up to 150 bar), temperature, solvents (THF, CH_2Cl_2, $PhCH_3$) and the catalyst (Ir, Rh or Ru based catalysts); however, we did not observe any significant improvement. For the N-containing substrates we eventually used $Pd(OH)_2$. Although these hydrogenations gave diastereomeric mixtures with the ratio of ca. 2:1, in favor of the desired epimers, the diastereomers were in all cases separable by chromatography. Final deprotection of hydrogenated intermediates **22b**-**22g** with

sodium methoxide proceeded uneventfully and provided the corresponding target compounds **4b-4g**. Compounds **4d** and **4e** were converted into amides **4h** and **4i** - heretofore unknown carbocyclic analogs of furanfurin and thiophenfurin.[17] This route also provided another heretofore unknown carbocyclic C-analog of tubercidine (compound **4g** in Scheme 6), which we than prepared optically active and briefly tested for cytotoxicity (see below).

The fact, that the orthogonality of TIPS and pivaloate protecting groups can be utilized to further selectively manipulate the position 5′, is briefly illustrated in Scheme 6. Cleavage of the pivaloate in **21a** followed by tosylation provided tosylate **25**, which proved to be a versatile intermediate for manipulation of position 5′ via nucleophilic substitution: it underwent substitutions with ammonia or primary amines; amine **27** was used for subsequent reactions with different electrophiles, which ultimately provided target compounds **28a-c** (Scheme 6). In the future, we will use the methodology to install more elaborated nitrogen-containing substituents that are associated with biological activity in classical nucleoside analogs.[18]

Scheme 6. Modifications of Position 5′[e]

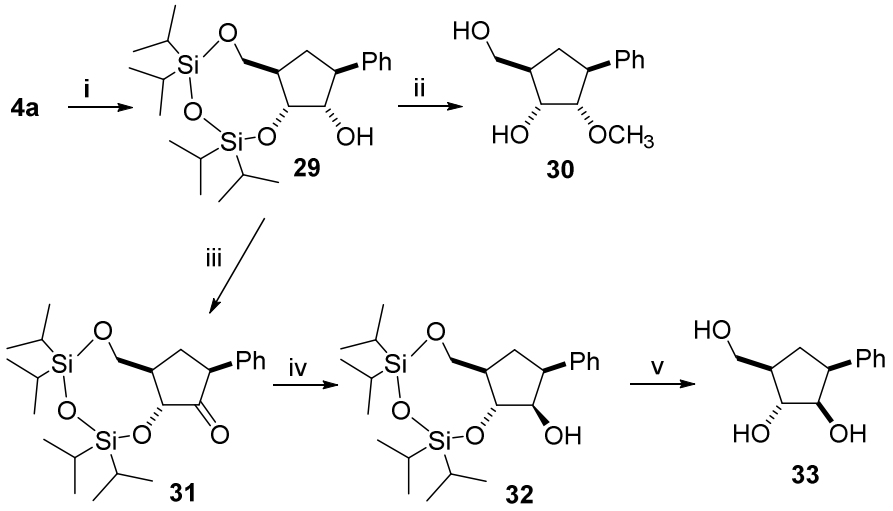


[e]Reagents and conditions: i) DIBAL-H, CH_2Cl_2, -78 °C to rt then TsCl, TEA, DMAP, CH_2Cl_2 rt, (88%); ii) a) 2-methoxyethylamine, DIPEA, DMF 100 °C, (69 %); b) TBAF, THF, rt, (90%); iii) NH_3 in IPA, aq. NH_3, 75 °C, (87 %); iv) a) AcCl, DIPEA, CH_2Cl_2, rt, (73%); b) TBAF, THF, rt, (89%, **28a**); v) a) phenylisocyanate, TEA, CH_2Cl_2, rt, (93%); b) TBAF, THF, rt, (67%, **28b**); vi) a) *N,N*-dimethylsulfamoyl chloride, TEA, DMF, rt, (86%); b) TBAF, THF, rt, (89%, **28c**).

We also attempted to manipulate position 2′ utilizing compound **4a**, which we were able to produce in gram quantities by the routes depicted in Schemes 4 and 5 above. Standard di-protection of 5′- and 3′- hydroxyls by TIPDS[19] provided cyclic siloxane **29** (Scheme 7). Alkylation of the remaining free hydroxyl at position 2′ followed by final deprotection yielded target compound **30**, whose

structural integrity was confirmed by X-ray crystallography (see the Supporting Information). Our attempts to invert the stereochemistry at position 2′ by Mitsunobu reaction[20] failed and we recovered only unreacted **29**. However, we were able to perform the inversion via diastereoselective reduction of ketone **31** (Scheme 7). While with typically used $NaBH_4$[21] the reduction proceeded with no diastereoselectivity, the results were more satisfactory with sterically demanding agents: for $LiAlH(O\text{-}t\text{Bu})_3$, the ratio of **32** to its epimer was 90:10 and for $LiAlH[O\text{-}C(CH_2CH_3)_3]_3$ the formation of **32** was exclusive (for the crystal structure of **32**, see the Supporting Information). Subsequent removal of the protecting group produced triol **33** in high overall yield.

Scheme 7. **Manipulation of Position 2′**[f]

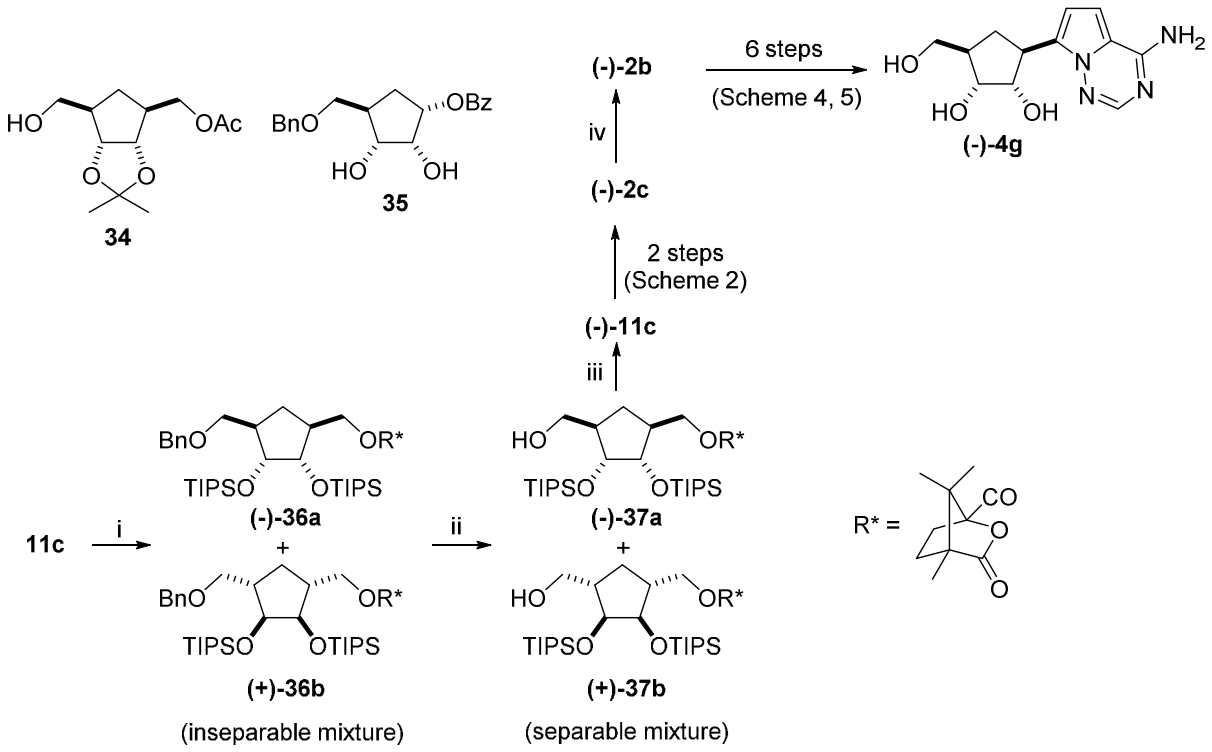


[f]Reagents and conditions: i) TIPDSCl, Pyr, 0 °C, (88%); ii) a) *n*-BuLi, MeOTf, -78 °C, (49%); b) TBAF, THF, rt, 64 %; iii) IBX, CH_3CN, 80 °C, (81%); iv) $LiAlH[O\text{-}C(CH_2CH_3)_3]_3$, THF, 0 °C, (92%); v) TBAF, THF, rt, (73%).

Ultimately, we attempted to develop a route that would allow enantioselective synthesis of all three sub-series **1**, **3**, and **4**. The utility of known chiral precursors proved to be limited: monoacetate **34**[22] was not optimal due to the presence of difficult to remove acetonide, while the synthesis of compound **35**[23] (especially the alkylation of cyclopentadienide[24]) was in our hands extremely irreproducible. Similarly, attempted desymmetrization of diol **7b** by enantioselective silylation[25] or by pivaloylation with chiral variant of DMAP[26] also failed. Fortunately, upon extensive experimentation we found a suitable chiral auxiliary that allowed preparation of non-racemic **11c**. Racemic **11c** was first converted into an inseparable mixture of diastereomeric camphanates **(-)-36a** and **(+)-36b**. Subsequent hydrogenolysis afforded compounds **(-)-37a** and **(+)-37b**, which we were able to separate by standard chromatography and re-benzylate[27] without the loss of stereochemical integrity to obtain individual **(-)-36a** and **(+)-36b**, respectively (Scheme 8). The absolute configuration of the crystalline camphanate **(-)-37a** was confirmed by X-ray crystallography (see

the Supporting Information). Interestingly, attempts to prepare the camphanates **(-)-37a** and **(+)-37b** directly from diol **7b** failed and provided mixtures containing substantial amounts of poorly separable dicamphanate. Subsequent removal of camphanate from (-)-**36a** provided (-)-**11c**, which was converted into optically pure (-)-**2c** and then into (-)-**2b**. Optically active cyclopentanone (-)-**2b** was then elaborated into two compounds with defined absolute configuration: (+)-**3b** and tubercidine analog (-)-**4g** (Scheme 8), whose enantiomeric purity was confirmed by HPLC on chiral stationary phase. Compared to tubercidine, (-)-**4g** was found to be less active against tumorigenic MCF7 cells (IC_{50} values 96 nM for tubercidine and 13.3 μM for (-)-**4g**), but the compound was comparatively less toxic to human foreskin fibroblast HFF1 cells (21 nM for tubercidine and 10.4 μM for (-)-**4g**). In contrast, the opposite enantiomer (+)-**4g**, racemic 1′-epimer of **4g** and the unsaturated analog **3h** were inactive (description of the assays is given in the Supporting Information.

Scheme 8. Enantioselective Synthesis of Tubercidine Analog (-)-**4g**[g]



[g]Reagents and conditions*:* i) a) (1*S*)-(-)-camphanic chloride, DIPEA, DMAP, CH_2Cl_2, rt (97%, 1:1 diastereomeric mixture of **(-)-36a** and **(+)-36b**); ii) $Pd(OH)_2/C$, H_2, THF, 65 °C, (67%, **(-)-37a** and 76%, **(+)-37b**); iii) a) TriBOT, TfOH, 5Å MS, 1,4-dioxane, rt, (93%, **(-)-36a** and 80%, **(+)-36b**), b) MeONa, MeOH, rt, (90%, **(-)-11c** and 90%, **(+)-11c**); iv) $Pd(OH)_2/C$, H_2, THF, 65 °C then PivCl, DMAP, DIPEA, CH_2Cl_2, rt (80%, **(-)-2c** over two steps).

In summary, our methodology enables flexible and diastereoselective synthesis of new carbocyclic C-nucleosides with a variety of substituents at position 1′ and selective manipulations of positions 2′ and 5′ of the cyclopentane core. Identification of suitable versatile intermediates (i. e. TIPS-protected cyclopentanones **2b** and **2c**) required extensive optimization of the protecting groups. We have prepared a series of new carbocyclic C-nucleosides, which included new carbocyclic analogs of furanfurin and thiophenfurin (compounds **4h** and **4i**, respectively), as well as new tubercidine analog (-)-**4g**. Compared to tubercidine, analog (-)-**4g** was found to be less potent, but more selectively toxic to MCF7 cells (breast cancer) than to HFF1 (human foreskin fibroblasts). A detailed account of the compounds‘ biological activity will be reported elsewhere in the near future.

Experimental Section

General

All reagents were of reagent grade and were used without further purification. The used solvents were anhydrous, stored over 4Å molecular sieves as received from commercial suppliers. All reactions were carried out in oven-dried glasware and under nitrogen atmosphere unless stated otherwise. Flash chromatography was carried on silica gel (230-400 mesh). TLC plates were visualized under UV and/or with phosphomolybdic acid, $KMnO_4$, CAM or H_2SO_4 in MeOH.

NMR spectra were recorded on a 500 MHz spectrometer (with operating frequencies, 500.13 MHz for ^{1}H, 125.77 MHz for ^{13}C, 470.53 MHz for ^{19}F and 160.46 MHz for ^{11}B) and a 300 MHz spectrometer (with operating frequencies 300.13 MHz for ^{1}H and 75.48 MHz for ^{13}C). The ^{1}H, and ^{13}C NMR chemical shifts (δ in ppm) were referenced to the residual signals of solvents: $CDCl_3$ [7.26 (^{1}H) and 77.23 (^{13}C)], CD_2Cl_2 [5.32 (^{1}H) and 53.50 (^{13}C)], CD_3OD [3.35 (^{1}H) and 49.30 (^{13}C)], acetone-d_6 [2.09 (^{1}H) and 29.90, 206.7 (^{13}C)], and DMSO-d_6 [2.50 (^{1}H) and 39.51 (^{13}C)]. ^{19}F NMR chemical shifts (δ in ppm) were referenced to the signal of trifluorotoluene (-63.72). Structural assignment of resonances have been performed with the help of 2D NMR gradients experiments (COSY, multiplicity edited ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC, NOESY, ^{1}H-^{15}N HSQC and ^{1}H-^{15}N HMBC).

The diffraction data were collected with a partial χ geometry diffractometer equipped with a CCD detector. Cu Kα radiation (λ= 1.54184 Å, rotating anode source, multilayer optic) was used. Data reduction and final cell refinement were carried out using the CrysAlisPro software (CrysAlisPRO, Agilent Technologies UK Ltd).

High resolution mass spectra were measured on TOF LC-MS with dual electrospray/chemical ionization mode or MALDI-TOF MS with mass accuracy greater than 2 ppm, applied mass range from 25 to 20,000 Da.

IR spectra (4000-400 cm^{-1}) were collected on anATR spectrometer. Solid samples were measured neat or in KBr pellets and oily samples as films.

Melting points were measured in capillary and are uncorrected. Optical rotations were measured in cuvettes with the path length of 10 cm.

CD spectra were recorded at 25 °C. Data were collected in the range from 195 nm to 280 nm in a 1 cm quartz cuvette.

(1*R,2*R**,3*S**,4*S**)-Bicyclo[2.2.1]hept-5-ene-2,3-diol (5).**

NMO (19.06 g, 162.8 mmol) and $K_2OsO_4.2H_2O$ (294 mg, 0.81 mmol) were added to a solution of norbornadiene (15.0 g, 162.8 mmol) in acetone and H_2O (200 + 50 mL) and the reaction mixture was stirred at 40 °C for 14 h. After cooling to 25 °C, $Na_2S_2O_5$ (1.0 g) was added and the reaction mixture was stirred at 25 °C for another 30 min. All volatiles were removed under reduced pressure and the black residue was purified by flash chromatography (hexane/EtOAc = 2:1) to afford **5** as a white crystalline solid (11.29 g, 55%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.04 (m, 2H), 3.71 (m, 2H), 2.95 (m, 2H), 2.70 m (2H), 1.89 (dm, *J* = 9.2 Hz, 1H), 1.63 (dm, *J* = 9.2 Hz, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.6, 69.2, 48.2, 42.4 ppm. The spectral data were consistent with the literature.[7]

(exo, exo)-5,6-Dimethylmethylendioxy-bicyclo[2.2.1]hept-2-ene (6a).

2,2-dimethoxypropane (26.0 mL, 196.6 mmol) and TsOH (5 mg) were added to a solution of **5** (6.2 g, 49.2 mmol) in acetone (75 mL). The reaction mixture was stirred at 25 °C for 20 min., the solvent was evaporated and the residue was purified on a short pad of silica gel (hexane/EtOAc = 20:1) to afford **6a** as a colorless oil which solidified upon standing at -20 °C (7.86 g, 95 %). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.05 (m, 2H), 4.18 (d, *J* = 1.6 Hz, 2H), 2.76 (m, 2H), 1.97 (m, 1H), 1.67 (m, 1H), 1.47 (s, 3H), 1.32 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.9, 113.8, 80.6, 45.4, 43.0, 26.3, 24.6 ppm. The spectral data were consistent with the literature.[7]

(1*R,4*S**,5*S**,6*R**)-5,6-bis(Triisopropylsilyloxy)bicyclo[2.2.1]hept-2-ene (6b).**

Imidazole (14.88 g, 218.73 mmol) and DMAP (870 mg, 7.14 mmol) were added to a solution of **5** (6.0 g, 47.55 mmol) in anhydrous DMF (60 mL), followed by dropwise addition of TIPSOTf (29.4 mL, 109.38 mmol) at 25 °C. The reaction mixture was stirred at 65 °C for 5 days. The reaction

mixture was cooled to 25 °C, quenched with H_2O (60 mL), and extracted with Et_2O (3 × 70 mL). The organic extracts were dried over Na_2SO_4, filtered, and the solvent was evaporated. The residual yellow oil was purified by flash chromatography (hexane) to afford **6b** as a colorless oil (20.1 g, 88 %). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.00 (m, 2H), 3.84 (d, *J* = 1.7 Hz, 2H), 2.62 (m, 2H), 2.20 (dm, *J* = 8.4 Hz, 1H), 1.60 (dm, *J* = 8.4 Hz, 1H), 1.12-1.07 (m, 42H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.9, 71.4, 49.8, 43.5, 18.5, 18.4, 13.1 ppm. IR ($\tilde{\nu}_{max}$) = 2927 (w), 2800 (w), 1403 (m), 1049 (s), 1111 (s), 702 (m), 646 (m) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{51}O_2Si_2$ 439.3422; Found 439.3427.

(3a*R,4*R**,7*S**,7a*S**)-2,2-Diphenyl-3a,4,7,7a-tetrahydro-4,7-methanobenzo[*d*][1,3]dioxole (6c).**

Dimethoxydiphenylmethane (2.08 g, 9.15 mmol) was added to a solution of **5** (800 mg, 6.34 mmol) in CH_2Cl_2 (8 mL), followed by addition of TsOH (1 mg), and the reaction mixture was stirred at 25 °C for 18 h. The solvent was evaporated and the residue was purified by flash chromatography (hexane/EtOAc = 20:1) to afford **6c** (1.60 g) contaminated with residual benzophenone and benzophenone dimethyl ketal as a white crystalline solid. An analytical sample could be obtained by repeated flash chromatography with slow gradient elution (hexane to hexane/EtOAc = 20:1) as a white crystalline solid. m.p. = 123-127 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.58-7.56 (m, 2H), 7.51-7.49 (m, 2H), 7.37-7.34 (m, 2H), 7.31-7.26 (m, 4H), 6.05 (m, 2H), 4.13 (d, *J* = 1.6 Hz, 2H), 2.97 (m, 2H), 2.21 (dm, *J* = 8.9 Hz, 1H), 1.77 (dm, *J* = 8.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 143.0, 141.7, 137.1, 128.5, 128.4, 128.3, 128.1, 126.7, 126.2, 114.4, 81.3, 45.4, 43.8 ppm. IR ($\tilde{\nu}_{max}$) = 2979 (w), 2946 (w), 2924 (w), 1489 (m), 1270 (m), 1203 (m), 1019 (s), 747 (s), 703 (s), 694 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M]^+$ Calcd for $C_{20}H_{18}O_2$ 290.1307; Found: 290.1311.

(3a*R,4*R**,7*S**,7a*S**)-3a,4,7,7a-Tetrahydro-4,7-methanobenzo[*d*][1,3]dioxol-2-one (6d).**

1,1′-carbonyldiimidazole (250 mg, 1.98 mmol) was added to a solution of **5** (200 mg, 1.58 mmol) in anhydrous toluene (6 mL) and the reaction mixture was stirred at 55 °C for 16 h. The reaction mixture was then cooled to 25 °C and the solvent was evaporated. The residue was purified by flash chromatography (hexane/EtOAc = 5:1) to afford **6d** as a white crystalline solid (191 mg, 80%). m.p. = 86-88 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.12 (m, 2H), 4.56 (d, *J* = 1.4 Hz, 2H), 3.14 (m, 2H), 1.90-1.82 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 156.5, 136.2, 78.9, 45.8, 41.2 ppm. IR ($\tilde{\nu}_{max}$) = 3011 (w), 1777 (s), 1367 (m), 1160 (s), 1055 (s), 1014 (s), 742 (s), 697 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_8H_8O_3Na$ 175.0371; Found: 175.0370.

(3a*R,4*R**,7*S**,7a*S**)-2,2-di-*tert*-Butyl-3a,4,7,7a-tetrahydro-4,7 methanobenzo[d][1,3,2]dioxasilole (6e).**

Imidazole (1.78 g, 26.16 mmol) was added to a cooled solution (0 °C, ice bath) of **5** (1.0 g, 7.93 mmol) in anhydrous DMF (10 mL) followed by dropwise addition of di-*tert*-butylsilyl bis(trifluoromethanesulfonate) (2.84 mL, 8.72 mmol). The reaction mixture was stirred while allowed to warm to 25 °C for 14 h. H_2O (60 mL) was added slowly and the mixture was extracted with Et_2O (3 × 50 mL). The organic extracts were dried over Na_2SO_4, filtered, and the solvent was evaporated. The residue was purified by flash chromatography (hexane/EtOAc = 20:1) to afford **6e** as a colorless oil (1.42 g, 78%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.06 (m, 2H), 4.15 (d, *J* = 1.5 Hz, 2H), 2.79 (m, 2H), 2.20 (dm, *J* = 9.2 Hz, 1H), 1.64 (dm, *J* = 9.2 Hz, 1H), 1.12 (s, 9H), 1.05 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 137.5, 78.5, 47.2, 42.5, 28.3, 27.7, 22.9, 20.6 ppm. IR ($\tilde{\nu}_{max}$) = 2933 (w), 2858 (w), 1475 (m), 1171 (w), 1036 (s), 1021 (s), 853 (s), 823 (s), 704 (m), 648 (m) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{27}O_2Si$ 267.1780; Found: 267.1779.

(1*R,4*S**,5*S**,6*R**)-5,6-bis(Benzyloxy)bicyclo[2.2.1]hept-2-ene (6f).**

A solution of **5** (4.88 g, 38.70 mmol) in DMF (40 mL) was added dropwise to a suspension of NaH (60% dispersion in mineral oil, 4.64 g, 116.11 mmol) in DMF (20 mL). The reaction mixture was stirred at 25 °C for 20 min, benzyl bromide (11.05 mL, 92.9 mmol) was slowly added, followed by a solution of tetra-n-butyl ammonium iodide (1.43 g, 3.87 mmol) in DMF (10 mL). The reaction mixture was stirred at 25 °C for additional 14 h and then quenched by dropwise addition of H_2O (5 mL). H_2O (100 mL) was added and the mixture was extracted with Et_2O (4 × 100 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and the solvent was evaporated. The resulting yellow oil was purified by flash chromatography (hexane/EtOAc = 20:1) to afford **6f** as a white crystalline solid (9.08 g, 77%), m.p. = 65.9-66.1 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37-7.26 (m, 10H), 6.01 (m, 2H), 4.69-4.63 (m, 4H), 3.53 (m, 2H), 2.85 (m, 2H), 2.20 (m, 1H), 1.67 (m, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.2, 137.0, 128.5, 128.0, 127.6, 77.2, 72.5, 45.9, 44.2 ppm. IR ($\tilde{\nu}_{max}$) = 3063 (w), 3029 (w), 1496 (w), 1453 (m), 1343 (w), 1114 (m), 733 (s), 696 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{22}O_2Na$ 329.1517; Found: 329.1524.

(1*R,4*S**,5*S**,6*R**)-5,6-bis(4-Methoxybenzyloxy)bicyclo[2.2.1]hept-2-ene (6g).**

A solution of **5** (1.18 g. 9.37 mmol) in DMF (20 mL), was added dropwise to a suspension of NaH (60% dispersion in mineral oil, 1.12 g, 28.11 mmol) in DMF (20 mL). The reaction mixture was stirred at 25 °C for 20 min, 4-methoxybenzyl chloride (2.8 mL, 20.62 mmol) was slowly added, followed by a solution of tetra-n-butyl ammonium iodide (346 mg, 0.94 mmol) in DMF (10 mL).

The reaction mixture was stirred at 25 °C for additional 14 h and then quenched by dropwise addition of H_2O (5 mL). H_2O (100 mL) was added and the mixture was extracted with Et_2O (4 × 100 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and the solvent was evaporated. The resulting yellow oil was purified by flash chromatography (hexane/EtOAc = 15:1) to afford **6g** as a white wax (3.2 g, 93%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27 (d, *J* = 8.6 Hz, 4H), 6.85 (d, *J* = 8.6 Hz, 4H), 5.99 (m, 2H), 4.58 (d, *J* = 11.7 Hz, 2H), 4.53 (d, *J* = 11.7 Hz, 2H), 3.80 (s, 6H), 3.48 (d, *J* = 1.8 Hz, 2H), 2.80 (m, 2H), 2.16-2.14 (m, 1H), 1.64-1.62 (m, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 159.3, 137.0, 131.4, 129.6, 113.9, 77.0, 76.8, 72.1, 55.5, 45.9, 44.2 ppm. IR ($\tilde{\nu}_{max}$) = 2991 (w), 2952 (w), 1402 (m), 1257 (m), 1109 (s), 741 (s), 694, 650 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{26}O_4Na$ 389.1723; Found: 389.1727.

(1*R,4*S**,5*S**,6*R**)-5,6-bis(*tert*-Butyldimethylsilyloxy)bicyclo[2.2.1]hept-2-ene (6h).**

Imidazole (558 mg, 8.21 mmol) and TBSCl (544 mg, 3.61 mmol) were added to a solution of **5** (207 mg, 1.64 mmol) in CH_2Cl_2 (15 mL) and the reaction mixture was stirred at 25 °C for 14 h. The solvent was evaporated and the residue was purified by flash chromatography (hexane/EtOAc = 10:1) to afford **6h** as a white semi-solid (440 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.00 (m, 2H), 3.64 (m, 2H), 2.53 (m, 2H), 2.14 (dm, *J* = 8.2 Hz, 1H), 1.56 (dm, *J* = 8.2 Hz, 1H) 0.91 (s, 18H), 0.07 (s, 6H), 0.05 (s, 6H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 137.0, 71.0, 49.7, 43.4, 26.3, 18.6, -4.0, -4.7 ppm. IR ($\tilde{\nu}_{max}$) = 1481 (w), 1103 (m), 759 (s), 693 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{39}O_2Si_2$ 355.2483; Found: 355.2486.

(1*R,4*S**,5*S**,6*R**)-5,6-bis(*tert*-Butyldiphenylsilyloxy)bicyclo[2.2.1]hept-2-ene (6i).**

TBDPSCl (1 mL, 3.96 mmol) and imidazole (433 mg, 6.36 mmol) were added to a solution of **5** (200 mg, 1.59 mmol) in CH_2Cl_2 (10 mL) and the reaction mixture was stirred at 25 °C for 14 h. The solvent was evaporated and the yellow residue was purified by flash chromatography (hexane/EtOAc = 20:1) to afford **6i** as a white crystalline solid (240 mg, 25 %), along with the mono-silylated side-product (417 mg, 43%). m.p. = 133-136 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.76-7.72 (m, 8H), 7.41-7.31 (m, 12H), 5.53 (m, 2H), 3.87 (d, *J* = 1.5 Hz, 2H), 2.32 (dm, *J* = 8.6 Hz, 1H), 2.24 (m, 2H), 1.38 (dm, *J* = 8.6 Hz, 1H), 1.10 (s, 18H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.6, 136.3, 136.2, 135.3, 134.7, 129.7, 129.6, 127.7, 127.7, 72.3, 48.9, 43.0, 27.4, 19.6 ppm. IR ($\tilde{\nu}_{max}$) = 1472 (w), 1102 (m), 1086 (m), 697 (s), 499 (s), 481 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{39}H_{46}O_2Si_2Na$ 625.2929; Found: 625.2928.

General Procedure A for ozonolysis of protected norbornenediols

A mixture of O_3/O_2 (O_2 flow = 5L/min, ozonolysis rate ~ 12 mmol/5 min) was bubbled into a cooled (–78 °C) solution of the starting material in CH_2Cl_2:MeOH (1:3, ~ 15 mmol of the starting material/10 mL). After completion of ozonolysis (indicated by persistent blue color of the reaction

mixture), excess of O_3 was removed by bubbling N_2 into the reaction mixture. Thiourea (6 eq.) was added in five portions and the reaction mixture was stirred at –78 °C for 1 h. $NaBH_4$ (0.25 eq.) was added in one portion and the reaction mixture was stirred at –78 °C for 1 h. Another portion of $NaBH_4$ (1.025 eq.) was added and the reaction mixture was stirred for additional 3-14 h while allowed to warm to 25 °C. The reaction mixture was concentrated under reduced pressure and the residual viscous oil was partitioned between dichloromethane (100 mL/15 mmol) and brine (50 mL). The aqueous phase was reextracted with CH_2Cl_2. The organic extracts were dried over Na_2SO_4, filtered, and the solvent was evaporated. The residue was purified by flash chromatography to afford the corresponding diol.

((3aR*,4*R,6*S**,6a*S**)-2,2-Dimethyltetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4,6-diyl)dimethanol (7a).**

The compound was prepared by General Procedure A using 6.2 g (37.32 mmol) of **6a**; flash chromatography (CH_2Cl_2/MeOH = 20:1 to 10:1) afforded **7a** as a colorless oil (5.11 g, 67%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.41 (m, 2H), 3.69 (m, 4H), 2.28 (m, 2H), 2.08 (m, 1H), 1.68 (br s, 2H), 1.51 (s, 3H), 1.32 (s, 3H), 1.26 (m, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 112.7, 83.7, 64.5, 47.6, 30.7, 27.8, 25.3 ppm. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{10}H_{19}O_4$ 203.1278; Found 203.1276. The spectral data were consistent with the literature.[7]

(1*R,3*S**,4*S**,5*R**)-4,5-bis(Triisopropylsilyloxy)cyclopentane-1,3-diyl)dimethanol (7b).**

The compound was prepared by General Procedure A using 10.09 g (22.80 mmol) of **6b**; flash chromatography (CH_2Cl_2/MeOH = 20:1) afforded **7b** as a white solid (10.03 g, 80%), m.p. = 107 – 109 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.05 (dd, *J* = 2.7, 7.4 Hz, 2H), 3.66 (dd, *J* = 10.6, 5.9 Hz, 4H), 3.60 (dd, *J* = 10.6, 5.9 Hz), 2.28 (m, 2H), 2.07 (m, 1H), 1.69 (br s, -OH, 2H), 1.16 (m, 1H), 1.09 (m, 42H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 77.7, 65.1, 45.0, 25.8, 18.5 ppm. IR ($\tilde{\nu}_{max}$) = 3301 (br), 2890 (m), 2859 (m), 1432 (m), 1039 (s), 825(m), 631 (m) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{54}O_4Si_2Na$ 497.3453; Found 497.3452.

((3a*S,4*S**,6*R**,6a*R**)-6-((*tert*-Butyldiphenylsilyloxy)methyl)-2,2-dimethyltetrahydro-3a*H*-cyclopenta[d][1,3]dioxol-4-yl)methanol (8a).**

A solution of **7a** in 15 mL of anhydrous THF (1.95 g, 9.64 mmol) was added to a suspension of NaH (464 mg, 11.60 mmol, 60 % dispersion in mineral oil) in THF (2 mL). The reaction mixture was stirred at 25 °C for 20 min, then TBDPSCl (2.63 mL, 10.12 mmol) was added and the reaction mixture was stirred for 14 h. The reaction mixture was quenched by addition of silica gel (500 mg) and adsorbed on silica gel (10 g). Flash chromatography (hexane/EtOAc = 3:1) afforded **8a** as a

colorless oil (3.24 g, 76 %). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.66-7.64 (m, 4H), 7.44-7.36 (m, 6H), 4.41-4.38 (m, 1H), 4.33-4.31 (m, 1H), 3.75-3.60 (m, 4H), 2.31-2.22 (m, 4H), 2.08-2.03 (m, 1H), 1.49 (s, 3H), 1.39 (dd, 10.9 Hz, 1H), 1.29 (s, 3H), 1.06 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 135.86, 135.85, 133.9, 129.9, 127.9, 112.6, 83.9, 82.9, 65.3, 65.1, 48.1, 47.4, 30.8, 27.9, 27.1, 25.4, 19.6 ppm. IR ($\tilde{\nu}_{max}$) = 3456 (br), 2930 (w), 2857 (w), 1471 (w), 1427 (w), 1110 (s), 1060 (s), 701 (s), 504 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{26}H_{36}O_4SiNa$ 463.2257; Found 463.2275.

(1*R, 2*R**, 3*S**, 4*S**)-4-(Hydroxymethyl)-2, 3 bis((triisopropylsilyl)oxy)cyclopentyl)methyl pivalate (11b).**

DMAP (153 mg, 1.26 mmol) and DIPEA (2.13 mL, 25.26 mmol) were added into a solution of **7b** (6.00 g, 12.63 mmol) in CH_2Cl_2 (30 mL). Pivaloyl chloride (1.55 mL, 12.63 mmol) was added dropwise and the reaction mixture was stirred at 25 °C for 14 h. The reaction mixture was quenched with water (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield the crude product, which was purified by flash chromatography (hexane/EtOAc = 10:1) to afford **11b** as white crystals (3.87 g, 71 %), m.p. = 63-65 °C. NMR (500 MHz, $CDCl_3$): δ = 4.10 (dd, *J* = 11.2, 6.0 Hz, 1H), 4.05 (apparent d, overlapped, 1H), 3.95 (dd, *J* = 11.2, 6.0 Hz, 1H), 3.64 (dd, *J* = 10.5, 6.2 Hz, 1H), 3.56 (dd, *J* = 10.5, 6.2 Hz, 1H), 2.40 (m, 1H), 2.29 (m, 1H), 2.07 (m, 1H), 1.20 (s, 9H), 1.09 (m, 1H, overlapped, resolved by ^{1}H-^{13}C HSQC experiment), 1.09 (m, 42H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.8, 77.2 (overlapped with $CDCl_3$ signal, resolved by ^{1}H-^{13}C HSQC experiment), 76.7, 65.8, 65.1, 45.0, 42.1, 39.1, 27.4, 26.0, 18.53, 18.50, 18.48, 18.44, 13.2 ppm. IR ($\tilde{\nu}_{max}$) = 2942 (m), 2865 (m), 1731 (m), 1713 (m), 1463 (m), 1143 (s), 881 (s), 677 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{30}H_{62}O_5Si_2Na$ 581.4033; Found 581.4033.

***tert*-butyl(((3a*R**,4*R**,6*R**,6a*S**)-6-(Iodomethyl)-2,2-dimethyltetrahydro-3a*H*cyclopenta[d][1,3]dioxol-4-yl)methoxy)diphenylsilane (9a).**

Iodine (1.96 g, 7.74 mmol) was added to a cooled (0 °C, ice bath) solution of PPh_3 (2.33 g, 8.88 mmol) and imidazole (1.44 g, 21.12 mmol) in CH_2Cl_2 (5 mL) and the reaction mixture was stirred at 0 °C for 20 min. A solution of **8a** (3.1 g, 7.04 mmol) in CH_2Cl_2 (15 mL) was added and the reaction mixture was stirred while allowed to warm to 25 °C for 14 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (hexane/EtOAc = 20:1 to 15:1) to afford **9a** as a colorless oil (3.29 g, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.67-7.64 (m, 4H), 7.45-7.37 (m, 6H), 4.45 (dd, *J* = 6.9, 4.9 Hz, 1H), 4.17 (dd, *J* = 6.9 Hz, 1H), 3.70 (d, *J* = 5.6 Hz, 2H), 3.34 (dd, *J* = 9.9, 5.3 Hz, 1H), 3.24 (dd, *J* = 9.9, 6.9 Hz, 1H), 2.30 (m, 1H), 2.18 (m,

1H), 2.10 (m, 1H), 1.48 (s, 3H), 1.48 (m, 1H), 1.29 (s, 3H), 1.07 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 135.9, 133.83, 133.81, 129.9, 127.9, 112.8, 85.5, 83.1, 64.8, 47.5, 46.9, 35.5, 27.9, 27.2, 25.5, 19.6, 10.4 ppm. IR ($\tilde{\nu}_{max}$) = 2930 (m), 2857 (m), 1471 (w), 1210 (w), 1111 (m), 1069 (m), 702 (s) cm^{-1}. HRMS (MALDI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{26}H_{35}IO_3SiNa$ 573.1292; Found: 573.1281.

((*1R*,2R*,3S*,4R)-4-(Iodomethyl)-2,3-bis((triisopropylsilyl)oxy)cyclopentyl)methyl pivalate (9b).**

By essentially same procedure used for compound **8a**, 850 mg (1.52 mmol) of **11b** afforded (purification by flash chromatography (hexane/EtOAc = 30:1)) **9b** as a pale yellow oil (880 mg, 87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.13 (dm, *J* = 3.9 Hz, 1H), 4.06 (dd, *J* = 11.4, 6.8 Hz, 1H), 3.95 (dd, *J* = 11.4, 5.8 Hz, 1H), 3.89 (dd, *J* = 6.1, 3.3 Hz, 1H), 3.38 (dd, *J* = 9.6, 4.9 Hz, 1H), 3.14 (dd, *J* = 9.4, 8.2 Hz, 1H), 2.38 (m, 1H), 2.31 (m, 1H), 2.16 (m, 1H), 1.21 (s, 9), 1.08 (m, 42H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.7, 79.4, 76.7, 65.6, 44.9, 41.9, 39.1, 30.6, 27.5, 18.55, 18.49, 13.3, 12.6 ppm. IR ($\tilde{\nu}_{max}$) = 2932 (m), 2861 (m), 1492 (w), 1224 (w), 1100 (m), 1069 (m), 721 (s) cm^{-1}. HRMS (MALDI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{30}H_{61}IO_4Si_2Na$ 691.3045; Found: 691.3051.

((1*S,2*S**,3*R**,4*R**)-4-((Benzyloxy)methyl)-2,3 bis((triisopropylsilyl)oxy)cyclopentyl) methanol (11c).**

To a stirred suspension of NaH (590 mg, 14.76 mmol, 60% dispersion in mineral oil) in THF (10 mL) was added a solution of compound **7b** (5.01 g, 10.54 mmol) in THF (15 mL). After stirring for 30 min and cooling to 0 °C, benzyl bromide (1.28 mL, 10.54 mmol) was added dropwise over the period of 2 h and the resulting mixture was stirred for 36 h at 25 °C. The reaction was quenched by addition of silica gel (10 g) and the solvent was evaporated. The crude mixture was then purified by flash chromatography (hexane/EtOAc = 10:1) to afford **11c** as a pale yellow oil (4.55 g, 77%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37-7.27 (m, 5H), 4.51 (AB d, *J* = 12.1 Hz, 1H), 4.44 (AB d, *J* = 12.1 Hz, 1H), 4.11 (m, 1H), 4.00 (dd, *J* = 6.6, 3.5 Hz, 1H), 3.67 (dd, *J* = 10.6, 5.8 Hz, 1H), 3.58 (dd, *J* = 10.6, 5.8 Hz, 1H), 3.41 (m, 2H), 2.36-2.24 (m, 2H), 2.12-2.04 (m, 1H), 1.19 (m, 1H), 1.13-0.97 (m, 42H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.6, 128.5, 127.9, 127.7, 77.9, 77.5, 73.4, 72.4, 65.4, 44.9, 43.5, 43.6, 26.4, 18.52, 18.49, 18.4, 13.4, 13.2 ppm. IR ($\tilde{\nu}_{max}$) = 3438 (br w), 2941 (m), 2864 (m), 1496 (m), 1067 (m), 882 (s), 677 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{32}H_{61}O_4Si_2$ 565.4103; Found 565.4099.

***tert*-butyl(((3a*R**,4*R**,6a*S**)-2,2-Dimethyl-6-methylenetetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4-yl)methoxy)diphenylsilane (10a).**

DBU (1.04 mL, 7.54 mmol) was added to a solution of **9a** (1.54 g, 2.78 mmol) in toluene (10 mL) and the reaction mixture was stirred at 90 °C for 4 h. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (hexane/EtOAc = 20:1) to afford **10a** as a colorless oil (855 mg, 72%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.65-7.63 (m, 4H), 7.45-7.36 (m, 6H), 5.17 (m, 1H), 5.07 (m, 1H), 4.63 (d, *J* = 5.6 Hz, 1H), 4.50 (d, *J* = 5.6 Hz, 1H), 3.48 (m, 2H), 2.78-2.73 (m, 1H), 2.38 (m, 1H), 2.15 (m, 1H), 1.47 (s, 3H), 1.32 (s, 3H), 1.05 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 149.8, 135.8, 133.77, 133.75, 129.91, 129.90, 127.9, 112.7, 110.6, 82.7, 82.0, 64.6, 45.9, 32.7, 27.1, 27.0, 24.7, 19.5 ppm. IR ($\tilde{\nu}_{max}$) = 2930 (m), 1732 (w), 1478 (w), 1222 (w), 1127 (s), 679 (s) cm^{-1}. HRMS (MALDI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{26}H_{34}O_3SiNa$ 445.2169; Found: 445.2183.

(1*R,2*R**,3*S**)-4-Methylene-2,3-bis(triisopropylsilyloxy)cyclopentyl)methyl pivalate (12b**

2-Nitrophenyl selenocyanate (1.88 g, 8.28 mmol) and Bu_3P (3.22 mL, 12.88 mmol) were added to a solution of **11b** (2.58 g, 4.6 mmol) in THF (15 mL) and the reaction mixture was stirred at 25 °C for 14 h. Aqueous H_2O_2 (30% solution, 15.5 mL) was added at 0 °C (ice bath) and the reaction mixture was stirred at 25 °C for 2 h. The crude mixture was concentrated, diluted by saturated aqueous $NaHCO_3$ (20 mL) and extracted with EtOAc (3 × 30 mL). The organic extracts were dried over Na_2SO_4 and the brown residue was purified by flash chromatography (hexane/EtOAc = 50:1) to afford **12b** as a pale yellow oil (1.99 g, 80% over the two steps). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.12 (m, 1H), 4.92 (m, 1H), 4.40 (d, *J* = 2.7 Hz, 1H), 4.17 (dd, *J* = 11.2, 5.9 Hz, 1H), 4.00 (dd, *J* = 5.0, 2.7 Hz, 1H), 3.97 (dd, *J* = 11.2, 5.9 Hz, 1H), 2.63 (apparent dd, *J* = 16.7, 10.2 Hz, 1H), 2.49 (m, 1H), 2.00 (dm, *J* = 16.7 Hz, 1H), 1.19 (s, 9H), 1.11-1.06 (m, 42 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.8, 149.5, 109.4, 78.0, 76.4, 65.6, 42.2, 39.1, 29.9, 27.4, 18.50, 18.47, 18.45, 18.4, 13.1 ppm. IR ($\tilde{\nu}_{max}$) = 2942 (m), 2865 (m), 1732 (m), 1463 (w), 1282 (w), 1139 (s), 881 (s), 678 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{30}H_{60}O_4Si_2Na$ 563.3930; Found 563.3929.

((1*S,2*R**,3*R**)-3-((Benzyloxy)methyl)-5-methylenecyclopentane-1,2-diyl)bis(oxy))bis (triisopropylsilane) (12c).**

By essentially same procedure used for compound **12b**, 4.52 g (8.01 mmol) of **11c** afforded (purification by flash chromatography (hexane/EtOAc = 50:1)) **12c** as a pale yellow oil (3.28 g, 75% over the two steps). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35-7.26 (m, 5H), 5.08 (m, 1H), 4.89 (m, 1H), 4.52 (AB d, *J* = 12.0 Hz, 1H), 4.45 (AB d, *J* = 12.0 Hz, 1H), 4.41 (d, *J* = 2.8 Hz, 1H), 4.00 (dd, *J* = 3.7 Hz, 1H), 3.47 (dd, *J* = 9.1, 5.4 Hz, 1H), 3.41 (dd, *J* = 9.1, 5.4 Hz, 1H), 2.61 (m, 1H), 2.39 (m, 1H), 2.11 (m, 1H), 1.08-0.91 (m, 42H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 150.6, 138.8, 128.5, 127.8, 127.7, 108.2, 77.9, 76.9, 73.4, 72.4, 43.4, 30.4, 18.49, 18.48, 18.45, 18.4, 13.1,

13.0 ppm. IR ($\tilde{\nu}_{max}$) = 2942 (m), 2865 (m), 1463 (m), 1110 (s), 882 (s), 679 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{37}O_2Si$ 373.2563; Found 373.2551.

General Procedure B for ozonolysis of exocyclic alkenes

A mixture of O_3/O_2 (O_2 flow = 5L/min, ozonolysis rate ~ 12 mmol/5 min) was bubbled into a cooled (–78 °C) solution of the starting material in CH_2Cl_2:MeOH (1:3, 3 mmol of starting material/25 mL). After after complete ozonolysis (indicated by persistent blue color of the reaction mixture), excess of O_3 was removed by bubbling N_2 into the reaction mixture. Thiourea (2 eq.) was added and the reaction mixture was stirred for 3 h at 25 °C. The solvents were removed and the solid residue was purified by flash chromatography to afford the desired ketone.

(3a*R,6*R**,6a*R**)-6-((*tert*-Butyldiphenylsilyloxy)methyl)-2,2-dimethyldihydro-3a*H*-cyclopenta[d][1,3]dioxol-4(5*H*)-one (2a).**

The compound was prepared by General Procedure B using **10a** (3.25 g, 7.69 mmol); flash chromatography (hexane/EtOAc = 5:1) afforded **2a** as a white crystalline solid (3.0 g, 92%), m.p. = 96-97 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.62-7.59 (m, 4H), 7.47-7.38 (m, 6H), 4.63 (d, *J* = 5.4 Hz, 1H), 4.35 (d, *J* = 5.4 Hz, 1H), 3.80 (dd, *J* = 10.2, 2.8 Hz, 1H), 3.61 (dd, *J* = 10.2, 2.8 Hz, 1H), 2.75 (dd, *J* = 18.4, 9.0 Hz, 1H), 2.49 (m, 1H), 2.19 (m, 1H), 1.43 (s, 3H), 1.34 (s, 3H), 1.02 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 213.4, 135.9, 135.8, 132.8, 132.6, 130.2, 130.2, 128.1, 111.5, 81.8, 79.3, 77.5, 77.2, 76.9, 66.1, 39.3, 37.5, 27.1, 27.0, 24.9, 19.4. IR (KBr, $\tilde{\nu}_{max}$) = 3486, 2933, 1755, 1589, 1429, 1108, 705.85 cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{32}O_4SiNa$ 447.1962; Found 447.1962. The spectral data were consistent with those reported.[5]

(1*R,2*R**,3*R**)-4-Oxo-2,3-bis(triisopropylsilyloxy)cyclopentyl)methyl pivalate (2b).**

The compound was prepared by General Procedure B using **12b** (5.74 g, 10.57 mmol); flash chromatography (hexane/EtOAc = 30:1) afforded **2b** as a colorless oil (5.46 g, 95%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.41 (dd, *J* = 3.9, 1.5 Hz, 1H), 4.37 (m, *J* = 3.9 Hz, 1H), 4.13 (dd, *J* = 11.6, 8.6 Hz, 1H), 4.05 (dd, *J* = 11.6, 6.2 Hz, 1H), 2.62 (m, 1H), 2.51 (dd, *J* = 18.9, 10.1 Hz, 1H), 1.96 (dm, *J* = 18.9, 1H), 1.20 (s, 1H), 1.10-1.05 (m, 42H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 212.0, 178.5, 78.8, 74.3, 65.4, 39.6, 39.1, 34.3, 27.4, 18.3, 18.3, 18.3, 18.2, 12.81, 12.78 ppm. IR ($\tilde{\nu}_{max}$) = 2942 (m), 2866, 1763 (m), 173 (s), 1463 (m), 1132 (s), 881 (s), 676 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{59}O_5Si_2$ 543.3896; Found 543.3892.

(2*R,3*R**,4*R**)-4-((Benzyloxy)methyl)-2,3-bis((triisopropylsilyl)oxy)cyclopentanone (2c).**

The compound was prepared by General Procedure B using **12c** (4.0 g, 7.31 mmol); flash chromatography (hexane/EtOAc = 25:1) afforded **2c** as a yellow oil (3.41 g, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35-7.25 (m, 5H), 4.61 (dd, *J* = 4.1, 1.6 Hz, 1H), 4.52 (AB d, *J* = 11.8 Hz, 1H), 4.46 (AB d, *J* = 11.8 Hz, 1H), 4.36 (d, *J* = 4.1 Hz, 1H), 3.61 (dd, *J* = 9.4, 4.0 Hz, 1H), 3.49 (dd, *J* = 9.4, 5.1 Hz, 1H), 2.49-2.41 (m, 2H), 2.14-2.06 (m, 1H), 1.09-1.00 (m, 42H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 213.9, 138.0, 128.6, 128.0, 127.9, 79.5, 75.7, 73.7, 71.8, 40.9, 34.5, 18.33, 18.31, 18.27, 18.2, 12.82, 12.78. IR ($\tilde{\nu}_{max}$) = 2942 (m), 2865 (m), 1760 (m), 1463 (m), 1064 (s), 882 (s), 676 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{57}O_4Si_2$ 549.3790; Found 549.3783.

(1*R,2*R**,3*R**,4*R**)-4-((Benzyloxy)methyl)-1-phenyl-2,3-bis((triisopropylsilyl)oxy)cyclopentanol (13a).**

Phenyllithium (1.8 M in dibutyl ether, 1.54 mL, 2.77 mmol) was added to a cooled (0 °C, ice bath) solution of **2c** (1.01 g, 1.84 mmol) in THF (10 mL). The reaction mixture was stirred for 6 h while allowed to warm to 25 °C. The reaction was quenched with aqueous saturated NH_4Cl (5 mL) and extracted with EtOAc (4 × 20 mL). The combined organic extracts were washed with brine (20 mL), dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc = 50:1) to afford **13a** as a viscous brown oil (628 mg, 55%) and recovered starting material (147 mg, 15%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 (m, 2H), 7.39-7.34 (m, 4H), 7.34-7.29 (m, 1H), 7.25-7.20 (m, 2H), 7.18-7.13 (m, 1H), 4.56 (d, AB, *J* = 11.7 Hz, 1H), 4.53 (d, AB, *J* = 11.7 Hz, 1H), 4.44 (s, 1H), 4.38 (d, *J* = 4.3 Hz, 1H), 4.34 (d, *J* = 4.3 Hz, 1H), 3.62 (ddm, *J* = 9.3, 4.1 Hz, 1H), 3.46 (ddm, *J* = 9.3, 4.1 Hz, 1H), 2.52-2.44 (m, 2H), 2.11 (m, *J* = 10.0 Hz, 1H), 1.19-1.09 (m, 21H), 0.89-0.79 (m, 18H), 0.62-0.54 (m, 3H).^{13}C NMR (126 MHz, $CDCl_3$): δ = 145.7, 138.3, 128.6, 128.2, 128.0, 127.7, 126.5, 126.2, 82.7, 81.5, 80.7, 73.9, 72.9, 44.2, 43.5, 18.51, 18.48, 18.4, 18.2, 13.11, 13.08, 1.2 ppm. IR ($\tilde{\nu}_{max}$) = 3511 (br w), 2915 (s), 2866 (s), 1730 (m), 1495 (m), 1047 (m), 883 (s), 681 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{37}H_{60}O_3Si_2$ 609.4153; Found 609.4152.

(1*R,2*R**,3*R**,4*R**)-4-((Benzyloxy)methyl)-1-(2,4-bis(benzyloxy)pyrimidin-5-yl)-2,3-bis((triisopropylsilyl)oxy)cyclopentanol (13b).**

n-BuLi (1.6 M in hexanes, 1.83 mL, 2.93 mmol) was added dropwise to a cooled (–78 °C) solution of 2,4-bis(benzyloxy)-5-bromopyrimidine (1.09 g, 2.93 mmol) in THF (4 mL) and the reaction mixture was stirred at –78 °C for 1 h. A solution of ketone **2c** (1.08 g, 1.97 mmol) in THF (4 mL) was added dropwise and the reaction mixture was stirred at –78 °C for 1 h. The mixture was

allowed to warm to 25 °C, quenched with saturated aqueous NH_4Cl (10 mL) and extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in a vacuum. The residue was purified by flash chromatography (hexane/EtOAc = 10:1) to afford **13b** as a yellow crystalline solid (741 mg, 45%), m.p. = 75-77 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.62 (s, 1H), 7.42-7.38 (m, 2H), 7.29- 7.17 (m, 11H), 7.14-7.11 (m, 2H), 5.37 (s, 2H), 5.34 (d, *J* = 11.7 Hz, 1H), 5.10 (d, *J* = 11.7 Hz, 1H), 4.72 (s, 1H,-OH), 4.45 (d, *J* = 4.0 Hz, 1H), 4.19 (d, *J* = 4.0 Hz, 1H), 4.11 (d, *J* = 12.0 Hz, 1H), 3.97 (d, *J* = 12.0 Hz, 1H), 2.95-2.91 (m, 1H), 2.84-2.79 (m, 1H), 2.41-2.34 (m, 1H), 2.10-1.99 (m, 2H), 1.01-0.95 (m, 21H), 0.87-0.72 (m, 18H), 0.68-0.60 (m, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 166.5, 164.1, 159.7, 138.7, 137.2, 135.8, 129.8, 128.9, 128.6, 128.4, 128.2, 128.1, 127.6, 127.5, 117.0, 79.9, 79.1, 75.1, 73.1, 72.9, 69.1, 69.1, 43.4, 39.2, 18.43, 18.42, 18.3, 18.0, 13.1, 12.9 ppm. IR ($\tilde{\nu}_{max}$) = 3457 (br w), 2942 (m), 2865 (m), 1559 (m), 1422 (s), 825 (s), 685 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{49}H_{72}N_2O_6Si_2$ 841.5002; Found 841.4999.

(1*S,2*R**,3*R**,4*R**)-4-(Benzyloxymethyl)-1-butyl-2,3-bis(triisopropylsilyloxy) cyclopentanol (13c).**

Butylmagnesium chloride (2M in THF, 0.20 mL, 0.41 mmol) was slowly added into a solution of **2c** (150 mg, 0.27 mmol) in THF (2 mL) at 0 °C. The reaction mixture was allowed to warm to 25 °C, stirred for 14 h, then quenched with saturated aqueous NH_4Cl (15 mL), and extracted with EtOAc (3 × 15 mL). The organic extracts were dried over $MgSO_4$, filtered, and solvent was evaporated. The residual oil was purified by flash chromatography (hexane/ EtOAc = 25:1) to afford **13c** as a colorless oil (620 mg, 38%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35-7.27 (m, 5H), 4.47 (d, AB, *J* = 12.1 Hz, 1H), 4.43 (d, AB, *J* = 12.1 Hz, 1H), 4.24 (d, *J* = 3.9 Hz, 1H), 3.90 (s, 1H, -OH), 3.77 (d, *J* = 3.9 Hz, 1H), 3.38 (dd, *J* = 8.7, 5.1 Hz, 1H), 3.23 (dd, *J* = 9.0, 6.6 Hz, 1H), 2.36 (m, 1H), 2.14 (dd, *J* = 14.2, 10.5 Hz, 1H), 1.77 (m, 1H), 1.49 (dd, *J* = 14.3, 5.2 Hz, 1H), 1.36-1.25 (m, 4H), 1.24-1.16 (m, 2H), 1.12-1.05 (m, 42H), 0.9 (t, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.5 128.5, 127.9 127.8, 80.5, 79.7, 78.6, 73.5, 72.7, 43.1, 39.5, 38.3, 26.4, 23.7, 18.6, 18.5, 14.3, 13.4, 13.1 ppm. IR ($\tilde{\nu}_{max}$) = 2942 (m), 2865 (s), 1463 (m), 1154 (m), 825 (s), 679 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{35}H_{66}O_4Si_2Na$ 629.4392; Found 629.4391.

(1*R,2*R**,3*R**,4*R**)-1-Benzyl-4-(benzyloxymethyl)-2,3-bis(triisopropylsilyloxy)cyclopentanol (13d).**

The compound was prepared by essentially same procedure used for **13c**, using benzylmagnesium chloride (2M in THF, 0.21 ml, 0.41 mmol) and ketone **2c** (150 mg, 0.27 mmol); flash chromatography (hexane/ EtOAc = 25:1) afforded **13d** as a colorless oil (63 mg, 38%). ^{1}H NMR

(500 MHz, $CDCl_3$): δ = 7.35-7.22 (m, 9H), 7.18 (m, 1H), 4.47 (d, AB, *J* = 12.1 Hz, 1H), 4.43 (d, AB, *J* = 12.1 Hz, 1H), 4.26 (dd, *J* = 4.0, 1.4 Hz, 1H), 3.91 (d, *J* = 4.0 Hz, 1H), 3.75 (d, *J* = 1.0 Hz, 1H, -OH), 3.40 (dd, *J* = 9.1, 4.8 Hz, 1H), 3.23 (dd, *J* = 9.1, 5.8 Hz, 1H), 3.13 (d, *J* = 13.1 Hz, 1H), 2.44 (d, *J* = 13.1 Hz, 1H), 2.29 (m, 1H), 1.87 (dd, *J* = 14.3, 10.5 Hz, 1H), 1.63 (dd, *J* = 14.3, 5.5 Hz, 1H), 1.20-0-96 (m, 42H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.0, 138.5, 130.6, 128.6, 128.0, 127.9, 127.8, 126.2, 80.5, 79.5, 79.3, 73.5, 72.4, 46.0, 43.2, 38.3, 18.6, 18.53, 18.50, 13.6, 13.1 ppm. IR ($\tilde{\nu}_{max}$) = 2942 (m), 2865 (m), 1463 (m), 1153 (m), 881 (s), 678 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{38}H_{64}O_4Si_2$ 641.4416; Found 641.4417.

(1*R,2*R**,3*R**,4*R**)-4-((Benzyloxy)methyl)-1-(thiazol-4-yl)-2,3-bis((triisopropylsilyl)oxy)cyclopentanol (13e).**

Isopropylmagnesium chloride - lithium chloride complex (1.3 M in THF, 0.34 mL, 0.44 mmol) was added dropwise into a solution of 4-bromothiazole (0.04 mL, 0.41 mmol) in THF (1.5 mL). The reaction mixture was stirred at 25 °C for 30 min, then a solution of **2c** (150 mg, 0.27 mmol) in THF (1.5 mL) was added and the reaction mixture was stirred at 25 °C for 14 h. The solvent was evaporated, aqueous saturated NH_4Cl (15 mL) was added to the residue and the mixture was extracted with EtOAc (3 × 15 mL). The organic extracts were dried over $MgSO_4$, filtered, and the solvent was evaporated. The residual yellow oil was purified by flash chromatography (hexane/EtOAc = 25:1) to afford **13e** as a yellow oil (156 mg, 90%). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.40-7.33 (m, 4H), 7.28 (m, 1H), 7.13 (s, 1H), 4.86 (s, 1H), 4.43 (d, *J* = 4.0 Hz, 1H), 4.55 (d, AB, *J* = 11.4 Hz, 1H), 4.50 (d, AB, *J* = 11.4 Hz, 1H), 3.95 (d, *J* = 3.8 Hz, 1H), 2.53-2.48 (m, 1H, overlapped), 2.48 (d, AB, *J* = 10.7 Hz, 1H, partially overlapped), 2.43 (d, AB, *J* = 10.7 Hz, 1H), 2.24 (dd, *J* = 13.5, 4.1 Hz, 1H), 1.14-1.08 (m, 21H), 0.97-0.93 (m, 9H), 0.89-0.86 (m, 21H), 0.82-0.73 (m, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.4, 138.5, 128.5, 127.9, 127.7, 124.5, 117.6, 83.9, 79.6, 79.5, 73.6, 72.4, 43.5, 42.0, 18.48, 18.45, 18.3, 18.1, 13.1 ppm. IR ($\tilde{\nu}_{max}$) = 2942 (s), 2865 (s), 1463 (m), 1256 (m), 1089 (s), 882 (s), 680 (s) cm^{-1}. HRMS (MALDI-TOF) m/z: $[M+H]^+$ Calcd for $C_{34}H_{60}NO_4SSi_2$ 634.3776; Found: 634.3753.

General Procedure C for hydrogenolytic cleavage of benzyl ethers

Pd/C (10%, 10 mol %) or $Pd(OH)_2$ (10%-20%, 10 mol%) was added to a solution of the starting material in EtOH (0.1 mmol/5 mL) or THF (0.1 mmol/ 5 mL). The reaction mixture was thoroughly purged with H_2 and heated to 80 °C under H_2 atmosphere (1-50 bar, depending on the substrate) for 2-14 h (monitored by TLC and/or by ^1H NMR). The reaction mixture was cooled to 25 °C, filtered through Celite and concentrated under reduced pressure. The residue was purified by flash chromatography to afford the desired product.**5-((1*R**,2*R**,3*R**,4*R**)-**

1-Hydroxy-4-(hydroxymethyl)-2,3-bis(triisopropylsilyloxy) cyclopentyl)pyrimidine-2,4(1*H*,3*H*)-dione (14b).

The compound was prepared by General Procedure C using compound **13b** (376 mg, 0.45 mmol), Pd/C (5 mg, 0.05 mmol), H_2 (1 bar) in EtOH. The solid residues were removed by filtration through a pad of Celite and the resulting crude product was used in the next step without further purification. Analytical sample of **14b** was obtained by flash chromatography (hexane/EtOAc = 1:1) to afford **14b** as a white crystalline solid, m.p. > 200 °C (dec). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.05 (s, 1H), 10.80 (d, *J* = 5.9 Hz, 1H), 7.31 (d, *J* = 6.0 Hz, 1H), 4.68-4.66 (m, 1H), 4.47 (s, 1H), 4.32 (d, *J* = 3.9 Hz, 1H), 3.46-3.39 (m, 2H, partially overlapped with residual H_2O), 2.30-2.16 (m, 1H), 2.03 (dd, *J* = 14.3, 3.8 Hz, 1H), 1.87 (dd, *J* = 14.3, 10.3 Hz, 1H), 1.14-1.04 (m, 21H), 1.02-0.88 (m, 21H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 163.3, 151.1, 139.3, 113.1, 78.8, 73.8, 63.3, 45.0, 30.6, 18.97, 17.95, 17.9, 17.7, 12.3, 12.1 ppm. IR ($\tilde{\nu}_{max}$) = 3507 (br w), 3234 (br w), 3159 (br w), 2943 (m), 2866 (m), 1714 (s), 1652 (s), 1147 (m), 881 (s), 679 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{28}H_{54}N_2O_6Si_2Na$ 593.3413; Found 593.3413.

(1*R,2*R**,3*R**,4*R**)-4-(Hydroxymethyl)-1-phenyl-2,3-bis((triisopropylsilyl)oxy) cyclopentanol (15).**

The compound was prepared by General Procedure C using compound **13a** 100 mg (0.16 mmol), Pd/C (2 mg, 0.02 mmol) and H_2 (1 bar) in EtOH; flash chromatography (hexane/EtOAc = 20:1) afforded **15** as a white crystalline solid (65 mg, 75%), m.p. = 87-89 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58-7.52 (m, 2H), 7.32-7.24 (m, 2H), 7.22-7.15 (m, 1H), 4.48 (s, 1H), 4.41 (d, AB, *J* = 4.1 Hz, 1H), 4.33 (d, AB, *J* = 4.1 Hz, 1H) 3.78 (dd, *J* = 10.1, 4.7 Hz, 1H), 3.68 (dd, *J* = 10.1, 4.7 Hz, 1H), 2.55-2.38 (m, 2H), 2.06 (ddm, *J* = 13.4, 3.2 Hz, 1H), 1.18-1.10 (m, 21H), 0.94-0.81 (m, 18H), 0.72-0.54 (m, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.6, 128.5, 127.9, 127.8, 77.9, 77.6, 73.5, 72.4, 65.4, 44.9, 43.5, 26.4, 18.53, 18.49, 18.45, 13.4, 13.2 ppm. IR ($\tilde{\nu}_{max}$) = 3435 (br w), 3251 (br w), 2942 (s), 2865 (s), 1498 (m), 1151 (s), 867 (s), 680 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{55}O_3Si_2$ 519.3684; Found 519.3682.

(1*R,2*R**,3*R**,4*R**)-4-(Methoxymethyl)-1-phenyl-2,3-bis((triisopropylsilyl)oxy) cyclopentanol (16).**

To a stirred suspension of NaH (60% dispersion in mineral oil,16 mg, 0.24 mmol) in THF (1.5 mL) was added a solution of **15** (65 mg, 0.12 mmol) in THF (1 mL) at 25 °C. After stirring for 30 min and cooling to 0 °C (ice bath), methyl iodide (53 µL, 0.85 mmol) was added dropwise and the resulting mixture was stirred at 25 °C for 24 h. The reaction was quenched by addition of silica gel (0.15 g) and the solvent was evaporated under reduced pressure. The residue was then purified by

flash chromatography (hexane/EtOAc = 75:1 to 10:1) to afford **16** as a colorless crystalline solid (44 mg, 67%), m.p. = 61-69 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.57-7.54 (m, 2H), 7.30-7.26 (m, 2H), 7.20-7.15 (m, 1H), 4.36 (d, AB, *J* = 4.0 Hz, 1H), 4.34 (d, AB, *J* = 4.0 Hz, 1H), 3.48 (dd, *J* = 9.1, 4.5 Hz, 1H), 3.39 (s, 3H), 3.36 (dd, *J* = 9.1, 5.2 Hz, 1H), 2.52-2.41 (m, 2H, overlapped), 2.05 (dd, *J* = 13.7, 3.6 Hz, 1H), 1.16-1.11 (m, 21H), 0.95-0.81 (m, 18H), 0.67-0.57 (m, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 145.7, 127.8, 126.6, 126.2, 82.6, 81.4, 80.6, 77.4, 59.3, 44.2, 43.4, 18.50, 18.48, 18.42, 13.1 ppm. IR ($\tilde{\nu}_{max}$) = 3511 (m), 2939 (s), 2865 (s), 1461 (m), 1148 (m), 1067 (m), 882 (s), 681 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{31}H_{58}O_4Si_2Na$ 573.3765; Found 573.3764.

General Procedure D for removal of TIPS protecting groups

TBAF (1M in THF, 1.1-1.3 eq.) was added to a stirred solution of starting material in THF (0.3 mmol/mL). The reaction mixture was stirred at 25 °C for 14-24 h. The solvent was evaporated and the residue was purified by flash chromatography to afford the product.

5-((1*R,2*R**,3*R**,4*R**)-1,2,3-Trihydroxy-4-(hydroxymethyl)cyclopentyl)pyrimidine-2,4(1*H*,3*H*)-dione (1b).**

The compound was prepared by General Procedure D using compound **14b** (235 mg, 0.41 mmol); flash chromatography (CH_2Cl_2 to CH_2Cl_2/MeOH = 10:1 to 1:1) afforded compound **1b** (90 mg, 85 %) slightly contaminated by residual TBAF. Analytically pure sample of **1b** was obtained by RP-HPLC (Nucleodur® C18 HTec, details given in Supporting Information) as a white solid, m.p. > 250 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.96 (bs, 1H, -NH), 10.71 (bs, 1H, -NH), 7.29 (s, 1H), 4.54 (s, 1H, -OH), 4.42-4.50 (m, 3H, -3 x OH), 4.11 (m, 1H), 3.74 (dd, *J* = 10.5, 6.0 Hz, 1H), 3.43 (m, 1H), 3.34 (m, 1H), 2.13 (m, 1H), 1.89 (dd, *J* = 13.3, 9.7 Hz, 1H), 1.63 (dd, *J* = 13.3, 8.4 Hz, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 163.3, 151.3, 138.6, 114.5, 78.3, 72.9, 72.6, 63.2, 46.7, 36.3 ppm. IR ($\tilde{\nu}_{max}$) = 3088 (w), 3077 (w), 1704 (s), 1654 (s), 1015 (m), 849 (m), 542 (m) cm^{-1}. HRMS (ESI-TOF) m/z: $[M-H]^-$ Calcd for $C_{10}H_{13}N_2O_6$ 257.0779; Found 257.0775.

(1*R,2*R**,3*R**,4*R**)-4-(Benzyloxymethyl)-1-phenylcyclopentane-1,2,3-triol (14a).**

The compound was prepared by General Procedure D using compound **13a** (256 mg, 0.41 mmol); flash chromatography (CH_2Cl_2/MeOH = 20:1) afforded compound **14a** as a colorless oil (123 mg, 96%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48 (m, 2H), 7.38-7.27 (m, 7H), 7.26 (m, 1H, overlapped with $CHCl_3$), 4.56 (d, AB, *J* = 12.0 Hz, 1H), 4.53 (d, AB, *J* = 12.0 Hz, 1H), 4.19 (d, *J* = 6.4 Hz, 1H), 4.06 (dd, *J* = 6.3, 3.7 Hz, 1H), 3.63 (dd, *J* = 9.1, 4.9 Hz, 1H), 3.47 (dd, *J* = 9.1, 6.1 Hz, 1H), 3.35-2.77 (br s, 1H, -OH), 2.58-2.50 (m, 1H), 2.28 (dd, *J* = 14.1, 8.7 Hz, 1H), 1.81 (dd, *J* = 14.1, 9.7 Hz, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 144.1, 138.4, 128.7, 128.6, 127.94, 127.85, 127.5,

125.5, 82.3, 77.5, 75.9, 73.5, 72.2, 45.0, 39.8 ppm. IR ($\tilde{\nu}_{max}$) = 2955 (s), 2849 (s), 1729 (s), 1254 (m), 1065 (m), 702 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M-H]^-$ Calcd for $C_{19}H_{21}O_4$ 313.1445; Found 313.1442.

(1*R,2*R**,3*R**,4*R**)-4-(Hydroxymethyl)-1-phenylcyclopentane-1,2,3-triol (1a).**

The compound was prepared by prepared by General Procedure C using compound **14a** (61 mg, 0.19 mmol), $Pd(OH)_2/C$ (0.3 mg, 0.02 mmol), H_2 (50 bar) in THF; flash chromatography (CH_2Cl_2 to CH_2Cl_2/CH_3OH = 3:1) afforded compound **1a** as a white solid (40 mg, 92 %), m.p. = 141-143 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.49-7.44 (m, 2H), 7.33-7.27 (m, 2H), 7.22-7.17 (m, 1H), 4.66 (s, 1H), 4.58 (d, *J* = 6.1 Hz, 1H), 4.55 (m, 1H), 4.44 (d, *J* = 7.7 Hz, 1H), 3.82 (dd, *J* = 14.1, 6.8 Hz, 1H), 3.79 (m, 1H), 2.22 (m, 1H), 1.95 (dd, *J* = 13.5, 8.4 Hz, 1H), 1.66 (dd, *J* = 13.5, 10.1 Hz, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 146.3, 127.6, 126.0, 125.3, 80.7, 77.9, 72.9, 62.7, 46.9 ppm. The spectral data were consistent with those reported.[5]

(1*S,2*R**,3*R**,4*R**)-4-(Benzyloxymethyl)-1-butylcyclopentane-1,2,3-triol (14c).**

The compound was prepared by General Procedure D using compound **13c** (198 mg, 0.33 mmol); flash chromatography (CH_2Cl_2/MeOH = 20:1) afforded **14c** as a slightly yellow wax (78 mg, 82%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37-7.26 (m, 5H), 4.53 (d, AB, *J* = 12 Hz, 1H), 4.50 (d, AB, *J* = 12 Hz, 1H), 3.90 (m, 1H), 3.64 (d, *J* = 6.4 Hz, 1H), 3.53 (dd, *J* = 9.1, 5.2 Hz, 1H), 3.38 (dd, *J* = 9.1, 6.7 Hz, 1H), 3.16 (br s, 1H, -OH), 2.93 (br s, 1H, -OH), 2.70 (br s, 1H, -OH), 2.44-2.35 (m, 1H), 1.95 (dd, *J* = 14.0, 8.8 Hz, 1H), 1.62-1.53 (m, 1H), 1.49-1.28 (m, 6H), 0.90 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.4, 128.6, 127.9, 127.8, 80.8, 76.3, 76.2, 73.4, 72.5, 44.3, 39.1, 36.8, 26.2, 23.4, 14.2 ppm. IR ($\tilde{\nu}_{max}$) = 3260 (m), 2937 (m), 1409 (w), 1096 (s), 802 (s), 698 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M-H]^-$ Calcd for $C_{17}H_{26}O_4$ 293.1758; Found 293.1758; $[M+Cl]^-$ Calcd for $C_{17}H_{26}O_4Cl$ 329.1525; Found 329.1529.

(1*S,2*R**,3*R**,4*R**)-1-Butyl-4-(hydroxymethyl)cyclopentane-1,2,3-triol (1c).**

The compound was prepared by prepared by General Procedure C using compound **14c** (39 mg, 0.13 mmol) and $Pd(OH)_2/C$ (2 mg, 0.01 mmol), H_2 (50 bar) in THF; flash chromatography (CH_2Cl_2 to CH_2Cl_2/CH_3OH = 5:1) afforded **1c** as a white wax (25 mg, 93 %). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 4.42 (apparent t, *J* = 5.1 Hz, 1H), 4.34 (dd, *J* = 15.4, 6.3 Hz, 2H), 3.91 (s, 1H), 3.61 (dd, *J* = 5.4, 11.3 Hz, 1H), 3.39-3.32 (m, 3H), 2.02 (m, 1H), 1.69 (dd, *J* = 8.8, 13.3 Hz, 1H), 1.49-1.41 (m, 1H), 1.40-1.32 (m, 1H), 1.32-1.22 (m, 4H), 1.19 (dd, *J* = 9.0, 13.3 Hz, 1H), 0.86 (t, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 78.7, 76.0, 73.3, 62.8, 45.9, 36.8, 25.7, 22.8, 14.0 ppm.

IR ($\tilde{\nu}_{max}$) = 3424 (br w), 3235 (br w), 2955 (m), 2854 (m), 1376 (m), 1131 (s), 1020 (s), 867 (s), 529 (m) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Cl]^-$ Calcd for $C_{10}H_{20}O_4Cl$ 239.1056; Found 239.1056.

(1*R,2*R**,3*R**,4*R**)-1-Benzyl-4-(benzyloxymethyl)cyclopentane-1,2,3-triol (14d).**

The compound was prepared by General Procedure D using compound **13d** (218 mg, 0.33 mmol); flash chromatography (hexane/EtOAc = 20:1) afforded **14d** as a white semi-solid (98 mg, 90%). ^1H NMR (500 MHz, DMSO-d_6): δ = 7.36-7.22 (m, 10H), 4.49 (d, AB, *J* = 12.3 Hz, 1H), 4.46 (d, AB, *J* = 12.3 Hz, 1H), 3.90 (dd, *J* = 6.0, 4.0 Hz, 1H), 3.72 (d, *J* = 6.0 Hz, 1H), 3.49 (dd, *J* = 9.1, 5.1 Hz, 1H), 3.33 (dd, *J* = 9.1, 6.4 Hz, 1H), 3.03 (br s, 1H, -OH), 2.92 (d, *J* = 13.5 Hz, 1H), 2.80 (d, *J* = 13.5 Hz, 1H), 2.67 (br s, 1H, -OH), 2.36 (m, 1H), 1.83 (dd, *J* = 14.0, 8.8 Hz, 1H), 1.47 (dd, *J* = 14.0, 9.7 Hz, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 138.4, 137.2, 130.5, 128.6, 128.5, 127.9, 127.7, 126.8, 81.1, 77.2, 77.0, 75.7, 75.6, 73.4, 72.1, 44.8, 44.4, 36.4 ppm. IR ($\tilde{\nu}_{max}$) = 3432 (br w), 2844 (br w), 2955 (m), 1354 (m), 1183 (m), 1090 (s), 755 (m), 695 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M-H]^-$ Calcd for $C_{20}H_{23}O_4$ 327.1602; Found 327.1604.

(1*R,2*R**,3*R**,4*R**)-1-Benzyl-4-(hydroxymethyl)cyclopentane-1,2,3-triol (1d).**

The compound was prepared by prepared by General Procedure C using compound **14d** (30 mg, 0.09 mmol), $Pd(OH)_2/C$ (1 mg, 0.01 mmol), H_2 (50 bar) in THF; flash chromatography (CH_2Cl_2/CH_3OH = 20:1 to 1:1) afforded **1d** as a white semi-solid (20 mg, 92 %). ^1H NMR (500 MHz, DMSO-d_6): δ = 7.27-7.21 (m, 4H), 7.19-7.15 (m, 1H), 4.43 (d, *J* = 6.7 Hz, 1H, -OH), 4.40 (app t, *J* = 5.1 Hz, 1H, -OH), 4.35 (d, *J* = 7.1 Hz, 1H), 4.10 (s, 1H, -OH), 3.64 (dd, *J* = 11.8, 5.8 Hz, 1H), 3.38 (apparent t, *J* = 6.4 Hz, 1H), 3.32-3.26 (m, 2H, overlapped with H_2O), 2.77 (d, *J* = 13.1 Hz, 1H), 2.61 (d, *J* = 13.1 Hz, 1H), 2.03-1.97 (m, 1H), 1.49 (dd, *J* = 13.5, 8.9 Hz, 1H), 1.25 (dd, 13.5, 8.9 Hz, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 138.4, 130.2, 127.5, 125.7, 79.3, 75.3, 72.8, 62.7, 46.0, 44.5, 36.0 ppm. IR ($\tilde{\nu}_{max}$) = 3528 (m), 2912 (w), 2862 (w), 1366 (w), 1018 (s), 697 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M-H]^-$ Calcd for $C_{13}H_{17}O_4$ 237.1132; Found 237.1132; $[M+Cl]^-$ Calcd for $C_{13}H_{18}O_4Cl$ 273.0899; Found 273.0898.

(1*R,2*R**,3*R**,4*R**)-4-(Hydroxymethyl)-1-(thiazol-4-yl)cyclopentane-1,2,3-triol (1e).**

Lithium (10 mg, 1.43 mmol) in several pieces was added into a solution of naphthalene (244 mg, 1.91 mmol) in THF (9 mL). The reaction mixture was stirred at 25 °C under until the lithium was completely dissolved (2-3 h). The resulting dark green solution of lithium naphthalenide was slowly added into a solution of **13e** (150 mg, 0.24 mmol) in THF (2 mL). The reaction mixture was stirred at 25 °C for 1 h. The reaction mixture was quenched with saturated aqueous NH_4Cl (10 mL) and

extracted with EtOAc (3 × 15 mL). The organic extracts were dried over $MgSO_4$, filtered, and the solvent was evaporated. The crude product was dissolved in THF (3 mL) and TBAF (1 M in THF, 0.42 mL, 0.42 mmol) was added. The reaction mixture was stirred for 14 h at 25 °C. The solvent was evaporated and the crude product was purified by flash chromatography (CH_2Cl_2/MeOH = 30:1 to 1:1) to afford **1e** (29 mg, 53 %) slightly contaminated by residual TBAF. Analytically pure sample of **1e** was obtained by RP-HPLC (Nucleodur® C18 HTec, details given in Supporting Information) as a colorless glassy solid. ^{1}H NMR (500 MHz, CD_3OD): δ = 7.77 (d, *J* = 3.4 Hz, 1H), 7.50 (d, *J* = 3.4 Hz, 1H), 4.19 (d, *J* = 6.5 Hz, 1H), 4.06 (dd, *J* = 6.5, 4.7 Hz, 1H), 3.71 (ddm, *J* = 10.6, 6.1 Hz, 2H), 2.45 (m, 1H), 2.23 (dd, *J* = 13.9, 8.5 Hz, 1H), 2.08 (dd, *J* = 13.9, 10.2 Hz, 1H) ppm. ^{13}C NMR (126 MHz, CD_3OD): δ = 180.1, 143.7, 120.9, 83.6, 79.6, 74.7, 64.9, 40.7 ppm. IR ($\tilde{\nu}_{max}$) = 3345 (w), 2932 (w), 2873 (w), 1499 (w), 1063 (s), 1024 (s), 727 (m) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Cl]^-$ Calcd for $C_9H_{13}NO_4SCl$ 266.0259; Found 266.0259.

(1*R,2*R**,3*R**,4*R**)-4-(Methoxymethyl)-1-phenylcyclopentane-1,2,3-triol (17).**

The compound was prepared by General Procedure D using **16** (68 mg, 0.12 mmol); flash chromatography (hexane/EtOAc = 1:5) afforded **17** as a pale yellow crystalline solid (12 mg, 42%), m.p. = 59-60 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.52-7.49 (m, 2H), 7.38-7.34 (m, 2H), 7.29-7.26 (m, 1H), 4.19 (d, *J* = 6.5 Hz, 1H), 4.06 (dd, *J* = 6.4, 3.9 Hz, 1H), 3.55 (dd, *J* = 9.1, 4.9 Hz, 1H), 3.39 (dd, *J* = 9.1, 6.4 Hz, 1H), 3.38 (s, 3H), 2.56-2.49 (m, 1H), 2.28 (dd, *J* = 14.1, 8.5 Hz, 1H), 1.78 (dd, *J* = 14.1, 10.0 Hz, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 144.1, 128.6, 127.6, 125.5, 82.2, 77.4, 75.8, 74.8, 59.3, 45.0, 39.5 ppm. IR ($\tilde{\nu}_{max}$) = 3427 (br w), 3333 (br w), 3209 (br m), 2932 (w), 2857 (w), 1443 (m), 1066 (s), 1031 (s), 699 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M-H]^-$ Calcd for $C_{13}H_{17}O_4$ 237.1132; Found 237.1129.

(3a*R,6*R**,6a*R**)-6-((*tert*-Butyldiphenylsilyloxy)methyl)-2,2-dimethyl-6,6a-dihydro-3a*H*-cyclopenta[d][1,3]dioxol-4-yl trifluoromethanesulfonate (18a).**

LDA (2M solution in THF, 1.21 mL, 2.42 mmol) was added dropwise to a cooled solution (–78 °C) of compound **2a** (790 mg, 1.86 mmol) in THF (6 mL). The reaction mixture was stirred at –78 °C for 2 h. A solution of *N*-phenyl-bis(trifluoromethansulfonimide (0.790 mg, 2.22 mmol) in THF (5 mL) was added and the reaction mixture was stirred for 14 h while allowed to warm to 25 °C. The reaction mixture was quenched with saturated aqueous NH_4Cl (20 mL), diluted with water (30 mL), and extracted with EtOAc (3 × 50 mL). The organic extracts were dried over Na_2SO_4, filtered, and the solvent was evaporated. The dark brown residue was purified by flash chromatography (hexane/EtOAc = 20:1) to afford **18a** as a colorless oil (832 mg, 80%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.64-7.60 (m, 4H), 7.45-7.38 (m, 6H), 5.64 (d, *J* = 2.5 Hz, 1H), 5.05 (dd, *J* = 5.8, 1.8

Hz, 1H), 4.56 (d, *J* =1.8 Hz, 1H), 3.77 (dd, *J* = 10.3, 4.9 Hz, 1H), 3.66 (dd, *J* = 10.3, 4.4 Hz, 1H), 2.94 (m, 1H), 1.45 (s, 3H), 1.35 (s, 3H), 1.05 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 149.2, 135.8, 133.2, 133.1, 130.2, 128.1, 128.0, 118.92, 118.90 (q, $^{C\text{-}F}J$ = 320.7 Hz), 111.9, 81.0, 79.7, 64.2, 49.6, 27.3, 27.0, 25.9, 19.4 ppm. ^{19}F (470 MHz, $CDCl_3$): δ = –73.3 ppm. IR ($\tilde{\nu}_{max}$) = 2933 (w), 2860 (w), 1443 (m), 1424 (s), 1209 (s), 1129 (m), 1111 (m), 702 (m), 601 (m), 504 (m) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{26}H_{32}F_3O_6SSi$ 557.1635; Found 557.1636.

(1*R,4*R**,5*R**)-3-(Trifluoromethylsulfonyloxy)-4,5-bis(triisopropylsilyloxy)cyclopent-2-enyl)methyl pivalate (18b).**

KHMDS (1 M in THF, 1.21 mL, 1.21 mmol) was added at –78 °C to a solution of compound **2b** (550 mg, 1.01 mmol) and Comins' reagent (CAS# 145100-51-2, 476 mg, 1.21 mmol) in THF (4 mL) and the mixture was stirred at –78 °C for 1 h. The reaction mixture was then allowed to warm to 25 °C, stirred for 1 h, then quenched with saturated aqueous solution of NH_4Cl (10 mL), and extracted with EtOAc (3 × 20 mL). The combined extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (hexane/EtOAc = 50:1) to afford **18b** as a colorless wax (54 mg, 79%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.71 (d, *J* = 1.7 Hz), 4.61 (apparent d, *J* = 4.8 Hz, 1H), 4.47 (dd, *J* = 11.6, 3.4 Hz, 1H), 4.18 (dd, *J* = 6.3, 4.9 Hz, 1H), 4.06 (dd, *J* = 11.6, 4.1 Hz, 1H), 3.08 (m, 1H), 1.17 (s, 9H), 1.12-1.04 (m, 42H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.5, 150.9, 120.9, 118.8 (q, $^{C\text{-}F}J$ = 319.8 Hz), 75.5, 74.2, 61.8, 47.3, 39.1, 27.3, 18.39, 18.36, 18.33, 18.30, 13.3, 13.1 ppm. ^{19}F (470 MHz, $CDCl_3$): δ = –73.4 ppm. IR ($\tilde{\nu}_{max}$) = 2944 (m), 2867 (m), 1735 (m), 1427 (m), 1211 (s), 1138 (s), 882 (m), 825 (m), 682 (m), 609 (m) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{57}F_3O_7SSi_2$ 675.3388; Found 675.3389.

General Procedure E for the Suzuki coupling

A solution of enol triflate in DME/H_2O 4:1 (0.1 mmol/mL) was added to a mixture of hetero(aryl) boronic acid or boronate (1.5 eq.), K_3PO_4 (3 eq.) and $Pd(dppf)Cl_2.CH_3CN$ (10 mol %). The reaction mixture was then stirred at 80 °C for 2-14 h. After cooling to 25 °C, the reaction mixture was partitioned between H_2O (10 mL/0.5 mmol) and EtOAc (20 mL/0.5 mmol). The organic extracts were dried over Na_2SO_4, evaporated, and the residue was purified by flash chromatography to afford the product.

***tert*-Butyl(((3a*R**,4*R**,6a*S**)-2,2-dimethyl-6-phenyl-4,6a-dihydro-3a*H*-cyclopenta[d][1,3]dioxol-4-yl)methoxy)diphenylsilane (19).**

The compound was prepared by General Procedure E using enol triflate **18a** (440 mg, 0.79 mmol) and $PhB(OH)_2$ (145 mg, 1.18 mmol); flash chromatography (hexane/EtOAc = 20:1) afforded **19** as a colorless oil (326 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.65-7.60 (m, 6H), 7.42-7.29 (m, 9H), 6.05 (d, *J* = 2.6 Hz, 1H), 5.50 (dd, *J* = 5.8, 1.8 Hz, 1H), 4.71 (dm, *J* = 5.8 Hz, 1H), 3.84 (dd, *J* = 10.3, 4.9 Hz, 1H), 3.69 (dd, *J* = 10.3, 4.4 Hz, 1H), 3.09 (m, 1H), 1.42 (s, 3H), 1.39 (s, 3H), 1.02 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.8, 135.9, 135.8, 134.8, 133.8, 133.6, 129.9, 128.7, 128.1, 127.91, 127.88, 126.6, 110.6, 85.4, 81.9, 65.2, 53.8, 27.7, 27.1, 26.2, 19.5 ppm. IR ($\tilde{\nu}_{max}$) = 1588 (m), 1557 (m), 1401 (s), 1335 (w), 1239 (w), 1212 (s), 1098 (m), 708 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{31}H_{36}O_3SiNa$ 507.2326; Found 507.2325.

***tert*-Butyl(((3a*R**,4*R**,6a*S**)-2,2-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,6a-dihydro-3a*H*-cyclopenta[d][1,3]dioxol-4-yl)methoxy)diphenylsilane (20).**

Bis(pinacolato)diboron (140 mg, 0.55 mmol), KBr (90 mg, 0.75 mmol), and KOPh (99 mg, 0.75 mmol) were added to a solution of **18a** (278 mg, 0.50 mmol) in toluene (5 mL). The solution was evacuated and backfilled with argon (3 cycles). $Pd(Ph_3P)_2Cl_2$ (11 mg, 0.015 mmol, 3 mol %) and Ph_3P (8 mg, 0.03 mmol, 6 mol %) were added and the reaction mixture was stirred at 60 °C for 3 h. The reaction mixture was cooled to 25 °C, diluted with saturated aqueous $NaHCO_3$ (30 mL) and extracted with EtOAc (4 × 10 mL). The organic extracts were dried over Na_2SO_4, the solvent was evaporated and the brown residue was purified by flash chromatography (hexane/EtOAc = 20:1 to 10:1) to afford **20** as a colorless oil (187 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.65-7.59 (m, 4H), 7.45-7.35 (m, 6H), 6.44 (d, *J* = 2.8 Hz, 1H), 5.29 (d, *J* = 5.8 Hz, 1H), 4.59 (d, *J* = 6.2 Hz, 1H), 3.77 (dd, *J* = 10.1, 4.6 Hz, 1H), 3.59 (dd, *J* = 10.1, 4.6 Hz, 1H), 3.02 (m, 1H), 1.37 (s, 3H), 1.35 (s, 3H), 1.30 (s, 6H), 1.28 (s, 6H), 1.02 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 149.1, 137.7 (C-B observed indirectly by ^{1}H-^{13}C HMBC), 135.9, 135.8, 133.8, 133.5, 129.91, 129.90, 127.90, 127.88, 110.0, 87.6, 83.7, 82.4, 64.5, 56.2, 27.8, 27.0, 26.1, 25.0, 19.5 ppm. ^{11}B NMR (160.5 MHz, $CDCl_3$): δ = 29.9 ppm. IR ($\tilde{\nu}_{max}$) = 1592 (m), 1542 (m), 1328 (m), 1248 (m), 828 (s), 745 (m) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{31}H_{43}O_5BSiNa$ 557.2865; Found 557.2866.

((1*R,4*S**,5*R**)-3-Phenyl-4,5-bis(triisopropylsilyloxy)cyclopent-2-enyl)methyl pivalate (21a).**

The compound was prepared by General Procedure E using enol triflate **18b** (540 mg, 0.8 mmol) and $PhB(OH)_2$ (126 mg, 1.04 mmol); flash chromatography (hexane/EtOAc = 25:1) afforded **21a** as a colorless oil (455 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42-7.39 (m, 2H), 7.31 (m, 2H), 7.25 (m, 1H), 6.02 (apparent s, 1H), 5.10 (d, *J* = 4.2 Hz, 1H), 4.63 (dd, *J* = 11.2, 3.3 Hz, 1H), 4.13 (dd, *J* = 6.7, 4.6 Hz, 1H), 4.02 (dd, *J* = 11.2, 5.6 Hz, 1H), 3.24 (m, 1H), 1.15-1.13 (m, 30H), 0.98-0.89 (m, 18), 0.86-0.77 (m, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.7, 145.7, 135.9, 130.3,

128.5, 127.9, 126.3, 77.4, 77.0, 63.2, 49.5, 39.1, 27.4, 18.6, 18.53, 18.46, 13.8, 13.2 ppm. IR ($\tilde{\nu}_{max}$) = 2943 (m), 2866 (m), 1733 (m), 1141 (s), 882 (m), 682 (m) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{35}H_{62}O_4Si_2Na$ 625.4079; Found 625.4079.

((1*R,4*S**,5*R**)-3-(2,4-Difluorophenyl)-4,5-bis(triisopropylsilyloxy)cyclopent-2-enyl)methyl pivalate (21b).**

Degassed dimethoxyethane and water (10+5 mL) were added under argon to a mixture of **18b** (2.7 g, 3.99 mmol), 2,4-difluorophenylboronic acid (1.3 g, 7.98 mmol), LiCl (12 mg, 0.28 mmol), Na_2CO_3 (1.7 g, 16.15 mmol) and $Pd(PPh_3)_4$ (322 mg, 0.28 mmol) and the reaction mixture was stirred at 85 °C for 18 h. The reaction mixture was cooled to 25 °C, mixed with brine (80 mL) and extracted with EtOAc (3 × 80 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc = 15:1) to afford **21b** as a pale yellow oil (2.3 g; 89%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31 (td, *J* = 8.6, 6.5 Hz, 1H), 6.84 (ddd, *J* = 8.6, 3.4, 1.7 Hz, 1H), 6.79 (ddd, *J* = 11.2, 8.6, 2.5 Hz, 1H), 6.02 (apparent s, 1H), 5.08 (d, *J* = 4.4 Hz, 1H), 4.59 (dd, *J* = 11.3, 3.8 Hz, 1H), 4.17 (dd, *J* = 6.8, 4.4 Hz, 1H), 4.03 (dd, *J* = 11.3, 5.5 Hz, 1H), 3.21 (m, 1H), 1.18-1.06 (m, 32H), 0.97-0.91 (m, 16H), 0.86-0.77 (m, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.7, 162.6 (dd, ^{C-F}J = 231.6, 11.6 Hz), 160.5 (dd, ^{C-F}J = 232.7, 12.1 Hz), 140.3 (d, ^{C-F}J = 1.6 Hz), 134.5 (d, ^{C-F}J = 4.8 Hz), 130.5 (dd, ^{C-F}J = 5.6, 9.6 Hz), 120.7 (dd, ^{C-F}J = 4.1, 13.1 Hz), 111.2 (dd, ^{C-F}J = 3.1, 21.4 Hz), 104.4 (apparent t, ^{C-F}J = 26.2 Hz), 78.1 (d, ^{C-F}J = 3.4 Hz), 77.5 (detected by ^{1}H-^{13}C HSQC, overlapped with $CDCl_3$), 63.0, 49.4, 39.1, 27.4, 18.5, 18.44, 18.41, 17.9, 13.7, 13.3, 12.5 ppm. ^{19}F{^{1}H} NMR (471MHz, $CDCl_3$): δ = –109.2 (d, *J* = 7.8 Hz), –110.9 (d, *J* = 7.9 Hz) ppm. IR ($\tilde{\nu}_{max}$) = 2943 (m), 2886 (m), 1732 (s), 1501 (s), 1463 (w), 1137 (s), 881 (m), 679 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na^+]$ Calcd for $C_{35}H_{60}F_2O_4Si_2Na$ 661.3890; Found 661.3886.

((1*R,4*S**,5*R**)-3-(1-Methyl-1*H*-pyrazol-4-yl)-4,5-bis(triisopropylsilyloxy)cyclopent-2-enyl)methyl pivalate (21c).**

The compound was prepared by General Procedure E using triflate **18b** (575 mg, 0.85 mmol) and 1-methylpyrazole-4-boronic acid pinacol ester (194 mg, 0.94 mmol); flash chromatography (hexane/EtOAc = 20:1) afforded **21c** as a colorless wax (450 mg, 87 %). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 (s, 1H), 7.38 (s, 1H), 5.75 (s, 1H), 4.81 (d, *J* = 4.2 Hz, 1H), 4.56 (dd, *J* = 11.2, 3.8 Hz, 1H), 4.09 (dd, *J* = 6.1, 4.6 Hz, 1H), 3.98 (dd, *J* = 11.2, 5.5 Hz, 1H), 3.88 (s, 3H), 3.15 (m, 1H), 1.16 (s, 9H), 1.11 (s, 22H), 1.03-0.89 (m, 22H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.7, 137.6, 137.4, 127.7, 127.0, 118.8, 78.5, 77.2 (overlapped with $CDCl_3$), 63.3, 49.2, 39.1, 39.1, 27.4, 18.6, 18.6, 18.5, 18.4, 13.8, 13.2 ppm. IR ($\tilde{\nu}_{max}$) = 2941 (w), 2893 (w), 1721 (s), 1462 (m), 1256

(s), 1239 (s), 679 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{33}H_{62}N_2O_4Si_2$ 607.4321; Found 607.4322.

Methyl 5-((3*R,4*R**,5*S**)-3-(pivaloyloxymethyl)-4,5-bis(triisopropylsilyloxy)cyclopent-1-enyl)furan-3-carboxylate (21d).**

The compound was prepared by General Procedure E using **18b** (700 mg, 1.04 mmol) and methyl 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)furan-3-carboxylate (287 mg, 1.14 mmol); flash chromatography (hexane/EtOAc = 25:1) afforded **21d** as a colorless oil (550 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.92 (s, 1H), 6.67 (s, 1H), 6.10 (d, *J* = 1.4 Hz, 1H), 4.92 (d, *J* = 4.1 Hz, 1H), 4.62 (dd, *J* = 11.3, 3.6 Hz, 1H), 4.06 (dd, *J* = 7.4, 4.2 Hz, 1H), 4.01 (dd, *J* = 11.3, 5.6 Hz, 1H), 3.84 (s, 3H), 3.23 (m, 1H), 1.16 (s, 9H), 1.13-0.98 (m, 42H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.6, 163.6, 152.4, 146.9, 135.6, 130.8, 120.8, 106.3, 77.1, 76.4, 62.8, 51.9, 49.1, 39.1, 27.4, 18.6, 18.5, 18.4, 13.7, 13.1 ppm. IR ($\tilde{\nu}_{max}$) = 1730 (s), 1580 (w), 1281 (s), 881 (m), 679 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{35}H_{62}O_7Si_2Na$ 673.3926; Found 673.3927.

Methyl 5-((*3R*,4R*,5S)-3-(pivaloyloxymethyl)-4,5-bis(triisopropylsilyloxy)cyclopent-1-enyl)thiophene-3-carboxylate (21e).**

The compound was prepared by General Procedure E using **18b** (670 mg, 0.99 mmol) and methyl 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene-3-carboxylate (291 mg, 1.09 mmol); flash chromatography (hexane/EtOAc = 30:1) afforded **21e** as a colorless wax (650 mg, 99%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 1.4 Hz, 1H), 7,44 (apparent s, 1H), 5.98 (d, *J* = 1.9 Hz, 1H), 4.98 (d, *J* = 4.3 Hz, 1H), 4.61 (dd, *J* = 11.3, 3.8 Hz, 1H), 4.40 (m, 1H), 4.12 (dd, *J* = 7.0, 4.3 Hz, 1H), 4.01 (dd, *J* = 11.4, 5.3 Hz), 3.87 (s, 3H), 3.21 (m, 1H), 1.15 (s, 9H), 1.13-0.96 (m, 42H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.6, 163.2, 140.6, 139.4, 133.6, 132.1, 124.7, 78.0, 77.3, 62.7, 52.0, 49.5, 27.4, 27.4, 18.64, 18.57, 18.49, 18.43, 13.8, 13.2 ppm. IR ($\tilde{\nu}_{max}$) = 1715 (s), 1452 (m), 1286 (s), 1143 (s), 864 (s), 679 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{26}H_{41}O_5SSi$ 493.2438; Found 493.2444.

((1*R,4*S**,5*R**)-3-(3a,7a-Dihydrobenzo[*b*]thiophen-3-yl)-4,5-bis(triisopropylsilyloxy)cyclopent-2-enyl)methyl pivalate (21f).**

The compound was prepared by General Procedure E using **18b** (1.2 g, 1.83 mmol) and benzothiophen-2-ylboronic acid (490 mg, 2.75 mmol); flash chromatography (hexane/EtOAc = 15:1) afforded compound **21f** as a pale yellow oil (913 mg; 75%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.89 (dd, *J* = 6.8, 1.4 Hz, 1H), 7.85 (dd, *J* = 6.8, 1.4 Hz, 1H), 7.39-7.32 (m, 2H), 7.36 (s, 1H), 6.09 (d, *J* = 2.0 Hz, 1H), 5.13 (d, *J* = 4.3 Hz, 1H), 4.57 (dd, *J* = 11.3, 4.3 Hz, 1H), 4.30 (dd, *J* = 5.7, 4.5

Hz, 1H), 4.10 (dd, *J* = 11.3, 5.4 Hz, 1H), 1.16 (m, 30H), 0.92-0.87 (m, 21 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.7, 141.0, 140.5, 138.3, 132.6, 130.7, 124.6, 124.4, 124.0, 123.5, 123.0, 79.4, 77.1, 63.3, 49.9, 39.1, 27.4, 18.6, 18.50, 18.45, 13.6, 13.4 ppm. IR ($\tilde{\nu}_{max}$) = 2942 (m), 2865 (m), 1730 (m), 1460 (m), 1139 (s), 881 (s), 679 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{37}H_{62}O_4SSi_2Na$ 681.3800; Found 681.3803.

7-Bromo-*N*,*N*-bis((2-(trimethylsilyl)ethoxy)methyl)pyrrolo[2,1-*f*][1,2,4]triazin-4-amine.

A solution of 7-bromopyrrolo[1,2-f][1,2,4]triazin-4-amine (500 mg, 2.34 mmol) in DMF (4 mL) was added to a suspension of NaH (60 % in mineral oil, 234 mg, 5.86 mmol) in DMF (1.5 mL) and the mixture was stirred at 25 °C for 30 min. SEM-Cl (0.872 mL, 4.92 mmol) was added dropwise and the mixture was stirred at 25 °C for 5 h. The reaction mixture was quenched with water (10 mL) and extracted with EtOAc (3 × 25 mL). The organic phase was washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (hexane/EtOAc = 20 : 1) to afford the title compound (650 mg, 58%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.08 (s, 1H), 7.08 (d, AB, *J* = 4.8 Hz, 1H), 6.76 (d, AB, *J* = 4.8 Hz, 1H), 5.21 (s, 4H), 3.68 (m, 4H), 0.98 (m, 4H), 0.01 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 156.1, 147.5, 116.0, 114.0, 106.9, 102.1, 77.8, 66.3, 18.4, -1.2 ppm. IR ($\tilde{\nu}_{max}$) = 2954 (w), 1582 (w), 1517 (w), 1264 (m), 1074 (m), 858 (m), 732 (s) cm^{-1}. HR-MS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{34}N_4O_2Si_2Br$ 473.1403; Found: 473.1402.

(4-(bis((2-(Trimethylsilyl)ethoxy)methyl)amino)pyrrolo[2,1-*f*][1,2,4]triazin-7-yl)boronic acid (23).

n-BuLi (1.6 M in hexanes, 2.4 mL, 3.84 mmol) was added to a solution of 7-bromo-*N*,*N*-bis((2-(trimethylsilyl)ethoxy)methyl)pyrrolo[2,1-*f*][1,2,4]triazin-4-amine (909 mg, 1.92 mmol) in THF (6 mL) at -78 °C and the mixture was stirred at -78 °C for 30 min. 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (515 µL, 2.30 mmol) was added dropwise to the reaction mixture at -78 °C. The reaction mixture was then allowed to warm to 25 °C and stirred for 1 h. Saturated aqueous solution of NH_4Cl (10 mL) was added and the mixture was extracted with EtOAc (3 × 30 mL). The organic phase was washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to yield the crude boronate. The boronate hydrolyzed during the purification by flash chromatography on silica gel (CH_2Cl_2/EtOAc = 9:1) to afford **23** (418 mg, 50%) as a yellow wax . ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.35 (s, 2H, -$B(OH)_2$), 8.16 (s, 1H), 7.20 (d, AB, *J* = 4.5 Hz, 1H), 7.01 (d, AB, *J* = 4.8 Hz, 1H), 5.22 (s, 4H), 3.65 (apparent t, *J* = 8.1 Hz, 4H), 0.91

(apparent t, J = 8.1 Hz, 4H), – 0.03 (s, 18H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 155.7, 146.1, 126.3 (br, C-B(OH)$_2$, detected through ^{1}H-^{13}C HMBC), 120.2, 116.9, 106.2, 77.6, 65.1, 17.5, – 1.5 ppm. ^{11}B NMR (160.5 MHz, DMSO-d_6): δ = 25.9 (br) ppm. IR ($\tilde{\nu}_{max}$) = 2952 (m), 1585 (m), 1517 (w), 1370 (m), 1248 (m), 1075 (s), 856 (s), 832 (s) cm^{-1}. HRMS (ESI-TOF) m/z: [M-H]$^-$ Calcd for $C_{18}H_{34}N_4O_4BSi_2$ 437.2217; Found 437.2211.

((1*R,4*S**,5*R**)-3-(4-(bis((2-(Trimethylsilyl)ethoxy)methyl)amino)pyrrolo[1,2-*f*][1,2,4]triazin-7-yl)-4,5-bis(triisopropylsilyloxy)cyclopent-2-enyl)methyl pivalate (21g).**

The compound was prepared by General Procedure E from **18b** (162 mg, 0.24 mmol) and boronic acid **23** (137 mg, 0.31 mmol); flash chromatography (hexane/EtOAc = 20:1) afforded **21g** as a yellow semi-solid (164 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.98 (s, 1H), 6.98 (d, J = 4.8 Hz, 1H), 6.76 (apparent s, 1H), 6.74 (d, J = 4.8 Hz, 1H), 5.24-5.17 (m, 5H), 4.64 (dd, J = 11.3, 3.4 Hz, 1H), 4.12 (dd, J = 7.5, 4.3 Hz, 1H), 4.05 (dd, J = 11.3, 5.4 Hz, 1H), 3.67 (m, 4H), 1.12 (m, 30H), 1.07-0.79 (m, 29H), -0.01 (s, 18H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.7, 156.2, 146.5, 135.4, 133.3, 127.2, 115.8, 111.7, 105.5, 78.0, 77.9, 76.8, 66.2, 63.1, 49.1, 39.1, 27.4, 18.6, 18.5, 18.43, 18.41, 13.7, 13.1, -1.2 ppm. IR ($\tilde{\nu}_{max}$) = 2945 (w), 2858 (w), 1732 (s), 1582 (s), 1513 (s), 1248 (w), 1142 (s), 1079 (s), 855 (s), 681 (m) cm^{-1}. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd for $C_{47}H_{90}N_4O_6Si_4$ 919.6012; Found 919.6012.

((1*R,4*S**,5*R**)-4,5-Dihydroxy-3-phenylcyclopent-2-enyl)methyl pivalate (22a).**

The compound was prepared by general procedure D using **21a** (120 mg, 0.20 mmol); flash chromatography (CH_2Cl_2/EtOAc = 10:3) afforded **22a** as a colorless wax (55 mg, 95%). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.56-7.53 (m, 2H), 7.35-7.31 (m, 2H), 7.24 (dt, J = 9.1, 4.3 Hz, 1H), 6.26 (d, J = 2.2 Hz, 1H), 4.67 (m, 2H), 4.57 (dd, J = 9.2, 5.2 Hz, 2H, overlapped), 3.82 (dm, J = 4.9 Hz, 1H), 3.66 (m, 1H), 3.38 (m, 1H), 2.73 (dm, J = 5.9 Hz, 1H), 1.17 (s, 9H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 142.5, 135.3, 129.6, 128.2, 127.0, 125.7, 73.9, 72.7, 61.8, 53.6 ppm. IR ($\tilde{\nu}_{max}$) = 2985 (w), 1729 (s), 1569 (m), 1507 (s), 1282 (s), 1107 (s), 857 (s) cm^{-1}. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for $C_{17}H_{22}O_4Na$ 313.1411; Found 313.1410.

((1*R,4*S**,5*R**)-3-(2,4-Difluorophenyl)-4,5-dihydroxycyclopent-2-enyl)methyl pivalate (22b).**

The compound was prepared by General Procedure D using **21b** (178 mg, 0.28 mmol); flash chromatography (CH_2Cl_2/EtOAc = 3:1 to 1:1) afforded **22b** as a colorless oil (88 mg, 97%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55-7.50 (ddm, J = 6.6, 2.2 Hz, 1H), 6.91-6.87 (dm, J = 2.6, 1.0 Hz,

1H), 6.87-6.81 (m, *J* = 9.9, 2.6 Hz, 1H), 6.24 (apparent t, *J* = 1.8 Hz, 1H), 4.96 (dm, *J* = 5.9 Hz, 1H), 4.35 (dd, *J* = 11.1, 5.6 Hz, 1H), 4.19 (dd, *J* = 7.0, 4.1 Hz, 1H), 4.17 (m, 1H), 3.11 (m, 1H), 1.19 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.7, 162.6 (dd, $^{C\text{-}F}J$ = 250.2, 11.8 Hz), 161.0 (dd, $^{C\text{-}F}J$ = 252.8, 11.3 Hz), 138.3 (d, $^{C\text{-}F}J$ = 2.4 Hz), 132.7 (dd, *J* = 8.4, 1.7 Hz), 130.3 (dd, $^{C\text{-}F}J$ = 9.9, 5.9 Hz), 119.0 (dd, $^{C\text{-}F}J$ = 12.8, 4.8 Hz), 111.7 (dd, $^{C\text{-}F}J$ = 21.1, 3.5 Hz), 104.7 (apparent t, $^{C\text{-}F}J$ = 25.8 Hz), 76.3 (d, $^{C\text{-}F}J$ = 1.6 Hz), 73.9, 64.4, 51.7, 39.1, 27.4, 17.9, 12.5 ppm. ^{19}F{^{1}H} NMR (471MHz, $CDCl_3$): δ = – 109.5 (d, *J* = 7.8 Hz), – 110.3 (d, *J* = 7.9 Hz) ppm. IR ($\tilde{\nu}_{max}$) = 2973, 1727 (s), 1591 (m), 1504 (s), 1282 (s), 1104 (s), 848 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{20}F_2O_4Na$ 349.1222; Found 349.1219.

((1*R,4*S**,5*R**)-4,5-Dihydroxy-3-(1-methyl-1*H*-pyrazol-4-yl)cyclopent-2-enyl)methyl pivalate (22c).**

The compound was prepared by General Procedure D using **21c** (378 mg, 0.62 mmol); flash chromatography (CH_2Cl_2/EtOAc = 1:1) afforded **22c** as a yellow wax (167 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.62 (s, 1H), 7.54 (s, 1H), 5.78 (d, *J* = 2.2 Hz, 1H), 4.76 (d, *J* = 5.8 Hz, 1H), 4.27 (dd, *J* = 11.0, 5.8 Hz, 1H), 4.13 (dd, *J* = 5.8, 4.3 Hz, 1H), 4.09 (dd, *J* = 11.0, 5.5 Hz, 1H), 3.87 (s, 2H), 3.04 – 2.99 (m, 1H), 1.17 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.7, 137.7, 136.2, 128.2, 124.1, 117.3, 77.2, 74.0, 64.8, 51.8, 39.1, 39.0, 27.4 ppm. IR ($\tilde{\nu}_{max}$) = 3416 (w), 2952 (w), 1717 (s), 1284 (s), 1167 (s), 1151 (s), 622 (m) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Cl]^-$ Calcd for $C_{15}H_{22}N_2O_4Cl$ 329.1274; Found 329.1273.

Methyl 5-((3*R,4*R**,5*S**)-4,5-dihydroxy-3-(pivaloyloxymethyl)cyclopent-1-enyl)furan-3-carboxylate (22d).**

The compound was prepared by General Procedure D using **21d** (415 mg, 0.64 mmol); flash chromatography (CH_2Cl_2/EtOAc = 3:1) afforded **22d** as a yellow wax (185 mg, 86%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.96 (s, 1H), 6.81 (s, 1H), 6.12 (d, *J* = 2.3 Hz, 1H), 4.86 (m, 1H), 4.33 (dd, *J* = 11.1, 5.6 Hz, 1H), 4.13 (m, 2H, overlapped), 3.84 (s, 3H), 3.10 (dm, *J* = 4.7 Hz, 1H), 1.18 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.7, 163.6, 151.5, 147.6, 134.0, 128.0, 120.8, 107.5, 75.0, 74.2, 64.4, 51.9, 51.7, 39.1, 27.4 ppm. IR ($\tilde{\nu}_{max}$) = 3427 (m), 2958 (m), 1719 (m), 1235 (s), 760 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Cl]^-$ Calcd for $C_{17}H_{22}O_7Cl$ 373.1060; Found 373.1058.

Methyl 5-((*3R*,4R*,5S)-4,5-dihydroxy-3-(pivaloyloxymethyl)cyclopent-1-enyl)thiophene-3-carboxylate (22e).**

The compound was prepared by General Procedure D using **21e** (673 mg, 1.01 mmol); flash chromatography (CH_2Cl_2/EtOAc = 4:1) afforded **22e** as a white wax (265 mg, 74%). ^{1}H NMR (500

MHz, $CDCl_3$): δ = 7.98 (d, *J* = 1.3 Hz, 1H), 7.59 (apparent s, 1H), 6.01 (d, *J* = 2.4 Hz, 1H), 4.91 (d, *J* = 5.4 Hz, 1H), 4.34 (dd, *J* = 11.1, 5.5 Hz, 1H), 4.19 (apparent t, *J* = 5.0 Hz, 1H), 4.14 (dd, *J* = 11.1, 5.4 Hz, 1H), 3.86 (s, 3H), 3.08 (m, 1H), 2.82-2.67 (br s, 2H, -OH), 1.18 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.7, 163.3, 139.1, 137.9, 134.0, 132.5, 128.3, 125.4, 76.1, 74.2, 64.3, 52.1, 51.9, 39.1, 27.4 ppm. IR ($\tilde{\nu}_{max}$) = 3412 (w), 2969 (w), 1711 (s), 1451 (m), 1227 (s), 1152 (s), 1088 (m), 736 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{21}O_5S$ 337.1104; Found 337.1107.

((1*R,4*S**,5*R**)-3-(3a,7a-Dihydrobenzo[*b*]thiophen-3-yl)-4,5-dihydroxycyclopent-2-enyl)methyl pivalate (22f).**

The compound was prepared by General Procedure D using **21f** (873 mg, 0.64 mmol); flash chromatography (CH_2Cl_2/EtOAc = 3:1) afforded **22f** as a yellow oil (378 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.99 (dd, *J* = 7.3, 0.6 Hz, 1H), 7.88 (dd, *J* = 7.3, 0.6 Hz, 1H), 7.43-7.36 (m, 2H), 6.24 (d, *J* = 2.4 Hz, 1H), 4.97 (dd, *J* = 5.7, 1.0 Hz, 1H), 4.43 (dd, *J* = 11.1, 5.4 Hz, 1H), 4.25 (m, 2H, overlapped), 3.18 (m, 1H), 1.20 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.8, 140.8, 139.1, 137.8, 131.2, 129.2, 125.2, 124.8, 124.8, 123.2, 77.7, 73.8, 64.4, 51.9, 39.1, 27.4, 17.9, 12.5 ppm. IR ($\tilde{\nu}_{max}$) = 2958 (m), 2939 (m), 2865 (m), 1726 (s), 1282 (s), 1150 (s), 758 (s), 731 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{22}O_4SNa$ 369.1131; Found 369.1128.

((1*R*,4*S*,5*R*)-3-(4-(bis((2-(Trimethylsilyl)ethoxy)methyl)amino)pyrrolo[1,2-*f*][1,2,4]triazin-7-yl)-4,5-dihydroxycyclopent-2-enyl)methyl pivalate (22g).

The compound was prepared by General Procedure D using **21g** (140 mg, 0.15 mmol); flash chromatography (CH_2Cl_2 to CH_2Cl_2/MeOH = 20:1) afforded **22g** as a yellow semi-solid (75 mg, 81 %). ^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.99 (s, 1H), 7.08 (d, *J* = 4.8 Hz, 1H), 6.86 (d, *J* = 4.8 Hz, 1H), 6.44 (d, *J* = 2.2 Hz, 1H), 5.22 (m, 4H), 4.97 (dd, *J* = 6.0, 0.9 Hz, 1H), 4.40 (dd, *J* = 11.0, 5.2 Hz), 4.15 (m, 2H), 3.69 (m, 4H), 3.13 (m, 1H), 1.19 (s, 9H), 0.99 (m, 4H), -0.02 (s, 18H) ppm. ^{13}C NMR (126 MHz, CD_2Cl_2): δ = 178.3, 156.4, 146.9, 135.2, 131.3, 127.6, 115.2, 111.5, 106.8, 77.8, 74.5, 74.1, 66.1, 64.3, 51.5, 38.8, 29.8, 27.1, 18.2, –1.4, –1.6 ppm. IR ($\tilde{\nu}_{max}$) = 3278 (w), 2954 (w), 2918 (w), 1725 (m), 1578 (m), 1160 (w), 1084 (s), 1008 (m), 858 (s), 833 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{51}N_4O_6Si_2$ 607.3352; Found 607.3352.

General Procedure F for the cleavage of the pivaloate

Sodium methoxide (5 eq.) was added into a solution of the starting material in MeOH (0.1 mmol/mL) and the reaction mixture was stirred at 65 °C for 14 h. The reaction mixture was cooled to 25 °C, the solvent was evaporated and the residue was purified by flash chromatography.

(1*R,2*S**,5*R**)-5-(Hydroxymethyl)-3-phenylcyclopent-3-ene-1,2-diol (3a).**

The compound was prepared by General Procedure F using **22a** (334 mg, 1.15 mmol); flash chromatography (CH_2Cl_2/MeOH = 20:1 to 10:1) afforded **3a** as a white solid (0.211 g, 89 %), m.p. = 99-101 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.56-7.53 (m, 2H), 7.33 (tm, *J* = 7.2 Hz, 2H), 7.23 (tt, *J* = 7.2, 1.0 Hz, 1H), 6.26 (d, *J* = 2.2 Hz), 4.67 (m, 2H), 4.57 (m, 2H), 3.82 (apparent d, *J* = 4.5 Hz, 1H, -OH), 3.66 (m, 1H), 3.38 (m, 1H), 2.73 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 142.5, 135.3, 129.6, 128.2, 127.0, 125.7, 73.9, 72.7, 61.8, 53.6 ppm. IR ($\tilde{\nu}_{max}$) = 2927 (m), 2855 (m), 1471 (m), 1427 (m), 1104 (s), 699 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Cl]^-$ Calcd for $C_{12}H_{14}O_3Cl$ 241.0637; Found 241.0637.

(1*R,2*S**,5*R**)-3-(2,4-Difluorophenyl)-5-(hydroxymethyl)cyclopent-3-ene-1,2-diol (3b).**

The compound was prepared by General Procedure F using **22b** (126 mg, 0.39 mmol); flash chromatography (CH_2Cl_2/MeOH = 10:1 to 5:1) afforded **3b** as a white solid (83 mg, 89%), m.p. = 122-124 °C. NMR (500 MHz, DMSO-d_6): δ = 7.61 (ddm, *J* = 6.8, 2.1 Hz, 1H), 7.22 (ddd, *J* = 11.9, 9.3, 2.6 Hz, 1H), 7.09 (ddm, *J* = 8.6, 2.8 Hz, 1H), 6.29 (apparent t, *J* = 2.1 Hz, 1H), 4.73 (m, 1H, -OH), 4.68 (apparent t, *J* = 5.9, 1H,-OH), 4.63-4.59 (m, 2H, overlapped), 3.81 (dd, *J* = 12.0, 5.8 Hz, 1H), 3.64 (m, 1H), 3.40-3.35 (m, 1H), 2.76 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 160.9 (dd, $^{C\text{-}F}J$ = 246.9, 12.5 Hz), 160.4 (dd, $^{C\text{-}F}J$ = 251.8, 11.9 Hz), 136.5 (d, $^{C\text{-}F}J$ = 3.3 Hz), 134.2 (dd, *J* = 10.1, 1.9 Hz), 130.3 (dd, $^{C\text{-}F}J$ = 9.8, 6.0 Hz), 119.8 (dd, $^{C\text{-}F}J$ = 13.0, 3.5 Hz), 111.3 (dd, $^{C\text{-}F}J$ = 20.9, 3.5 Hz), 104.2 (apparent t, $^{C\text{-}F}J$ = 26.1 Hz), 74.9, 72.0, 61.6, 54.1 ppm. ^{19}F{^{1}H} NMR (471MHz, DMSO-d_6): δ= – 108.8 (d, *J* = 8.3 Hz), – 111.9 (d, *J* = 7.8 Hz) ppm. IR ($\tilde{\nu}_{max}$) = 3072 (w), 3051 (w), 2931 (w), 2858 (w), 1613 (m), 1254 (m), 849 (m), 821 (m), 739 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{12}O_3F_2Na$ 265.0652; Found 265.0657. Crystal data for **3b**: Crystallized from MeOH, $C_{12}H_{12}F_2O_3$, M_{rel} = 242.22, T = 120 K, space group P-1, a = 5.2120(4) Å, b = 7.4380(5) Å, c = 14.3549(9) Å, α = 80.834(6), β = 85.227(6), γ = 74.865(6), V = 529.826 Å^3. CCDC ref. No. 1452238.

(1*R,2*S**,5*R**)-5-(Hydroxymethyl)-3-(1-methyl-1*H*-pyrazol-4-yl)cyclopent-3-ene-1,2-diol (3c).**

The compound was prepared by General Procedure F using **22c** (96 mg, 0.33 mmol); flash chromatography (CH_2Cl_2/MeOH = 10:1 to 4:1) afforded **3c** as a white wax (63 mg, 91%). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.73 (s, 1H), 7.56 (s, 1H), 5.82 (d, *J* = 2.1 Hz, 1H), 4.60 (d, *J* = 6.0 Hz, 1H, -OH), 4.54 (dd, *J* = 4.9 Hz, 1H), 4.49-4.44 (m, 2H, overlapparented), 3.80 (s, 3H), 3.78 (dd, *J* = 11.5, 5.5 Hz, 1H), 3.55 (m, 1H), 2.65 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 136.6, 135.4, 127.9, 124.8, 117.6, 75.2, 72.6, 62.3, 53.9, 38.3 ppm. IR ($\tilde{\nu}_{max}$) = 2956 (m), 2923 (s), 1727

(s), 1461 (m), 1260 (s), 1071 (m), 798 (m) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Cl]^-$ Calcd for $C_{10}H_{14}N_2O_3Cl$ 245.0698; Found 245.0698.

Methyl 5-((3*R*,4*R*,5*S*)-4,5-dihydroxy-3-(hydroxymethyl)cyclopent-1-enyl)furan-3-carboxylate (3d).

The compound was prepared by General Procedure F using **22d** (120 mg, 0.35 mmol); flash chromatography (CH_2Cl_2/MeOH = 10:1 to 4:1) afforded **3d** as a white wax (0.077 g, 86%). ^1H NMR (500 MHz, DMSO-d_6): δ = 8.35 (s, 1H), 6.72 (s, 1H), 6.13 (d, *J* = 2.2 Hz, 1H), 4.92 (d, *J* = 6.7 Hz, 1H), 4.60 (m, 2H), 4.70 (d, *J* = 6.7 Hz, 1H), 3.82 (dd, *J* = 12.2, 5.8 Hz, 1H), 3.78 (s, 3H), 3.60 (ddd, *J* = 10.3, 5.1 Hz, 1H), 3.40 – 3.34 (m, 1H), 2.72 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 162.7, 152.2, 147.7, 133.3, 129.4, 119.7, 105.8, 73.7, 72.5, 61.5, 53.9, 51.5 ppm. IR ($\tilde{\nu}_{max}$) = 3203 (m), 1724 (s), 1580 (m), 1515 (m), 1233 (s), 760 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Cl]^-$ Calcd for $C_{12}H_{14}O_6Cl$ 289.0484; Found 289.0483.

Methyl 5-((*3R*,4R*,5S)-4,5-dihydroxy-3-(hydroxymethyl)cyclopent-1-enyl)thiophene-3-carboxylate (3e).**

The compound was prepared by General Procedure F using **22e** (110 mg, 0.31 mmol); flash chromatography (CH_2Cl_2/MeOH = 9:1) afforded **3e** as a white wax (42 mg, 50%). ^1H NMR (500 MHz, DMSO-d_6): δ = 8.20 (d, *J* = 1.3 Hz, 1H), 7.48 (apparent s, 1H), 6.11 (d, *J* = 2.1 Hz, 1H), 4.94 (d, *J* = 6.8 Hz, 1H), 4.64 - 4.59 (m, 3H), 3.85 (m, 1H), 3.80 (s, 3H), 3.59 (m, 1H), 3.37 (m, 1H), 2.71 (m, 1H), 3.40 – 3.34 (m, 1H), 2.72 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 162.3, 140.4, 136.9, 132.6, 132.4, 129.9, 123.8, 75.0, 72.6, 61.6, 54.1, 51.7 ppm. IR ($\tilde{\nu}_{max}$) = 3350 (w), 3228 (w), 1678 (s), 1527 (m), 1256 (s), 1055 (s), 739 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Cl]^-$ Calcd for $C_{12}H_{14}O_5SCl$ 305.0256; Found 305.0251.

(1*R,2*S**,5*R**)-3-(3a,7a-Dihydrobenzo[*b*]thiophen-3-yl)-5-(hydroxymethyl)cyclopent-3-ene-1,2-diol (3f).**

The compound was prepared by General Procedure F using **22f** (70 mg, 0.20 mmol); flash chromatography (CH_2Cl_2/MeOH = 10:1 to 5:1) afforded **3f** as a white solid (44 mg, 83%). m.p. = 123-125 °C. ^1H NMR (500 MHz, DMSO-d_6): δ = 7.94 (tm, *J* = 6.8 Hz, 2H), 7.43 (apparent s, 1H), 7.40-7.33 (m, 2H), 4.59 (d, *J* = 6.1 Hz, 1H), 4.55 (dd, *J* = 5.2 Hz, 1H), 4.43 (d, *J* = 4.8 Hz, 1H), 3.92 (m, 1H), 3.76 (dd, *J* = 9.9, 4.9 Hz, 1H), 3.50 (m, 1H), 3.45-3.36 (m, 2H, overlapped), 2.22 (ddm, *J* = 12.8, 8.22 Hz, 1H), 2.12-2.04 (m, 1H), 1.42 (ddd, *J* = 12.9, 10.2, 8.9 Hz) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 139.8, 139.2, 139.1, 124.1, 123.7, 122.7, 122.4, 120.3, 77.0, 73.3, 62.8,

46.3, 42.9, 30.4 ppm. IR ($\tilde{\nu}_{max}$) = 3311 (m), 1254 (m), 1126 (m), 1029 (s), 1018 (m), 737 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{14}O_3SNa$ 285.0556; Found 285.0554.

(1*R,2*S**,5*R**)-3-(4-(bis((2-(Trimethylsilyl)ethoxy)methyl)amino)pyrrolo[1,2-*f*][1,2,4]triazin-7-yl)-5-(hydroxymethyl)cyclopent-3-ene-1,2-diol (3g).**

The compound was prepared by General Procedure F using **22g** (66 mg, 0.11 mmol); flash chromatography (CH_2Cl_2 to CH_2Cl_2/MeOH = 10:1) afforded **3g** as a yellow solid (55 mg, 98%). m.p. = 250 °C. ^{1}H NMR (500 MHz, CD_3OD): δ = 8.10 (s, 1H), 7.18 (d, *J* = 4.8 Hz, 1H), 7.13 (d, *J* = 2.2 Hz, 1H), 7.03 (d, *J* = 4.8 Hz, 1H), 5.32 (apparent s, 4H), 5.01 (dd, *J* = 5.8, 0.6 Hz, 1H), 4.11 (m, 1H), 3.96 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.80 (m, 4H), 3.73 (dd, *J* = 10.8, 6.6 Hz, 1H), 3.09 m (1H), 1.06 (m, 4H), -0.08 (s, 18H) ppm. ^{13}C NMR (126 MHz, CD_3OD): δ = 157.5, 147.7, 134.8, 133.5, 128.6, 116.9, 113.4, 107.8, 79.6, 77.4, 74.6, 67.2, 64.0, 55.2, 19.3, –1.0 ppm. IR ($\tilde{\nu}_{max}$) = 3280 (w), 2920 (m), 1725 (m), 1579 (w), 1087 (s), 833 (s), 759 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{43}N_4O_5Si_2$ 523.2772; Found 523.2776.

(1*R,2*S**,5*R**)-3-(4-Aminopyrrolo[1,2-*f*][1,2,4]triazin-7-yl)-5-(hydroxymethyl)cyclopent-3-ene-1,2-diol (3h).**

Pyridinium 4-toluenesulfonate (360 mg, 1.44 mmol) was added into a solution of **3g** (150 mg, 0.28 mmol) in MeOH : H_2O (5+1 mL), the reaction mixture was stirred at 55 °C for 12 h, then cooled to 25 °C and the solvents were evaporated. The residue was purified by preparative TLC (SiO_2, CH_2Cl_2/MeOH 10:1, repeated elution) to afford **3h** (115 mg) slightly contaminated by TsOH. Analytically pure sample of **3h** was obtained by RP-HPLC (Nucleodur® C18 HTec, details given in Supporting Information) as a white solid, m.p. > 250 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.92 (s, 1H), 7.64 (br s, 2H, -NH_2), 7.13 (d, *J* = 2.2 Hz, 1H), 6.90 (d, *J* = 4.5 Hz, 1H), 6.88 (d, *J* = 2.1 Hz, 1H), 6.76 (d, *J* = 4.5 Hz, 1H), 4.74 (d, *J* = 6.5 Hz, 1H), 4.70 (apparent t, *J* = 5.8 Hz, 1H), 4.60 (apparent t, *J* = 5.3 Hz, 1H), 4.51 (d, *J* = 7.2 Hz), 3.78 (dd, *J* = 13.1, 6.5 Hz, 1H), 3.68 (m, 1H), 3.40-3.35 (m, 1H), 2.80 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 155.5, 148.0, 133.1, 130.2, 125.9, 115.4, 110.6, 101.4, 75.2, 72.2, 62.0, 53.9 ppm. IR ($\tilde{\nu}_{max}$) = 3333 (w), 3218 (w), 2924 (m), 1651 (m), 1602 (m), 1122 (m), 1010 (m), 731 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{12}H_{15}N_4O_3$ 263.1139; Found 263.1139; $[M-H]^-$ Calcd for $C_{12}H_{13}N_4O_3$ 261.0993; Found 261.0991.

General Procedure G for the directed hydrogenation

H_2 was gently bubbled into a solution of Crabtree´s catalyst (CAS# 64536-78-3) (1 mol %) and the starting material in CH_2Cl_2 (0.2 mmol/mL) at 25 °C till the full conversion was observed by TLC or

^{1}H NMR (0.5-3 h). The solvent was evaporated and the residue was purified by flash chromatography.

((1*R,2*R**,3*S**,4*S**)-2,3-Dihydroxy-4-phenylcyclopentyl)methyl pivalate (24a).**

The compound was prepared by General Procedure G using **22a** (466 mg, 1.6 mmol); flash chromatography (CH_2Cl_2/EtOAc = 1:1) afforded **24a** as a pale yellow oil (439 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.33 (m, 2H), 7.27-7.22 (m, 3H), 7.43-7.36 (m, 2H), 4.22 (dd, *J* = 11.1, 5.6 Hz, 1H), 4.16 (dd, *J* = 11.1, 5.8 Hz, 1H), 4.04-3.97 (m, 2H), 3.16 (m, 1H), 2.55 (brs, 1H), 2.40 (m, 1H), 2.31 (brs, 1H), 2.25 (m, 1H), 1.48 (m, *J* = 11.5 Hz), 1.23 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.9, 142.2, 128.9, 127.5, 127.0, 78.9, 74.7, 65.8, 50.2, 44.3, 39.1, 31.9, 27.5 ppm. IR ($\tilde{\nu}_{max}$) = 3452 (m), 2955 (m), 2892 (m), 1724 (s), 1283 (m), 719 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{25}O_4$ 293.1747; Found 293.1747.

((1*R,2*R**,3*S**,4*S**)-4-(2,4-Difluorophenyl)-2,3-dihydroxycyclopentyl)methyl pivalate (24b).**

The compound was prepared by General Procedure G using **22b** (290 mg, 0.89 mmol); flash chromatography (CH_2Cl_2/EtOAc = 3:1) afforded **24b** as a colorless wax (269 mg, 92 %). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.19 (ddm, *J* = 8.5, 6.4 Hz, 1H), 6.87-6.78 (m, 2H), 4.22 (dd, *J* = 11.5, 5.7 Hz, 1H), 4.15 (dd, *J* = 11.5, 5.7 Hz, 1H), 4.12 (m, 1H), 3.99 (apparent t, *J* = 5.6 Hz, 1H), 3.32 (ddm, *J* = 11.3, 7.8 Hz, 1H), 2.44-2.35 (m, 1H), 2.21 (m, 1H), 1.47 (m, 1H), 1.22 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.9, 161.8 (dd, $^{C\text{-}F}J$ = 246.7, 11.8 Hz), 161.5 (dd, $^{C\text{-}F}J$ = 247.8, 11.4 Hz), 129.7 (dd, $^{C\text{-}F}J$ = 9.8, 7.3 Hz), 125.0 (dd, $^{C\text{-}F}J$ = 14.2, 4.0 Hz), 111.5 (dd, $^{C\text{-}F}J$ = 20.9, 3.8 Hz), 104.4 (apparent t, $^{C\text{-}F}J$ = 26.2 Hz), 77.4, 74.3, 65.4, 44.6, 44.4, 39.1, 30.8, 27.5 ppm. ^{19}F{^{1}H} NMR (471MHz, $CDCl_3$): δ= – 112.7 (d, *J* = 6.6 Hz), – 113.2 (d, *J* = 7.1 Hz). IR ($\tilde{\nu}_{max}$) = 3365 (w), 2970 (w), 2931 (w), 1703 (s), 1601 (m), 1505 (s), 1287 (s), 1175 (s), 964 (s), 849 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{22}F_2O_4Na$ 351.1378; Found 351.1376.

(1*R,2*R**,3*S**,4*S**)-2,3-Dihydroxy-4-(1-methyl-1*H*-pyrazol-4-yl)cyclopentyl)methyl pivalate (24c).**

The compound was prepared by General Procedure C using **22c** (91 mg, 0.31 mmol), $Pd(OH)_2$/C (4 mg, 0.03 mmol), H_2 (1 bar) in EtOH; flash chromatography (EtOAc/MeOH = 99:1) afforded **24c** (40 mg, 44%) as a pale yellow solid. m.p. = 80-83 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (s, 1H), 7.24 (s, 1H), 4.13 (ddm, *J* = 11.2, 5.8 Hz, 2H), 3.92 (dd, *J* = 5.8, 4.6 Hz, 1H), 3.85 (s, 3H), 3.80 (dd, *J* = 8.2, 5.8 Hz, 1H), 3.05 (dd, *J* = 11.1, 7.9 Hz, 1H), 2.41 – 2.32 (m, 1H), 2.22 (ddm, *J* = 13.0, 8.0 Hz, 1H), 1.31 (m, 1H), 1.20 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.8, 137.6, 128.1, 123.1, 79.1, 74.3, 65.9, 44.3, 40.2, 39.1, 39.0, 31.4, 27.4 ppm. IR ($\tilde{\nu}_{max}$) = 3449 (m), 2955

(m), 2889 (m), 1723 (s), 1283 (m), 1158 (s), 711 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{25}N_2O_4$ 297.1809; Found 297.1806.

Methyl 5-((1*R,2*S**,3*R**,4*R**)-2,3-dihydroxy-4-(pivaloyloxymethyl)cyclopentyl)furan-3-carboxylate (24d).**

The compound was prepared by General Procedure G using **22d** (312 mg, 0.92 mmol); flash chromatography (CH_2Cl_2/EtOAc = 2:1) afforded **24d** as a colorless wax (298 mg, 95%). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 0.7 Hz, 1H), 6.45 (s, 1H), 4.19 (dd, *J* = 11.2, 5.5 Hz, 1H), 4.13 (dd, *J* = 11.2, 5.7 Hz, 1H), 4.08 (m, 1H), 3.95 (m, 1H), 3.08 (s, 3H), 3.24 (m, 1H), 2.40 (m, 1H), 2.26 (m, 1H), 1.53 (m, 1H), 11.21 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.9, 163.8, 157.7, 147.0, 120.0, 105.5, 76.9, 74.6, 65.4, 51.8, 43.7, 43.3, 39.1, 29.0, 27.4 ppm. IR ($\tilde{\nu}_{max}$) = 3434 (m), 2956 (m), 1580 (m), 1515 (m), 1233 (s), 760 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Cl]^-$ Calcd for $C_{17}H_{24}O_7Cl$ 375.1216; Found 375.1216.

Methyl 5-((*1R*,2S*,3R*,4R)-2,3-dihydroxy-4-(pivaloyloxymethyl)cyclopentyl)thiophene-3-carboxylate (24e).**

The compound was prepared by General Procedure G using **22e** (102 mg, 0.29 mmol); flash chromatography (CH_2Cl_2/EtOAc = 2:1) afforded **24e** as a pale yellow wax (102 mg, 99%). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 1.3 Hz, 1H), 7.31 (m, 1H), 4.19 (dd, *J* = 11.2, 5.2 Hz, 1H), 4.13 (dd, *J* = 11.1, 5.5 Hz, 1H), 3.99 (m, 1H), 3.93 (m, 1H), 3.85 (s, 3H), 3.38 (m, 1H), 2.45-2.32 (m, 2H), 1.52 (m, 1H), 1.23 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.8, 163.5, 146.9, 133.4, 131.3, 124.5, 79.4, 74.4, 65.5, 52.0, 45.4, 44.2, 39.1, 32.1, 27.5 ppm. IR ($\tilde{\nu}_{max}$) = 2956 (w), 1714 (s), 1460 (m), 1228 (s), 1152 (s), 737 (m) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{25}O_6S$ 357.1366; Found 357.1369.

((1*R,2*R**,3*S**,4*S**)-4-(3a,7a-Dihydrobenzo[*b*]thiophen-3-yl)-2,3-dihydroxycyclopentyl)methyl pivalate (24f).**

The compound was prepared by General Procedure G using **22f** (102 mg, 0.29 mmol); flash chromatography (CH_2Cl_2/EtOAc = 2:1) afforded **24f** as a pale yellow wax (88 mg, 86%). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.93-7.90 (m, 1H), 7.87-7.85 (m, 1H), 7.42-7.34 (m, 2H), 7.16 (d, *J* = 0.8 Hz, 1H), 4.27 (dd, *J* = 11.2, 5.4 Hz, 1H), 4.21-4.16 (m, 2H), 4.00 (dd, *J* = 5.6 Hz, 1H), 3.61 (m, 1H), 2.54-2.46 (m, 1H), 2.44-2.37 (m, 1H), 1.65-1.57 (m, 1H), 1.23 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.7, 140.8, 139.0, 137.4, 124.6, 124.1, 122.9, 122.2, 120.1, 77.6, 74.5, 65.4, 43.62, 43.5, 30.3, 27.3, 17.7 ppm. IR ($\tilde{\nu}_{max}$) = 3434 (m), 2956 (m), 1712 (s), 1580 (m), 1515 (m),

1233 (s), 760 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{25}O_4S$ 349.1468; Found 349.1472.

((1*R,2*R**,3*S**,4*S**)-4-(4-Aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-2,3-dihydroxycyclopentyl)methyl pivalate (24g).**

The compound was prepared by General Procedure C using **22g** (405 mg, 0.67 mmol), $Pd(OH)_2/C$ (94 mg, 0.07 mmol), H_2 (1 bar) in EtOH; flash chromatography (CH_2Cl_2/EtOAc = 1:1) afforded the reduced compound as a diastereomeric mixture (400 mg, 98%). The mixture was dissolved in MeOH : H_2O (10+2 mL), PPTS (825 mg, 3.28 mmol) was added and the reaction mixture was stirred at 55 °C for 12 h, then cooled to 25 °C and the solvents were evaporated. The residue was purified by flash chromatography (CH_2Cl_2/MeOH = 10:1) and then preparative TLC (SiO_2, CH_2Cl_2/MeOH 10:1, repeated elution) to afford **24g** (103 mg, 45%) and its epimer (0.070 g, 30%) as white solids, m.p. > 250 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.78 (s, 1H), 7.53 (br s, 2H, -NH_2) 6.82 (d, *J* = 4.6 Hz, 1H), 6.45 (d, *J* = 4.6 Hz, 1H), 4.62 (br s, 1H, -OH), 4.58 (br s, 1H, -OH), 4.11 (dd, *J* = 10.8, 5.2 Hz, 1H), 4.06 (apparent t, *J* = 5.9 Hz, 1H), 4.01 (dd, *J* = 10.8, 5.9 Hz, 1H), 3.77 (apparent t, *J* = 5.5 Hz, 1H), 3.55 (m, 1H), 2.27-2.16 (m, 2H), 1.32 (m, 1H), 1.14 (s, 9H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 177.4, 155.5, 147.4, 132.5, 114.0, 107.4, 100.6, 75.6, 73.1, 65.3, 43.1, 39.2, 39.0, 38.2, 29.6, 26.8 ppm. IR ($\tilde{\nu}_{max}$) = 3324 (m), 2928 (m), 1726 (m), 1602 (s), 1522 (s), 1477 (s) 1150 (s), 728 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{25}N_4O_4$ 349.1875; Found 349.1874.

(1*S,2*R**,3*R**,5*S**)-3-(Hydroxymethyl)-5-phenylcyclopentane-1,2-diol (4a).**

The compound was prepared by General Procedure F using **24a** (578 mg, 1.97 mmol); flash chromatography (CH_2Cl_2/MeOH = 10:1) afforded **4a** as a white solid (365 mg, 89%). m.p. = 105-106 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.30-7.24 (m, 4H), 7.16 (m, 1H), 4.53 (apparent t, *J* = 5.1 Hz, 1H, -OH), 4.40 (d, *J* = 6.0 Hz, 1H, -OH), 4.35 (d, *J* = 2.7 Hz, 1H, -OH), 3.72 (m, 1H), 3.48-3.37 (m, overlapped, 2H), 2.97 (m, 1H), 2.07-1.95 (m, 2H), 1.32-1.22 (m, 2H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 144.0, 128.0, 127.4, 125.7, 78.1, 73.5, 63.1, 49.0, 46.7, 31.7 ppm. IR ($\tilde{\nu}_{max}$) = 3290 (m), 2938 (w), 1396 (w), 1213 (s), 1111 (s), 1178 (s), 759 (s), 697 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+NH_4]^+$ Calcd for $C_{12}H_{20}O_3N$ 226.1438; Found 226.1436. Crystal data for **4a**: Crystallized from MeOH, $C_{12}H_{16}O_3$, M_{rel} = 601.51, T = 120 K, space group Pbca, a = 9.8445(4) Å, b = 6.9522(5) Å, c = 30.4659(12) Å, α = 90.00, β = 90.00, γ = 90.00, V = 2085.11 $Å^3$. CCDC ref. No. 1452773.

(1*R,2*S**,3*S**,5*R**)-3-(2,4-Difluorophenyl)-5-(hydroxymethyl)cyclopentane-1,2-diol (4b).**

The compound was prepared by General Procedure F using **24b** (173 mg, 0.53 mmol); flash chromatography (CH_2Cl_2/MeOH = 10:1 to 5:1) afforded **4b** as a white solid (115 mg, 90%). m.p. = 101-103 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ = 7.41 (ddm, J = 8.6, 6.9 Hz, 1H), 7.12 (dddd, J = 12.0, 10.7, 9.7, 2.7 1H), 7.03 (apparent td, J = 8.5, 2.7 Hz, 1H), 4.55 (apparent t, J = 5.2 Hz, 1H), 4.46 (d, J = 6.5 Hz, 1H), 4.40 (d, J = 4.6 Hz, 1H), 3.74 (dd, J = 7.2, 3.6 Hz, 1H), 3.45-3.36 (m, 2H), 3.23 (m, 1H), 2.07-1.95 (m, 2H, overlapped), 1.25-1.17 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 160.5 (dd, $^{C\text{-}F}J$ = 246.1, 11.9 Hz), 160.4 (dd, $^{C\text{-}F}J$ = 244.0, 12.5 Hz), 129.6 (dd, $^{C\text{-}F}J$ = 10.0, 7.2 Hz), 126.7 (dd, $^{C\text{-}F}J$ = 14.6, 3.8 Hz), 111.1 (dd, $^{C\text{-}F}J$ = 19.7, 4.5 Hz), 103.4 (dd, $^{C\text{-}F}J$ = 26.8, 25.2 Hz), 76.7, 73.1, 63.0, 46.6, 41.6, 31.0 ppm. ^{19}F{^{1}H} NMR (471MHz, $CDCl_3$): δ = – 114.08 (AB d, J = 6.05 Hz), –114.13 (AB d, J = 6.7 Hz). IR ($\tilde{\nu}_{max}$) = 3276 (m), 1453 (m), 1272 (m), 1208 (m), 1043 (s), 963 (s), 849 (s), 606 (m) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{22}F_2O_4Na$ 351.1378; Found 351.1376.

(1*S,2*R**,3*R**,5*S**)-3-(Hydroxymethyl)-5-(1-methyl-1*H*-pyrazol-4-yl)cyclopentane-1,2-diol (4c).**

The compound was prepared by General Procedure F using **24c** (212 mg, 0.38 mmol). Flash chromatography (CH_2Cl_2/MeOH = 5:1) afforded **4c** as a yellow solid (43 mg, 53%). m.p. = 112-114 °C. ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6): δ = 7.44 (s, 1H), 7.25 (s, 1H), 4.50 (dd, J = 5.1 Hz, 1H, -OH), 4.41 (d, J = 6.4 Hz, 1H,-OH), 4.28 (d, J = 4.1 Hz, 1H,-OH), 3.76 (s, 3H), 3.65 (dd, J = 9.2, 4.5 Hz, 1H), 3.50 (dd, J = 14.0, 5.8 Hz, 1H), 3.42 – 3.35 (m, 2H), 2.83 (ddm, J = 10.6, 8.1 Hz, 1H), 2.06 – 1.97 (m, 1H), 1.94 (m, 1H), 1.17 (ddd, J = 12.4, 10.8, 8.4 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6): δ = 137.4, 128.4, 124.2, 79.1, 73.8, 63.7, 47.2, 38.7, 31.7 ppm. IR ($\tilde{\nu}_{max}$) = 3415 (m), 2926 (m), 2870 (m), 1265 (s), 1118 (s), 1015 (s), 839 (m), 670 (w) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Cl]^-$ Calcd for $C_{10}H_{16}N_2O_3Cl$ 247.0855; Found 247.0854. Crystal data for **5c**: Crystallized from MeOH, $C_{10}H_{16}N_2O_3$, M_{rel} = 212.25, T = 120 K, space group P-1, a = 7.2069(4) Å, b = 7.7420(3), c = 9.5826(4) Å, α = 80.466(4), β = 79.403(4), γ = 77.127(4), V = 507.987 Å^3. CCDC ref. No. 1452237.

Methyl 5-((1*R*,2*S*,3*R*,4*R*)-2,3-dihydroxy-4-(hydroxymethyl)cyclopentyl)furan-3-carboxylate (4d).

The compound was prepared by General Procedure F using **24d** (254 mg, 0.75 mmol); flash chromatography (CH_2Cl_2/MeOH = 6:1) afforded **4d** as a yellow wax (140 mg, 73%). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.23 (d, J = 0.8 Hz, 1H), 6.44 (s, 1H), 4.54 (m, 3H), 3.78 (m, 1H), 3.75 (s, 3H), 3.67 (m, 1H), 3.38 (m, 2H), 3.07 (dd, J = 18.2, 8.2 Hz, 1H), 2.00 (m, overlapped, 2H), 1.34 (ddd, J = 12.5, 10.2, 7.8 Hz, 1H), 1.53 (m, 1H), 11.21 (s, 9H) ppm. ^{13}C NMR (126 MHz, DMSO-

d_6): δ = 163.0, 159.5, 146.8, 118.9, 104.2, 76.3, 73.2, 62.7, 51.3, 46.1, 42.3, 28.8 ppm. IR ($\tilde{\nu}_{max}$) = 3284 (m), 1707 (s), 1607 (m), 1515 (m), 1438 (m), 1110 (s), 760 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Cl]^-$ Calcd for $C_{12}H_{16}O_6Cl$ 291.0641; Found 291.0641.

Methyl 5-((*1R*,2S*,3R*,4R)-2,3-dihydroxy-4-(hydroxymethyl)cyclopentyl)thiophene-3-carboxylate (4e).**

The compound was prepared by General Procedure F using **24e** (100 mg, 0.28 mmol); flash chromatography (CH_2Cl_2/MeOH = 13:1) afforded **4e** as a white wax (46 mg, 61%). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.12 (d, *J* = 1.4 Hz, 1H), 7.23 (m, 1H), 4.72 (d, *J* = 7.2 Hz, 1H), 4.58 (apparent t, *J* = 5.3 Hz, 1H), 4.45 (d, *J* = 5.1 Hz, 1H), 3.77 (s, 3H), 3.71 (m, 1H), 3.60 (m, 1H), 3.39 (m, 2H), 3.20 (m, 1H), 2.15 (m, 1H), 1.99 (m, 1H), 1.34 (ddd, *J* = 12.7, 11.1, 8.3 Hz) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 162.5, 149.0, 131.9, 131.2, 123.2, 78.8, 73.2, 62.9, 51.5, 46.6, 44.0, 31.4 ppm.IR ($\tilde{\nu}_{max}$) = 3339 (w), 3094 (w), 1714 (s), 1429 (m), 1239 (s), 990 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Cl]^-$ Calcd for $C_{12}H_{16}O_5SCl$ 307.0412; Found 307.0410.

(1*R,2*S**,3*S**,5*R**)-3-(3a,7a-Dihydrobenzo[*b*]thiophen-3-yl)-5-(hydroxymethyl)cyclopentane-1,2-diol (4f).**

The compound was prepared by General Procedure F using **24f** (173 mg, 0.53 mmol); flash chromatography (CH_2Cl_2/MeOH = 5:1) afforded **4f** as a yellow solid (123 mg, 88%). m.p. = 102-104 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.98-7.92 (m, 2H), 7.43 (s, 1H), 7.42-7.32 (m, 2H), 4.59 (d, *J* = 5.8 Hz, 1H, -OH), 4.55 (dd, *J* = 5.3 Hz, 1H, -OH), 4.43 (d, *J* = 4.8 Hz, 1H, -OH), 3.92 (dd, *J* = 12.8, 5.8 Hz, 1H), 3.75 (dd, *J* = 9.8, 4.8 Hz, 1H), 3.49 (m, 1H), 3.46-3.36 (m, 2H, overlapped), 2.22 (ddd, *J* = 12.8, 7.5 Hz, 1H), 2.08 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 139.8, 139.2, 139.1, 124.1, 123.74, 122.70, 122.4, 120.3, 77.0, 73.3, 62.8, 46.3, 42.9, 30.4 ppm. IR ($\tilde{\nu}_{max}$) = 3260 (w), 1426 (m), 1318 (m), 1097(m), 1082 (m), 1068 (m), 1022 (m), 960 (m), 906 (m), 708 (m), 634 (m) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{24}O_4SNa$ 371.1288; Found 371.1286.

(1*R,2*S**,3*S**,5*R**)-3-(4-Aminopyrrolo[1,2-*f*][1,2,4]triazin-7-yl)-5-(hydroxymethyl)cyclopentane-1,2-diol (4g).**

The compound was prepared by General Procedure F using **24g** (84 mg, 0.24 mmol); flash chromatography (CH_2Cl_2/CH_3OH = 10:3) afforded **4g** as a white solid (53 mg, 84%), m.p. > 250 °C decomp. ^{1}H NMR (500 MHz, CD_3OD): δ = 7.90 (s, 1H), 7.15 (d, *J* = 4.6 Hz, 1H), 6.73 (d, *J* = 4.6 Hz, 1H), 4.23 (dd, *J* = 7.9, 5.1 Hz, 1H), 4.00 (apparent t, *J* = 5.1 Hz), 3.79 (m, 1H), 3.70 (dd, *J* = 10.7, 6.1 Hz), 3.64 (dm, *J* = 10.7, 6.1 Hz, 1H), 2.40 (m, 1H), 2.27 (m, 1H), 1.55 (dm, *J* = 10.5, 8.8

Hz, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 155.5, 147.3, 133.1, 113.9, 107.3, 100.6, 76.0, 73.2, 62.9, 46.4, 30.0 ppm. IR ($\tilde{\nu}_{max}$) = 3362 (w), 3225 (w), 1679 (m), 1606 (m), 1108 (m), 1019 (m), 725 (m) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{12}H_{17}O_3N_4$ 265.1295; Found 265.1297.

5-((1*R,2*S**,3*R**,4*R**)-2,3-Dihydroxy-4-(hydroxymethyl)cyclopentyl)furan-3-carboxamide (4h)**

A mixture of **4d** (59 mg, 0.23 mmol) and 7 M NH_3 in CH_3OH (2 mL) was stirred in a pressure tube at 100 °C for 24 h. After cooling to 25 °C, the reaction mixture was concentrated under reduced pressure and the residue was purified by preparative TLC (CH_2Cl_2/MeOH/ = 9 : 1) to afford **4h** as a yellow wax (12 mg, 22%). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.00 (d, *J* = 0.9 Hz, 1H), 7.52 (br s, 1H), 7.05 (br s, 1H), 6.47 (apparent s, 1H), 4.62 (br s, 1H, -OH), 4.54 (m, 1H), 4.43 (br s, 1H), 3.76 (m, 1H), 3.66 (m, 1H), 3.44-3.39 (m, 1H), 3.38-3.32 (m, 1H), 3.03 (m, 1H), 2.03 (m, 1H), 2.00-1.94 (m, 1H), 1.33 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 163.6, 158.4, 143.6, 123.2, 104.1, 76.3, 73.3, 62.8, 46.1, 42.5, 29.0 ppm. IR ($\tilde{\nu}_{max}$) = 3378 (m), 3173 (m), 1642 (m), 1617 (m), 1101 (m), 795 (m) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{11}H_{16}NO_5$ 242.1023; Found 242.1027.

5-((*1R*,2S*,3R*,4R)-2,3-Dihydroxy-4-(hydroxymethyl)cyclopentyl)thiophene-3-carboxamide (4i)**

A mixture of **4e** (40 mg, 0.14 mmol) and 7 M NH_3 in CH_3OH (2 mL) was stirred in a pressure tube at 100 °C for 24 h. After cooling to 25 °C, the reaction mixture was concentrated under reduced pressure and the residue was purified by preparative TLC (CH_2Cl_2/MeOH/ = 6 : 1) to afford **4i** as a white wax (15 mg, 43%). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.90 (d, *J* = 1.4 Hz, 1H), 7.69 (br s, 1H), 7.26 (m, 1H), 7.08 (br s, 1H), 4.69 (d, *J* = 6.7 Hz, 1H), 4.59 (apparent t, *J* = 5.0 Hz, 1H), 4.45 (d, *J* = 4.6 Hz, 1H), 3.70 (m, 1H), 3.60 (m, 1H), 3.44-3.34 (m, 1H), 3.20-3.13 (m, 1H), 2.13 (m, 1H), 1.99 (m, 1H), 1.34 (m, 1H), 1.33 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 163.8, 147.9, 137.2, 126.3, 123.3, 78.9, 73.2, 63.0, 46.6, 44.2, 31.8 ppm. IR ($\tilde{\nu}_{max}$) = 3401 (m), 3170 (w), 1642 (s), 1609 (m), 1464 (m), 727 (m), 604 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{11}H_{15}NO_4SCl$ 292.0416; Found 292.0416.

((1*R,4*S**,5*R**)-3-Phenyl-4,5-bis(triisopropylsilyloxy)cyclopent-2-enyl)methyl 4-methylbenzenesulfonate (25).**

DIBAL-H (1M in hexane, 538 μL, 0.54 mmol) was added to a solution of **21a** (130 mg, 0.22 mmol) in CH_2Cl_2 (4 mL) at –78 °C and the reaction mixture was stirred at –78 °C for 30 min. The mixture

was then allowed to warm to 25 °C, stirred for 1 h, then quenched with saturated aqueous solution of sodium potassium tartrate (3 mL), and extracted with CH_2Cl_2 (3 × 15 mL). The organic extracts were washed with brine (5 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to yield the crude product, which was purified by flash chromatography (hexane/EtOAc = 10:1) to afford the de-pivaloylated intermediate (a colorless wax, 100 mg, 90%), which was directly used in the next step. Tosyl chloride (49 mg, 0.26 mmol), triethylamine (83 μL, 0.60 mmol) and DMAP (2 mg, 0.02 mmol) were added to a solution of the intermediate (100 mg, 0.20 mmol) in CH_2Cl_2 (4 mL). The reaction mixture was stirred at 25 °C for 3 h, quenched with saturated aqueous $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure to yield a pale yellow residue, which was purified by flash chromatography (hexane/EtOAc = 15 : 1) to afford **25** (131 mg, 98%) as a colorless wax. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 8.3 Hz, 2H), 7.38 – 7.26 (m, 7 H), 5.93 (apparent s, 1H), 5.04 (d, *J* = 4.6 Hz, 1H), 4.39 (dd, *J* = 9.7, 3.7 Hz, 1H), 4.05 (dd, *J* = 9.7, 7.2 Hz, 1H), 3.99 (dd, *J* = 7.3, 4.4 Hz, 1H), 3.20 (m, 1H), 2.44 (s, 3H), 1.09-1.01 (m, 21H), 0.95-0.85 (m, 18H), 0.77 (m, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 146.2, 145.0, 135.4, 133.2, 130.0, 129.2, 128.5, 128.24, 128.16, 126.3, 77.1, 76.6, 70.2, 49.1, 21.9, 18.6, 18.5, 18.44, 18.38, 13.7, 13.1 ppm. IR ($\tilde{\nu}_{max}$) = 2943, 2866, 1729, 1495, 1381, 1178 cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{37}H_{60}O_5SSi_2Na$ 695.3592; Found 695.3588.

(1*R,2*S**,5*R**)-5-((2-Methoxyethylamino)methyl)-3-phenylcyclopent-3-ene-1,2-diol (26).**

2-Methoxyethylamine (33 μL, 0.39 mmol) and DIPEA (0.100 mL, 0.58 mmol) were added to a solution of **25** (130 mg, 0.19 mmol) in DMF (2 mL). The reaction mixture was stirred at 100 °C for 3 h, then quenched with water (10 mL) and extracted with EtOAc (2 × 20 mL). The combined extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield crude product, which was purified by flash chromatography (hexane/EtOAc 4 : 1) to afford the substitution intermediate (77 mg, 69%) as a pale yellow wax. TBAF (1 M in THF, 267 μL, 0.7 mmol) was added to a solution of the intermediate (70 mg, 0.12 mmol) in THF (5 mL) at 0 °C. The reaction mixture was stirred at 25 °C for 14 h, then quenched with water (15 mL) and concentrated under reduced pressure to yield the crude product, which was purified by preparative TLC (CH_2Cl_2/7M NH_3 in MeOH = 8 : 1) to afford **26** (28 mg, 90%) as a yellow wax. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.55 (d, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.7 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 1H), 6.29 (apparent s, 1H), 4.73 (m, 1H), 4.67 (m, 1H), 3.78 (t, *J* = 5.4 Hz, 1H), 3.44 (t, *J* = 5.4 Hz, 2H), 3.26 (s, 3H, partially overlapped with residual H_2O), 2.86-2.75 (m, 4H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 142.5, 135.1, 129.5, 128.2, 127.1, 125.7, 75.1, 73.8, 70.8, 58.0, 51.4, 50.1, 48.5

ppm. IR ($\tilde{\nu}_{max}$) = 3345 (m), 2959 (m), 2875 (m), 1448 (m), 804 (s), 693 (m) cm^{-1}. HRMS (APCI-TOF) m/z: $[M-H]^-$ Calcd for $C_{15}H_{22}NO_3$ 264.1594; Found 264.1593.

(1*R,4*S**,5*R**)-3-Phenyl-4,5-bis(triisopropylsilyloxy)cyclopent-2-enyl)methanamine (27).**

A mixture of **25** (75 mg, 0.11 mmol) and 2 M NH_3 in 2-propanol (2.5 mL) was stirred in a pressure tube at 50 °C for 24 h. Then, aqueous NH_3 solution (25–29%, 1 mL) was added and the reaction mixture was stirred at 75 °C for additional 24 h, after which the TLC showed full consumption of the starting material. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography (CH_2Cl_2/MeOH/NH_3 in MeOH = 95 : 5: 0.5) to afford **27** as a yellow wax (50 mg, 70%). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.44 (m, 2H), 7.35 (apparent t, *J* = 7.5 Hz, 2H), 7.27 (apparent t, *J* = 7.1 Hz, 1H), 6.40 (s, 1H), 5.07 (d, *J* = 4.3 Hz, 1H), 3.97 (dd, *J* = 7.0, 4.3 Hz, 1H), 3.07 (dd, *J* = 12.1, 3.4 Hz, 1H), 2.96 (m, 1H), 2.55 (dd, *J* = 11.5, 8.9 Hz, 1H), 1.16-1.05 (s, 21H), 0.94-0.86 (m, 18H), 0.83-0.75 (m, 3H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 143.9, 135.3, 131.9, 128.2, 127.6, 125.7, 77.8, 76.4, 51.1, 41.7, 18.16, 18.11, 18.05, 18.01, 12.9, 12.3 ppm. IR ($\tilde{\nu}_{max}$) = 2943, 2866, 1464, 1155, 1118 cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{30}H_{55}NO_2Si_2Na$ 540.3664; Found 540.3660.

***N*-(((1*R**,4*S**,5*R**)-4,5-Dihydroxy-3-phenylcyclopent-2-enyl)methyl)acetamide (28a).**

DIPEA (30 µL, 0.17 mmol) and AcCl (4.5 µL, 0.07 mmol) were added dropwise into cooled (0 °C) solution of **27** (30 mg, 0.06 mmol) in CH_2Cl_2 (1.5 mL). The reaction mixture was stirred at 25 °C for 2 h, then mixed with saturated aqueous $NaHCO_3$ (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in THF (2 mL) and TBAF in THF (1 M, 86 µL) was added dropwise at 0 °C. The reaction mixture was allowed to warm to 25 °C and stirred for 14 h. The solvent was evaporated and the residue was purified by preparative TLC (CH_2Cl_2/MeOH = 15:1) to afford **28a** (8 mg, 89%) as a yellow wax. ^{1}H NMR (500 MHz, acetone-d_6): δ = 7.63 (dm, *J* = 8.5 Hz, 2H), 7.36 (m, 2H), 7.30 – 7.26 (m, 1H), 7.21 (br s, 1H, -NH), 6.28 (d, *J* = 2.2 Hz, 1H), 4.88 (dd, *J* = 5.8, 1.1 Hz, 1H), 4.02 (apparent t, *J* = 5.7 Hz, 1H), 3.49 – 3.43 (m, 1H), 3.42-3.35 (m, 1H), 2.93 (apparent dd, *J* = 11.8, 5.9 Hz, 1H), 1.91 (s, 3H) ppm. ^{13}C NMR (126 MHz, Acetone-d_6): δ = 170.3, 144.5, 136.5, 130.3, 129.2, 128.2, 127.0, 76.0, 75.7, 52.8, 41.8, 23.1 ppm. IR ($\tilde{\nu}_{max}$) = 3308, 2922, 2852, 1655, 1633, 1109 cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{17}NO_3Na$ 270.1101; Found 270.1104.

1-(((1*R,4*S**,5*R**)-4,5-Dihydroxy-3-phenylcyclopent-2-enyl)methyl)-3-phenylurea (28b).**

TEA (28 μL, 0.20 mmol) and phenyl isocyanate (12 μL, 0.11 mmol) were added dropwise at 0°C into a solution of **27** (52 mg, 0.10 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was stirred at 25 °C for 2.5 h, then mixed with H_2O (10 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in THF (3 mL) and TBAF in THF (1 M, 0.18 mL) was added. The reaction mixture was stirred at 25 °C for 14 h. The solvent was removed in vacuo and the crude product was purified by flash chromatography (CH_2Cl_2/MeOH = 95:5) to afford **28b** (17 mg, 67%) as a white semi-solid.^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.60 (s, 1H,- NH), 7.56 (apparent d, *J* = 7.6 Hz, 2H), 7.39 (apparent d, *J* = 7.7 Hz, 2H), 7.34 (apparent d, *J* = 7.7 Hz, 2H), 7.27-7.17 (m, 3H) 6.87 (apparent t, *J* = 7.3 Hz, 1H), 6.32 (apparent t, *J* = 5.7 Hz, 1H, -NH), 6.22 (d, *J* = 2.0 Hz, 1H), 4.75 (br s, 2H, -OH), 4.70 (m, 1H), 3.81 (m, 1H), 3.35-3.23 (m, 2H, overlapped with residual H_2O signal), 2.81 (apparent dd, *J* = 11.9, 5.20 Hz) ppm.^{13}C NMR (126 MHz, DMSO-d_6): δ = 155.3, 143.0, 140.6, 135.1, 129.0, 128.5, 128.2, 127.2, 125.8, 120.8, 117.5, 74.4, 73.9, 51.1, 40.8 ppm. IR ($\tilde{\nu}_{max}$) = 3340, 3284, 3058, 3031, 2959, 2923, 2853, 1649, 1555, 1257 cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{21}N_2O_3$ 325.1547; Found 325.1545.

_N_-(((1_R_*,4_S_*,5_R_*)-4,5-Dihydroxy-3-phenylcyclopent-2-en-1-yl)methyl)-_N_,_N_-dimethylsulfuric diamide (28c).

TEA (50 μL, 0.36 mmol) and *N,N*-dimethylsulfamoyl chloride (20 μL, 0.18 mmol) were added at 0 °C to a solution of **27** (62 mg, 0.12 mmol) in DMF (3 mL). The reaction mixture was stirred for 30 min at 0 °C and then at 25 °C for 3 h. The reaction mixture was quenched with H_2O (10 mL) and extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was dissolved in THF (2 mL) and TBAF in THF (1 M, 0.19 mL) was added. The reaction mixture was stirred at 25 °C for 14 h. The solvent was removed in vacuo and the crude product was purified by flash chromatography (CH_2Cl_2/MeOH = 15:1 to 5:1) to afford **28c** (24 mg, 89%) as a colorless wax. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.53 (apparent d, *J* = 8.0 Hz, 2H), 7.36 (m, 2H), 7.30 (m, 1H), 6.12 (d, *J* = 2.0 Hz, 1H), 4.94 (dd, *J* = 5.9, 1.3 Hz, 1H), 4.67 (br s, 1H), 4.10 (apparent t, *J* = 5.8 Hz, 1H), 3.36 (m, 1H), 3.19 (dd, *J* = 12.6, 7.9 Hz, 1H), 3.02 (dd, *J* = 12.1, 6.0 Hz, 1H), 2.83 (m, 6H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 144.3, 134.0, 129.0, 128.6, 128.3, 126.3, 76.2, 75.3, 51.1, 38.3 ppm. IR ($\tilde{\nu}_{max}$) = 3445, 3301, 2924, 1457, 1320, 1145, 1093 cm^{-1}. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{20}N_2O_4SNa$ 335.1036; Found 335.1032.

(6a_R_*,8_S_*,9_S_*,9a_R_*)-2,2,4,4-Tetraisopropyl-8-phenylhexahydrocyclopenta[_f_][1,3,5,2,4]trioxadisilocin-9-ol (29).

1,3-Dichloro-1, 1, 3, 3-tetraisopropyldisiloxane (307 μL, 0.96 mmol) was added to a solution of **4a** (200 mg, 0.96 mmol) in pyridine (4 mL) at 0 °C. The reaction mixture was stirred at 25 °C for 16 h, then quenched with 2 M aqueous HCl (15 mL), and extracted with EtOAc (2 × 40 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield the crude product, which was purified by flash chromatography (hexane/EtOAc = 20:1) to afford **29** (380 mg, 88%) as a colorless wax. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.31-7.25 (m, 2H), 7.23-7.16 (m, 3H), 4.29 (br s, 1H, -OH), 4.07 (dd, J = 7.6, 5.9 Hz, 1H), 3.90 (dd, J = 11.6, 3.6 Hz, 1H), 3.79 (apparent t, J = 5.3 Hz, 1H), 3.75 (dd, J = 11.6, 3.6 Hz, 1H), 2.95 (m, 1H), 2.19 (m, 1H), 1.97 (ddm, J = 12.5, 7.7 Hz, 1H), 1.09 – 0.95 (m, 28H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ = 144.1, 128.2, 127.0, 125.9, 77.6, 73.7, 62.1, 49.8, 46.3, 30.3, 17.4, 17.3, 17.24, 17.21, 17.03, 17.00, 16.96, 16.91, 12.9, 12.80, 12.3, 12.1 ppm. IR ($\tilde{\nu}_{max}$) = 2943 (m), 2886 (m), 1028 (m), 883 (m), 694 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{41}O_3Si_2$ 433.2588; Found 433.2584.

(1*R,2*S**,3*S**,5*R**)-5-(Hydroxymethyl)-2-methoxy-3-phenylcyclopentanol (30).**

n-BuLi (70 μL, 0.11 mmol) was added to a solution of **29** (50 mg, 0.11 mmol) in THF (1.5 mL) at –78 °C and the mixture was stirred for 15 min. Methyl trifluoromethanesulfonate (12 μL, 0.110 mmol) was added dropwise at –78 °C and the reaction mixture was stirred for 3 h while allowed to warm to 25 °C. The mixture was mixed with saturated aqueous solution of NH_4Cl (5 mL) and extracted with EtOAc (2 × 20 mL). The combined extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was dissolved in THF (2 mL) and TBAF (1 M in THF, 0.220 mL) was added. The reaction mixture was stirred at 25 °C for 14 h. The solvent was removed in vacuo and the crude product was purified by flash chromatography (CH_2Cl_2/CH_3OH = 15:1 to 5:1) to afford **30** (8 mg, 32% over the 2 steps) as a colorless solid. m.p. = 103-105 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34-7.29 (m, 2H), 7.25-7.20 (m, 3H), 4.08 (apparent t, J = 5.8 Hz, 1H), 3.80 (dd, J = 10.6, 4.9 Hz, 1H), 3.71 (d, J = 10.6, 6.7 Hz, 1H), 3.64 (apparent t, J = 6.2 Hz, 1H), 3.34 (s, 3H), 3.21 (m, 1H), 2.24 (m, 2H), 1.38 (m, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 143.6, 128.8, 127.4, 126.7, 88.0, 75.0, 65.4, 58.1, 48.6, 47.0, 32.4 ppm. IR ($\tilde{\nu}_{max}$) = 3251 (m), 2925 (w) 2907 (w), 1350 (w), 1193 (s), 1055 (s), 697 (s), 551 (s) cm^{-1} HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{13}H_{19}O_3$ 223.1329; Found 223.1330. Crystal data for **26**: Crystallized from MeOH, $C_{13}H_{18}O_3$, M_{rel} = 222.28, T = 120 K, space group $P2_1/n$, a = 12.5947(2) Å, b = 6.74830(10) Å, c = 14.1169(3) Å, α = 90.00, β = 105.382(2), γ = 90.00, V = 1156.86 Å^3. CCDC ref. No. 1452235.

(6a*R,8*S**,9a*R**)-2,2,4,4-Tetraisopropyl-8-phenyltetrahydrocyclopenta[*f*][1,3,5,2,4]trioxadisilocin-9(9a*H*)-one (31).**

IBX (102 mg, 0.37 mmol) was added to a solution of **29** (110 mg, 0.24 mmol) in acetonitrile (2.5 mL) and the reaction mixture was stirred at 80 °C for 4 h, then cooled down to 25 °C, diluted with Et_2O (20 mL) and filtered through a pad of Celite. The filtrate was washed with saturated aqueous solution of $NaHCO_3$ (15 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (hexane/EtOAc = 20 : 1) to afford **31** (88 mg, 81 %) as a colorless wax. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32 (m, 2H), 7.23 (m, 3H), 4.32 (d, *J* = 11.6 Hz, 1H), 4.12 (dd, *J* = 11.6, 2.6 Hz, 1H), 3.93 (d, *J* = 11.6 Hz, 1H), 3.41 (m, 1H), 2.34-2.28 (m, 1H), 2.19-2.05 (m, 2H), 1.14-0.96 (m, 28H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 212.6, 138.5, 128.9, 127.8, 127.2, 76.9, 60.2, 51.9, 43.7, 27.1, 17.7, 17.62, 17.58, 17.3, 17.22, 17.15, 17.13, 13.8, 13.5, 13.0, 12.7 ppm. IR ($\tilde{\nu}_{max}$) = 2944 (m), 2866 (m), 1726 (m), 1449 (m), 1025 (m), 856 (m), 688 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+CH_3OH]^+$ Calcd for $C_{25}H_{45}O_5Si_2$ 481.2800; Found 481.2796.

(6a*R,8*S**,9*R**,9a*R**)-2,2,4,4-Tetraisopropyl-8-phenylhexahydrocyclopenta[*f*][1,3,5,2,4]trioxadisilocin-9-ol (32).**

$LiAlH[OC(C_2H_5)_3]_3$ (0.5 M in THF, 459 μL, 0.23 mmol) was added dropwise to a solution of **31** (103 mg, 0.23 mmol) in THF (4 mL) at 0 °C. The reaction mixture was stirred at 25 °C for 3 h, then quenched with saturated aqueous NH_4Cl (6 mL), and extracted with EtOAc (3 × 30 mL). The combined extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by preparative TLC (hexane/EtOAc = 10 : 1) to afford **32** (95 mg, 92%) as a white solid, m.p. = 61-63 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36-7.31 (m, 2H), 7.31-7.28 (m, 2H), 7.25 (m, *J* = 1H), 4.20 (dd, *J* = 5.5, 2.7 Hz, 1H), 4.16 (m, 1H), 4.04 (dd, *J* = 11.3, 3.9 Hz, 1H), 3.77 (dd, *J* = 11.3, 8.6 Hz, 1H), 3.44 (m, 1H), 2.19 (m, 1H), 2.02 (m, 1H), 1.85 (m, 1 H), 1.15-1.04 (m, 28H) ppm.^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.4, 128.9, 128.8, 127.1, 81.4, 81.3, 65.6, 49.7, 47.5, 30.2, 17.9, 17.78, 17.75, 17.7, 17.5, 17.42, 17.41, 17.36, 13.9, 13.8, 13.3, 12.8 ppm. IR ($\tilde{\nu}_{max}$) = 2941 (w), 2864 (m), 1060 (m), 551 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{41}O_3Si_2$ 433.2588; Found 433.2584. Crystal data for **32**: Crystallized from MeOH, $C_{24}H_{42}O_4Si_2$, M_{rel} = 450.76, T = 120 K, space group $P2_1/n$, a = 9.6577(2) Å, b = 26.6774(5) Å, c = 10.5938(2) Å, *α* = 90.00, *β* = 109.914(2), *γ* = 90.00, V = 2566.21 Å^3. CCDC ref. No. 1452236.

(1*R,2*R**,3*R**,5*S**)-3-(Hydroxymethyl)-5-phenylcyclopentane-1,2-diol (33).**

The compound was prepared by General Procedure D using compound **32** (70 mg, 0.16 mmol); flash chromatography (CH_2Cl_2/MeOH = 10:1) afforded **33** as a white wax (24 mg, 73%). ^{1}H NMR (500 MHz, acetone-d_6): δ = 7.38 (dm, *J* = 7.3 Hz, 2H), 7.29 (apparent t, *J* = 7.0 Hz, 2H), 7.19 (tm, *J* = 7.40 Hz), 4.01 (m, 2H), 3.94 (br s, 1H), 3.74 (m, 2H), 3.61 (d, *J* = 5.6 Hz, 1H), 3.44 (m, 1H),

2.24-2.17 (m, 1H), 2.16-2.11 (m, 1H), 2.04-1.95 (m, 1H) ppm. ^{13}C NMR (126 MHz, Acetone-d_6): δ = 142.1, 129.8, 128.7, 126.7, 82.4, 81.6, 65.2, 50.3, 49.1, 31.4 ppm. IR ($\tilde{\nu}_{max}$) = 3310 (w), 2964 (m), 1154 (s), 798 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{12}H_{17}O_3$ 209.1172; Found 209.1167.

(1*S*,4*S*)-((1*R*,2*R*,3*S*,4*S*)-4-(Hydroxymethyl)-2,3-bis(triisopropylsilyloxy)cyclopentyl)methyl 4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxylate ((+)-37b)

and

(1*S*,4*S*)-((1*S*,2*S*,3*R*,4*R*)-4-(Hydroxymethyl)-2,3-bis(triisopropylsilyloxy)cyclopentyl)methyl 4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxylate ((−)-37a).

DMAP (457 mg, 3.75 mmol) and DIPEA (2.61 mL, 15.02 mmol) were added to a cooled (0 °C, ice bath) solution of **11c** (4.24 g, 7.51 mmol) in CH_2Cl_2 (15 mL) followed by dropwise addition of (1*S*)-(-)-camphanic chloride solution in CH_2Cl_2 (10 mL). The reaction mixture was stirred at 25 °C for 14 h. The solvent was evaporated and the resulting yellow oil was purified by flash chromatography (SiO_2, hexane/EtOAc = 10:1) to afford inseparable mixture of the diastereomeric camphanates **(-)-36a** and **(+)-36b** as a colorless oil (5.43 g, 97 %), which was used directly in the next step.

$Pd(OH)_2$/C (0.321 g, 2.57 mmol) was added to a degassed solution of the mixture of the diastereomeric camphanates (5.43 g 7.28 mmol) in THF (50 mL). The reaction mixture was stirred in a hydrogenation apparatus at 65 °C under H_2 atmosphere (50 bar) for 24 h. The reaction mixture was cooled to 25 °C and filtered through pad of Celite, which was washed with additional THF (3 × 20 mL). The filtrate was concentrated in a vacuum and the resulting colorless oil was purified by flash chromatography (hexane/EtOAc = 10:1 to 4:1).

The less polar diastereomer **(+)-37b** was obtained as a colorless oil (1.70 g, 76%). $[\alpha]_D^{25}$ + 7.5 (*c* 0.1, $CHCl_3$). IR ($\tilde{\nu}_{max}$) = 2942 (m), 2865 (m), 1791 (s), 1735 (m), 1464 (m), 1102 (s), 1061 (s), 882 (s) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.30 (dd, *J* = 4.9, 11.3 Hz, 1H), 4.14 (d, *J* = 6.0, 11.3 Hz, 1H), 4.06 (ddm, *J* = 13.1, 6.1 Hz, 2H), 2.50-2.39 (m, 2H), 2.24 (m, 1H), 2.09 (m, 1H), 2.02-1.88 (m, 2H), 1.69 (m, 1H), 1.20 (m, 2H), 1.08 (s, 40H), 0.95 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.3, 167.9, 91.4, 77.4, 76.5, 67.0, 64.7, 55.0, 54.4, 45.2, 41.9, 30.9, 29.2, 26.2, 18.5, 18.5, 17.0, 16.9, 13.3, 13.2, 9.9 ppm. HRMS (APCI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{35}H_{66}O_7Si_2Na$ 677.4239; Found 677.4239.

The more polar diastereomer **(−)-37a** (1.60 g, 67%) was obtained as a white crystalline compound. m.p. = 91-93 °C. $[\alpha]_D^{25}$ -7.6 (*c* 0.1, $CHCl_3$). IR ($\tilde{\nu}_{max}$) = 2941 (m), 2867 (m), 1790 (s), 1735 (m), 1465 (m), 1102 (s), 1058 (s), 882 (s) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.36 (dd, *J* = 5.2, 11.0 Hz, 1H), 4.11 (d, *J* = 6.7, 11.0 Hz, 1H), 4.07 (m, 1H), 4.03 (m, 1H), 3.59 (ddm, 6.0, 15.5 Hz, 2H),

2.51-2.38 (m, 1H), 2.26 (m, 1H), 2.11 (m, 1H), 2.02 (m, 1H), 1.91 (m, 1H), 1.69 (m, 1H), 1.09 (m, 42H), 0.96 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.2, 167.9, 91.4, 77.3, 76.7, 67.3, 64.7, 55.0, 54.3, 45.2, 42.0, 31.0, 29.2, 26.3, 18.51, 18.46, 16.99, 16.97, 13.3, 13.2, 9.9 ppm. HRMS (APCI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{35}H_{66}O_7Si_2Na$ 677.4239; Found 677.4239. Crystal data for **(-)-37a**: Crystallized from EtOAc, $C_{35}H_{66}O_7Si_2$, M_{rel} = 655.07, T = 120 K, space group $P2_12_12$ a = 11.0527(3) Å, b = 44.5049(19) Å, c = 7.8273(3) Å, α = 90.00, β = 90 γ = 90.00, V = 3850.24 Å^3. CCDC ref. No. 1452234.

General Procedure H for benzylation

TriBOT (0.8 eq.) and dried MS 5Å (30 mg/mL of 1,4-dioxane) were added into a solution (1,4-dioxane, 0.2 M) of the starting material. TfOH (0.4 eq.) was added dropwise and the reaction mixture was stirred at 25 °C for 2 h. The reaction mixture was quenched by addition of DIPEA (50 μL/0.5 mmol), diluted with brine (15 mL/1 mmol), and extracted with EtOAc (3 × 20 mL/ 1 mmol). The organic extracts were dried over $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography.

(1*S*,4*S*)-((1*R*,2*R*,3*S*,4*S*)-4-(Benzyloxymethyl)-2,3-bis(triisopropylsilyloxy)cyclopentyl)methyl 4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxylate ((+)-36b).

The compound was prepared by General Procedure H using compound **(+)-37b** (1.70 g, 2.60 mmol); flash chromatography (hexane/EtOAc = 7:1) afforded **(+)-36b** as a colorless oil (1.55 g, 80%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34-7.26 (m, 5H), 4.48 (d, AB, *J* = 12.5 Hz, 2H), 4.35 (dd, *J* = 11.0, 5.1 Hz, 1H), 4.14-4.07 (m, 2H), 4.01 (d, *J* = 7.0, 3.6 Hz, 1H), 3.37 (d, *J* = 6.3 Hz, 2H), 2.47 (m, 1H), 2.40 (ddd, *J* = 13.4, 10.7, 4.2 Hz, 1H), 2.28 (m, 1H), 2.01-1.86 (m, 2H), 2.11 (m, 1H), 1.67 (ddd, *J* = 13.4, 9.3, 4.2 Hz, 1H), 1.19 (m, 2H), 1.06 (m, 42H), 0.94 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.3, 167.9, 138.7, 128.5, 127.8, 127.6, 91.4, 76.4, 73.4, 72.2, 67.5, 55.0, 54.3, 43.5, 41.8, 30.9, 29.2, 27.1, 18.51, 18.49, 18.47, 18.44, 17.0, 16.9, 13.3, 13.1, 10.0 ppm. IR ($\tilde{\nu}_{max}$) = 2942 (m), 2867 (m), 1794 (s), 1734 (m), 1463 (m), 1098 (s), 1060 (s), 882 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{42}H_{72}O_7Si_2$ 745.4889; Found 745.4892.

(1*S*,4*S*)-((1*S*,2*S*,3*R*,4*R*)-4-(Benzyloxymethyl)-2,3-bis(triisopropylsilyloxy)cyclopentyl)methyl 4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxylate ((−)-36a).

The compound was prepared by General Procedure H using compound **(−)-37a** (1.60 g, 2.45 mmol); flash chromatography (hexane/EtOAc = 7: 1) afforded **(−)-36a** as a colorless oil (1.70 g, 93%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35-7.25 (m, 5H), 4.47 (d, AB, *J* = 11.7 Hz, 2H), 4.37 (dd, *J* = 10.9, 5.0 Hz, 1H), 4.14-4.06 (m, 2H), 3.99 (d, *J* = 7.2, 3.4 Hz, 1H), 3.37 (m, 2H), 2.48 (m, 1H),

2.38 (m, 1H), 2.28 (m, 1H), 2.12 (m, 1H), 1.97 (m, 1H), 1.88 (m, 1H), 1.66 (m, 1H), 1.19 (m, 2H), 1.06 (m, 40H), 0.94 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.3, 167.8, 138.7, 128.5, 127.8, 127.7, 91.3, 77.2, 76.5, 73.4, 72.1, 67.6, 55.0, 54.2, 43.5, 41.9, 30.9, 29.2, 27.1, 18.51, 18.49, 18.47, 18.44, 17.0, 16.9, 13.3, 13.1, 9.9 ppm. IR ($\tilde{\nu}_{max}$) = 2944 (m), 2862 (m), 1794 (s), 1734 (m), 1463 (m), 1098 (s), 1060 (s), 882 (s) cm^{-1}. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{42}H_{72}O_7Si_2$ 745.4889; Found 745.4892.

(1*R*,2*R*,3*S*,4*S*)-4-(Benzyloxymethyl)-2,3-bis(triisopropylsilyloxy)cyclopentyl)methanol ((+)-11c).

Sodium methoxide (0.584 g, 10.82 mmol) was added to a solution of **(+)-36b** (1.55 g, 2.08 mmol) in MeOH (20 mL) and the mixture was stirred at 25 °C for 14 h. The solvent was removed in a vacuum, the residue was diluted with saturated aqueous NH_4Cl (70 mL) and the mixture was extracted with EtOAc (4 × 100 mL). The organic extracts were dried over $MgSO_4$, filtered, and the solvent was evaporated. The crude mixture was purified by flash chromatography (hexane/EtOAc = 15:1) to afford product **(+)-11c** as colorless oil (1.06 g, 90%). The spectral data were identical to those of the racemic compound **11c**. $[\alpha]_D^{25}$ +3.3 (*c* 0.1, $CHCl_3$).

(1*S*,2*S*,3*R*,4*R*)-4-(Benzyloxymethyl)-2,3-bis(triisopropylsilyloxy)cyclopentyl)methanol ((−)-11c).

Using the procedure described above for compound **(+)-11c**, 1.70 g (2.28 mmol) of (−)-**36a** afforded **(−)-11c** as a colorless oil (1.16 g, 90%). The spectral data were identical to those of the racemic compound **11c**. $[\alpha]_D^{25}$ −3.4 (*c* 0.1, $CHCl_3$).

(2*R*,3*R*,4*R*)-4-((Benzyloxy)methyl)-2,3-bis((triisopropylsilyl)oxy)cyclopentanone ((–)-2c).

The compound was prepared from **(−)-11c** by the procedure used for racemic **2c**. $[\alpha]_D^{25}$ −21.5 (*c* 0.1, $CHCl_3$).

(2*S*,3*S*,4*S*)-4-((Benzyloxy)methyl)-2,3-bis((triisopropylsilyl)oxy)cyclopentanone ((+)-2c).

The compound was prepared from **(+)-11c** by the procedure used for racemic **2c**. $[\alpha]_D^{25}$ +21.2 (*c* 0.1, $CHCl_3$).

(1*R*,2*R*,3*R*)-4-Oxo-2,3-bis(triisopropylsilyloxy)cyclopentyl)methyl pivalate ((−)-2b).

$Pd(OH)_2$/C (64 mg, 0.45 mmol) was added to a degassed solution of **(−)-2c** (830 mg, 1.51 mmol) in THF (25 mL). The reaction mixture was stirred in a hydrogenation apparatus at 65 °C under H_2 atmosphere (50 bar) for 24 h. The reaction mixture was cooled to 25 °C and filtered through pad of

Celite, which was washed with additional THF (3 × 30 mL). The filtrate was concentrated in a vacuum and the residue was dissolved in CH_2Cl_2 (25 mL). DIPEA (569 μL, 3.44 mmol) and PivCl (225 μL, 1.81 mmol) were added into the reaction mixture and the mixture was stirred at 25 ℃ for 14 h. The solvent was removed in a vacuum and the residue was purified by flash chromatography (hexane/EtOAc = 30:1) to afford **(−)-2b** as a colorless oil (656 mg, 80%). The spectral data were identical to those of racemic **2b**. $[\alpha]_D^{25}$ −16 (*c* 0.1, $CHCl_3$).

(1*S*,2*S*,3*S*)-4-Oxo-2,3-bis(triisopropylsilyloxy)cyclopentyl)methyl pivalate ((+)-2b).

The compound was prepared from **(+)-2c** by the procedure used for **(–)-2b**. $[\alpha]_D^{25}$ +18 (*c* 0.1, $CHCl_3$).

((1*R*,4*S*,5*R*)-3-(2,4-Difluorophenyl)-4,5-dihydroxycyclopent-2-enyl)methyl pivalate ((+)-22b).

The compound was prepared from **(−)-2b** by the procedure used for racemic **22b**. $[\alpha]_D^{25}$ +63.5 (*c* 0.05, $CHCl_3$).

((1*S*,4*R*,5*S*)-3-(2,4-Difluorophenyl)-4,5-dihydroxycyclopent-2-enyl)methyl pivalate ((−)-22b).

The compound was prepared from **(+)-2b** by the procedure used for racemic **22b**. $[\alpha]_D^{25}$ −63.0 (*c* 0.05, $CHCl_3$).

(1*R*,2*S*,5*R*)-3-(2,4-Difluorophenyl)-5-(hydroxymethyl)cyclopent-3-ene-1,2-diol ((+)-3b).

The compound was prepared from **(+)-22b** by the procedure used for racemic **3b**. $[\alpha]_D^{25}$ +62.5 (*c* 0.05, MeOH).

(1*R*,2*S*,3*S*,5*R*)-3-(4-Aminopyrrolo[1,2-*f*][1,2,4]triazin-7-yl)-5-(hydroxymethyl)cyclopentane-1,2-diol ((-)-4g).

The compound (53 mg) was prepared from **(-)-2b** (656 mg) by the procedure used for racemic **4g**. $[\alpha]_D^{25}$ −52.0 (*c* 0.25, DMSO).

(1*S*,2*R*,3*R*,5*S*)-3-(4-Aminopyrrolo[1,2-*f*][1,2,4]triazin-7-yl)-5-(hydroxymethyl)cyclopentane-1,2-diol ((+)-4g).

The compound (30 mg) was prepared from **(+)-2b** (515 mg) by the procedure used for racemic **4g**. $[\alpha]_D^{25}$ +52.0 (*c* 0.25, DMSO).

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Supporting Information: The supporting information is available on the ACS Publications website at DOI: …… . Copies of ^{1}H and ^{13}C NMR spectra of all compounds; selected IR spectra; chromatogram of HPLC purification of compound**1b**; HPLC analysis and CD spectra of **(+)-22b**, **(-)-22b, (+)-4g** and **(-)-4g**; crystallographic data (CIF files) for compounds **3b**, **4a**, **4c**, **30**, **32**, and **(-)-37a**; description of the cell-based assays.

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