# A Pauson–Khand Approach to New Carbocyclic Nucleoside Analogs

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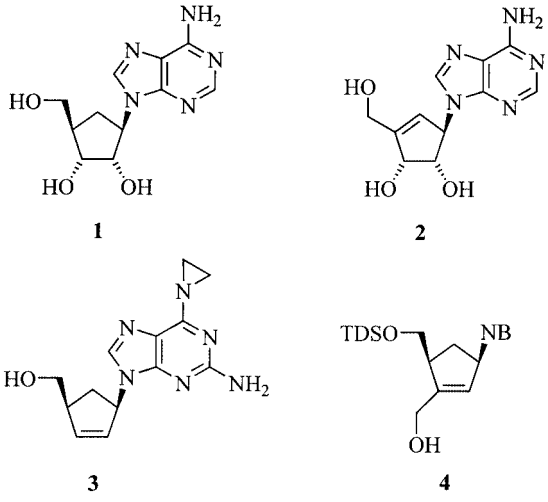
**Keywords:** Cobalt / Palladium / Kinetic resolution / Nucleosides / Pauson–Khand reaction

The synthesis of three new carbocyclic nucleoside analogs (CNAs) with the nucleobase attached to a 3′-hydroxymethylcyclopent-2′-en-1′-yl scaffold is reported. A variety of symmetric dienynes (propargylic acetals of type **11**) were used as substrates in a cobalt-mediated Pauson–Khand (PK) reaction to give bicyclic cyclopentenone derivatives of type *rac*-**12** with high diastereoselectivity. These compounds are valuable building blocks for the synthesis of structurally diverse CNAs with a high biological potential as apoptosis-inducing agents. Starting from the PK product *rac*-**12a**, the synthesis of 4′-trialkylsilyloxyethyl-substituted nucleosides *rac*-**18** and *rac*-**19** (with 5-bromouracil and 6-chloropurine as a nucleobase, respectively) was accomplished in seven steps (28 % and 37 % overall yield). The regio- and diastereoselective nucleobase (NB) introduction was achieved by $Pd^0$-catalyzed allylic substitution. Starting from the PK product *rac*-**12e**, the 2′-phenyl-4′-trialkylsilyloxymethyl-substituted CNA *rac*-**17** was prepared (6 steps, 29 % yield)by exploitingan alternative protocol – a Mitsunobu reaction – for the NB introduction. The key intermediates **12a** and **12e** were obtained in virtually enantiopure form by kinetic resolution by means of oxazaborolidine-catalyzed borane reduction (CBS reduction) in the presence of a (*R*)-diphenylprolinol-derived *B*-methyl oxazaborolidine catalyst.


## Introduction

Carbocyclic nucleosides (CNAs), where the furanose oxygen atom of the normal nucleoside is replaced by a methylene group, have received a great deal of attention over the last two decades. They play an important role as antiviral or antitumoral drugs,[1] and synthetic strategies towards such compounds have been highlighted in various review articles.[2] Aristeronmycin[3,4] (**1**) and neplanocin A[5] (**2**) are natural products that have a carbocyclic backbone and show antiviral and anticancer activity (Scheme 1). Due to their biological properties and their interesting structures they have often been chosen as target molecules for chemical syntheses. Abacavir[6] (**3**), which is the cyclopropylamine derivative of Carbovir,[7] has entered into clinical use for the treatment of HIV. Several methods for the construction of cyclopentyl skeletons have been developed.[2,8] However, many of them do not allow for a (diversity-oriented[9]) variation of substituents at the carbocyclic backbone.




Scheme 1. Selected examples of CNAs (carbocyclic nucleoside analogs). NB = nucleobase.

We have recently reported a convergent and enantioselective synthesis of monoprotected, 2′,3′-unsaturated carbocyclic nucleoside analogs of type **4** with a hydroxymethyl substituent in the 3′-position.[10] The synthesis centrally exploits transition metal organic chemistry, i.e. a Co-mediated Pauson–Khand (PK) reaction and a Pd-catalyzed allylic substitution, the latter of which allows the introduction of various nucleobases with virtually complete regio- and diastereocontrol. Enantiomerically pure compounds are accessible by kinetic resolution of the PK products. The potential of this new class of compounds as *anti*-tumoral agents was first shown in a series of biological assays,[10b] with cytotoxic activities at concentrations in the lower micromolar range resulting from apoptosis induction. Evidence for an apoptotic pathway of cell death was provided by microscope (characteristic membrane blebbing and cell shrinkage), by measuring the DNA fragmentation (hypoploidity) and by probing the activation of caspases 3, 8 and 9 (Western blot analysis).

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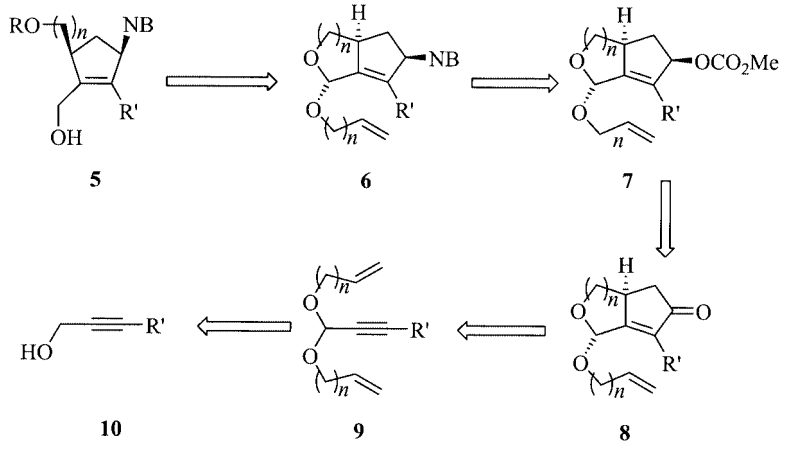



Scheme 2. Retrosynthetic analysis for CNAs of type **5**.

Challenged by these promising results, we decided to carry out further structural variations of the above-mentioned type of nucleosides. In this article, we now describe the synthesis of further CNAs having a modified backbone, thereby demonstrating the flexibility of our strategy and thus expanding the scope of possible target structures. In a first part we focus on general investigations concerning the selectivity of Pauson–Khand reactions in order to obtain potential CNA precursors, and in a second part, selected PK products are exploited as building blocks for the synthesis of the envisioned target structures of type **5** (Scheme 2).

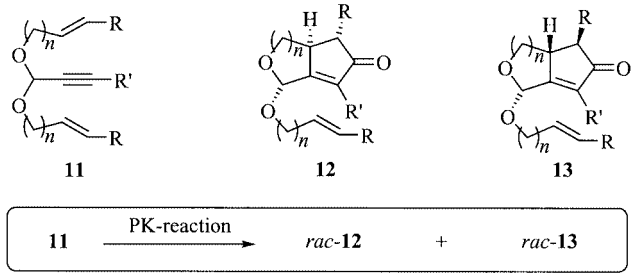
## Results and Discussion

A retrosynthetic analysis revealed that compounds of type **5** could be traced back to bicyclic acetals of type **6**,[10] thus allowing the differentiation of the two oxygen functionalities after acetal hydrolysis (Scheme 2). It was envisioned that the nucleobase could be introduced by $Pd^0$-catalyzed allylic substitution.[11,12] Bicyclic compounds of type **7** could be derived from α,β-unsaturated ketones of type **8**, which should be accessible by an intramolecular PK reaction from symmetric acetals **9**. Such acetals are easily obtained from propargylic alcohols of type **10**.

By systematically varying the substitution pattern of the acetals of type **9** we wanted to evaluate the scope and limitations of our PK-based strategy. Other key issues to be addressed concerned the preparation of the PK products **8** in nonracemic form, as well as the diastereoselective introduction of the two additional stereocenters.

### Pauson–Khand Reaction

The formation of three new bonds in an inter- or intramolecular [2+2+1]-cycloaddition makes the PK reaction one of the most powerful tools in the repertoire of organic chemists.[13] It has found various applications in the synthesis of complex organic molecules and extensive investigations are constantly being reported, also in the field of catalytic PK-type reactions.[14–16] Against this background, it was interesting to carefully evaluate the generality (and diastereoselectivity) of this reaction as a key step in our approach towards new CNAs (Scheme 2 and Scheme 3).

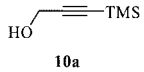
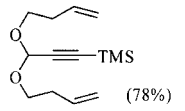
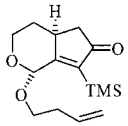
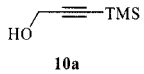
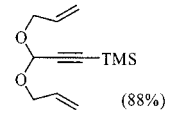
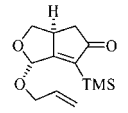
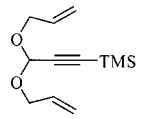
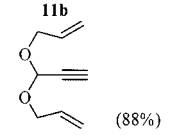
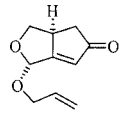
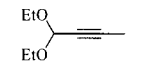
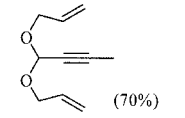
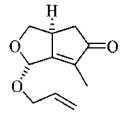
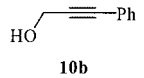
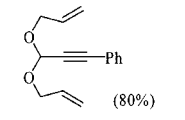
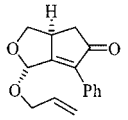
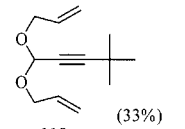
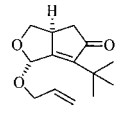
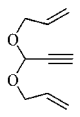
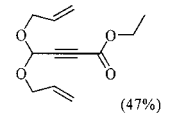
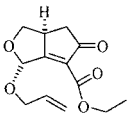
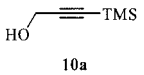
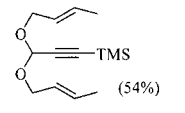
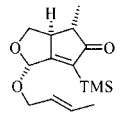
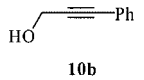
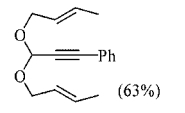
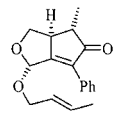
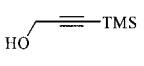
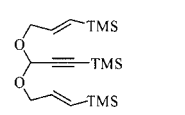
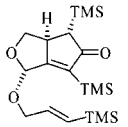



Scheme 3. General pattern of the Pauson–Khand reactions investigated (see Table 1 for yields and diastereoselectivities).

Pauson–Khand precursors of type **11** were synthesized following established acetalization protocols.[17] In the case of propargylic alcohols **10a** and **10b** PCC oxidation[18] gave the corresponding (highly sensitive) aldehydes, which were only isolated as crude products and then directly converted into the acetals of type **11** by acid-catalyzed acetalization with PPTS (entries 1, 2, 5, 8, 9, and 10). A modified protocol had to be used for the synthesis of **11e** because of the high volatility of the respective aldehyde (entry 4). Here, the commercially available diethylacetal **14** was converted into **11e** by acid-catalyzed transacetalization with azeotropic removal of EtOH. For the preparation of acetal **11f**, the alkyne **15** was first deprotonated with *n*BuLi and methyl formate was added. The resulting mixture of the desired aldehyde and the corresponding dialkynylcarbinol (2,2,8,8-tetramethylnona-3,6-diyn-5-ol) was directly subjected to the standard acetalization procedure to afford **11f** in 33% yield after chromatographic purification. The ester **11g** was obtained from acetal **13h** in a deprotonation/acylation sequence (*n*BuLi, $ClCO_2Et$).

Table 1. Results of the Pauson–Khand reaction according to Scheme 3.

| Entry | Starting material | Method | Acetal intermediates of type **11** (yield) | PK-products of type **12** (all racemic) | Yield (*dr*) |
|---|---|---|---|---|---|
| 1 |  **10a** | A[b] |  (78%) **11a** |  **12a** | 93% (>99:1) |
| 2[a] |  **10a** | A |  (88%) **11b** |  **12b** | 72% (>99:1) |
| 3[a] |  **11b** | B[c] |  (88%) **11c** |  **12c** | 45% (72:28) |
| 4 |  **14** | C[d] |  (70%) **11d** |  **12d** | 81% (98:2) |
| 5 |  **10b** | A |  (80%) **11e** |  **12e** | 88% (>99:1) |
| 6 |  **15** | D[e] |  (33%) **11f** |  **12f** | 59% (>99:1) |
| 7 |  **11c** | E[f] |  (47%) **11g** |  **12g** | 0% |
| 8 |  **10a** | A |  (54%) **11h** |  **12h** | 32% (>99:1) |
| 9 |  **10b** | A |  (63%) **11i** |  **12i** | 71% (>99:1) |
| 10 |  **10a** | A |  (50%) **11j** |  **12j** | 0% |

[a] Reported previously.[10] [b] Method A: a) PCC (1.5 equiv.), $CH_2Cl_2$, room temp., 3 h; b) allyl-OH (5 equiv.) or homoallyl-OH (10 equiv.), cat. TsOH, benzene, reflux, $-H_2O$, 16 h. [c] Method B: TBAF (1 equiv.) in THF, $H_2O$/allyl-OH (2:1), room temp., 1 h. [d] Method C: allyl-OH (5 equiv.), cat. TsOH, benzene, reflux, –EtOH, 16 h. [e] Method D: a) *n*BuLi (1.1 equiv.), $HCO_2Me$ (2 equiv.), THF, 0 °C, 1.5 h; b) allyl-OH (10 equiv.), cat. TsOH, benzene, reflux, $-H_2O$, 16 h. [f] Method E: *n*BuLi (1.1 equiv.), $ClCO_2Et$ (1.1 equiv.), THF, –78 °C to room temp., 16 h; PK reaction: $Co_2(CO)_8$ (1.15 equiv.), 4 Å mol. sieves (8 wt. equiv.), $CH_2Cl_2$, room temp., 2 h; then TMANO (8 equiv.), air, –20 °C to room temp., 16 h.

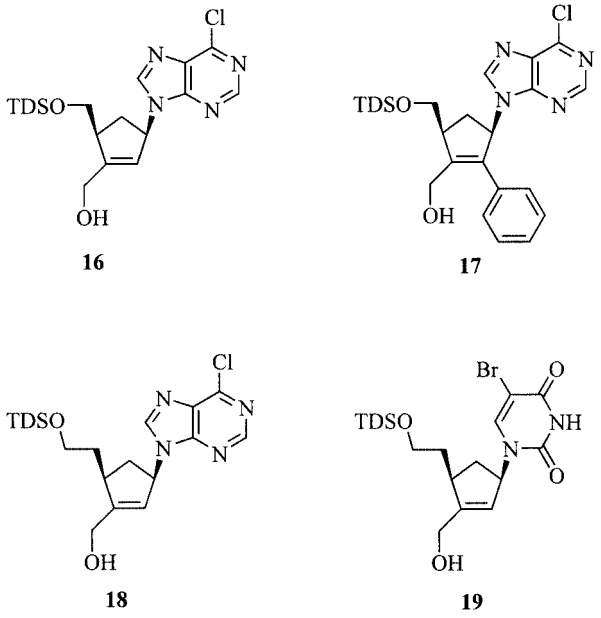
Having prepared a variety of dienynes (**11a**–**j**), we next investigated the $Co_2(CO)_8$-mediated PK reaction using these substrates. As a standard protocol, we used the same conditions optimized for substrate **11b** in the course of our previous study.[10] Here, an amine *N*-oxide is used as an activator, a concept independently introduced by Jeong and Schreiber.[19] The *N*-oxide acts by oxidizing a CO ligand to $CO_2$, thus generating a vacant coordination site at a cobalt center. All reactions (Table 1) were performed by first stirring the substrates with $Co_2(CO)_8$ (1.1 equiv.) and molecular sieves (4 Å) for two hours at room temp. in dichloromethane (in situ formation of alkyne–$Co_2(CO)_6$ complexes), before trimethylamine *N*-oxide (8 equiv.) was added at –20 °C and the mixture was exposed to air and stirring was continued overnight.

The results of the various experiments (Table 1) show that most of the enynes of type **11** afford the expected products in moderate to excellent yields. While the relative configuration of *rac*-**12b** has previously been assigned by X-ray crystallography,[10b] the configuration of the main diastereomers was assigned in all other cases by $^1$H NMR spectroscopy, especially NOE measurements and/or correlation with data from known compounds. The assignments are in agreement with those of Jeong and coworkers,[20] who have prepared such compounds in a related fashion starting from isolated alkyne–$Co_2(CO)_6$ precursors.

Two of the substrates, the electron-deficient enyne **11g** (entry 7) and the one bearing three bulky TMS groups (**11j**; entry 10), could not be converted into the corresponding PK products. The diastereoselectivities proved to be strongly dependant on the bulkiness of the terminal substituent at the triple bond. Whereas for bulky substituents virtually complete diastereoselectivity was obtained (TMS, Ph, *t*Bu, see entries 3, 4, and 9), a slight drop (*dr* = 98:2) was observed for R′ = Me (Scheme 3). Significantly lower selectivities were observed for R′ = H (*dr* = 72:28; entry 10), matching the observations made by Jeong et al.[20] The highest yields were achieved for the transformation of the 1,7-dienyne **11a** into the hydroindanone derivative *rac*-**12a**.

## Synthesis of New CNAs

As reported previously, compound *rac*-**16** (Scheme 4) exhibited particularly promising results in preliminary biological assays.[10b] Therefore, we chose this compound as a starting point for further structural optimization. We envisioned the CNAs **17**–**19** as promising target structures as they feature a silyl protecting group as well as chloropurine as the nucleobase (**17** and **18**). We were interested in how the backbone variation, i.e. the increased chain length of the substituent in the 4′-position (**18** and **19**) or the introduction of a phenyl substituent in the 2′-position (**17**) would effect the biological activity. The CNAs **17**–**19** were derived from the readily synthesized PK products *rac*-**12a** and *rac*-**12e** (Scheme 2, Table 1).



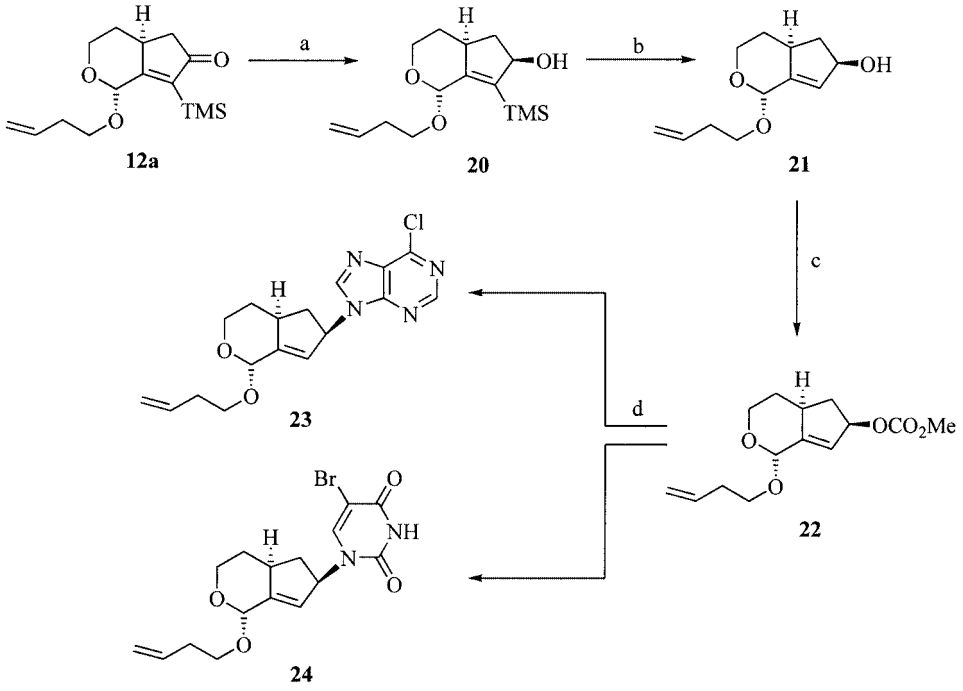

Scheme 4. The apoptosis-inducing CNA **16**[10a] and the envisioned structural analogs **17**–**19** (as target structures).

The elaboration of the synthetic routes described here was carried out in the racemic series. Additionally, the access to the nonracemic compounds was achieved by kinetic resolution of the PK products *rac*-**12a** and *rac*-**12e** as described in the latter part of this paper.

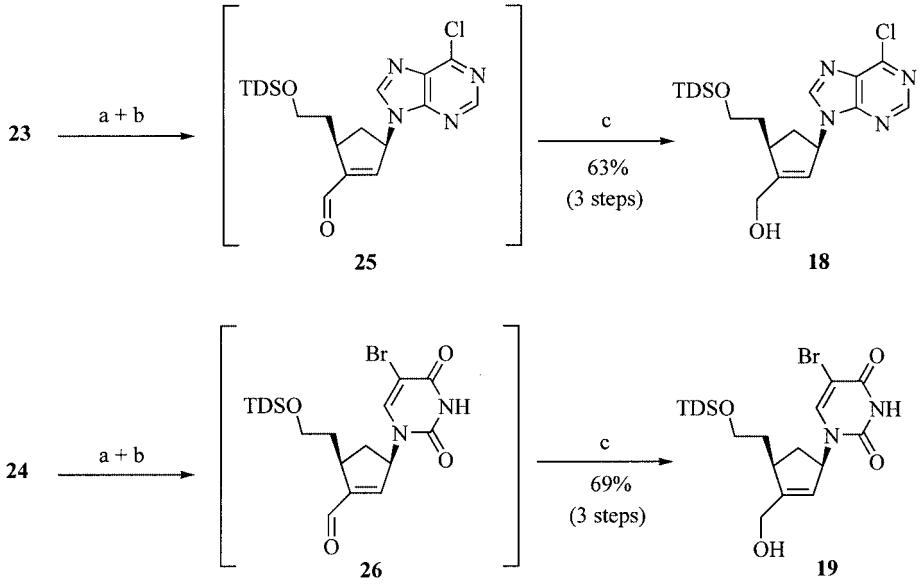
Following our general synthetic strategy (Scheme 2), the PK product *rac*-**12a** was first reduced under Luche conditions[21] to afford the allylic alcohol *rac*-**20** (99%; Scheme 5). After removal of the TMS group by treatment with KO*t*Bu (81%),[22] the resulting product (*rac*-**21**) was treated with methylchloroformate to afford the carbonate *rac*-**22** in high yield (91%). Having thus set up the system for the planned nucleobase introduction by Pd-catalyzed allylic substitution,[12] *rac*-**22** was treated with bromouracil and chloropurine, respectively, in the presence of 5 mol-% [$Pd_2(dba)_3$] and 10 mol-% dppp. The expected substitution products were obtained in good yields (*rac*-**23a**: 60%; *rac*-**23b**: 73%).

Unexpectedly, the hydrolysis of the acetal moiety in compounds *rac*-**23** and *rac*-**24** proved to be rather difficult. Under the standard conditions (PPTS, acetone, $H_2O$, reflux[23]) only low conversion was observed, possibly due to a high stability of the six-membered heterocycle (and the intermediate oxenium cation) and the tendency of the lactol (hydroxyaldehyde) to react with homoallylic alcohol back to the starting material during workup. This problem was solved by using polymer-supported reagents, i.e. Amberlyst-15, as a strongly acidic catalyst[24] in the hydrolysis step and neutralization of the filtrate with an excess of poly(4-vinylpyridine) (Scheme 6). After evaporation of the solvent, the crude product was directly *O*-silylated by addition of pyridine and thexyldimethylsilyl chloride (TDS-Cl) to afford the aldehydes *rac*-**25** and *rac*-**26**, respectively. A small amount of remaining acetal (*rac*-**23** or *rac*-**24**) was easily separated




Scheme 5. Synthesis of the CNA precursors *rac*-**23** and *rac*-**24**. Reaction conditions: a) $NaBH_4$ (5 equiv.), $CeCl_3$ (1 equiv.), MeOH, –20 °C to room temp., 2 h, 99%; b) *t*BuOK (1 equiv.), DMSO/$H_2O$ (19:1), room temp., 2 h, 81%; c) $ClCO_2Me$ (3 equiv.), py, 0 °C, 1 h, 91%; d) [$Pd_2(dba)_3$] (5 mol-%), dppp (10 mol-%), chloropurine or bromouracil (1.5 equiv.), DMF, room temp., 16 h, 60% for *rac*-**23**; 73% for *rac*-**24**.

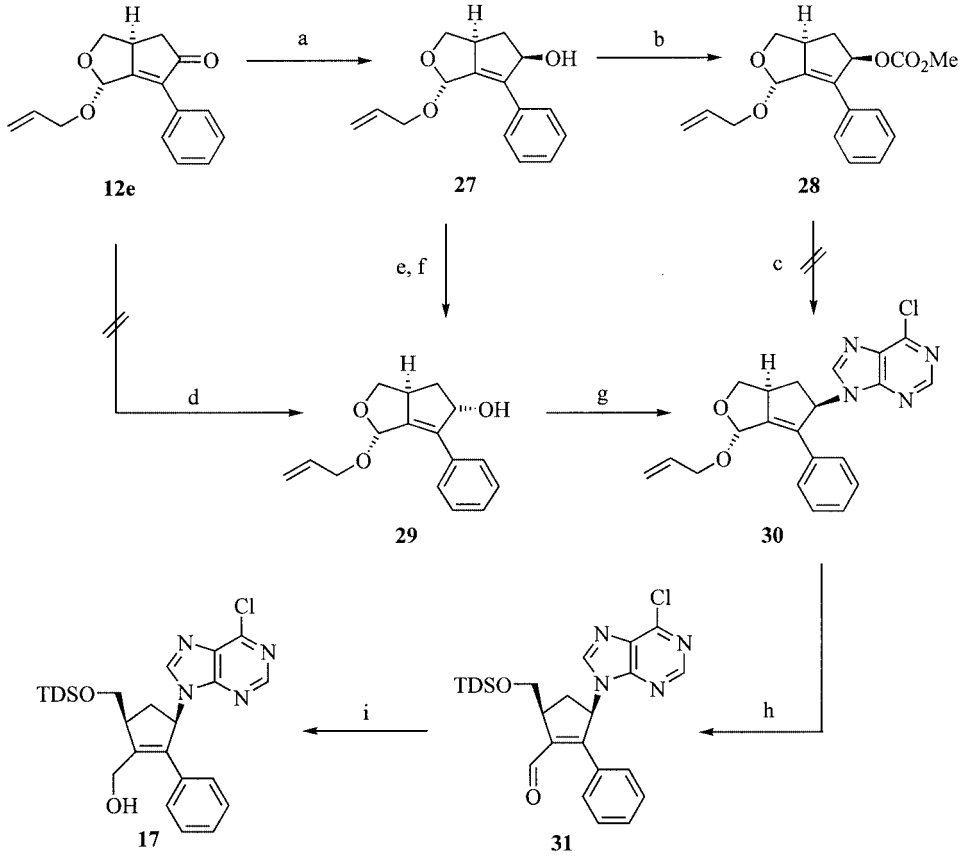



Scheme 6. Preparation of the CNAs *rac*-**18** and *rac*-**19**. Reaction conditions: a) Amberlyst-15 (0.1 wt. equiv.), wet acetone, room temp., 1 h, then poly(4-vinylpyridine) (2 wt. equiv.); b) TDSCl (3 equiv.), py, room temp., 16 h; c) $NaBH_4$ (10 equiv.), MeOH/$CH_2Cl_2$, –78 °C, 1 h.

after borohydride reduction, and the CNAs *rac*-**18** and *rac*-**19** were obtained in good overall yields (63–69% over three steps).

The synthesis of the target compound *rac*-**17** (Scheme 4), which bears a phenyl substituent in the 2′-position, was attempted following a similar strategy (Scheme 7). While reduction of the ketone *rac*-**12e** (99%) and carbonate formation (84%) proceeded smoothly under these conditions, all our attempts to introduce the nucleobase by Pd-catalyzed substitution failed.[10b,12] Obviously, the tetra-substituted double bond in substrate *rac*-**28** is not sufficiently reactive towards the $Pd^0$ catalyst. As a consequence, we decided to




Scheme 7. Synthesis of the 2′-phenyl-substituted nucleoside analog *rac*-**17**. Reaction conditions: a) $NaBH_4$ (4 equiv.), $CeCl_3$ (1 equiv.), MeOH, –20 °C to room temp., 2 h, 99%; b) $ClCO_2Me$ (3 equiv.), py, 0 °C, 1 h, 84%; c) $[Pd_2(dba)_3]$ (5 mol-%), dppp (10 mol-%), chloropurine (1.5 equiv.), DMF, room temp., 16 h; d) Yamamoto's reagent (from 2,6-di-*tert*-butyl-4-methylphenol and DIBAH),[27a] toluene, –78 °C to –40 °C, 5 h; e) DEAD (5 equiv.), $PPh_3$ (5 equiv.), *p*-nitrobenzoic acid (4.4 equiv.), toluene, room temp., 16 h, 79%; f) $K_2CO_3$ (2 equiv.), MeOH, room temp., 16 h, 82%; g) DEAD (2 equiv.), $PPh_3$ (2 equiv.), chloropurine (2 equiv.), THF, room temp., 16 h, 62%; h) PPTS (0.3 equiv.), wet acetone, reflux, 6 h; then TDSCl (4 equiv.), py, room temp., 16 h, 73% over 2 steps; i) $NaBH_4$ (10 equiv.), MeOH/$CH_2Cl_2$, –78 °C, 1 h, 99%.

introduce the nucleobase in this case by means of a Mitsunobu-type reaction.[25,26] To access the required epimeric alcohol *rac*-**29**, we initially tried to reduce **12e** with Yamamoto's reagent, which often shows an inverted diastereoselectivity in the reduction of ketones.[27] However, this Lewis-acidic reagent predominantly led to acetal cleavage and none of the reduction products (*rac*-**27** or *rac*-**29**) could be isolated (Scheme 7).

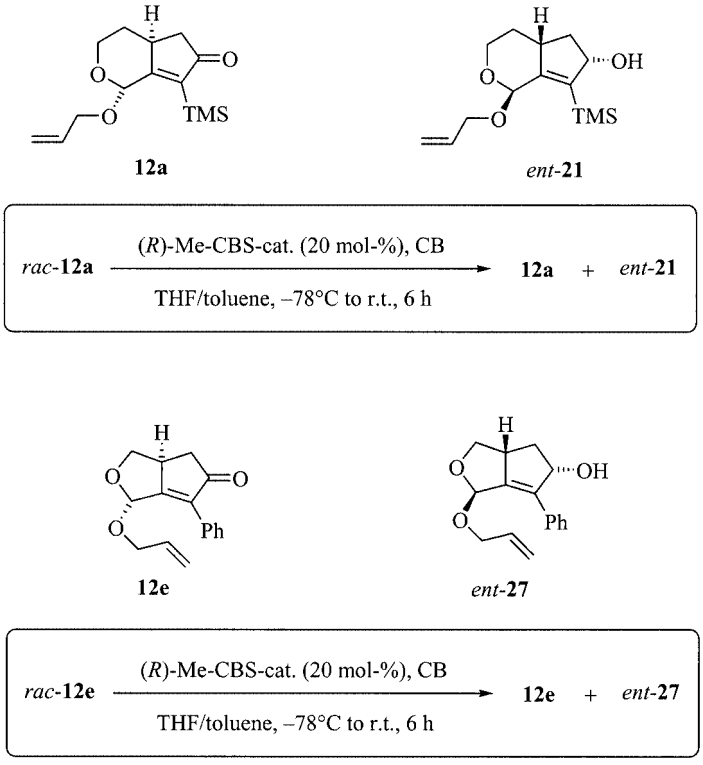
To overcome these problems, alcohol *rac*-**27** was converted into its epimer *rac*-**29** in a Mitsunobu reaction (*p*-nitrobenzoic acid in the presence of DIAD and triphenylphosphane) and subsequent ester hydrolysis in 65% overall yield (Scheme 7).[25] Chloropurine was then introduced in a second Mitsunobu reaction to yield the bicyclic CNA precursor *rac*-**30** (62%). Hydrolysis of the acetal ring was easily accomplished in this case by treatment of *rac*-**30** with PPTS in wet acetone.[23] After removal of the solvent, the 5′-OH group was directly protected as a silyl ether. Reduction of the aldehyde intermediate *rac*-**31** with $NaBH_4$ then proceeded smoothly (99%) to give the desired 2′-phenyl-substituted CNA *rac*-**17.**

### Kinetic Resolution of the Key Intermediates *rac*-15a and *rac*-15c

Having successfully elaborated efficient synthetic routes towards the target compounds in the racemic series, an important goal was to pave the way for the synthesis of the new CNAs in the nonracemic series as well.

As all attempts to perform the chirogenic step (i.e. the PK reaction of substrates of type **11**; see Table 1) in an enantioselective manner[14,15] were not successful, we had to resolve the chiral products. In analogy to our previous work,[10b] we investigated the possibility to kinetically resolve the ketones *rac*-**12a** and *rac*-**12e**, respectively, by means of an asymmetric oxazaborolidine-catalyzed borane reduction (CBS reduction).[28]




Scheme 8. Preparation of nonracemic **15a** and **15c** by kinetic resolution (see Table 2 for details).

Table 2. Results of the kinetic resolution by means of CBS reduction according to Scheme 8.

| Entry | Substrate | Catecholborane | Unreacted ketone of type **12** | Alcohols *ent*-**21**/*ent*-**27** |
|---|---|---|---|---|
| 1 | *rac*-**12a** | 0.50 equiv. | 62% (53% *ee*) | 22% (90% *ee*) |
| 2 | *rac*-**12a** | 0.65 equiv. | 43% (83% *ee*) | 36% (85% *ee*) |
| 3 | *rac*-**12a** | 0.80 equiv. | 30% (98% *ee*) | 51% (78% *ee*) |
| 4 | *rac*-**12e** | 0.65 equiv. | 38% (96% *ee*) | n.d. |
| 5 | *rac*-**12e** | 0.80 equiv. | 29% (>99% *ee*) | n.d. |

Following our established protocol, a solution containing the racemic ketone (*rac*-**12a** and *rac*-**12e**, respectively) and the (*R*)-diphenylprolinol-derived *B*-methyl oxazaborolidine (20 mol-%) in toluene at –78 °C was treated with 0.5 to 0.8 equivalents of catecholborane in THF. The mixture was allowed to warm up to room temp. over a period of 6 h and then quenched by addition of MeOH (Scheme 8).

As the results summarized in Table 2 show, the kinetic resolutions proceeded with high efficiency. Using 0.80 equiv. of catecholborane the recovered ketones were obtained after ca. 60% conversion in 30% isolated yield in virtually enantiopure form (Table 2). The enantiomeric purities were determined by means of GLC (**12a**) or HPLC (**12e**) on chiral stationary phases. The enantiomeric purity of the reduction product *ent*-**21** was determined after reoxidation with $MnO_2$. Attempts to reoxidize *ent*-**27** under such conditions failed (decomposition).

These results nicely demonstrate the generality of the CBS protocol for the kinetic resolution of PK products of type **8** (see also Scheme 2).

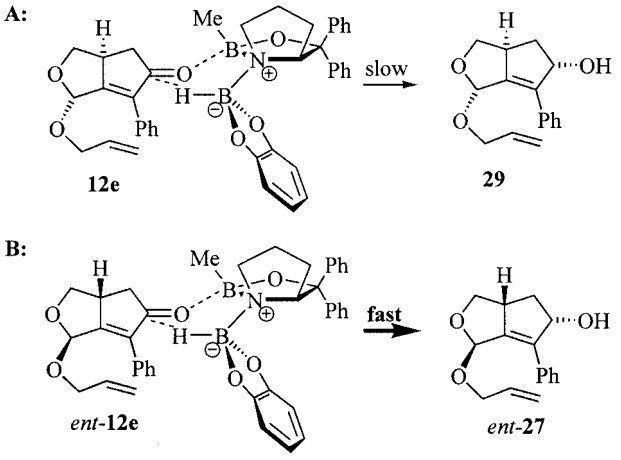
The stereochemical assignments of the nonracemic products were made applying the Corey model, i.e. by analyzing the (competing) transition states for the CBS reduction of the two enantiomeric substrates assuming a strong catalyst control (Scheme 9).[28a,10b]

As shown in Scheme 9 for the resolution of *rac*-**12e**, the reduction of **12e** (case A) should be less favored (slower) because hydride transfer has to occur from the concave side of the substrate, which violates the natural preference. In contrast, the reduction of *ent*-**12e** (case B) is highly favored because substrate and catalyst control are matched. It should be mentioned that the configurational assignments drawn by this type of analysis have been validated carefully in our previous work for the resolution of *rac*-**12b**.[10b]

## Conclusions

In summary, we have developed an efficient and practical protocol for the synthesis of new, monoprotected, 2′,3′-un-




Scheme 9. Two competing transition structures for the kinetic resolution of *rac*-**12e** by CBS reduction assuming catalyst control. A: mismatched case (violation of substrate preference); B: matched case.

saturated carbocyclic nucleoside analogs having a hydroxymethyl side chain in 3′-position, as exemplified by structures **17**, **18**, and **19**. Such compounds are analogs of strongly apoptosis-inducing CNAs. The synthesis described herein demonstrates the flexibility of our Pauson–Khand-based approach, which allows the variation of the substitution pattern at the pseudosugar backbone. Using a variety of dieneynes as substrates, we found high diastereoselectivities in the Co-mediated key reaction. Two of the resulting cyclopentanoid building blocks (*rac*-**12a** and *rac*-**12e**) were used for the elaboration of the further synthetic routes. Special attention was given to the nucleobase introduction. Starting from **12a**, an established protocol based on Pd-catalyzed allylic substitution was applied. In contrast, two subsequent Mitsunobu reactions were needed to achieve a stereocontrolled NB introduction in the 2′-phenyl-substituted series. Finally, we have shown that the key intermediates (**12a** and **12e**) can be obtained in enantiomerically pure form through a highly efficient kinetic resolution by means of CBS reduction.

The biological activity (apoptosis induction) of the new CNAs prepared is currently under investigation. The results will be reported separately. In any case, the (diversity-oriented) synthetic schemes disclosed here will provide a reliable basis for the preparation of various new CNSs of type **5** in the future.

## Experimental Section

**General Remarks:** Anhydrous solvents were obtained by distillation from sodium/benzophenone (THF), from $CaH_2$ ($CH_2Cl_2$), from KOH (pyridine, $Et_3N$), or by storage over 4 Å mol. sieves (DMSO). Reagents (generally ≥ 99%) were used as purchased unless otherwise stated. The concentration of organolithium reagents was determined by titration against menthol in THF using 1,10-phenanthroline as an indicator.[29] TMANO (trimethylamine *N*-oxide) was dried by azeotropic removal of water with toluene. Water- and/or air-sensitive compounds were handled under an atmosphere of argon using Schlenk techniques. Reactions were monitored by analytical thin-layer chromatography (TLC) using Merck silica gel 60 F 254 aluminum plates. Chromatograms were visualized either with UV light, by staining with iodine, or with a "cerium reagent" [prepared by dissolving 2 g of phosphomolybdic acid and 1 g of $Ce(SO_4)_2$ in 100 mL of 10% aqueous $H_2SO_4$] and subsequent heating. Flash chromatography:[30] silica gel 60 (230–400 mesh) from Merck. Gas chromatography (GLC): HP-6890, with $H_2$ as a carrier gas, FID (flame ionization detector). Merck–Hitachi HPLC-system: L6200A pump, L-4000A UV-detector. NMR spectroscopy: Bruker DPX 300, DRX 500 and AC 250 instruments. Chemical shifts ($\delta$) are given in ppm relative to the solvent reference. $^{13}C$ NMR spectra were measured with proton decoupling and the number of bound protons (multiplicities) determined by DEPT. IR spectroscopy: Perkin–Elmer FT-IR Paragon 1000 using the ATR technique. Mass spectrometry: Finnigan MAT Incos 50 Galaxy System (DIP-MS) or a Finnigan MAT 900 spectrometer; high resolution mass spectra (HRMS) were recorded on a Finnigan HSQ-30 (HR-EI-MS) or on a Finnigan MAT 900 (HR-ESI-MS). The method of ionization is given in parentheses. Melting points were measured on a Büchi B-545 apparatus and are uncorrected. Specific optical rotations were recordedon a Perkin–Elmer 343 plus polarimeter; concentrations, *c*, are given in grams per 100 mL; the cell length was 100 mm.

**3,3-Bis(but-3-enyloxy)-1-propynyltrimethylsilane (11a):** A solution of alcohol **10a** (1.00 g, 7.80 mmol) in dry $CH_2Cl_2$ (5 mL) was added dropwise to a stirred suspension of pyridinium chlorochromate (2.52 g, 11.70 mmol) in dry $CH_2Cl_2$ (15 mL) at 0 °C. The mixture was allowed to warm to room temp. for 3 h and was then carefully filtered through a plug of silica. After evaporation of the solvent, the sensitive 3-trimethylsilyl-2-propyne-1-al was immediately further converted as follows. The crude aldehyde (approx. 7.80 mmol), homoallyl alcohol (3.40 mL, 39 mmol), and *p*TsOH (74 mg, 39 μmol) were dissolved in benzene (15 mL), and the mixture was heated to reflux for 16 h with azeotropic removal of water (Dean–Stark trap). After cooling to room temp., the mixture was neutralized by addition of $NaHCO_3$ before it was filtered through a plug of silica and concentrated under reduced pressure. The residue was purified by flash chromatography (CyHex/EtOAc, 20:1) to afford the acetal **11a** as a light-yellow oil (1.54 g, 78% over two steps). TLC: $R_f$ = 0.63 (CyHex/EtOAc, 20:1). $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 5.89–5.72 (m, 2 H, C*H*=$CH_2$), 5.23 (s, 1 H, H-3), 5.07 (d, $J$ = 17.2 Hz, 2 H, CH=CH–$H_{cis}$), 5.18 (d, $J$ = 10.2 Hz, 2 H, CH=CH–$H_{trans}$), 3.70 (td, $J$ = 6.8, 9.5 Hz, 2 H, O–$CH_2$), 3.54 (td, $J$ = 6.7, 9.5 Hz, 2 H, O–C$H_2$), 2.33 (td, $J$ = 6.7, 6.7 Hz, 4 H, C$H_2$–CH=$CH_2$), 0.17 (s, 9 H, $SiCH_3$) ppm. $^{13}C$ NMR (63 MHz, $CDCl_3$): $\delta$ = 135.0 (*C*H=$CH_2$), 116.5 (CH=*C*$H_2$), 99.8 (C3), 91.5 and 90.7 (C1 and C2), 64.7 (O–*C*$H_2$), 33.9 (*C*$H_2$CH=$CH_2$), –0.3 (TMS) ppm. IR (ATR): $\tilde{\nu}$ = 2956 (m), 1640 (m), 1352 (m), 1327 (m), 1249 (m), 1103 (s), 1037 (s), 913 (m), 842 (s), 759 $cm^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 251 (14) [M – $H^+$], 181 (57), 151 (23), 123 (18), 111 (19), 99 (22), 73 (68), 59 (35), 55(100). HRMS (EI) calcd. for [M – $H^+$] $C_{14}H_{23}O_2Si$: 251.1467; found 251.146.

**1,1-Diallyloxy-2-butyne (11d):** A solution of 1,1-diethoxy-2-propyne (**14**; 2.00 g, 14.06 mmol), allyl alcohol (4.74 mL, 70 mmol), and *p*TsOH (134 mg, 0.7 mmol) in benzene (50 mL) was heated to reflux. Using a distillation head, the benzene/ethanol azeotrope was constantly removed from the system and benzene was added (5 × 20 mL), until no further azeotrope formed (16 h). The mixture was cooled to room temp. and neutralized by addition of $K_2CO_3$. The solvent and excess of allyl alcohol were removed under reduced pressure and the residue was purified by flash chromatography (CyHex/EtOAc, 10:1) to give the product **11d** as a colorless oil

(1.64 g, 70%).TLC: $R_f$ = 0.56 (CyHex/EtOAc, 10:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 5.91 (dddd, $J$ = 5.4, 11.5, 10.3, 6.0 Hz, 2 H, C*H*=$CH_2$), 5.31 (q, $J$ = 1.6 Hz, 1 H, H-1), 5.26 (tdd, $J$ = 1.6, 1.6,11.5 Hz, 2 H, CH=CH–$H_{trans}$), 5.16 (tdd, $J$ = 1.6, 1.6, 10.3 Hz, 2 H, CH=CH–$H_{cis}$), 4.18 (tdd, $J$ = 1.6, 12.6, 5.4 Hz, 2 H, C$H_2$–CH=$CH_2$), 4.04 (tdd, $J$ = 1.4, 12.6, 6.0 Hz, 2 H, C$H_2$–CH=$CH_2$), 1.85 (d, $J$ = 1.6 Hz, 3 H, $CCH_3$) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 134.1 (*C*H=$CH_2$), 117.3 (CH=*C*$H_2$), 90.6 (C1), 82.7 and 74.5 (C2 and C3), 66.0 (*C*$H_2$CH=$CH_2$), 3.5 (C4) ppm. IR (ATR): $\tilde{\nu}$ = 2875 (w), 1725 (m), 1424 (m), 1363 (m), 1246 (m), 1157 (s), 1036 cm$^{-1}$ (s). MS (EI, 70 eV): *m*/*z* (%) = 166 (6) [M$^+$], 165 (59), 109 (100), 81 (45), 79 (51), 67 (37), 53 (38).

**3,3-Diallyloxy-1-propynylbenzene (11e):** Following the two-step procedure described for **11a**, **10b** (6.00 g, 45.4 mmol) afforded the acetal **11e** (9.22 g, 80% yield) as a yellow oil. TLC: $R_f$ = 0.58 (CyHex/EtOAc, 20:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 7.48–7.44 (m, 2 H, $H_{ar}$), 7.33–7.29 (m, 3 H, $H_{ar}$), 5.97 (tdd, $J$ = 5.5, 17.2, 10.3 Hz, 2 H, C*H*=$CH_2$), 5.57 (s, 1 H, H-3), 5.33 (tdd, $J$ = 1.6, 1.6,17.2 Hz, 2 H, CH=CH–$H_{trans}$), 5.20 (tdd, $J$ = 1.3, 1.7, 10.3 Hz, 2 H, CH=CH–$H_{cis}$), 4.29 (tdd, $J$ = 1.4, 12.6, 5.5 Hz, 2 H, C$H_2$–CH=$CH_2$), 4.15 (tdd, $J$ = 1.4, 12.6, 6.0 Hz, 2 H, C$H_2$–CH=$CH_2$) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 134.0 (*C*H=$CH_2$), 131.9, 128.9, 128.2 (d, $C_{ar}$), 121.7 (s, $C_{ar}$), 117.5 (CH=*C*$H_2$), 91.0 (C3), 85.7 and 83.9 (C1 and C2), 66.3 (*C*$H_2$CH=$CH_2$) ppm. IR (ATR): $\tilde{\nu}$ = 2865 (w), 2228 (w), 1488 (m), 1355 (m), 1323 (m), 1254 (w), 1087 (s), 1026 (s), 921 (s), 755 (s), 689 cm$^{-1}$ (s). MS (EI, 70 eV): *m*/*z* (%) = 227 (5) [M – H$^+$], 198 (23), 171 (24), 142 (100), 141 (94), 129 (53), 128 (96), 11 5 (24), 102 (28), 77 (14). HRMS (EI) calcd. for [M – H]$^+$ $C_{15}H_{15}O_2$: 227.1072; found 227.106.

**1,1-Diallyloxy-4,4-dimethyl-2-pentyne (11f):** 3,3-Dimethyl-but-1-yne (**15**; 2.00 g, 24.35 mmol) was dissolved in dry THF (25 mL) and *n*BuLi (18.59 mL, 26.78 mmol) was slowly added at 0 °C. After stirring for 30 min the mixture was added to ethyl formate (3.92 mL, 48.69 mmol) in dry THF (25 mL) at 0 °C. After 1 h the reaction was quenched by addition of ice water (50 mL) and acetic acid (2.2 mL, 36.5 mmol) was added. The mixture was extracted with MTBE (3×30 mL) and the combined organic layers were washed with brine and dried with $MgSO_4$. After removal of the solvent, the crude mixture was directly subjected to the acetalization conditions, as described for the preparation of **11a**, to afford the acetal **11f** (1.65 g, 33% yield) as a colorless oil after flash chromatography (CyHex/EtOAc, 20:1). TLC: $R_f$ = 0.43 (CyHex/EtOAc, 20:1). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.93 (dddd, $J$ = 5.5, 17.3, 10.3, 6.0 Hz, 2 H, C*H*=$CH_2$), 5.31 (s, 1 H, H-1), 5.28 (tdd, $J$ = 1.6, 1.7,17.3 Hz, 2 H, CH=CH–$H_{trans}$), 5.16 (tdd, $J$ = 1.2, 1.7, 10.3 Hz, 2 H, CH=CH–$H_{cis}$), 4.17 (tdd, $J$ = 1.5, 12.7, 5.5 Hz, 2 H, C$H_2$–CH=$CH_2$), 4.04 (tdd, $J$ = 1.4, 12.7, 6.0 Hz, 2 H, C$H_2$–CH=$CH_2$), 1.21 (s, 9 H, $CCH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 134.2 (*C*H=$CH_2$), 117.3 (CH=*C*$H_2$), 91.0 (C3), 85.7 and 83.9 (C1 and C2), 66.3 (*C*$H_2$CH=$CH_2$), 30.7 (C5), 27.3 (C4) ppm. IR (ATR): $\tilde{\nu}$ = 2968 (m), 2204 (m), 1628 (m), 1456 (w), 1362 (m), 1262 (m), 1109 (m), 1033 (s), 922 cm$^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 208 (1) [M$^+$], 177 (10), 151 (100), 135 (21), 121 (27), 107 (46), 90 (46), 81 (84), 67 (69), 57 (79), 41 (99). HRMS (EI) calcd. for [M]$^+$ $C_{13}H_{20}O_2$: 208.1463; found 208.146.

**Ethyl 4,4-Diallyloxy-2-butynoate (11g):** Acetal **11c** (1.60 g, 10.51 mmol) was dissolved in THF (10 mL) and the mixture was cooled to 0 °C. A 1.44 M solution of *n*BuLi in hexane (8.03 mL, 11.56 mmol) was added and the reaction mixture was stirred for another 30 min, before it was added to a solution of ethyl chloroformate (1.10 mL, 11.56 mmol) in THF (10 mL) at –78 °C. The mixture was allowed to warm to room temp. during 16 h. Water (30 mL) was added and it was extracted with EtOAc (4×30 mL). The combined organic phases were washed with water (3×20 mL) and brine (20 mL), dried ($MgSO_4$), and the solvent was removed under reduced pressure. After purification by flash chromatography (CyHex/EtOAc, 20:1) the product **11g** was obtained as a colorless oil (1.10 g, 47% yield). TLC: $R_f$ = 0.31 (CyHex/EtOAc, 20:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 5.89 (dddd, $J$ = 5.4, 17.2, 10.3, 6.0 Hz, 2 H, C*H*=$CH_2$), 5.42 (s, 1 H, H-4), 5.29 (tdd, $J$ = 1.3, 1.7,17.2 Hz, 2 H, CH=CH–$H_{trans}$), 5.16 (tdd, $J$ = 1.3, 1.7, 10.3 Hz, 2 H, CH=CH–$H_{cis}$), 4.22 (q, $J$ = 7.1 Hz, 2 H, O–C$H_2$CH$_3$), 4.22 (m, 2 H, C$H_2$–CH=$CH_2$), 4.08 (tdd, $J$ = 1.3, 12.6, 6.0 Hz, 2 H, C$H_2$–CH=$CH_2$), 1.28 (t, $J$ = 7.1 Hz, 3 H, O–$CH_2$C$H_3$) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 152.7 (C1), 133.3 (*C*H=$CH_2$), 117.9 (CH=*C*$H_2$), 89.9 (C4), 80.4 and 76.5 (C2 and C3), 66.7 (*C*$H_2$CH=$CH_2$), 62.3 (O*C*$H_2$CH$_3$), 13.9 (OCH$_2$*C*H$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 2983 (w), 1715 (s), 1366 (w), 1242 (s), 1109 (m), 1044 (s), 1014 (m), 930 (m), 750 cm$^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 224 (2) [M$^+$], 223 (7), 167 (48), 127 (24), 111 (46), 93 (100), 81 (43), 67 (26), 53 (47).

**3,3-Bis(but-2-enyloxy)-1-propynyltrimethylsilane (11h):** Following the two-step procedure described for **11a** [(*E*)-2-butenol was used instead of allyl alcohol], **10a** (2.00 g, 15.6 mmol) afforded the acetal **11h** (2.12 g, 54% yield) as a colorless oil after flash chromatography (CyHex/EtOAc, 20:1). TLC: $R_f$ = 0.42 (CyHex/EtOAc, 50:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 5.77–5.66 (m, 2 H, CH=C*H*CH$_3$), 5.63–5.52 (m, 2 H, C*H*=CHCH$_3$), 5.26 (s, 1 H, H-3), 4.11 (tdd, $J$ = 4.2, 6.4, 12.4 Hz, 2 H, O–C$H_2$), 3.97 (tdd, $J$ = 1.3, 7.5, 12.4 Hz, 2 H, O–C$H_2$), 1.69 (dd, $J$ = 1.2, 6.2 Hz, 6 H, $CH_3$), 0.16 (s, 9 H, $SiCH_3$) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 130.2 and 126.9 (*C*H=*C*H), 100.0 and 90.8 (C1 and C2), 90.0 (C3), 65.9 (O–*C*$H_2$), 17.7 (*C*$H_3$CH=$CH_2$), –0.3 (TMS) ppm. IR (ATR): $\tilde{\nu}$ = 2958 (m), 2915 (w), 1448 (w), 1350 (m), 1249 (m), 1097 (s), 1020 (s), 963 (m), 842 (s), 759 cm$^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 251 (1) [M – 1$^+$], 237 (3) [M – $CH_3^+$], 223 (4), 181 (16), 137 (18), 127 (71), 111 (19), 99 (26), 73 (38), 55 (100). HRMS (EI) calcd. for [M – $CH_3^+$] $C_{13}H_{21}O_2Si$: 237.1311; found 237.130.

**3,3-Bis(but-2-enyloxy)-1-propynylbenzene (11i):** Following the two-step procedure as described for **11a** [(*E*)-2-butenol was used instead of allyl alcohol], **10b** (1.00 g, 7.57 mmol) afforded the acetal **11i** (1.07 g, 63% yield) as a yellow oil. TLC: $R_f$ = 0.47 (CyHex/EtOAc, 20:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 7.47–7.43 (m, 2 H, $H_{ar}$), 7.32–7.26 (m, 3 H, $H_{ar}$), 5.84–5.71 (m, 2 H, CH=C*H*CH$_3$), 5.68–5.60 (m, 2 H, C*H*=CHCH$_3$), 5.53 (s, 1 H, H-3), 4.20 (tdd, $J$ = 1.3, 6.5, 12.4 Hz, 2 H, O–C$H_2$), 4.06 (tdd, $J$ = 1.3, 6.2, 12.4 Hz, 2 H, O–C$H_2$), 1.71 (dd, $J$ = 1.2, 6.1 Hz, 6 H, $CH_3$) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 131.9, 130.3 128.8, 128.2, 126.9 (d, $C_{ar}$ and *C*H=*C*H), 121.9 (s, $C_{ar}$), 90.7 (C3), 85.5 and 84.3 (C1 and C2), 66.0 (O–*C*$H_2$), 17.8 (*C*$H_3$CH=$CH_2$) ppm. IR (ATR): $\tilde{\nu}$ = 2913 (m), 2233 (w), 1488 (m), 1442 (m), 1353 (m), 1092 (s), 1016 (s), 964 (s), 755 (m), 690 cm$^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 256 (<1) [M$^+$], 195 (8), 185 (15), 167 (9), 156 (41), 131 (100), 115 (41), 102 (65), 77 (27), 55 (79), 39 (51).

**3,3-Bis(3-trimethylsilanylallyloxy)-1-propynyltrimethylsilane (11j):** Following the two-step procedure described for **11a** [(*E*)-2-(3-trimethylsilany)propenol[31] was used instead of allyl alcohol], **10a** (1.13 g, 9.08 mmol) afforded the acetal **11j** (1.66 g, 50% yield) as a colorless oil after flash chromatography (CyHex/EtOAc, 20:1). TLC: $R_f$ = 0.74 (CyHex/EtOAc, 20:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 6.09 (ddd, $J$ = 4.7, 5.1, 18.7 Hz, 2 H, C*H*=CHTMS), 5.92 (td, $J$ = 1.2, 18.7 Hz, 2 H, CH=C*H*TMS) 5.30 (s, 1 H, H-3), 4.22 (ddd, $J$ = 1.2, 4.7, 13.0 Hz, 2 H, C$H_2$–CH=$CH_2$), 4.07 (ddd, $J$ = 1.2, 5.1, 13.0 Hz, 2 H, C$H_2$–CH=$CH_2$), 0.17 (s, 9 H, C≡C–

$SiCH_3$), 0.05 (s, 18, C=CH–Si$CH_3$) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 141.3 and 132.8 (CH=CH), 99.6 and 91.1 (C1 and C2), 90.7 (C3), 68.3 ($CH_2$CH=CH), –0.3 and –1.4 (TMS) ppm. IR (ATR): $\tilde{\nu}$ = 2954 (m), 1247 (s), 1103 (m), 1028 (m), 837 (s), 760 (m), 699 cm$^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 368 (<1) [$M^+$], 295 (9), 239 (6) [M – $OCH_2CH$=$CHTMS^+$], 225 (7), 155 (19), 147 (24), 133 (27), 85 (42), 73 (100), 59 (68).

**General Procedure for Pauson–Khand Reactions:** A 50-mL flask was charged with dry, degassed $CH_2Cl_2$ (25 mL), activated 4-Å molecular sieves (8 wt. equiv.), and $Co_2(CO)_8$ (393 mg, 1.15 mmol) under argon. [**Note:** the $Co_2(CO)_8$ must be of high quality, i.e. red and nonsticky crystals, to obtain good yields.] Then, the dieneyne (1 mmol) was added all at once and the mixture was stirred at room temp. for 2 h under argon. After cooling the mixture to –20 °C, dry TMANO (600 mg, 8 mmol) was added in small portions over a period of 10 min. A stream of air was bubbled through the dark solution for 20 min before stirring was continued for 16 h at room temp. (open flask). The mixture was filtered through a plug of silica (in order to remove blue- and violet-colored cobalt by-products) before the solvent was evaporated and the residue purified by flash chromatography.

**(5*SR*,9*RS*)-9-(But-3-enyloxy)-2-trimethylsilyl-8-oxabicyclo[3.4.0]-non-1-ene-3-one (*rac*-12a):** Following the general procedure for PK reactions, compound **11a** (252 mg, 1 mmol) gave *rac*-**12a** (264 mg, 0.93 mmol, 93%) as a white solid. TLC: $R_f$ = 0.31 (CyHex/EtOAc, 2:1). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.81 (tdd, *J* = 6.7, 10.4, 17.3 Hz, 1 H, C*H*=$CH_2$), 5.54 (s, 1 H, H-9), 5.10 (tdd, *J* = 1.5, 1.7, 17.3 Hz, 1 H, CH=CH–$H_{trans}$), 5.04 (dd, *J* = 1.5, 10.4 Hz, 1 H, CH=CH–$H_{cis}$), 4.01 (ddd, *J* = 11.9, 11.4, 2.0 Hz, 1 H, H-7a), 3.83 (td, *J* = 6.9, 9.5 Hz, 1 H, O–CH*Ha*), 3.65 (ddd, *J* = 1.4, 4.6, 11.4 Hz, 1 H, H-7b), 3.53 (td, *J* = 6.7, 9.5 Hz, 1 H, O–CH*Hb*), 3.15–3.06 (m, 1 H, H-5), 2.52 (dd, *J* = 6.9, 18.6 Hz, 1 H, H-4a), 2.37 (ttd, *J* = 1.2, 6.7, 6.7 Hz, 2 H, $CH_2$–CH=$CH_2$), 2.02 (dd, *J* = 4.6, 11.3 Hz, 1 H, H-6a), 1.92 (dd, *J* = 2.9, 18.6 Hz, 1 H, H-4b), 1.56 (ddd, *J* = 4.6, 12.6, 12.6 Hz, 1 H, H-6b), 0.19 [s, 9 H, Si($CH_3$)$_3$] ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 212.0 (C3), 180.1 (C1), 138.8 (C2), 134.8 (*C*H=$CH_2$), 116.8 (CH=*C*$H_2$), 95.2 (C9), 66.9 and 59.0 (C7 and O–*C*$H_2$CH$_2$CH=$CH_2$), 42.0 (C4), 37.1 (C5), 35.4 and 34.0 (C6 and O–$CH_2$*C*$H_2$CH=$CH_2$), –0.6 (TMS) ppm. IR (ATR): $\tilde{\nu}$ = 2948 (m), 2874 (w), 1694 (s), 1610 (m), 1247 (m), 1143 (m), 1102 (s), 1034 (s), 967 (m), 841 (s), 762 cm$^{-1}$ (w). MS (EI, 70 eV): *m*/*z* (%) = 280 (<1) [$M^+$], 265 (3), 225 (90), 209 (48), 195 (28), 151 (14), 135 (47), 109 (18), 91 (16), 75 (100), 73 (92), 59 (18), 55 (58). HRMS (EI) calcd. for [M + $CH_3$]$^+$ $C_{14}H_{21}O_3Si$: 265.1260; found 265.126.

**(5*SR*,8*RS*)-8-Allyloxy-2-methyl-7-oxabicyclo[3.3.0]oct-1-ene-3-one (*rac*-12d):** Following the general procedure for PK reactions (carried out on a 2 mmol scale), compound **11d** (332 mg, 2 mmol) gave *rac*-**12d** (315 mg, 1.62 mmol, 81%) as a light-yellow oil. The diastereomeric ratio was 98:2 according to $^1$H NMR spectroscopy. TLC: $R_f$ = 0.15 (CyHex/EtOAc, 4:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 5.90 (dddd, *J* = 17.2, 10.4, 6.1, 5.2 Hz, 1 H, C*H*=$CH_2$), 5.57 (s, 1 H, H-8), 5.31 (dd, *J* = 1.3, 17.2 Hz, 1 H, CH=CH–$H_{trans}$), 5.21 (dd, *J* = 1.3, 10.4 Hz, 1 H, CH=CH–$H_{cis}$), 4.36 (dd, *J* = 7.6, 7.6 Hz, 1 H, H-6a), 4.25 (tdd, *J* = 1.3, 5.2, 12.7 Hz, 1 H, CH*H*a–CH=$CH_2$), 4.11 (tdd, *J* = 1.2, 6.1, 12.7 Hz, 1 H, CH*H*b–CH=$CH_2$), 3.42–3.35 (m, 1 H, H-5), 3.35 (dd, *J* = 7.6, 7.6 Hz, 1 H, H-6b), 2.68 (dd, *J* = 6.2, 18.0 Hz, 1 H, H-4a), 2.11 (dd, *J* = 2.9, 18.0 Hz, 1 H, H-4b), 1.77 (d, *J* = 2.3 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 209.4 (C3), 170.6 (C1), 133.8 (*C*H=$CH_2$), 133.2 (C2), 117.7 (CH=*C*$H_2$), 95.9 (C8), 71.4 (C6), 68.5 (*C*$H_2$CH=$CH_2$), 40.1 (C4), 39.2 (C5), 8.9 ($CH_3$) ppm. IR (ATR): $\tilde{\nu}$ = 2878 (m), 1717 (s), 1684 (s), 1409 (w), 1280 (m), 1151 (m), 1063 (m), 991 (s), 944 (m), 894 cm$^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 193 (1) [M – 1$^+$], 165 (21), 137 (79), 123 (61), 109 (29), 95 (37), 79 (74), 67 (50), 53 (26), 41 (100).

**(5*SR*,8*RS*)-8-Allyloxy-2-phenyl-7-oxabicyclo[3.3.0]oct-1-ene-3-one (*rac*-12e):** Following the general procedure for PK reactions, compound **11e** (228 mg, 1 mmol) gave *rac*-**12e** (226 mg, 0.88 mmol, 88%) as a yellow oil. TLC: $R_f$ = 0.25 (CyHex/EtOAc, 4:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 7.63–7.59 (m, 2 H, $H_{ar}$), 7.43–7.35 (m, 3 H, $H_{ar}$), 6.02 (dddd, *J* = 17.2, 10.3, 5.4, 6.3 Hz, 1 H, C*H*=$CH_2$), 5.61 (s, 1 H, H-8), 5.36 (tdd, *J* = 1.6, 1.6, 17.2 Hz, 1 H, CH=CH–$H_{trans}$), 5.26 (tdd, *J* = 1.2, 1.6, 10.3 Hz, 1 H, CH=CH–$H_{cis}$), 4.45 (dd, *J* = 7.9, 7.9 Hz, 1 H, H-6a), 4.38 (tdd, *J* = 1.4, 5.4, 12.7 Hz, 1 H, CH*H*a–CH=$CH_2$), 4.21 (tdd, *J* = 1.2, 6.3, 12.7 Hz, 1 H, CH*H*b–CH=$CH_2$), 3.62–3.48 (m, 1 H, H-5), 3.44 (dd, *J* = 7.6, 8.8 Hz, 1 H, H-6b), 2.90 (dd, *J* = 6.4, 17.9 Hz, 1 H, H-4a), 2.35 (dd, *J* = 3.3, 17.9 Hz, 1 H, H-4b) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 207.2 (C3), 174.7 (C1), 138.2 (C2), 133.3 (*C*H=$CH_2$), 129.7, 129.1, 128.7, 128.1 ($C_{ar}$), 117.9 (CH=*C*$H_2$), 98.7 (C8), 70.3 and 69.5 (C6 and *C*$H_2$CH=$CH_2$), 40.1 (C5), 40.4 (C4) ppm. IR (ATR): $\tilde{\nu}$ = 2914 (m), 1711 (s), 1446 (w), 1273 (m), 1122 (m), 987 (s), 907 (s), 728 (s), 697 (s), 647 cm$^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 256 (5) [$M^+$], 215 (14), 199 (34), 173 (27), 141 (32), 129 (50), 128 (100), 115 (34), 77 (21). HRMS (EI) calcd. for [$M^+$] $C_{16}H_{16}O_3$: 256.1099; found 256.110.

**(5*SR*,8*RS*)-8-Allyloxy-2-*tert*-butyl-7-oxabicyclo[3.3.0]oct-1-ene-3-one (*rac*-12f):** Following the general procedure for PK reactions (carried out on a 2 mmol scale), compound **11f** (416 mg, 2 mmol) gave *rac*-**12f** (280 mg, 1.18 mmol, 59%) as a colorless oil. TLC: $R_f$ = 0.15 (CyHex/EtOAc, 4:1). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.92 (dddd, *J* = 17.2, 10.4, 5.4, 6.6 Hz, 1 H, C*H*=$CH_2$), 5.83 (s, 1 H, H-8), 5.31 (tdd, *J* = 1.9, 2.3, 17.2 Hz, 1 H, CH=CH–$H_{trans}$), 5.22 (tdd, *J* = 1.9, 2.3, 10.4 Hz, 1 H, CH=CH–$H_{cis}$), 4.34 (dd, *J* = 7.4, 7.4 Hz, 1 H, H-6a), 4.28 (dddd, *J* = 1.9, 1.9, 5.4, 13.5 Hz, 1 H, CH*H*a–CH=$CH_2$), 4.09 (dddd, *J* = 1.9, 1.9, 6.6, 13.5 Hz, 1 H, CH*H*b–CH=$CH_2$), 3.38 (dd, *J* = 7.4, 7.8 Hz, 1 H, H-6b), 3.36–3.30 (m, 1 H, H-5), 2.62 (dd, *J* = 6.3, 17.6 Hz, 1 H, H-4a), 2.08 (dd, *J* = 3.4, 17.6 Hz, 1 H, H-4b), 1.24 [s, 9 H, C($CH_3$)$_3$] ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 209.1 (C3), 168.2 (C1), 144.1 (C2), 133.9 (*C*H=$CH_2$), 118.1 (CH=*C*$H_2$), 97.0 (C8), 71.0 and 68.8 (C6 and *C*$H_2$CH=$CH_2$), 41.1 (C4), 39.6 (C5), 33.3 (*C*$CH_3$), 28.6 (C*C*$H_3$) ppm. IR (ATR): $\tilde{\nu}$ = 2955 (m), 2870 (w), 1710 (s), 1361 (w), 1289 (w), 1130 (m), 1072 (m), 992 cm$^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 236 (59) [$M^+$], 179 (73), 165 (16), 137 (100), 109 (55), 91 (28), 67 (26). HRMS (EI) calcd. for [$M^+$] $C_{14}H_{20}O_3$: 236.1412; found 236.141.

**(4*SR*,5*SR*,8*RS*)-8-(But-2-enyloxy)-4-methyl-2-trimethylsilyl-7-oxabicyclo[3.3.0]oct-1-ene-3-one (*rac*-12h):** Following the general procedure for PK reactions, compound **11h** (252 mg, 1 mmol) gave *rac*-**12h** (89 mg, 0.32 mmol, 32%) as a light-yellow oil. TLC: $R_f$ = 0.31 (CyHex/EtOAc, 4:1). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.83–5.71 (m, 1 H, CH=C*H*$CH_3$), 5.63–5.53 (m, 1 H, C*H*=CH$CH_3$), 5.58 (s, 1 H, H-8), 4.40 (dd, *J* = 8.5, 8.5 Hz, 1 H, H-6a), 4.21 (dd, *J* = 6.3, 11.1 Hz, 1 H, O–CH*H*a–CH=CH), 4.02 (dd, *J* = 7.4, 11.1 Hz, 1 H, O–CH*H*b–CH=CH), 3.50 (dd, *J* = 8.5, 8.5 Hz, 1 H, H-6b), 3.11 (td, *J* = 8.5, 4.2 Hz, 1 H, H-5), 2.14 (qd, *J* = 7.3, 4.2 Hz, 1 H, H-4), 1.70 (dd, *J* = 1.4, 6.2 Hz, 3 H, CH=CHC$H_3$), 1.20 [d, *J* = 7.3 Hz, 3 H, C(4)C$H_3$], 0.20 (s, 9 H, TMS) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 214.9 (C3), 182.4 (C1), 136.5 (C2), 131.1, 126.6 (*C*H=*C*H), 96.5 (C8), 70.6 and 68.5 (C6 and *C*$H_2$CH=$CH_2$), 50.8 and 59.5 (C5 and C4), 17.9 and 14.0 (C*C*$H_3$), –1.5 (Si*C*$H_3$) ppm. IR (ATR): $\tilde{\nu}$ = 2971 (m), 2894 (m), 1751 (s), 1704 (s), 1454 (w),

1377 (m), 1248 (m), 1182 (s), 1057 (s), 970 (m), 844 $cm^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 280 (1) [$M^+$], 226 (41), 195 (35), 165 (26), 137 (32), 107 (24), 73 (100), 55 (66).

**(4*SR*,5*SR*,8*RS*)-8-(But-2-enyloxy)-4-methyl-2-phenyl-7-oxabicyclo-[3.3.0]oct-1-ene-3-one (*rac*-12i):** Following the general procedure for PK reactions, compound **11i** (256 mg, 1 mmol) gave *rac*-**12i** (205 mg, 0.71 mmol, 71%) as a white solid. M.p. 82 °C. TLC: $R_f$ = 0.26 (CyHex/EtOAc, 4:1). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 7.61 (dd, *J* = 8.3, 2.1 Hz, 2 H, $H_{ar}$), 7.42–7.34 (m, 3 H, $H_{ar}$), 6.02 (qd, *J* = 6.9, 15.1 Hz, 1 H, CH=C*H*CH$_3$), 5.73–5.65 (m, 1 H, C*H*=CHCH$_3$), 5.63 (s, 1 H, H-8), 4.49 (dd, *J* = 8.4, 8.1 Hz, 1 H, H-6a), 4.29 (dd, *J* = 6.2, 11.2 Hz, 1 H, O–CH*H*a–CH=CH), 4.13 (dd, *J* = 7.3, 11.2 Hz, 1 H, O–CH*H*b–CH=CH), 3.53 (dd, *J* = 8.4, 8.4 Hz, 1 H, H-6b), 3.20 (td, *J* = 8.4, 3.4 Hz, 1 H, H-5), 2.35 (qd, *J* = 7.2, 3.4 Hz, 1 H, H-4), 1.74 (dd, *J* = 1.3, 6.9 Hz, 3 H, CH=CHC*H*$_3$), 1.32 [d, *J* = 7.2 Hz, 3 H, C(4)C*H*$_3$] ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 209.5 (C3), 169.3 (C1), 134.5 (C2), 131.1, 130.4, 128.9, 128.8, 128.5, 126.5 (*C*H=*C*H and $C_{ar}$), 97.1 (C8), 70.6 and 68.6 (C6 and *C*H$_2$CH=CH$_2$), 49.5 and 48.2 (C5 and C4), 17.9 and 14.0 (CH$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 2874 (w), 1711 (s), 1446 (m), 1274 (m), 1192 (m), 1124 (m), 1089 (m), 983 (s), 903 (m), 776 (m), 696 $cm^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 284 (3) [$M^+$], 253 (4), 228 (18), 213 (24), 141 (23), 128 (44), 115 (38), 91 (23), 77 (17), 55 (100). HRMS (EI) calcd. for [$M^+$] $C_{18}H_{20}O_3$: 284.1412; found 284.142.

**CBS Kinetic resolution of *rac*-12a and *rac*-12e:** A Schlenk flask was charged with the azeotropically dried ketone *rac*-**12a** (561 mg, 2 mmol) and a 0.1 M solution of freshly prepared (*R*)-diphenylprolinol-derived *B*-methyl oxazaborolidine[28a] in toluene (4 mL) was added at room temp. The mixture was cooled to –78 °C and after 30 min a freshly prepared solution of catecholborane (0.5 M in THF, various amounts, see Table 2) was added within 5 min. The mixture was allowed to warm to room temp. and stirred for another 6 h. The reaction was quenched by addition of a 2 M aqueous KOH (10 mL). After stirring for 30 min at room temp., the mixture was extracted with EtOAc (4×15 mL) and the combined organic layers were washed with a 2 M solution of KOH (2×20 mL), a saturated aqueous solution of $NH_4Cl$ (20 mL), and $CuSO_4$ (2×20 mL). After repeating the washing process it was finally washed with brine (2×20 mL). After drying ($MgSO_4$) and evaporation of the solvent, the residue was purified by flash chromatography (EtOAc/CyHex, 1:4) to afford the ketone **12a** and the alcohol *ent*-**21**. The kinetic resolution of ketone *rac*-**12e** was carried out in the same way. Determination of the *ee*: For compound **12a** a chiral GLC (Hydrodex β-PM, 120 °C, isotherm, 15 psi $H_2$; retention times **12b**: 95.65 min and *ent*-**12b**: 97.88 min) was used; for compound **12e** a chiral HPLC (Chiralpak AD-H, acetonitrile/hexane, 5:95, 1 mL $min^{-1}$ flow, retention times **12e**: 11.07 min and *ent*-**12e**: 12.60 min) was used. Ketone **12a** (>99% *ee*): $[\alpha]_D^{20}$ = –174.3 (*c* = 1.045 in $CHCl_3$); $[\alpha]_{546}^{20}$ = –211.5; $[\alpha]_{405}^{20}$ = –558.0.

**Oxidation of Alcohol *ent*-21:** A solution of alcohol *ent*-**21** in dry $CH_2Cl_2$ (2 mL) was added to a stirred suspension of $MnO_2$ (10 equiv.) in dry $CH_2Cl_2$ (5 mL) at 0 °C under argon. The mixture was allowed to warm to room temp. and stirred for 2 h. The suspension was filtered through a plug of Celite and the solvent was evaporated to give the ketone *ent*-**12a**. The *ee* analysis of the resulting ketone was carried out by chiral GLC as described previously.

**(3*RS*,5*SR*,9*RS*)-9-(But-3-enyloxy)-2-trimethylsilyl-8-oxabicyclo-[3.4.0]non-1-ene-3-ol (*rac*-20):** $NaBH_4$ (2.70 g, 71.3 mmol) was added portionwise to a solution of *rac*-**12a** (4.00 g, 14.3 mmol) and $CeCl_3 \cdot 7H_2O$ (5.31 g, 14.3 mmol) in MeOH (150 mL) at –20 °C (ice-salt bath) over a period of 30 min. After stirring the mixture at room temp. for 2 h, the reaction was quenched by addition of saturated aqueous $NaHCO_3$ (100 mL). The mixture was extracted with MTBE (4×75 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (2×50 mL) solution and brine (50 mL), dried ($MgSO_4$) and the solvents were evaporated. After purification by flash chromatography (CyHex/EtOAc = 2+1) compound *rac*-**20** was isolated in 99% yield (4.01 g, 14.2 mmol) as a colorless oil. TLC: $R_f$ = 0.34 (CyHex/EtOAc, 2:1). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 5.88–5.75 (m, 1 H, C*H*=CH$_2$), 5.23 (s, 1 H, H-9), 5.11 (tdd, *J* = 1.6, 1.8, 17.2 Hz, 1 H, CH=CH–$H_{trans}$), 5.02 (tdd, *J* = 1.2, 1.8, 10.3 Hz, 1 H, CH=CH–$H_{cis}$), 4.88 (t, *J* = 6.1 Hz, 1 H, H-3), 3.90 (ddd, *J* = 2.1, 11.8, 12.3 Hz, 1 H, H-7a), 3.76 (td, *J* = 7.1, 9.5 Hz, 1 H, O–CH*Ha*), 3.57 (ddd, *J* = 1.6, 5.4, 11.8 Hz, 1 H, H-7b), 3.45 (td, *J* = 6.8, 9.5 Hz, 1 H, O–CH*Hb*), 2.88–2.77 (m, 1 H, H-5), 2.57 (td, *J* = 13.3, 6.1 Hz, 1 H, H-4a), 2.39–2.32 (m, 2 H, *C*H$_2$–CH=CH$_2$), 1.86 (dd, *J* = 5.4, 12.3 Hz, 1 H, H-6a), 1.51 (tdd, *J* = 12.3, 12.3, 6.1 Hz, 1 H, H-6b), 1.17 (td, *J* = 6.1, 13.3 Hz, 1 H, H-4b), 0.17 [s, 9 H, Si(C*H*$_3$)$_3$] ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 152.5 (C1), 140.8 (C2), 135.5 (*C*H=CH$_2$), 116.9 (CH=*C*H$_2$), 96.7 (C9), 82.3 (C3), 66.9 and 59.4 (C7 and O–*C*H$_2$CH$_2$CH=CH$_2$), 42.3 (C4), 41.5 (C5), 36.0 and 34.6 (C6 and O–CH$_2$*C*H$_2$CH=CH$_2$), 0.4 (TMS) ppm. IR (ATR): $\tilde{\nu}$ = 3424 (w), 2951 (m), 1721 (m), 1695 (s), 1607 (m), 1247 (s), 1100 (m), 1033 (s), 840 (s), 761 $cm^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 282 (11) [$M^+$], 265 (10), 227 (23), 211 (13), 183 (27), 137 (67), 75 (62), 73 (100), 55 (49).

**(3*RS*,5*SR*,9*RS*)-9-(But-3-enyloxy)-8-oxabicyclo[3.4.0]non-1-ene-3-ol (*rac*-21):** *t*BuOK (3.80 g, 33.9 mmol) was added to a solution of *rac*-**20** (4.00 g, 33.9 mmol) in a 19:1 solvent mixture of DMSO and $H_2O$ (50 mL) at room temp.; the color of the mixture turned immediately to brown. After stirring for 2 h at room temp. the mixture was diluted by addition of water (100 mL) and extracted with EtOAc (4×50 mL). The combined organic phases were washed with water (3×50 mL) and brine (50 mL), dried ($MgSO_4$), and the solvent was removed under reduced pressure. The product *rac*-**21**, obtained as a colorless oil (2.41 g, 81% yield), was pure according to $^1H$ NMR spectroscopy and TLC and therefore no further purification was necessary. TLC: $R_f$ = 0.11 (CyHex/EtOAc, 2:1). $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 5.89–5.70 (m, 1 H, C*H*=CH$_2$), 5.61 (s, 1 H, H-2), 5.20 (s, 1 H, H-9), 5.08 (dd, *J* = 2.1, 17.2 Hz, 1 H, CH=CH–$H_{trans}$), 5.02 (dd, *J* = 2.1, 10.3 Hz, 1 H, CH=CH–$H_{cis}$), 4.88 (dd, *J* = 7.7, 7.7 Hz, 1 H, H-3), 3.91 (ddd, *J* = 12.2, 12.4, 2.6 Hz, 1 H, H-7a), 3.78–3.63 (m, 1 H, O–CH*Ha*), 3.59 (dd, *J* = 2.8, 12.2 Hz, 1 H, H-7b), 3.54–3.45 (m, 1 H, O–CH*Hb*), 2.90–2.77 (m, 1 H, H-5), 2.61 (td, *J* = 7.7, 13.4 Hz, 1 H, H-4a), 2.39 –2.29 (m, 2 H, CH$_2$–CH=CH$_2$), 1.86 (dd, *J* = 6.2, 12.4 Hz, 1 H, H-6a), 1.62 (br. s, 1 H, OH), 1.51 (tdd, *J* = 2.8, 6.2, 12.4 Hz, 1 H, H-6b), 1.29–1.19 (m, 1 H, H-4b) ppm. $^{13}C$ NMR (63 MHz, $CDCl_3$): $\delta$ = 144.2 (C1), 134.8 (*C*H=CH$_2$), 127.7 (C2), 116.5 (CH=*C*H$_2$), 95.8 (C9), 76.8 (C3), 66.3 and 59.4 (C7 and O–*C*H$_2$CH$_2$CH=CH$_2$), 41.3 (C4), 38.8 (C5), 35.7 and 34.0 (C6 and O–CH$_2$*C*H$_2$CH=CH$_2$) ppm. IR (ATR): $\tilde{\nu}$ = 3412 (m), 2927 (m), 2871 (m), 1440 (m), 1321 (m), 1246 (m), 1187 (m), 1162 (m), 1085 (s), 1032 (s), 1000 (s), 955 (m), 839 $cm^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 209 (<1) [M – $1^+$], 166 (20), 139 (60, 120 (40), 110 (19), 91 (100), 79 (29), 66 (49), 55 (29), 39 (82).

**(3*RS*,5*SR*,9*RS*)-9-(But-3-enyloxy)-8-oxabicyclo[3.4.0]non-1-ene-3-yl methyl carbonate (*rac*-22):** Pyridine (5 mL) and methyl chloroformate (2.30 mL, 29.7 mmol) were added to a solution of alcohol *rac*-**21** (2.08 g, 9.90 mmol) in $CH_2Cl_2$ (100 mL) at 0 °C and the mixture was stirred for 1 h under argon. The reaction was quenched with water (50 mL) and stirred for an additional 30 min. The phases were separated and the aqueous phase was extracted with

$CH_2Cl_2$ (3 × 100 mL). The combined organic phases were washed with brine (50 mL), followed by drying ($MgSO_4$) and removal of the solvent under reduced pressure. After purification by flash chromatography (CyHex/EtOAc, 2:1) compound *rac*-**22** was isolated in 91% yield (2.41 g, 9.00 mmol) as a colorless oil. TLC: $R_f$ = 0.56 (CyHex/EtOAc, 2:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 5.86–5.72 (m, 1 H, C*H*=$CH_2$), 5.61 (m, 1 H, H-2), 5.61–5.67 (m, 1 H, H-3), 5.21 (s, 1 H, H-9), 5.08 (dd, $J$ = 1.9, 17.2 Hz, 1 H, CH=CH–$H_{trans}$), 5.03 (dd, $J$ = 1.9, 10.7 Hz, 1 H, CH=CH–$H_{cis}$), 3.92 (ddd, $J$ = 12.0, 12.0, 2.0 Hz, 1 H, H-7a), 3.74 (s, 3 H, $OCH_3$), 3.76–3.62 (m, 1 H, O–CH*Ha*), 3.60 (ddd, $J$ = 1.4, 4.4, 12.0 Hz, 1 H, H-7b), 3.49 (td, $J$ = 6.7, 9.7 Hz, 1 H, O–CH*Hb*), 2.95–2.82 (m, 1 H, H-5), 2.64 (td, $J$ = 7.9, 14.1 Hz, 1 H, H-4a), 2.39–2.31 (m, 2 H, C$H_2$–CH=$CH_2$), 1.86 (dd, $J$ = 5.7, 12.0 Hz, 1 H, H-6a), 1.63–1.35 (m, 2 H, H-6b and H-4b) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 155.4 (C=O), 147.1 (C1), 134.9 (*C*H=$CH_2$), 122.6 (C2), 116.5 (CH=*C*$H_2$), 95.6 (C9), 83.0 (C3), 66.3 and 59.3 (C7 and O–*C*$H_2$CH$_2$CH=$CH_2$), 54.5 ($CH_3$), 38.7 (C5), 36.9 and 35.4 and 34.0 (C4 and C6 and O–$CH_2$*C*$H_2$CH=$CH_2$) ppm. IR (ATR): $\tilde{\nu}$ = 2936 (m), 1741 (s), 1441 (m), 1345 (m), 1261 (s), 1093 (m), 1037 (m), 970 (m), 793 cm$^{-1}$ (w). MS (EI, 70 eV): *m*/*z* (%) = 268 (8) [M$^+$], 197 (100), 153 (11), 139 (14), 121 (53), 109 (23), 91 (37), 77 (33), 59 (27), 55 (79). HRMS (EI) calcd. for [M$^+$] $C_{14}H_{20}O_5$: 268.1311; found 268.129.

**(3′*RS*,5′*SR*,9′*RS*)-9′-(But-3′′-enyloxy)-8′-oxabicyclo[3.4.0]non-1′-ene-3′-yl)-5-bromo-1*H*-pyrimidine-2,4-dione (*rac*-24):** dppp (116 mg, 0.280 mmol) was added to a solution of $[Pd_2(dba)_3]$ (62 mg, 0.067 mmol) in dry, degassed DMF (20 mL) at room temp. under argon. The solution was stirred for 5 min. Carbonate *rac*-**22** (720 mg, 2.69 mmol) in DMF (2 mL) and the bromouracil (770 mg, 4.03 mmol) in DMF (2 mL) were added to the mixture. After stirring at room temp. for 16 h, the reaction was quenched by addition of water (80 mL). The layers were separated and the aqueous phase was extracted with EtOAc (5 × 60 mL). The combined organic layers were washed with water (3 × 60 mL) and brine (30 mL), dried, and finally the solvent was removed under reduced pressure. The residue was purified by flash chromatography (CyHex/EtOAc, 2:1) to afford the product *rac*-**24** as a white solid (751 mg, 73%). M.p. 161 °C. TLC: $R_f$ = 0.14 (CyHex/EtOAc, 2:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 9.36 (s, 1 H, N*H*), 7.51 (s, 1 H, H-6), 5.89–5.73 (m, 1 H, C*H*=$CH_2$), 5.74–5.66 (m, 1 H, H-3′), 5.43–5.41 (m, 1 H, H-2′), 5.30 (s, 1 H, H-9′), 5.13–5.01 (m, 2 H, CH=C$H_2$), 3.97 (ddd, $J$ = 1.6, 10.2, 11.3 Hz, 1 H, H-7a′), 3.81–3.72 (m, 1 H, O–CH*Ha*), 3.67 (ddd, $J$ = 1.6, 5.7, 10.2 Hz, 1 H, H-7b′), 3.52 (td, $J$ = 6.6, 9.6 Hz, 1 H, O–CH*Hb*), 3.07–2.94 (m, 1 H, H-5′), 2.83 (td, $J$ = 8.1, 13.5 Hz, 1 H, H-4a′), 2.40–2.32 (m, 2 H, $CH_2$–CH=$CH_2$), 1.93 (dd, $J$ = 5.7, 12.1 Hz, 1 H, H-6a), 1.53 (tdd, $J$ = 5.0, 11.3, 12.1 Hz, 1 H, H-6b′), 1.25–1.14 (m, 1 H, H-4b′) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 159.0 (C4), 150.3 and 148.8 (C2 and C1′), 140.0 (C6), 134.8 (*C*H=$CH_2$), 121.5 (C2′), 116.7 (CH=*C*$H_2$), 97.0 (C9′), 95.1 (C5), 66.6 and 59.0 (C7′ and O–*C*$H_2$CH$_2$CH=$CH_2$), 61.5 (C3′), 38.8 (C5′), 38.7 and 35.2 and 33.9 (C4 and C6 and O–$CH_2$*C*$H_2$CH=$CH_2$) ppm. IR (ATR): $\tilde{\nu}$ = 3068 (w), 1694 (s), 1616 (m), 1442 (m), 1253 (m), 1094 (m), 1032 (m), 963 cm$^{-1}$ (w). MS (EI, 70 eV): *m*/*z* (%) = 384 (4) [M$^+$], 382 (4) [M$^+$], 311 (57), 313 (58), 193 (46), 139 (85), 121 (46), 109 (65), 93 (89), 77 (59), 55 (100). HRMS (EI) calcd. for [M$^+$] $C_{16}H_{19}{}^{81}BrN_2O_4$: 384.0509; found 384.052. $C_{16}H_{19}BrN_2O_4$ (383.24): calcd. C 50.14, H 5.00, N 7.31; found C 50.41, H 5.28, N 7.00.

**(3′*RS*,5′*SR*,9′*RS*)-9′-(But-3-enyloxy)-8′-oxabicyclo[3.4.0]non-1′-ene-3′-yl)-9*H*-6-chloropurine (*rac*-23):** Following the procedure for the preparation of *rac*-**24**, chloropurine was introduced. Compound *rac*-**22** (1.97 g, 7.35 mmol) afforded *rac*-**23** (1.55 g, 60%) as a white solid. M.p. 85 °C. TLC: $R_f$ = 0.58 (EtOAc). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 8.71 (s, 1 H, H-2), 8.16 (s, 1 H, H-8), 5.89–5.75 (m, 2 H, C*H*=$CH_2$ and H-3′), 5.67–5.66 (m, 1 H, H-2′), 5.33 (s, 1 H, H-9′), 5.13–5.01 (m, 2 H, CH=C$H_2$), 3.98 (ddd, $J$ = 1.2, 12.3, 12.8 Hz, 1 H, H-7a′), 3.78 (td, $J$ = 7.0, 9.7 Hz, 1 H, O–CH*Ha*), 3.67 (ddd, $J$ = 2.1, 4.9, 12.3 Hz, 1 H, H-7b′), 3.53 (td, $J$ = 6.6, 9.7 Hz, 1 H, O–CH*Hb*), 3.18–3.07 (m, 1 H, H-5′), 2.98 (ddd, $J$ = 8.2, 8.4, 13.8 Hz, 1 H, H-4a′), 2.41–2.34 (m, 2 H, $CH_2$–CH=$CH_2$), 1.95 (dd, $J$ = 6.2, 12.8 Hz, 1 H, H-6a′), 1.63 (tdd, $J$ = 4.9, 13.1, 13.8 Hz, 1 H, H-6b′), 1.61–1.49 (m, 1 H, H-4b′) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 151.8 (C2), 151.5 and 150.9 (C4 and C6), 148.1 (C1′), 143.1 (C8), 134.8 (*C*H=$CH_2$), 131.8 (C5), 121.2 (C2′), 116.7 (CH=*C*$H_2$), 95.2 (C9′), 66.5 and 59.0 (C7′ and O–*C*$H_2$CH$_2$CH=$CH_2$), 59.7 (C3′), 39.3 (C5′), 39.6 and 35.2 and 34.0 (C4 and C6 and O–$CH_2$*C*$H_2$CH=$CH_2$) ppm. IR (ATR): $\tilde{\nu}$ = 2935 (w), 2358 (s), 2339 (s), 1588 (m), 1558 (m), 1334 (m), 1195 (m), 1095 (m), 1032 (m), 950 (m), 848 (m), 667 cm$^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 346 (46) [M$^+$], 275 (93), 219 (11), 192 (54), 155 (49), 121 (30), 93 (62), 77 (56), 66 (38), 55 (100). HRMS (EI) calcd. for [M$^+$] $C_{17}H_{19}ClN_4O_2$: 346.1197; found 346.120. $C_{17}H_{19}ClN_4O_2$ (346.81): calcd. C 58.87, H 5.52, N 16.15; found C 59.29, H 5.92, N 15.66.

**(1′*RS*,4′*SR*)-6-Chloro-9-[4′-dimethyl-(1,1,2-trimethylpropyl)silanyloxyethyl]-3′-(hydroxymethylcyclopent-2′-enyl)-9*H*-purine (*rac*-18):** A solution of *rac*-**23** (104 mg, 0.3 mmol) in wet acetone (6 mL) was added to Amberlyst-15 (10 mg, 0.1 wt. equiv.) and the mixture was shaken for 1 h. After removal of Amberlyst-15 by filtration, poly(4-vinylpyridine) (208 mg, 2 wt. equiv.; 2% cross-linked) was added, the solvent was evaporated, and the flask was flushed with argon (3 times). Dry pyridine (2 mL) was added and, after stirring at room temp. for 5 min, $ThxMe_2SiCl$ (176 μL, 0.9 mmol) was added. After stirring at room temp. for 16 h, the reaction was quenched by addition of saturated aqueous $NaHCO_3$ (20 mL). After stirring the resulting mixture at room temp. for 30 min, the water phase was extracted with EtOAc (4 × 20 mL) and the combined organic layers were washed with 10% HCl (3 × 20 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (40 mL), dried ($MgSO_4$), and concentrated. After removal of the solvent the crude product was directly used for the next step. A mixture of MeOH (3 mL) and $CH_2Cl_2$ (6 mL) was added to $NaBH_4$ (113 mg, 3 mmol), the resulting mixture was stirred at room temp. for 3 min, and then cooled to –78 °C. A solution of the crude mixture in $CH_2Cl_2$ (2 mL) was added dropwise. After stirring the mixture at –78 °C for 1 h, acetone (5 mL) was added and the mixture was allowed to warm to room temp. and stirred for an additional 30 min. The mixture was poured onto a plug of silica, washed with EtOAc, and the solvents were removed under reduced pressure. After purification by flash chromatography the CNA *rac*-**18** was obtained (83 mg, 63%) as a white solid. M.p. 130 °C. TLC: $R_f$ = 0.16 (DCM/MeOH, 20:1). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.72 (s, 1 H, H-2), 8.14 (s, 1 H, H-8), 5.83 (m, 1 H, H-2′), 5.73–5.70 (m, 1 H, H-1′), 4.48 (d, $J$ = 15.1 Hz, 1 H, CH*H*aOH), 4.32 (d, $J$ = 15.1 Hz, 1 H, CH*H*bOH), 3.67–3.50 (m, 2 H, SiOC$H_2$), 3.02–2.91 (m, 2 H, H-4′ and H-5a′), 2.14 (br. s, 1 H, OH), 2.01–1.91 (m, 1 H, SiOCH$_2$CH*H*a), 1.75–1.67 (m, 1 H,H-5b′), 1.61 (septet, $J$ = 6.8, 1 H, $Me_2$C*H*), 1.47–1.36 (m, 1 H, SiOCH$_2$CH*H*b), 0.81 [d, $J$ = 6.8 Hz, 6 H, (C$H_3$)$_2$CH], 0.77 [s, 6 H, C(C$H_3$)$_2$], 0.03 and 0.02 (2s, 6 H, SiC$H_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 155.6 (C3′), 151.7 (C2), 151.5 and 150.9 (C4 and C6), 143.3 (C8), 132.0 (C5), 121.1 (C2′), 60.9 and 60.5 ($CH_2$*C*$H_2$OSi and *C*$H_2$OH), 59.3 (C1′), 41.6 (C4′), 39.1 and 36.7 (C5′ and *C*$H_2$CH$_2$OSi), 34.1 [(*C*H$_3$)$_2$*C*H], 25.1 ($Me_2$*C*Si), 20.3 [(*C*H$_3$)$_2$CH], 18.4 [(*C*H$_3$)$_2$CSi], –3.5 (*C*H$_3$Si) ppm. IR (ATR): $\tilde{\nu}$ = 3359 (m), 2955 (m), 2864 (w), 1588 (s), 1558 (m), 1401 (m), 1332 (m), 1249 (m), 1200 (m), 1087 (m), 954 (m), 828 (s), 773 cm$^{-1}$ (m).

MS (ESI): *m*/*z* (%) = 459 (25) [M + Na$^+$], 402 (6), 318 (39), 262 (100), 155 (7), 105 (32). HRMS (ESI) calcd. for [M + Na]$^+$ $C_{21}H_{33}ClN_4O_2SiNa$: 459.1959; found 459.197. $C_{21}H_{33}ClN_4O_2Si$ (437.05): calcd. C 57.71, H 7.61, N 12.82; found C 57.77, H 7.56, N 12.65.

**(1′*RS*,4′*SR*)-5-Bromo-1-[4′-[dimethyl-(1,1,2-trimethylpropyl)silanyloxyethyl]-3′-(hydroxymethylcyclopent-2′-enyl)-1*H*-pyrimidine-2,4-dione (*rac*-19):** Following the procedure for the preparation of *rac*-**18**, compound *rac*-**24** (115 mg, 0.3 mmol) afforded *rac*-**19** (99 mg, 69%) as a white solid. M.p. 134 °C. TLC: $R_f$ = 0.15 (DCM/MeOH, 20:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 9.06 (br. s, 1 H, NH), 7.52 (s, 1 H, H-6), 5.57–5.54 (m, 2 H, H-1′ and H-2′), 4.38 (d, *J* = 15.4 Hz, 1 H, CH*H*aOH), 4.26 (d, *J* = 15.4 Hz, 1 H, CH*H*bOH), 3.70–3.51 (m, 2 H, SiOC*H*$_2$), 2.88–2.76 (m, 2 H, H-4′ and H-5a′), 2.01–1.89 (m, 1 H, $SiOCH_2CH$*H*a), 1.58 (septet, *J* = 6.8 Hz, 1 H, $Me_2CH$), 1.44–1.28 (m, 2 H,H-5b′ and $SiOCH_2CH$*H*b), 0.84 [d, *J* = 6.8 Hz, 6 H, $(CH_3)_2CH$], 0.81 [s, 6 H, $C(CH_3)_2$], 0.06 (s, 6 H, $SiCH_3$) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 159.1 (C4), 156.0 (C3′), 150.2 (C2), 140.4 (C6), 121.3 (C2′), 96.5 (C5), 61.3 (C1′), 60.9 and 60.6 ($CH_2CH_2OSi$ and $CH_2OH$), 41.2 (C4′), 38.5 and 36.7 (C5′ and $CH_2CH_2OSi$), 34.1 [$(CH_3)_2CH$], 25.1 ($Me_2CSi$), 20.3 [$(CH_3)_2CH$], 18.5 [$(CH_3)_2CSi$], –3.4 and –3.5 ($CH_3Si$) ppm. IR (ATR): $\tilde{\nu}$ = 3396 (w), 2954 (m), 1693 (s),1616 (m), 1445 (m), 1248 (m), 1092 (m), 1034 (m), 828 (m), 776 cm$^{-1}$ (m). MS (ESI): *m*/*z* (%) = 633 (3), 569 (4), 495 (100) [M + Na$^+$], 475 (2), 407 (7), 305 (5). HRMS (ESI) calcd. for [M + Na$^+$] $C_{20}H_{33}{}^{79}BrN_2O_4SiNa$: 495.1291; found 495.128.

**(3*RS*,5*SR*,8*RS*)-8-Allyloxy-2-phenyl-7-oxabicyclo[3.3.0]oct-1-ene-3-ol (*rac*-27):** $NaBH_4$ (590 mg, 15.6 mmol) was added portionwise to a solution of *rac*-**12e** (1.00 g, 3.90 mmol) and $CeCl_3{\cdot}7H_2O$ (1.45 g, 3.90 mmol) in MeOH (340 mL) at –20 °C (ice-salt bath) over a period of 30 min. After stirring the mixture at room temp. for 2 h, the reaction was quenched by addition of a saturated aqueous $NaHCO_3$ (100 mL). The mixture was extracted with MTBE (4 × 100 mL) and the combined organic layers were washed with sat. $NaHCO_3$ (2 × 100 mL) and brine (100 mL), dried ($MgSO_4$), and the solvents evaporated. The alcohol *rac*-**27** was obtained as a colorless oil (1.00 g, 99%) that was pure according to $^1$H NMR spectroscopy and GLC analysis. TLC: $R_f$ = 0.21 (CyHex/EtOAc, 2:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 7.66–7.57 (m, 2 H, $H_{ar}$), 7.38–7.28 (m, 3 H, $H_{ar}$), 6.02 (dddd, *J* = 17.2, 10.3, 5.4, 6.1 Hz, 1 H, C*H*=$CH_2$), 5.60 (s, 1 H, H-8), 5.47–5.39 (m, 1 H, H-3), 5.25 (tdd, *J* = 1.6, 1.6, 17.2 Hz, 1 H, CH=CH–$H_{trans}$), 5.16 (tdd, *J* = 1.3, 1.6, 10.3 Hz, 1 H, CH=CH–$H_{cis}$), 4.29 (dd, *J* = 8.0, 8.0 Hz, 1 H, H-6a), 4.20 (tdd, *J* = 1.4, 5.4, 12.7 Hz, 1 H, CH*H*a–CH=$CH_2$), 4.05 (tdd, *J* = 1.4, 6.1, 12.7 Hz, 1 H, CH*H*b–CH=$CH_2$), 3.48 (dd, *J* = 8.0, 8.0 Hz, 1 H, H-6b), 3.37–3.25 (m, 1 H, H-5), 2.88–2.77 (m, 1 H, H-4a), 1.51 (ddd, *J* = 8.0, 8.0, 12.4 Hz, 1 H, H-4b) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 143.9 and 136.8 and 134.1 (s, C1, C2, and $C_{ar}$), 134.3 (*C*H=$CH_2$), 128.4, 128.2, 127.9, (d, $C_{ar}$), 117.5 (CH=*C*$H_2$), 97.1 (C8), 83.7 (C3), 72.3 and 68.1 (C6 and *C*$H_2$CH=$CH_2$), 43.8 (C5), 41.6 (C4) ppm. IR (ATR): $\tilde{\nu}$ = 3412 (m), 2914 (m), 2876 (m), 1444 (m), 1339 (m), 1203 (w), 1064 (s), 978 (s), 938 (m), 765 (m), 698 cm$^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 258 (2) [M$^+$], 201 (52), 194 (56), 159 (63), 143 (64), 131 (82), 128 (89), 115 (74), 105 (59), 91 (100), 77 (57). HRMS (EI) calcd. for [M$^+$] $C_{16}H_{18}O_3$: 258.1256; found 258.126.

**(3*RS*,5*SR*,8*RS*)-8-Allyloxy-2-phenyl-7-oxabicyclo[3.3.0]oct-1-ene-3-yl Methyl Carbonate (*rac*-28):** Following the procedure for the preparation of *rac*-**22**, compound *rac*-**27** (30 mg, 0.12 mmol) afforded *rac*-**28** (32 mg, 84%) as a colorless oil.TLC: $R_f$ = 0.45 (CyHex/EtOAc, 2:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 7.47–7.43 (m, 2 H, $H_{ar}$), 7.35–7.30 (m, 3 H, $H_{ar}$), 6.28–6.22 (m, 1 H, H-3), 5.92 (dddd, *J* = 5.4, 6.1, 10.3, 17.2 Hz, 1 H, C*H*=$CH_2$), 5.55 (s, 1 H, H-8), 5.26 (tdd, *J* = 1.6, 1.6, 17.2 Hz, 1 H, CH=CH–$H_{trans}$), 5.16 (tdd, *J* = 1.2, 1.3, 10.3 Hz, 1 H, CH=CH–$H_{cis}$), 4.30 (dd, *J* = 7.7, 7.7 Hz, 1 H, H-6a), 4.22 (tdd, *J* = 1.4, 5.4, 12.7 Hz, 1 H, CH*H*a–CH=$CH_2$), 4.05 (tdd, *J* = 1.3, 6.1, 12.7 Hz, 1 H, CH*H*b–CH=$CH_2$), 3.76 (s, 3 H, $CH_3$), 3.49 (dd, *J* = 7.7, 7.7 Hz, 1 H, H-6b), 3.46–3.33 (m, 1 H, H-5), 2.95 (ddd, *J* = 6.7, 6.7, 12.7 Hz, 1 H, H-4a), 1.70 (ddd, *J* = 7.6, 7.6, 12.7 Hz, 1 H, H-4b) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 155.0 and 146.1 and 133.2 (s, C1, C2, and $C_{ar}$), 134.1 (*C*H=$CH_2$), 128.4, 128.1, 127.9, (d, $C_{ar}$), 117.6 (CH=*C*$H_2$), 96.9 (C8), 88.2 (C3), 72.0 and 68.2 (C6 and *C*$H_2$CH=$CH_2$), 55.8 ($CH_3$), 44.2 (C5), 38.2 (C4) ppm. IR (ATR): $\tilde{\nu}$ = 2952 (w), 1741 (s), 1671 (m), 1441 (m), 1257 (s), 1045 (m), 934 (m), 790 (m), 700 cm$^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 316 (8) [M$^+$], 259 (30), 210 (18), 194 (68), 169 (61), 155 (100), 141 (73), 128 (66), 115 (69), 91 (35), 77 (39), 59 (32). HRMS (EI) calcd. for [M$^+$] $C_{18}H_{20}O_5$: 316.1311; found 316.130.

**(3*RS*,5*SR*,8*RS*)-8-Allyloxy-2-phenyl-7-oxabicyclo[3.3.0]oct-1-ene-3-yl 4-Nitrobenzoate (Derived from *rac*-27):** A mixture of *rac*-**27** (860 mg, 3.41 mmol), 4-nitrobenzoic acid (2.50 g, 15.0 mmol), and $PPh_3$ (4.47 mg, 17.05 mmol) in dry toluene (50 mL) was stirred at room temp. for 30 min. DEAD (2.65 mL, 17.05 mmol) was added dropwise and the resulting yellow mixture was stirred for another 16 h. The solvent was evaporated and the mixture was purified by column chromatography (CyHex/EtOAc = 4 +1) to give the *p*-nitrobenzoate as a light-yellow oil (1.096 g, 79%). TLC: $R_f$ = 0.47 (CyHex/EtOAc, 2:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 8.26–8.10 (m, 4 H, $H_{ar-NO2}$), 7.50–7.46 (m, 2 H, $H_{ar}$), 7.38–7.28 (m, 3 H, $H_{ar}$), 6.82 (dd, *J* = 1.5, 7.0 Hz, 1 H, H-3), 6.14–5.99 (m, 1 H, C*H*=$CH_2$), 5.51 (s, 1 H, H-8), 5.39 (tdd, *J* = 1.5, 1.6, 17.2 Hz, 1 H, CH=CH–$H_{trans}$), 5.27 (tdd, *J* = 1.1, 1.6, 10.3 Hz, 1 H, CH=CH–$H_{cis}$), 4.39–4.33 (m, 1 H, CH*H*a–CH=$CH_2$), 4.34 (dd, *J* = 8.4, 8.4 Hz, 1 H, H-6a), 4.20 (tdd, *J* = 1.2, 6.4, 12.5 Hz, 1 H, CH*H*b–CH=$CH_2$), 4.03–3.96 (m, 1 H, H-5), 3.41 (dd, *J* = 8.4, 8.4 Hz, 1 H, H-6b), 2.36 (ddd, *J* = 7.0, 14.5 Hz, 1 H, H-4a), 2.15 (ddd, *J* = 7.0, 7.0, 14.5 Hz, 1 H, H-4b) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 164.6 (C=O), 150.52, 150.48, 135.4, 133.6, 132.5 (C1 and C2 and s, $C_{ar}$), 134.1 (*C*H=$CH_2$), 130.8, 128.8, 128.5, 127.6, 123.4 (d, $C_{ar}$), 118.1 (CH=*C*$H_2$), 97.1 (C8), 85.6 (C3), 71.2 and 68.5 (C6 and *C*$H_2$CH=$CH_2$), 47.4 (C4), 36.5 (C5) ppm. IR (ATR): $\tilde{\nu}$ = 2919 (m), 1718 (s), 1526 (s), 1345 (m), 1266 (s), 1099 (m), 1076 (m), 994 (m), 939 (m), 852 (m), 718 cm$^{-1}$ (m). MS (EI, 70 eV): *m*/*z* (%) = 407 (16) [M$^+$], 350 (9), 321 (10), 194 (16), 171 (22), 155 (53), 150 (100), 115 (25), 104 (31), 92 (18), 76 (21). HRMS (EI) calcd. for [M$^+$] $C_{23}H_{21}NO_6$: 407.1369; found 407.138.

**(3*SR*,5*SR*,8*RS*)-8-Allyloxy-2-phenyl-7-oxabicyclo[3.3.0]oct-1-ene-3-ol (*rac*-29):** The *p*-nitrobenzoate derived from *rac*-**27** (710 mg, 1.74 mmol) was dissolved in MeOH (30 mL) and $K_2CO_3$ (480 mg, 3.48 mmol) was added. The mixture was stirred at room temp. for 16 h. Water (60 mL) and EtOAc (100 mL) were added and the organic phase was separated. After re-extracting the aqueous phase with EtOAc (3 × 60 mL), the combined organic phases were washed with water (50 mL) and brine (50 mL), and were finally dried ($MgSO_4$) and concentrated in vacuo to give a colorless oil. Purification by flash chromatography (CyHex/EtOAc, 2:1) gave alcohol *rac*-**29** (269 mg, 82%). TLC: $R_f$ = 0.13 (CyHex/EtOAc, 2:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 7.51–7.46 (m, 2 H, $H_{ar}$), 7.40–7.29 (m, 3 H, $H_{ar}$), 6.01 (dddd, *J* = 5.2, 6.2, 10.3, 17.2 Hz, 1 H, C*H*=$CH_2$), 5.57 (dd, *J* = 1.3, 6.4 Hz 1 H, H-3), 5.46 (s, 1 H, H-8), 5.35 (tdd, *J* = 1.6, 1.6, 17.2 Hz, 1 H, CH=CH–$H_{trans}$), 5.22 (tdd, *J* = 1.2, 1.6, 10.3 Hz, 1 H, CH=CH–$H_{cis}$), 4.27 (tdd, *J* = 1.6, 5.2, 12.6 Hz, 1 H, CH*H*a–CH=$CH_2$), 4.29 (dd, *J* = 8.4, 8.4 Hz, 1 H, H-6a), 4.15 (tdd, *J* = 1.3, 6.2, 12.6 Hz, 1 H, CH*H*b–CH=$CH_2$),

3.98–3.86 (m, 1 H, H-5), 3.30 (dd, $J$ = 8.4, 8.4 Hz, 1 H, H-6b), 2.26–2.18 (m, 1 H, H-4a), 1.93 (ddd, $J$ = 7.0, 7.0, 14.0 Hz, 1 H, H-4b) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 147.0 and 137.4 and 133.1 (C1 and C2 and s, $C_{ar}$), 134.3 (*C*H=$CH_2$), 128.8, 128.3, 127.8 (d, $C_{ar}$), 117.7 (CH=*C*$H_2$), 97.2 (C8), 83.2 (C3), 71.6 and 68.3 (C6 and *C*$H_2$CH=$CH_2$), 47.1 (C5), 38.7 (C4) ppm. IR (ATR): $\tilde{\nu}$ = 3387 (m), 2880 (m), 1496 (m), 1445 (m), 1356 (m), 1287 (m), 1203 (m), 1091 (s), 996 (s), 969 (s), 778 (m), 694 cm$^{-1}$ (m). MS (EI, 70 eV): $m/z$ (%) = 258 (2) [M$^+$], 214 (24), 201 (42), 171 (37), 159 (47), 143 (57), 131 (78), 128 (77), 115 (69), 105 (73), 91 (100), 77 (58). HRMS (EI) calcd. for [M$^+$] $C_{16}H_{18}O_3$: 258.1256; found 258.126.

**(3′*RS*,5′*SR*,8′*RS*)-9-(8′-Allyloxy-2′-phenyl-7′-oxabicyclo[3.3.0]oct-1′-ene-3′-yl)-9*H*-6-chloropurine (*rac*-30):** 6-Chloropurine (371 mg, 2.4 mmol) and $PPh_3$ (1.57 g, 2.4 mmol) were dissolved in dry THF (20 mL) and DEAD (467 μL, 2.4 mmol) was added dropwise. The resulting yellow mixture was stirred for 10 min and a solution of *rac*-**27** (300 mg, 1.2 mmol) in THF (2 mL) was slowly added. After stirring the reaction mixture for 15 h the solvent was evaporated and the mixture was purified by flash chromatography (EtOAc) to give compound *rac*-**30** as a sticky, yellow oil (294 mg, 62%, purity was ≈90% according to $^1$H NMR). TLC: $R_f$ = 0.30 (CyHex/EtOAc, 1:1). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.73 (s, 1 H, H-2), 7.98 (s, 1 H, H-8), 7.13–7.10 (m, 2 H, $H_{ar}$), 7.00–6.97 (m, 3 H, $H_{ar}$), 6.53 (ddd, $J$ = 1.6, 6.9, 8.7 Hz, 1 H, H-3′), 5.89 (s, 1 H, H-8), 5.81 (dddd, $J$ = 17.2, 10.3, 6.1, 5.3 Hz, 1 H, C*H*=$CH_2$), 5.20 (tdd, $J$ = 1.5, 1.6, 17.2 Hz, 1 H, CH=CH–$H_{trans}$), 5.13 (tdd, $J$ = 1.3, 1.6, 10.3 Hz, 1 H, CH=CH–$H_{cis}$), 4.41–4.36 (m, 1 H, H-6a′), 4.19 (tdd, $J$ = 1.4, 5.3, 12.7 Hz, 1 H, CH*H*a–CH=$CH_2$), 4.03 (tdd, $J$ = 1.3, 6.1, 12.7 Hz, 1 H, CH*H*b–CH=$CH_2$), 3.73–3.64 (m, 2 H, H-6b′ and H-5), 3.06 (ddd, $J$ = 6.9, 6.9, 12.5 Hz, 1 H, H-4a′), 2.03 (ddd, $J$ = 8.7, 8.7, 12.5 Hz, 1 H, H-4b′) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 152.5 (C2), 144.2 (C8), 147.8, 132.5, 132.3, 131.9, 129.3, 129.0, 128.9, 128.8, 127.1 (C4, C5, C6, C1′, C2′, $C_{ar}$), 134.3 (*C*H=$CH_2$), 118.2 (CH=*C*$H_2$), 96.5 (C8′), 72.1 (C6′), 68.6 (*C*$H_2$CH=$CH_2$), 66.5 (C3′), 45.9 (C5′), 40.2 (C4′) ppm. IR (ATR): $\tilde{\nu}$ = 2975 (m), 1725 (m), 1669 (m), 1588 (s), 1556 (s), 1400 (m), 1334 (s), 1195 (s), 1064 (m), 982 (m), 933 (s), 721 (m), 695 cm$^{-1}$ (m). MS (EI, 70 eV): $m/z$ (%) = 394 (6) [M$^+$], 337 (11), 240 (38), 199 (19), 181 (20), 171 (37), 155 (100), 141 (64), 128 (27), 115 (44), 77 (24). HRMS (EI) calcd. for [M$^+$] $C_{21}H_{19}O_2N_2Cl$: 394.1197; found 394.119.

**(3*RS*,5*SR*)-3-(6′-Chloropurin-9′-yl)-5-[2-dimethyl-(1,1,2-trimethylpropyl)silanyloxymethyl]-2-phenylcyclopent-1-enecarbaldehyde (*rac*-31):** A solution of *rac*-**30** (150 mg, 0.38 mmol) and PPTS (28 mg, 0.11 mmol) in wet acetone (5 mL) was stirred under reflux for 6 h. The solvent was evaporated and the flask was flushed with argon (3 times). Dry pyridine (2 mL) was added and, after stirring at room temp. for 5 min, ThxMe$_2$SiCl (299 μL, 1.52 mmol) was added. After stirring at room temp. for 16 h, the reaction was quenched by addition of saturated aqueous $NaHCO_3$(20 mL). After stirring the resulting mixture at room temp. for 30 min, the water phase was extracted with EtOAc (4×10 mL) and the combined organic layers were washed with 10% HCl (3×10 mL), sat. $NaHCO_3$ (10 mL), and brine (10 mL), dried ($MgSO_4$), and concentrated. The residue was then purified by flash chromatography (CyHex/EtOAc, 2:1) to give *rac*-**31** as a white solid (139 mg, 73%). M.p. 142 °C. TLC: $R_f$ = 0.40 (CyHex/EtOAc, 2:1). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 9.85 (s, 1 H, *H*C=O), 8.72 (s, 1 H, H-2′), 8.20 (s, 1 H, H-8′), 7.28–7.22 (m, 5 H, $H_{ar}$), 6.42 (ddd, $J$ = 6.9, 9.5, 1.8 Hz, 1 H, H-3), 4.41 (dd, $J$ = 3.7, 9.9 Hz, 1 H, SiOC*H*a), 3.75 (dd, $J$ = 2.5, 9.9 Hz, 1 H,SiOC*H*b), 3.50–3.42 (m, 1 H, H-5), 2.99 (ddd, $J$ = 9.5, 9.5, 14.1 Hz, 1 H,H-4a), 2.23 (ddd, $J$ = 6.9, 6.9, 14.1 Hz, 1 H, H-4b), 1.65 (septet, $J$ = 6.9 Hz, 1 H, Me$_2$C*H*), 0.89 [d, $J$ = 6.8 Hz, 6 H, (C$H_3$)$_2$CH], 0.88 [s, 6 H, C(C$H_3$)$_2$], 0.15 and 0.14 (2s, 6 H, SiC$H_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 190.7 (*C*H=O), 158.1 (C2), 151.9 (C2′), 151.7 and 151.0 (C4′+C6′), 143.9 (C8′), 141.3 (C1), 130.9 and 130.6 (C5′and s, $C_{ar}$), 130.3 and 129.0 and 128.6 (d, $C_{ar}$), 63.3 (*C*$H_2$OSi), 60.7 (C3), 45.5 (C5), 34.1 (Me$_2$*C*H), 33.5 (C4), 25.5 (Me$_2$*C*Si), 20.5 and 20.4 [(*C*$H_3$)$_2$CH], 18.6 and 18.5 [(*C*$H_3$)$_2$CSi], –3.3 and –3.4 (*C*$H_3$Si) ppm. IR (ATR): $\tilde{\nu}$ = 2955 (m), 1716 (m), 1671 (s), 1588 (s), 1558 (s), 1401 (m), 1333 (m), 1251 (m), 1197 (s), 1105 (m), 934 (m), 829 (s), 776 cm$^{-1}$ (m). MS (ESI): $m/z$ (%) = 519 (5) [M + Na$^+$], 497 (44), 343 (11), 318 (41), 262 (100), 183 (15). HRMS (ESI) calcd. for [M + H$^+$] $C_{26}H_{34}$: $ClN_4O_2SiNa$ 497.2139; found 497.213.

**(1′*RS*,4′*SR*)-9-{4′-[Dimethyl-(1,1,2-trimethylpropyl)silanyloxymethyl]-3′-hydroxymethyl-2′-phenylcyclopent-2′-enyl}-9*H*-6-chloropurine (*rac*-17):** A mixture of MeOH (3 mL) and $CH_2Cl_2$ (6 mL) was added to $NaBH_4$ (40 mg, 1.04 mmol), the resulting mixture was stirred at room temp. for 3 min, and then cooled to –78 °C. A solution of *rac*-**31** (52 mg, 0.104 mmol) in $CH_2Cl_2$ (2 mL) was added dropwise. After stirring the mixture at –78 °C for 1 h, acetone (5 mL) was added and the mixture was allowed to warm to room temp. and stirred for 30 min. The mixture was poured onto a plug of silica, washed with EtOAc, and the solvents were removed under reduced pressure to give the CNA *rac*-**17** (53 mg, 99%) in a high purity according to $^1$H NMR spectroscopy and TLC. M.p. 133 °C. TLC: $R_f$ = 0.24 (CyHex/EtOAc, 2:1). $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 8.72 (s, 1 H, H-2), 7.92 (s, 1 H, H-8),7.19–7.13 (m, 5 H, $H_{ar}$), 6.27 (dd, $J$ = 8.6, 6.9 Hz, 1 H, H-1′), 4.45–4.22 (m, 2 H, C*H*$_2$OH), 3.97 (dd, $J$ = 10.3, 3.8 Hz, 1 H, SiOC*H*a), 3.72 (dd, $J$ = 10.3, 6.9 Hz, 1 H,SiOC*H*b), 3.43 (t, $J$ = 5.5 Hz, 1 H, OH), 3.29–3.22 (m, 1 H, H-4′), 2.93 (ddd, $J$ = 8.6, 8.6, 13.6 Hz, 1 H,H-5a′), 1.73 (ddd, $J$ = 6.9, 6.9, 13.6 Hz, 1 H, H-5b′), 1.65 (septet, $J$ = 6.8, 1 H, Me$_2$C*H*), 0.90 [d, $J$ = 6.8 Hz, 6 H, (C$H_3$)$_2$CH], 0.89 [s, 6 H, C-(C$H_3$)$_2$], 0.18 and 0.16 (2s, 6 H, SiC$H_3$) ppm. $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ = 151.8 (C2), 151.7 and 150.8 (C4 and C6), 145.8 (C3′), 143.7 (C8), 137.6 and 132.9 (C2′and s, $C_{ar}$), 131.3 (C5), 128.7 and 128.4 and 127.8 (d, $C_{ar}$), 65.5 (*C*$H_2$OSi), 60.7 (C1′), 58.7 (*C*$H_2$OH), 48.1 (C4′), 34.2 (C5′), 34.1 (Me$_2$*C*H), 25.3 (Me$_2$*C*Si), 20.3 and 20.2 [(*C*$H_3$)$_2$CH], 18.5 [(*C*$H_3$)$_2$CSi], –3.4 and –3.5 (*C*$H_3$Si) ppm. IR (ATR): $\tilde{\nu}$ = 3382 (m), 2954 (m), 2864 (m), 1692 (m), 1588 (s), 1558 (m), 1333 (m), 1251 (m), 1195 (m), 1107 (m), 828 (s), 776 (s), 699 cm$^{-1}$ (m). MS (ESI): $m/z$ (%) = 705 (8), 619 (9), 521 (75) [M + Na$^+$], 367 (100), 209 (15), 185 (8). HRMS (ESI) calcd. for [M + Na$^+$] $C_{26}H_{35}ClN_4O_2SiNa$: 521.2115; found 521.211.

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