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Article

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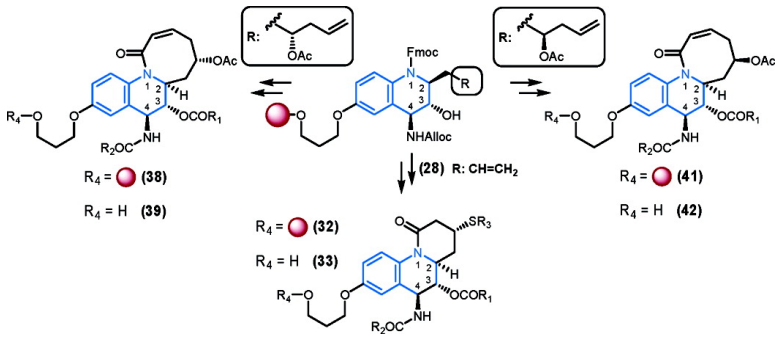


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# Part 2: Building Diverse Natural-Product-Like Architectures from a Tetrahydroaminoquinoline Scaffold. Modular Solution- and Solid-Phase Approaches for Use in High-Throughput Generation of Chemical Probes

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The solution- and solid-phase synthesis to obtain several natural-product-like, tetrahydroquinoline-based, polycyclic derivatives were developed. In one approach, two derivatives (**38** and **41**) having an eight-membered unsaturated lactam were successfully obtained both in solution and on solid support.

## Introduction

In the post-genomic chemical biology age, there is a growing desire to understand the role of macromolecular (i.e., protein−protein, protein−DNA/RNA) interactions-based signaling networks by small molecules.[1] Because protein−protein-based signaling networks are highly dynamic and complex in nature[2] and present tremendous challenges in their systematic dissection,[3] the use of small molecules as chemical probes to modulate macromolecular interactions in a temporal and reversible manner is an attractive strategy to understanding systems biology.[4] However, a wide access to structurally complex and diverse small molecules as chemical probes for biological systems remains a major limiting factor.[5] In particular, small molecules possessing features of complex bioactive natural products, such as richness in chiral functional groups and 3D architectures, would play an important role in dissecting macromolecular interactions, leading to a better understanding of various cellular responses, including normal and dysfunctional networks.[6]

With the goal of accessing alkaloid-like (natural-product-like) polycyclic compounds in search of chemical dissectors of macromolecular interactions, we have developed[7] a practical, enantioselective synthesis of a highly functionalized, tetrahydroaminoquinoline scaffold, **1** (Figure 1). A stereoselective aza-Michael reaction was the key step to reaching to this scaffold. Compound **1** is highly versatile because it contains several attractive features, which include (i) the presence of several orthogonally protected functional groups, (ii) $\beta$- and $\delta$-amino acid derivatives, (iii) a 1,2-*trans*-amino alcohol moiety, and (iv) a 1,3-hydroxycarboxyl ester functionality. In addition to these features, the presence of the phenolic hydroxyl group could serve as an anchoring site for solid-phase synthesis.

## Results and Discussion

Herein, we report the use of two tetrahydroaminoquinoline derivatives, **2** and **3**, that were easily obtained from **1**. The transformation of the side chain carboxyl ester at $C_2$ to the allylic functional groups opens several modular pathways to forming different ring skeletons by ring closing metathesis, as outlined in Figures 1 and 2. For example, the incorporation of the *N*-acryloyl group either at $N_1$- or $C_4$-$NH_2$ would allow the formation of two different tricyclic compounds, **4** and **5**, containing three diversity sites (see Figure 1). Compound **4** contains a six-membered ring lactam that could be subjected to a variety of nucleophilic reagents in cycloaddition reactions. The presence of the bridged eight-membered ring lactam moiety on compound **5** is an attractive feature that could be further subjected to diversification. In another approach, a simple replacement of the *N*-acryloyl group at either $N_1$- or $C_4$-$NH_2$ by a *N*-heptenoyl moiety followed by ring closing metathesis reaction would afford two structurally different tricyclic compounds, **6** and **7**. As discussed earlier, these derivatives have the potential to be utilized in introducing a wide variety of diverse groups during library generation. Both of these compounds incorporate additional 10- and 12-membered rings as part of their tricyclic architectures. The ring-closing metathesis approach could also be independently utilized with scaffolds **3a** and **3b** to provide polycyclic derivatives **8** and **9** containing a medium-sized unsaturated ring lactam. The unsaturated lactam functionality could be further explored in introducing an additional diversity site.

Our solution synthesis to obtain the desired scaffold **12** from compound **10** and the successful synthesis of two different tricyclic compounds **14** and **16** are shown in Scheme 1.

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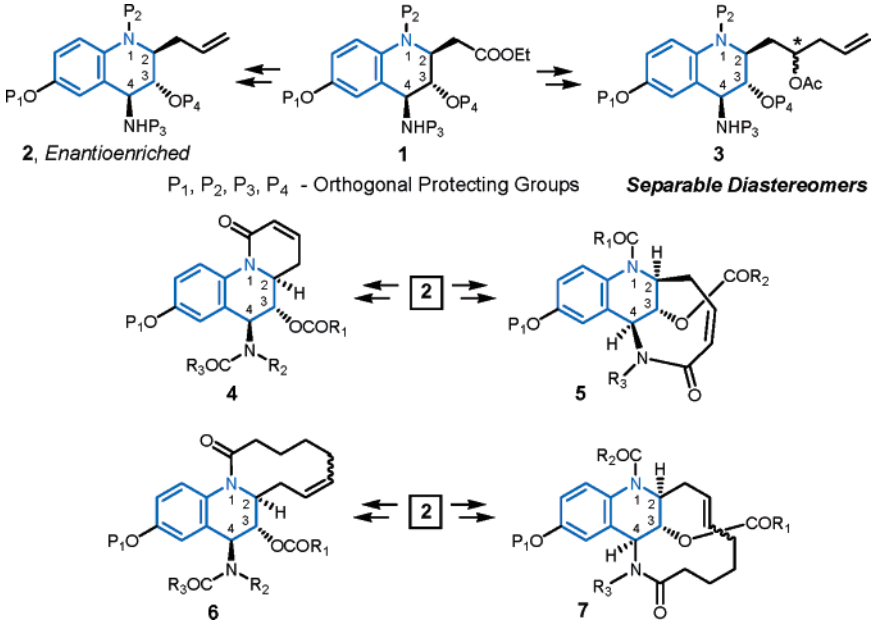



**Figure 1.** A modular approach to obtaining different, tetrahydroaminoquinoline-based, polycyclic architectures from an enantioenriched scaffold, **2**.

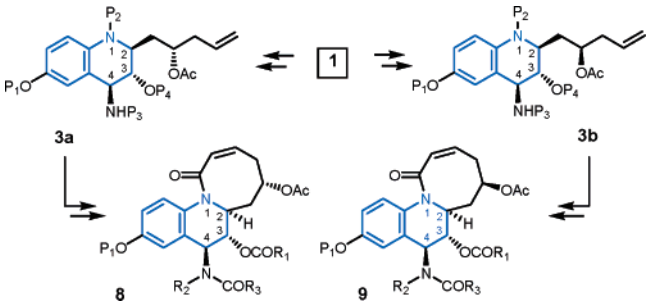


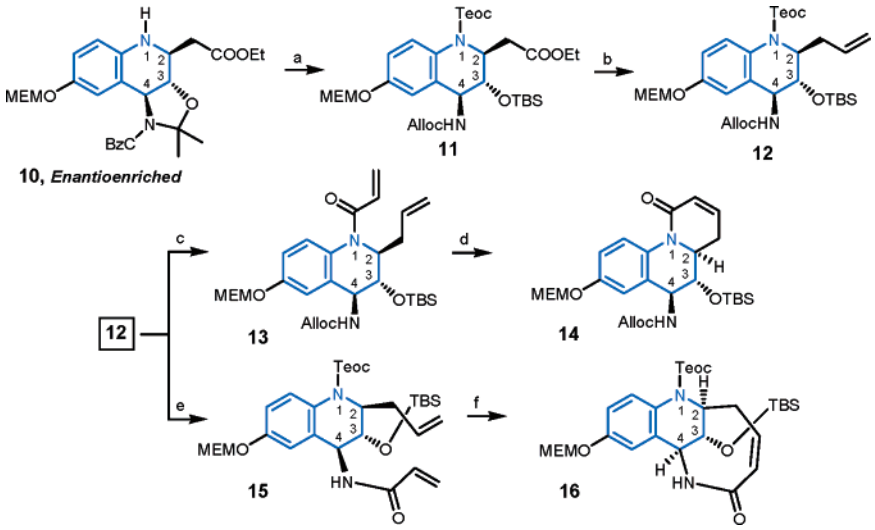

**Figure 2.** Tetrahydroaminoquinoline-based, polycyclic architectures having an unsaturated eight-membered ring lactam from enantioenriched scaffolds, **3a** and **3b**.

The orthogonally protected tetrahydroaminoquinoline derivative **14** was prepared from an enantioenriched cyclic amine derivative **10** in several steps. These included (i) *N*-Teoc protection (80%); (ii) deprotection of the *N*-Cbz and acetonide groups by hydrogenation using Pd/C, followed by *N*-Alloc protection at $C_4$ (60%); and (iii) −OTBS protection (80%), yielding product **11**. Compound **11** was then subjected to (i) side-chain carboxyl ester reduction (70%) and (ii) oxidation of the primary hydroxyl group and Wittig reaction (80%) to produce the desired scaffold **12** having a terminal olefinic moiety. The tricyclic derivative **14** was then obtained from **12** in four steps as follows: (i) *N*-Teoc and −OTBS removal (80%), (ii) selective N-acryloylation, (iii) −OTBS protection, and (iv) ring-closing metathesis (RCM) using 10.0 mol % second-generation Grubbs' catalyst (80%). The product was characterized by MS and NMR. When used on compound **15**, a similar RCM approach led to the successful synthesis of compound **16** containing a bridged, eight-membered, unsaturated, lactam functionality. The synthesis included the *N*-alloc removal from **12**, which was then subjected to N-acryloylation and subsequent RCM reaction to produce the bridged derivative **16**. Our successful attempts to obtain different tricyclic compounds with 10- and 12-membered rings are shown in Scheme 2.

In a model study to obtain polycyclic derivatives **18** and **20** containing medium sized rings,[8] compound **12** was subjected to (i) $C_4$-*N*−Alloc removal (70%), (ii) $C_4$-N-benzoylation (85%), (iii) *N*−Teoc/−OTBS removal, and (iv) N-heptenoylation/−OTBS protection (60% over two steps) to produce **17**. Upon treatment with Grubbs' second-generation catalyst in a RCM reaction, **17** was then successfully converted to the tricyclic derivative **18** having a 10-membered ring as a mixture of two isomers (confirmed by NMR studies). A similar RCM approach also produced compound **20** having a 12-membered ring as a single isomer from **19**. This reaction was very clean and high-yielding (85% from **19**), and the product **20** was fully characterized by NMR studies. The 2D-NMR studies revealed interesting results regarding the conformation of the bridged macrocycle in compound **18**. First, there was no sign of the other isomer (i.e., macrocyclic product was formed with the *trans*-olefin moiety only!), and second, as observed in compounds **12** and **19**, these products (which ones) show nOe between the two protons at $C_2$ and $C_4$, indicating the occupation of the functional groups at the pseudoequatorial positions. In contrast to **12** and **19**, compound **20** did not show any nOe between the two protons at $C_2$ and $C_4$. This observation was extremely useful in understanding the shape of the bridged macrocycle. One could envision that the two functional groups bearing the olefinic moiety would prefer to adopt a pseudoaxial orientation, leading to the successful RCM reaction in producing the bridged macrocyclic derivative **20** (see Scheme 2).

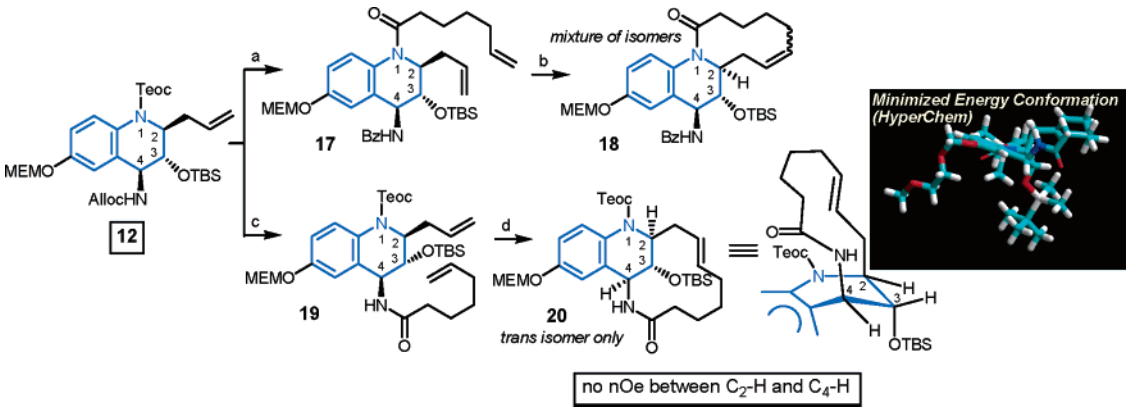
As shown in Scheme 3, the next study involved a methodology development leading to the generation of tetrahydoraminoquinoline-based tricyclic derivatives **23** and **26** containing an eight-membered unsaturated ring lactam. In reaching this objective, compounds **21** and **24** were easily obtained from enantioenriched **10** (not shown in Scheme 3), and the detailed reaction sequence is provided in the Supporting Information. With both diastereomers **21** and **24**

**Scheme 1**[a]




[a] (a) (i) TeocCl (2.0 equiv), pyridine (5.0 equiv), $CH_2Cl_2$, −10 °C, 80%; (ii) Pd/C, $H_2$, EtOH; (iii) DIPEA (1.8 equiv), AllocCl (1.6 equiv), $CH_2Cl_2$, −78 °C, 60%; (iii) 2,6-lutidine (1.5 equiv), TBSOTf (1.29 equiv), 80%; (b) (i) $LiBH_4$ (5.0 equiv), THF, RT, 70%; (ii) $Et_3N$ (4.7 equiv), $SO_3$·Py (3 equiv), RT, 3.5 h; (iii) methyltriphenylphosphonium bromide (1.8 equiv), NaHMDS (1.6 equiv) 80%; (c) (i) TBAF (3.0 equiv), THF 0 °C, 3.5 h, 90%; (ii) $Et_3N$ (1.8 equiv), acryloyl chloride (1.3 equiv), −10 C; (iii) 2,6-lutidine (2.0 equiv), TBSOTf (1.2 equiv), $CH_2Cl_2$, −78 °C, 60%; (d) Grubbs' catalyst (second-generation, 10 mol %), $CH_2Cl_2$, 80%; (e) (i) piperidine (4.3 equiv), $Pd(PPh_3)_4$ (10.0 mol %); (ii) $Et_3N$ (1.78 equiv), acryloyl chloride (1.4 equiv), $CH_2Cl_2$, −10 °C; (f) Grubbs' catalyst (second generation, 10.0 mol %), $CH_2Cl_2$, 70%.

**Scheme 2**[a]



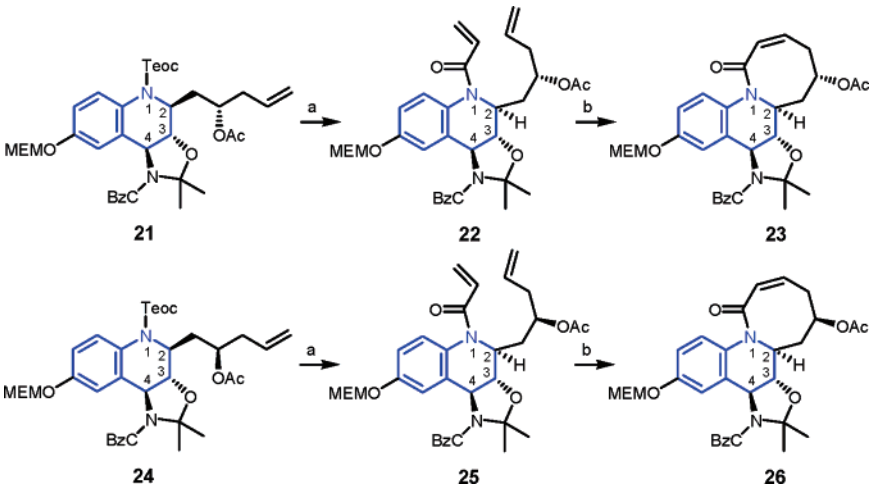

[a] (a) (i) piperidine (4.3 equiv), $Pd(PPh_3)_4$ (10.0 mol %); (ii) $Et_3N$ (5.0 equiv), benzoyl chloride (2.0 equiv), $CH_2Cl_2$, 90%, RT; (iii) TBAF (3.0 equiv), THF 0 °C, 3.5 h, 80%; (iv) $Et_3N$ (6.0 equiv), 5-heptenoyl chloride (1.3 equiv), $CH_2Cl_2$, −10 °C; (v) 2,6-lutidine (4.0 equiv); (vi) TBSOTf (3.0 equiv), $CH_2Cl_2$, −10 °C, 60%; (b) Grubbs' catalyst (second generation, 10.0 mol %), $CH_2Cl_2$, 68%; (c) (i) piperidine (4.3 equiv), $Pd(PPh_3)_4$ (10.0 mol %); (ii) 5-heptenoic acid (1.5 equiv), DIC (5.0 equiv), DMAP (1.0 equiv), $CH_2Cl_2$, RT; (d) Grubbs' catalyst (second generation, 10.0 mol %), $CH_2Cl_2$, 85%.

on hand, they were independently subjected to *N*-Teoc removal (94−96%), followed by N-acryloylation (61−69%) to produce the desired products **22** and **25**. When subjected to a ring-closing metathesis reaction using Grubbs' second-generation catalyst (10 mol %), cyclic products **23** (81%) and **26** (87%) were independently formed. In both cases, the reaction was very fast, cyclization occurred at the room temperature, and the products were clean and high-yielding. The presence of an unsaturated eight-membered ring lactam could be further utilized in introducing a diversity site for library generation. As a result, the successful method development of compounds **23** and **26** in solution synthesis prompted us to develop the solid-phase synthesis of these targets (see compounds **39** and **42**, Scheme 6).

As shown in Scheme 4, the next milestone was to obtain compound **27** for developing the solid-phase synthesis. Thus, compound **12** was converted to **27** in several synthetic transformations (note that the detailed synthetic steps are discussed in the Supporting Information).

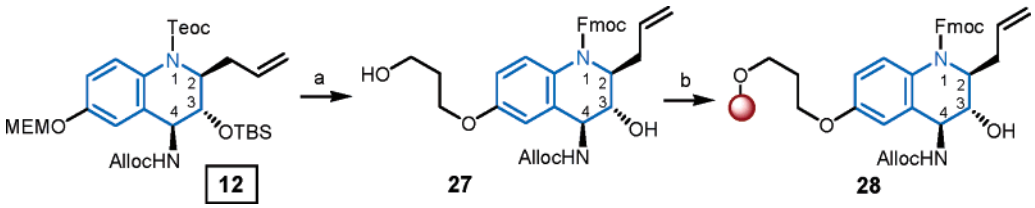
During this sequence, a three-carbon spacer containing a primary hydroxyl group was introduced at the phenolic hydroxyl position. Compound **27** was then immobilized onto alkylsilyl polystyrene macrobeads (500−560 $\mu$m, 1.29mmol/g, courtesy of Broad Institute).[9] The loading was determined to be 90% upon cleavage of the product from the solid support. The loading was also highly selective for the primary hydroxyl group because we did not observe any signs of immobilization of compound **27** on the secondary hydroxyl group at $C_3$. Our solid-phase synthesis strategy to obtain a tricyclic derivative with three potential diversity sites from **28** is shown in Scheme 5. Following the *N*-Fmoc removal (20% piperdine, HPLC yield >98%), compound **28** was subjected to N-acryloylation (98%) and subsequently to RCM using second-generation Grubbs' catalyst. The tricyclic product **30** possessing a six-membered ring lactam was produced in a high yield (HPLC yield >95%). As observed in solution synthesis, the reaction proceeded smoothly in the presence of the free hydroxyl group at $C_3$ and the *N*-Alloc

**Scheme 3**[a]



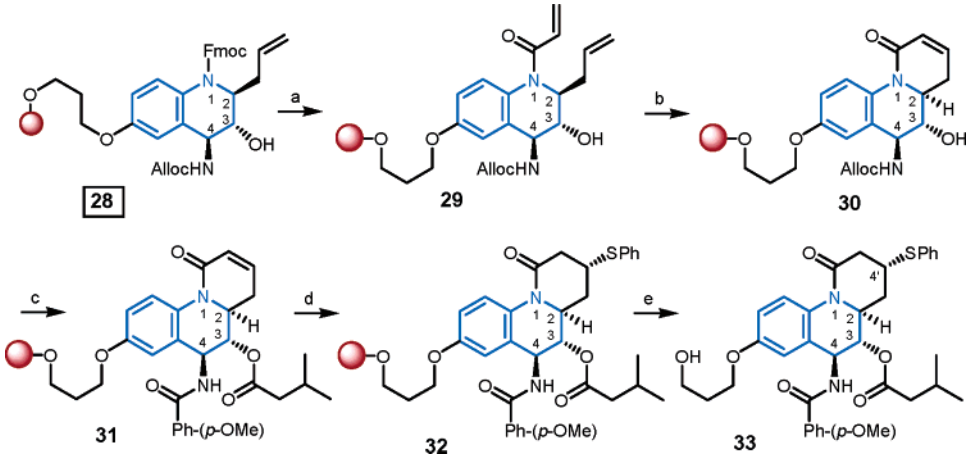

[a] (a) (i) TBAF (2.0 equiv), THF, RT, 50 min, 94−96%; (ii) $Et_3N$ (3.5−4.0 equiv), acryloyl chloride (3.0 equiv), $CH_2Cl_2$, RT, 61−68.5%; (b) Grubbs' catalyst (second-generation, 10.0 mol %), $CH_2Cl_2$, reflux, 1 h, 81−87%.

**Scheme 4**[a]




[a] (a) (i) *p*-TsOH (2.0 equiv), ethanol, (ii) toluene-4-sulfonic acid, 3-(tetrahydropyran-2-yloxy)-propyl ester (1.3 equiv), $CsCO_3$ (1.4 equiv), DMF; (iii) TBAF (2.0 equiv), THF 0 °C; (iv) FmocCl (2.0 equiv), 10% $NaHCO_3$, EtOAc, 70%; (b) alkylsilyl-linker-based polystyrene macrobeads (1.0 equiv), TfOH (6.0 equiv), 2,6-lutidine (10.0 equiv), **27** (0.5 equiv).

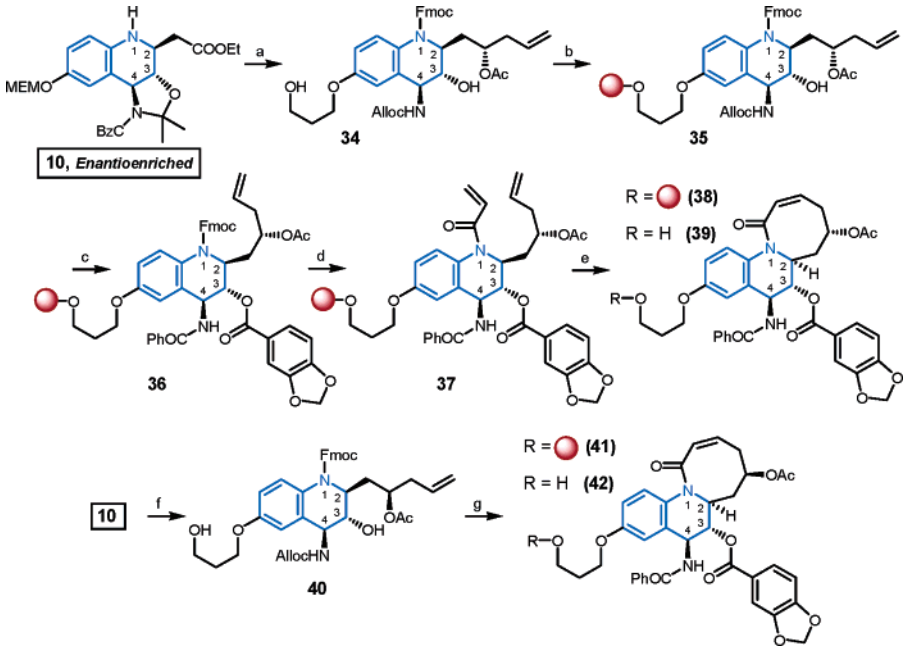
**Scheme 5**[a]




[a] (a) (i) 20% piperidine in $CH_2Cl_2$; (ii) $Et_3N$ (10.0 equiv), acryloyl chloride (5.0 equiv), −10 °C; (2.0 equiv), $CH_2Cl_2$; (b) Grubbs' catalyst (second generation, 30 mol %), $CH_2Cl_2$, HPLC yield 95%; (c) NaHMDS (10.0 equiv), valeryl chloride (5.0 equiv), THF; (d) (i) piperidine (4.0 equiv), $Pd(PPh_3)_4$ (10 mol %), $CH_2Cl_2$; (ii) $Et_3N$ (10.0 equiv), *p*-methoxybenzoyl chloride (5.0 equiv), $CH_2Cl_2$; (iv) $Et_3N$ (10.0 equiv), benzenethiol (5.0 equiv), $CH_2Cl_2$; (e) HF-pyridine.

group at $C_4$. After having performed a clean synthesis of the functionalized tricyclic system on solid support, the synthetic platform was set to explore diversity-based reactions. Compound **30** was subjected to hydroxyl group derivatization, but this proved to be difficult initially with several unsuccessful attempts. It turned out that reaction with NaHMDS and trapping the electrophile produced the desired ester derivative (as the first diversity site, HPLC yield >98%). Following the $C_4$-*N*-Alloc removal, the free amine was subjected to derivatization into N-benzoylation to incorporate the second diversity (HPLC yield >98%). The six-membered ring derivative containing the unsaturated lactam moiety was tested to introduce the third diversity. In this test study, compound **31** was reacted with thiophenol as the nucleophile in the presence of a mild base. The reaction proceeded very smoothly and produced only a single isomer with a complete selective facial attack in the Michael reaction. Finally, compound **33** was obtained after cleavage

**Scheme 6**[a]




[a] (a) See the experimental section; (b) alkylsilyl-linker based polystyrene macrobeads (33.8 mg, 0.046 mmol), TfOH (0.45 M sol, 0.62 mL, 0.277 mmol), 2,6-lutidine (43.3 μL, 0.37 mmol), **34** (62 mg, 0.092 mmol); (c) (i) 1,3-diisopropylcarbodiimide (13.6 μL, 0.086 mmol), 3,4-methylenedioxyphenylacetic acid (11.7 mg, 0.064 mmol), 4-(dimethylamino)-pyridine (0.5 mg, 0.004 mmol), RT, 23 h; (ii) triphenylphosphine (149.5 mg, 0.549 mmol), acetic acid, tetrakis(triphenylphosphine)palladium (133.8 mg, 0.114 mmol), RT; (iii) 2,4,6-collidine (57.5 μL, 0.431 mmol), benzoyl chloride (25.2 μL, 0.215 mmol); (d) (i) piperidine (4.0 equiv), (ii) 2,4,6-collidine (57.5 μL, 0.431 mmol), acryloyl chloride (18.2 μL, 0.215 mmol, dissolved in anhydrous $CH_2Cl_2$ (0.5 mL) and dropwise addition at the same temperature); (e) Grubbs' catalyst (second-generation, 7.3 mg, 0.008 mmol), $CH_2Cl_2$, reflux, 19 h; (f, and g) see the Supporting Information.

from the solid support, and it was fully characterized by MS and using 2D-NMR studies. There was no nOe between the two protons at $C_4$ and $C_4'$. In addition, the nOe between the protons at $C_3$ and $C_4'$ led us to conclude that the nucleophilic attack on compound **31** occurred from an α-face, producing **32** as a single diastereomer. As a result, following the loading step, the overall eight-step reaction sequence was very clean, producing the final product with three potential diversity sites in ~88−90% HPLC yield.

Our solid-phase synthesis to obtain compounds **38** and **40** containing eight-membered, unsaturated lactam rings is shown in Scheme 6. In achieving this goal, the required compounds **34** and **39** were obtained from **21** and **24**, respectively. As in our previous study, the independent loading of these two starting materials worked very well, and in both the cases, the loading was found to be 71−72%. In one study, compound **35** was subjected to (i) O-acylation, (ii) *N*-Alloc removal, and (iii) N-amidation, giving the product **36** anchored onto the solid support. Following the *N*-Fmoc removal by a piperidine wash, the free amine was then reacted with acryloyl chloride to obtain **37**, a required starting material for the ring-closing metathesis reaction. It was gratifying to note that when treated with the Grubbs' second-generation catalyst (10−15 mol %) in $CH_2Cl_2$ under refluxing conditions, the cyclic product having an unsaturated medium-sized lactam ring was formed very cleanly. The final product **39** after cleavage from the solid support was purified over silica gel and was then thoroughly characterized by HPLC/MS, $^1$H NMR, and 2D NMR. Following a similar series of steps using compound **40** as a starting material for loading onto the solid support, the product **41** was obtained in seven steps. Once again, to our great surprise, the ring-closing metathesis reaction with this isomer also worked very nicely onto the solid support. Finally, the product **42** obtained after the cleavage was purified and then subjected to thorough analysis (i.e., HPLC/MS, $^1$H and 2D NMR).

## Conclusion

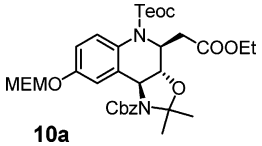
In summary, we have reported solution synthesis of several polycyclic compounds (**14**, **16**, **18**, **20**, **23**, and **26**) from a versatile, tetrahydroaminoquinoline scaffold, **10**. Compounds **16** and **20** contain bridged, functionalized 8- and 12-membered rings as part of their tricyclic architectures. In three series shown in Schemes 5 and 6, the solution synthesis was successfully transferred onto solid phase to produce the tricyclic derivatives **33**, **39**, and **42** containing diversity sites for library generation. The overall eight-step, solid-phase synthesis sequence to obtaining compound **33** from **29** was very clean and high-yielding. One of the key steps in the solid-phase synthesis included the formation of a six-membered ring lactam and its further utilization to produce a stereocontrolled thiol addition. Similarly, the multistep solid-phase sequence to obtain products **39** and **42** was very clean. As a result, the use of these diverse, solid-phase synthesis methods in library generation is in progress, and the biological studies with tetrahydroaminoquinoline-derived, natural-product-like library members will be reported as they become available.

## Experimental Section

All reactions were carried out in flame-dried glassware under an atmosphere of nitrogen with magnetic stirring. Thin-

layer chromatography was performed on EMD (Art. 5715-7) precoated silica gel 60 $F_{254}$ glass plates (layer thickness 0.25 mm). Visualization was effected with a UV lamp (254 nm) or by staining with Vanillin solution, $KMnO_4$ solution, or ammonium molybdate/ceric sulfate solution. Flash column chromatography was performed using silica gel 60 (40−63 $\mu$m, Silicycle) or a Biotage Horizon Flash Chromatography System. Solvents were purified as follows: trace amounts of water and oxygen from THF, DMF, and dichloromethane were removed using columns containing activated alumina and copper under $N_2$. Triethylamine, pyridine, ethyl ether, and toluene were obtained from commercial suppliers (EMD and Aldrich) and used without further purification. NMR spectra were recorded on a Bruker DRX 400-MHz spectrometer. All chemical shifts are reported in parts per million ($\delta$). $^1$H NMR (400-MHz) spectra were recorded at room temperature in $CDCl_3$ or $C_6D_6$ solutions and referenced to residual $CHCl_3$ (7.27 ppm) or $C_6H_6$ (7.16 ppm). Fully decoupled $^{13}$C NMR (100-MHz) spectra were recorded in $CDCl_3$ or $C_6D_6$ solutions. The center peaks of $CDCl_3$ (77.0 ppm) and $C_6D_6$ (128.7 ppm) were used as the internal reference. Mass spectra were carried out on a VG Quattro I (Micromass) mass spectrometer equipped with a pneumatically assisted electrospray ionization source operating in positive mode. HPLC were performed using a Hewlett-Packard (Agilent) 1100 Series equipped with a diode array detector and a NovaPack C18 (3.9 × 300 mm) column. The enantiomeric excess was determined by chiral HPLC using a Hewlett-Packard (Agilent) 1090 Series II liquid chromatograph equipped with a diode array detector and a Chiracel-OD column.

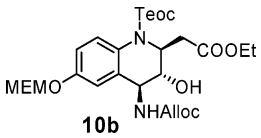
**Compound 11.**




**10a**

Triphosgene (475 mg) was taken in w 250-mL, round-bottom flask and was cooled to −78 °C under $N_2$. $CH_2Cl_2$ (30 mL) was added, and the mixture was stirred vigorously for 30 min. To this solution was added trimethylsilylethanol (0.64 mL) over 15 min. The reaction mixture was warmed to −10 °C, and pyridine (0.36 mL) was added to the reaction mixture slowly (over 30 min). The reaction mixture was stirred for 2 h at 0 °C. To the above reaction mixture a solution of free amine (1.19 g, 2.25 mmol) and pyridine (0.54 mL) in 10 mL of $CH_2Cl_2$ was added over 30 min at −30 °C and was stirred for 1.0 h at the same temperature. Then it was warmed to 0 °C and further stirred for 2 h at the same temperature. The reaction mixture was quenched with saturated $NaHCO_3$ solution, extracted with $CH_2Cl_2$ (3 × 50 mL), and dried over $MgSO_4$. The solvent was evaporated on a rotovap, and the crude product was purified by flash column chromatography using using 20% EtOAc in hexane to obtain 1.2 g (80%) of Teoc-protected amine derivative **10a**. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.34−7.28 (m, 6H), 6.96−6.76 (m, 2H), 5.28 (m, 2H), 5.18 (bs, 2H), 4.55 (bs, 1H), 4.31 (m, 2H), 4.27 (bs, 1H), 4.09 (m, 2H), 3.80 (bs, 2H), 3.72 (t, 1H, $J$ = 9.5 Hz), 3.56 (m, 2H), 3.39 (s, 3H), 2.76 (m, 2H), 1.62 (s, 6H) 1.18 (t, 3H, $J$ = 7 Hz); 1.05 (m, 2H), 0.03 (s, 9H); MS (EI) *m*/*z* (rel. intensity) 673 (M + 1).

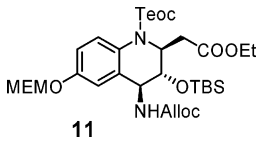
**Compound 10b.**




**10b**

To a solution of **10a** (1.0 g, 1.48 mmol) in 300 mL ethanol was added Pd/C (200 mg) and stirred vigorously for 6 h under hydrogen balloon. Pd/C was removed by filtration through celite pad. Ethanol was removed on a rotovap and dried over high vacuum pump. The crude was dissolved in $CH_2Cl_2$ (200 mL) and DIPEA (0.46 mL, 2.66 mmol) was added at −78 °C. To this solution allylchloroformate (0.25 mL, 2.35 mmol) was added slowly at −78 °C. The reaction mixture was warmed to −30 °C and stirred for 1 h at the same temperature. The reaction was quenched with saturated $NaHCO_3$ solution and extracted with $CH_2Cl_2$ (3 × 50 mL). The solvent was removed on a rotovap to give yellowish oil. The crude was separated by flash chromatography using 50% EtOAc in hexane to obtain 516 mg (60%) of *N*-Alloc protected amine, **10b**. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.30−6.95 (m, 3H), 5.98 (m, 1H), 5.38 (d, 1H, $J$ = 17.1 Hz), 5.31 (m, 3H), 4.67 (m, 3H), 4.28 (m, 2H), 4.09 (q, 2H, $J$ = 4.9 Hz), 3.83 (m, 3H), 3.58 (m, 3H), 3.39 (s, 3H), 2.94 (dd, 1H, $J_1$ = 15.4 Hz, $J_2$ = 4.6 Hz), 2.56 (dd, 1H, $J_1$ = 15.4 Hz, $J_2$ = 8.6 Hz), 1.82 (bs, 1H), 1.22 (t, 3H, $J$ = 7.1 Hz), 1.07 (t, 2H, $J$ = 8.6 Hz), 0.03 (s, 9H); MS (EI) *m*/*z* (rel. intensity) 583 (M + 1).

**Compound 11.**

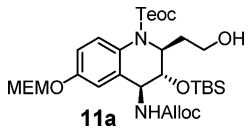



**11**

To a solution of **10b** (2.0 g, 3.43 mmol) in $CH_2Cl_2$ (100 mL), 2,6-lutidine (0.6 mL, 5.16mmol) followed by TBSOTf (1.02 mL, 4.44 mmol) was added slowly at −78 °C. The reaction mixture was warmed to −30 °C, stirred for 3 h, and quenched with saturated $NaHCO_3$ solution. The reaction mixture was extracted with $CH_2Cl_2$ (3 × 50 mL) and dried over anhydrous $MgSO_4$. The solvent was removed on a rotovap to give yellowish oil. The crude product was separated by flash chromatography using 20% EtOAc in hexane to obtain 1.9 g (80%) of compound **11**. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.34−6.97 (m, 3H), 5.96 (m, 1H), 5.36−5.31 (m, 2H), 5.26 (m, 2H), 4.93 (bs, 1H), 4.84 (d, 1H, $J$ = 7 Hz), 4.63 (bs, 2H), 4.57 (bs, 1H), 4.26 (t, 2H, $J$ = 7 Hz), 4.10 (q, 2H, $J$ = 7 Hz), 3.85 (m, 2H), 3.59 (m, 2H), 3.39 (s, 3H), 2.49 (m, 2H), 1.61 (bs, 1H), 1.24 (t, 3H, $J$ = 7 Hz), 1.08 (m, 2H), 0.87 (s, 9H), 0.19 (s, 3H), 0.17 (s, 3H), 0.04 (s, 9H); $^{13}$C NMR 170.7 (1C), 155.8 (1C), 155.5 (1C), 154.6 (1C), 133.0 (1C), 130.0 (1C), 128.7 (1C), 127.3 (1C), 118.3 (1C), 116.5 (1C), 115.2 (1C), 94.0 (1C), 73.1 (1C), 71.9 (1C), 68.0 (1C), 66.3 (1C), 64.8 (1C), 61.1 (1C), 59.4 (1C), 55.1 (1C), 53.4 (1C), 36.1 (1C), 26.0 (3C), 18.2

(1C), 18.0 (1C), 14.4 (1C), 0.89 (1C), −1.1 (1C), −1.4 (1C), −4.2 (1C), −4.5 (1C); MS (EI) *m*/*z* (rel. intensity) 697 (M + 1).

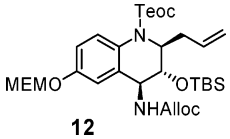
**Compound 11a.**



**11a**

To a solution of the carboxyl ester **11** (1.2 g, 1.72 mmol) in 30 mL of THF at 0 °C was added $LiBH_4$ (4.3 mL, 2M) slowly. The reaction mixture was stirred for 24 h at room temperature. The reaction was quenched with saturated $NH_4Cl$ solution, and it was then extracted with EtOAc. The extract was dried over $MgSO_4$ (anhydrous), concentrated on a rotovap to obtain yellow oil. The crude product was purified by flash column chromatography using 30% EtOAc in hexane to obtain 787 g (70%) of compound **11a**. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.28−6.90 (m, 3H), 5.99 (m, 1H), 5.37 (d, 1H, $J$ = 17.1), 5.27 (s, 3H), 4.80 (d, 1H, $J$ = 7.4 Hz), 4.64 (m, 5H), 4.24 (bs, 2H), 3.84 (t, 2H, $J$ = 4.0 Hz), 3.62 (m, 3H), 3.39 (s, 3H), 2.52 (bs, 2H), 1.81 (bs, 1H), 1.30 (bs, 1H), 1.07 (t, 2H, $J$ = 9.0), 0.88 (m, 9H), 0.16 (s, 6H), 0.04 (s, 9H); MS (EI) *m*/*z* (rel. intensity) 655 (M + 1).

**Compound 12.**

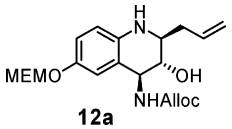


**12**

To a solution of the alcohol **11a** (500.0 mg, 0.763 mmol) in 40 mL $CH_2Cl_2$ was added triethylamine (0.5 mL, 3.58 mmol) at 0 °C. To the above solution $SO_3$*x*Py (364.0 mg, 2.28 mmol) in 2.5 mL DMSO was added over 15 min. The reaction mixture was warmed to room temperature and stirred for 3.5 h. The reaction was quenched with saturated $NH_4Cl$ solution, extracted with $CH_2Cl_2$ (3 × 50 mL), and dried over anhydrous $MgSO_4$. The organic solvent was evaporated on a rotovap, and the crude aldehyde derivative was separated by flash column chromatography using 20% EtOAc in hexane. It was then directly subjected to the Wittig reaction.

To a solution of methyltriphenylphosphonium bromide (492.0 mg, 1.37 mmol) in 10 mL of THF was added NaHMDS (1.22 mL, 1.22 mmol) at −78 °C. The reaction mixture was stirred for 1 h at 0 °C. The solution turned to yellow color. To this solution was added the aldehyde (500 mg, 0.763 mmol) in THF (20 mL) at −78 °C. The whole reaction mixture was warmed to 0 °C and then stirred at the same temperature for 1 h. The reaction was quenched with saturated $NH_4Cl$ solution and extracted with EtOAc (3 × 30 mL), dried over $MgSO_4$, and concentrated. The crude residue was purified by column chromatography using 20% EtOAc in hexane to obtain compound **12** (634 mg, 80%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.60−6.97 (m, 3H), 5.96 (m, 1H), 5.74 (m, 1H), 5.32 (d, 1H, $J$ = 17 Hz), 5.22 (m, 3H), 5.01 (d, 1H, $J$ = 10.1 Hz), 4.96 (d, 1H, $J$ = 17 Hz), 4.87 (d, 1H, $J$ = 7.9 Hz), 4.60 (d, 2H, $J$ = 5.4 Hz), 4.54 (m, 2H), 4.20 (bs, 2H), 3.85 (bs, 1H), 3.81 (m, 2H), 3.55 (m, 2H), 3.34 (s, 3H), 2.27 (m, 1H), 2.07 (m, 1H), 1.03 (m, 2H), 0.85 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H), 0.01 (s, 9H); MS (EI) *m*/*z* (rel. intensity) 651 (M + 1).

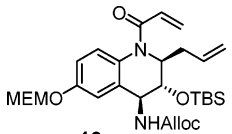
**Compound 12a.**



**12a**

To a solution of compound **12** (50 mg, 0.076 mmol) in 30.0 mL THF was added TBAF (0.23 mL, 0.230 mmol). The reaction mixture was warmed to 0 °C and then stirred for 30 min at the same temperature. The reaction was quenched with $NaHCO_3$ and extracted with EtOAc (3 × 30 mL) and concentrated to obtain yellowish oil. The crude product was separated by flash chromatography using 50% EtOAc in hexane to obtain **12a**. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.12−6.83 (m, 2H), 6.51 (d, 1H), 6.02 (m, 1H), 5.89 (m, 1H), 5.39 (dd, 1H, $J_1$ = 17, $J_2$ = 1.3 Hz), 5.29 (d, 1H, = 9 Hz), 5.23 (d, 1H, $J_1$ = 9.7 Hz), 5.16 (s, 3H), 4.90 (t, 1H, $J$ = 8 Hz), 4.67 (d, 2H, $J$ = 5 Hz), 3.83−3.81 (m, 3H), 3.60 (m, 3H), 3.39 (s, 3H), 3.25 (dt, 1H, $J_1$ = 9.3, $J_2$ = 2.4 Hz), 2.89 (d, 1H, $J$ = 13.8 Hz), 2.19 (m, 1H), 1.69 (bs, 1H); MS (EI) *m*/*z* (rel. intensity) 393 (M + 1).

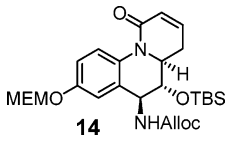
**Compound 13.**



**13**

The crude product was dissolved in 30 mL of $CH_2Cl_2$, and $Et_3N$ (0.04 mL, 0.286 mmol) was added to this solution at −45 °C. Following this, the acryloyl chloride (16 mL, 0.196 mmol) was then added slowly, and the reaction mixture was warmed to −10 °C and stirred for an additional 2 h. The reaction was quenched with saturated $NaHCO_3$ solution, extracted with $CH_2Cl_2$ (3 × 30 mL), and dried over anhydrous $MgSO_4$. The crude product was dissolved in $CH_2Cl_2$ and cooled to −78 °C. To this reaction mixture were added 2,6-lutidine (35 $\mu$L, 0.306 mmol) and TBSOTf (45 $\mu$L, 0.196 mmol) at −78 °C and the mixture was warmed to −50 °C. The reaction mixture was stirred for 4 h, quenched with saturated $NaHCO_3$, extracted with $CH_2Cl_2$ (3 × 30 mL), and dried over anhydrous $MgSO_4$. The solvent was removed on a rotovap, and the crude product was separated by flash column chromatography using 20% EtOAc in hexane to obtain compound **13** (51 mg, 60% over three steps). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.60−6.80 (m, 3H), 5.93 (m, 1H), 5.80 (m, 1H), 5.33 (d, 1H, $J$ = 17.1 Hz), 5.22 (m, 3H), 5.01 (d, 1H, $J$ = 10.1 Hz), 4.97 (d, 1H, $J$ = 17.1 Hz), 4.87 (d, 1H, $J$ = 7.9 Hz), 4.60 (d, 2H, $J$ = 5.4 Hz), 4.54 (m, 2H), 4.20 (bs, 1H), 3.84 (bs, 1H), 3.81 (m, 2H), 3.55 (m, 2H), 3.35 (s, 3H), 2.23 (m, 2H), 2.01 (m, 2H), 0.85 (m, 9H), 0.14 (s, 3H), 0.11 (s, 3H); MS (EI) *m*/*z* (rel. intensity) 561 (M + 1).

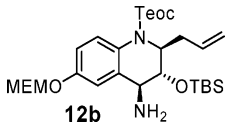
**Compound 14.**



**14**

To a solution of an olefin derivative **13** (30 mg, 0.0672 mmol) in $CH_2Cl_2$ was added 10 mol % second-generation Grubbs' catalyst (6.0 mg, 0.007 mmol). The reaction mixture was stirred for 30 min at room temperature. The solvent was removed on a rotovap, and the crude product was purified by flash column chromatography using 30% EtOAc in hexane to obtain the tricyclic product **14** (28 mg, 80%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.62 (d, 1H, $J$ = 8.5 Hz), 7.02 (m, 3H), 6.58 (m, 1H), 6.06 (d, 1H, $J$ = 9.8 Hz), 6.00 (m, 1H), 5.36 (d, 1H, $J$ = 17 Hz), 5.27 (m, 2H), 5.01 (m, 1H), 4.86 (t, 1H, $J$ = 7.7 Hz), 4.63 (d, 2H, $J$ = 5.6 Hz), 3.96 (t, 1H, $J$ = 8.6 Hz), 3.83 (m, 3H), 3.58 (m, 2H), 3.39 (s, 3H), 2.72 (t, 2H, $J$ = 4 Hz), 0.91 (m, 9H), 0.11 (s, 3H), 0.10 (s, 3H); $^{13}$C NMR 163.7 (1C), 156.6 (1C), 155.1 (1C), 139.0 (1C), 133.0 (1C), 132.4.1 (1C), 126.6 (1C), 126.0 (1C), 118.3 (1C), 116.1 (1C), 115.9 (1C), 94.0 (1C), 72.4 (1C), 71.9 (1C), 68.0 (1C), 67.9 (1C), 66.3 (1C), 60.8 (1C), 59.4 (1C), 57.8 (1C), 26.1 (3C), 25.8 (2C), 18.3 (1C), −3.9 (1C); MS (EI) $m/z$ (rel. intensity) 532 (M + 1).

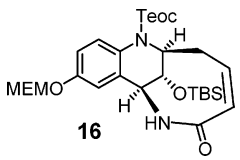
**Compound 12b.**



**12b**

To a solution of compound **12** (50.0 mg, 0.0769 mmol) in 30 mL of $CH_2Cl_2$ was added $Pd(PPh_3)_4$ (4.0 mg, 0.0076 mmol) at 0 °C, and the mixture was stirred vigorously. To this reaction mixture, piperidine (38 $\mu$L, 0.384 mmol) was added slowly, and the mixture was warmed to room temperature. The reaction mixture was stirred for 1 h at the same temperature. The solvent was removed on a rotovap, and the crude residue was purified by flash column chromatography using 1% MeOH in $CH_2Cl_2$ to give **12b**, 34.0 mg (80%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.41 (m, 1H), 7.14 (m, 1H), 6.96 (m, 1H), 5.73 (m, 1H), 5.31 (m, 2H), 5.01 (m, 2H), 4.41 (bs, 1H), 4.28 (bs, 2H), 3.85 (t, 2H, $J$ = 4.2 Hz), 3.73 (d, 1H, $J$ = 7.2 Hz), 3.61 (t, 2H, $J$ = 5.1 Hz), 3.39 (s, 3H), 3.30 (bs,1H), 2.47 (m, 1H), 2.07 (m, 1H), 1.64 (bs, 2H), 1.02 (bs, 2H), 0.96 (s, 9H), 0.17 (s, 6H), 0.02 (s, 9H); MS (EI) $m/z$ (rel. intensity) 567 (M + 1).

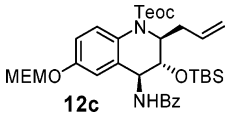
**Compound 16.**



**16**

To a solution of free amine (50 mg, 0.088 mmol) in 20 mL of $CH_2Cl_2$ was added triethylamine (22 $\mu$L, 0.157 mmol) at −78 °C. To this reaction mixture acryloyl chloride (10$\mu$L, 0.123 mmol) was added dropwise. The reaction mixture was warmed to −10 °C and then stirred for 30 min at the same temperature. The reaction mixture was quenched with saturated $NaHCO_3$ solution, extracted with $CH_2Cl_2$ (3 × 30 mL), and dried over anhydrous $MgSO_4$. The solvent was removed on a rotovap, and the residue was dried over a high vacuum pump. The crude product was further dissolved in 20 mL of $CH_2Cl_2$. To this reaction mixture was added second-generation Grubbs' catalyst (7 mg, 0.0082 mmol). The reaction mixture was refluxed for 24 h. The solvent was evaporated on a rotovap, and the crude product was purified by flash column chromatography using 30% EtOAc in hexane to obtain bridged tricyclic derivative **16** (36 mg, 70% over three steps). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.01−6.91 (m, 2H), 6.40 (m, 1H), 6.17 (dd, 1H, $J_1$ = 16.9, $J_2$ = 10.3 Hz), 5.73 (d, 1H, $J$ = 9.1 Hz), 5.60 (d, 1H, $J$ = 7.3 Hz), 5.26 (m, 2H), 5.05 (m, 1H), 4.87 (dd, 1H, $J_1$ = 7.2, $J_2$ = 3.0 Hz), 4.23 (bs, 2H), 4.03 (bs, 1H), 3.84 (t, 2H, $J$ = 4.6 Hz), 3.62 (m, 2H), 3.37 (s, 3H), 2.26 (m, 1H), 2.16 (m, 1H), 1.07 (t, 2H, $J$ = 9.2), 0.86 (m, 9H), 0.21 (s, 3H), 0.16 (s, 3H), 0.01 (m, 9H); $^{13}$C NMR 165.1 (1C), 155.9 (1C), 154.4 (1C), 134.4 (1C), 130.8 (1C), 130.5 (1C), 127.7 (1C), 117.9 (1C), 116.5 (1C), 115.5 (1C), 94.1 (1C), 72.0 (1C), 67.9 (1C), 64.6 (1C), 59.3 (1C), 58.1 (1C), 52.4 (1C), 35.2 (1C), 26.0 (3C), 18.3 (1C), 18.0 (1C), −1.1 (3C), −4.0 (2C), −4.5 (1C); MS (EI) $m/z$ (rel. intensity) 593 (M + 1) (see Figure 3).

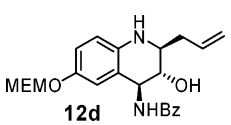
**Compound 12c.**



**12c**

To a solution of **12b** (50 mg, 0.088 mmol) in 20 mL of $CH_2Cl_2$ was added triethylamine (61 $\mu$L, 0.44 mmol) at −78 °C. To this reaction mixture was added benzoyl chloride (20 $\mu$L, 0.176 mmol); it was then allowed to warm to room temperature and stirred for an additional 12 h. The reaction mixture was quenched with saturated $NaHCO_3$ solution, extracted with $CH_2Cl_2$ (3 × 30 mL), and dried over $MgSO_4$ (anhydrous). The solvent was removed on a rotovap to obtain a yellowish oil. The crude product was purified by flash column chromatography using 10% EtOAc in hexane to obtain **12c** (53 mg, 90%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.10 (m, 1H), 7.79 (m, 2H), 7.62−7.35 (m, 4H), 7.07−6.96 (m, 2H), 6.16 (d, 1H), 5.83 (m, 1H), 5.23 (m, 2H), 5.04 (m, 2H), 4.66 (bs, 1H), 4.25 (bs, 2H), 4.14 (s, 1H), 3.82 (t, 2H, $J$ = 4.2 Hz), 3.57 (m, 2H), 3.31 (s, 3H), 2.32 (m, 1H), 2.23 (m, 1H), 1.08 (m, 2H), 0.87 (s, 9H), 0.23 (s, 3H), 0.17 (s, 3H), 0.05 (s, 9H); MS (EI) $m/z$ (rel. intensity) 671 (M + 1).

**Compound 12d.**



**12d**

To a solution of compound **12c** (50 mg, 0.074 mmol) in 20 mL THF was added TBAF (0.22 mL, 0.223 mmol). The reaction mixture was warmed to 0 °C and then stirred for 30 min at the same temperature. The reaction was quenched with $NaHCO_3$ and extracted with EtOAc (3 × 30 mL) and

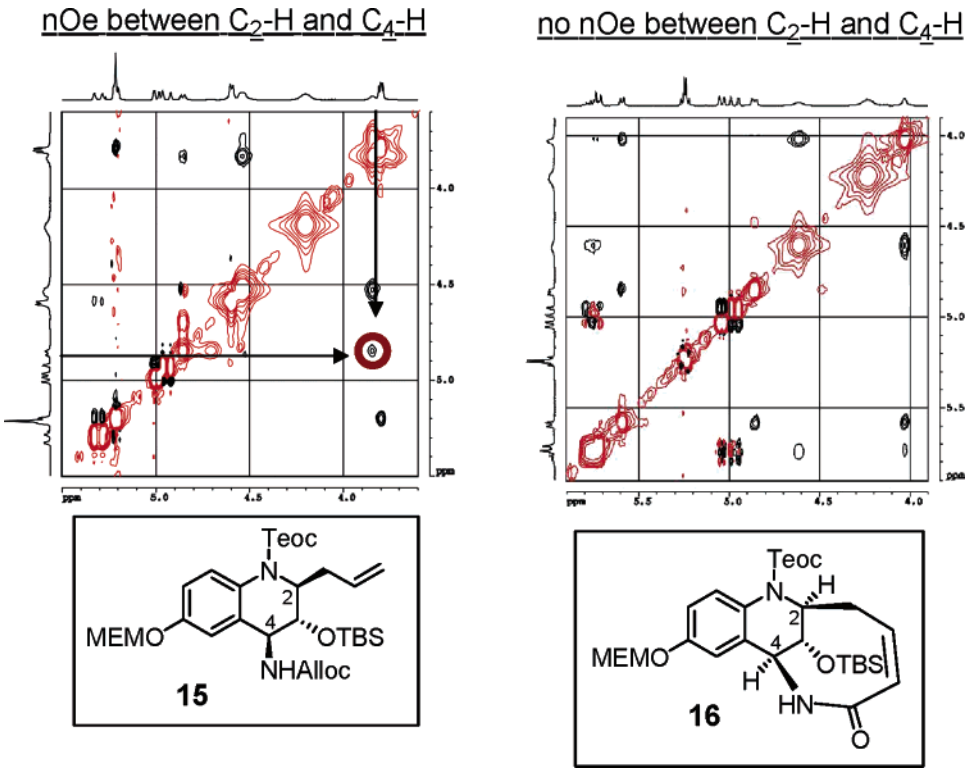
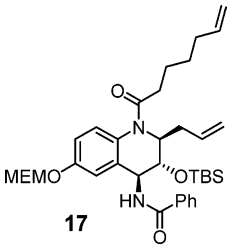



**Figure 3.**

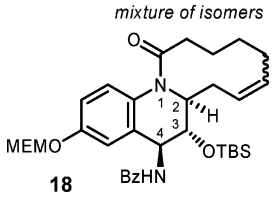
concentrated to obtain a yellowish oil. The crude product was separated by flash chromatography using 50% EtOAc in hexane to obtain **12d**, 24 mg (80%).

**Compound 17.**



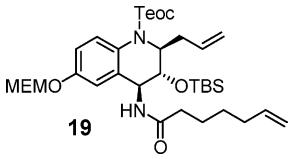

$SOCl_2$ (18 $\mu$L, 0.246 mmol) was added to 5-heptenoic acid (17 $\mu$L, 0.126 mmol) in 1.0 mL of $CH_2Cl_2$ at 0 °C and stirred for 12 h at room temperature. In another flask, to a solution of free amine (40 mg, 0.097 mmol) in 10 mL of $CH_2Cl_2$ was added triethylamine (86 $\mu$L, 0.62 mmol) at −78 °C. The acid chloride was added to the reaction mixture at −78 °C, and the mixture was warmed to −10 °C and stirred for an additional 30 min. The reaction mixture was quenched with saturated $NaHCO_3$ solution, extracted with $CH_2Cl_2$ (3 × 30 mL), and dried over $MgSO_4$ (anhydrous). The solvent was removed on a rotovap, and the crude product was dissolved in 20 mL of $CH_2Cl_2$. This was then directly submitted to the hydroxyl group protection. To this reaction mixture was added 2,6-lutidine (45.0 $\mu$L, 0.388 mmol) at −78 °C. Then TBSOTf (66.0 $\mu$L, 0.291 mmol was added slowly, and the mixture was stirred for 3 h at −10 °C. The reaction mixture was quenched with saturated $NaHCO_3$ solution, extracted with $CH_2Cl_2$ (3 × 30 mL), and dried over $MgSO_4$ (anhydrous). The solvent was evaporated on a rotovap. The crude product was purified by flash column chromatography using 10% EtOAc in hexane to obtain compound **17** (37 mg, 60% over 2 steps). MS (EI) *m*/*z* (rel. intensity) 636 (M+).

**Compound 18.**



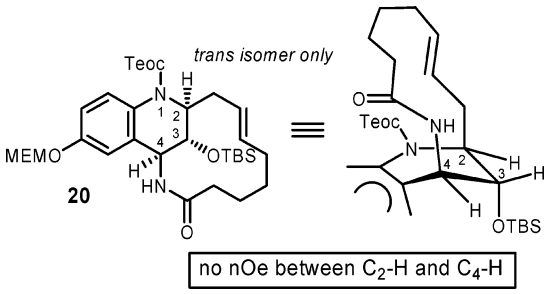

To a solution of compound **17** (30 mg, 0.0471 mmol) in $CH_2Cl_2$ was added 10 mol % of second-generation Grubbs' catalyst (0.4 mg, 0.00047 mmol). The reaction mixture was stirred for 1.5 h. The solvent was removed in a rotovap. The product was purified by flash column chromatography using 30% EtOAc in hexane to obtain **18** (19 mg, 68%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.80 7.20 (m, 6H), 7.03 (m, 2H), 5.56 (d, 1H, $J$ = 5.1 Hz), 5.45 (d, 1H, $J$ = 9.1 Hz), 5.26 (s, 2H), 4.66 (d, 1H, $J$ = 5.5 Hz), 4.66 (m, 1H), 4.26 (s, 2H), 3.87 (t, 2H, $J$ = 4.6 Hz), 3.62 (m, 2H), 3.38 (s, 3H), 2.49 (m, 2H), 2.21−1.85 (m, 4H), 1.44 (m, 2H), 1.08 (m, 2H), 0.84 (s, 9H), 0.21 (s, 3H), 0.15 (s, 3H); $^{13}$C NMR 165.0 (1C), 155.9 (1C), 154.4 (1C), 134.4 (2C), 130.7 (2C), 130.5 (1C), 127.7 (1C), 127.4 (2C), 118.0 (1C), 116.5 (1C), 115.5 (1C), 94.1 (1C), 72.0 (2C), 67.9 (2C), 64.6 (1C), 59.3 (1C), 58.0 (1C), 52.4 (1C), 35.2 (1C), 26.0 (3C), 18.2 (1C), 18.0 (1C), −1.1 (2C), −4.0 (2C), −4.5 (1C); MS (EI) *m*/*z* (rel. intensity) 532 (M + 1).

**Compound 19.**



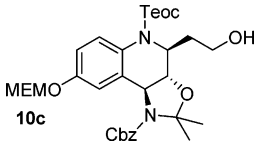

To a solution of the above amine derivative (50 mg, 0.088 mmol) in $CH_2Cl_2$ (20 mL) was added 5-heptenoic acid (18 $\mu$L, 0.132 mmol), DIC (70 mL, 0.44 mmol), and DMAP (11.0 mg, 0.09 mmol) at 0 °C. The reaction mixture was warmed to 0 °C and stirred for 24 h at the same temperature. The reaction mixture was quenched with saturated $NaHCO_3$ solution, extracted with $CH_2Cl_2$ (3 × 30 mL), and dried over $MgSO_4$ (anhydrous). The solvent was evaporated on a rotovap to obtain a yellowish oil. The crude product was purified by flash column chromatography using 10% EtOAc in hexane to obtain compound **19** (53 mg. 90%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.62−6.86 (m, 3H), 5.84 (m, 2H), 5.49 (d, 1H, $J$ = 7.2 Hz), 5.25 (m, 2H), 5.04 (d, 1H, $J$ = 17.3 Hz), 4.98 (d, 1H, $J$ = 10.8 Hz), 4.79 (d, 1H, $J$ = 4.8 Hz), 4.60 (bs, 1H), 4.22 (bs, 2H), 3.96 (bs, 1H), 3.84 (t, 2H, $J$ = 4.5 Hz), 3.62 (m, 2H), 3.37 (s, 3H), 2.37 (t, 2H, $J$ = 7.3 Hz), 2.25 (t, 2H, $J$ = 7.5 Hz), 2.10 (t, 2H, $J$ = 6.5 Hz), 1.71 (m, 2H), 1.47 (m, 2H), 1.05 (t, 2H, $J$ = 9.0 Hz), 0.86 (m, 9H), 0.19 (s, 3H), 0.14 (s, 3H), 0.04 (m, 9H).

**Compound 20.**




To a solution of compound **19** (30.0 mg, 0.0443 mmol) in $CH_2Cl_2$ was added 10 mol % of second-generation Grubbs' catalyst. The reaction mixture was stirred for 1.5 h. The solvent was removed on a rotovap, and the crude product was purified by flash column chromatography using 30% EtOAc in hexane to obtain bridged macrocycle **20** (24 mg, 85%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.80 (bs, 1H), 7.03 (m, 2H), 5.53 (d, 1H, $J$ = 15 Hz), 5.38 (d, 1H, $J$ = 15 Hz), 5.26 (s, 2H), 5.16 (d, 1H, $J$ = 6.7 Hz), 4.74 (s, 1H), 4.59 (d, 1H, $J$ = 6.7 Hz), 4.37 (q, 1H, $J$ = 1.3 Hz), 4.24 (bs, 2H), 3.87 (t, 2H, $J$ = 4.6 Hz), 3.61 (m, 2H), 3.39 (s, 3H), 2.65 (m, 1H), 2.72 (dt, 1H, $J_1$ = 15.1, $J_2$ = 4.5 Hz), 2.24 (m, 1H), 2.11 (m, 1H), 1.93 (m, 2H), 1.63 (m, 4H), 1.08 (t, 2H, $J$ = 10 Hz), 0.84 (s, 9H), 0.24 (s, 3H), 0.18 (s, 3H), 0.06 (s, 9H); $^{13}$C NMR 163.7 (1C), 156.6 (1C), 155.1 (1C), 139.0 (1C), 133.0 (1C), 132.4.1 (1C), 126.6 (1C), 126.0 (1C), 118.3 (1C), 116.1 (1C), 115.9 (1C), 94.0 (1C), 72.4 (1C), 71.9 (1C), 68.0 (1C), 67.9 (1C), 66.3 (1C), 60.8 (1C), 5.9.4 (1C), 57.8 (1C), 26.1 (3C), 25.8 (2C), 18.3 (1C), −3.9 (1C); $C_{33}H_{56}N_2O_7Si_2$. MS (EI) $m/z$ (rel. intensity) 649 (M + 1) (see Figure 4).

**Compound 10c.**




To a solution of ester **10a** (134 mg, 0.19 mmol) in 5 mL of anhydrous THF was added a 2 M lithium borohydride solution in THF (149.4 L, 0.29 mmol) at 0 °C, and the mixture was allowed to warm from 0 °C to RT and was stirred for an additional 15 h. Then it was again cooled to 0 °C, and more 2 M lithium borohydride solution in THF (50 $\mu$L, 0.09 mmol) was added, and the mixture was stirred for another 20 h. The reaction mixture was quenched by reverse addition onto ice-cold saturated $NH_4Cl$ solution. The aqueous layer was extracted with ethyl acetate (3 × 20 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude product was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 25% ethyl acetate/hexane to obtain the title **10c** compound (53.2 mg, 42%) as a colorless oil. MS ($ES^+$) $m/z$ 631 (M + 1); mol. formula $C_{32}H_{46}N_2O_9Si$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.33 (m, 5H, Ph), 7.17 (m, 1H, CHC*H*=C−N), 6.97 (dd, 1H, $J$ = 8.8 Hz and 2.7 Hz, C*H*CH=C−N), 6.81 (m, 1H, MEMOC−C*H*=C), 5.25 (m, 2H, C$H_2$Ph), 5.20 (m, 2H, MEM), 4.45 (m, 1H, C*H*Ncbz), 4.29 (m, 2H, $CH_2CH_2$OCON), 4.19 (m, 1H, NC*H*$CH_2$), 3.81 (m, 2H, MEM), 3.76 (m, 1H, C*H*O$CCMe_2$), 3.56 (m, 2H, MEM), 3.41 (s, 3H, MEM), 1.95 (m, 1H, C*H*OH), 1.73 (m, 1H, C*H*OH), 1.64 (brs, 3H, C$CH_3$), 1.57 (brs, 3H, C$CH_3$), 1.39 (m, 1H, C*H*$CH_2$OH), 1.27 (m, 1H, C*H*$CH_2$OH), 1.00 (m, 2H, $CH_2CH_2$TMS), 0.003 (s, 9H, TMS); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 155.38, 155.06, 154.75, 136.45, 132.81,

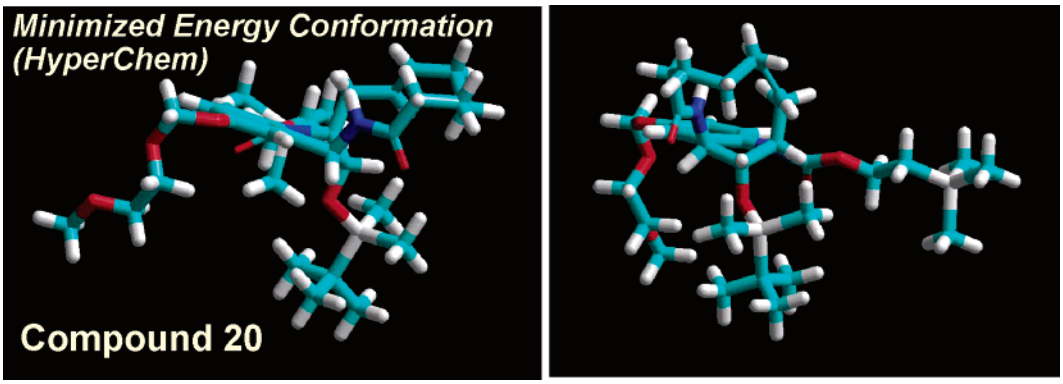
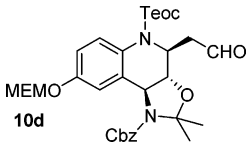



**Figure 4.**

128.87 (3C), 128.69, 128.58 (2C), 127.35, 114.17, 111.36, 102.08, 93.95, 83.55, 71.89, 68.01, 67.38, 65.16, 64.63, 59.85, 59.32, 54.55, 38.12, 25.71, 24.44, 17.97, −1.22 (3C).

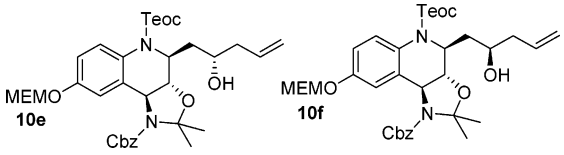
**Compound 10d.**



**10d**

To a solution of alcohol (53 mg, 0.08 mmol) in 5 mL of anhydrous $CH_2Cl_2$ was added Dess−Martin reagent (44.1 mg, 0.1 mmol) at room temperature, and the mixture was stirred for 1 h. Then 10 mL of a saturated solution of $NaHCO_3$ was added, the aqueous layer was extracted with $CH_2Cl_2$ (3 × 10 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude aldehyde **10d** (60 mg) was used for the next reaction without purification. MS ($ES^+$) *m*/*z* 629 (M + 1).

**Compounds 10e and 10f.**

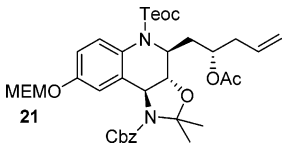



The crude aldehyde (53 mg, 0.08 mmol) was dissolved in 20 mL of anhydrous THF and cooled to −78 °C. Then 1 M $ZnCl_2$ solution in ether (337.2 $\mu$L, 0.33 mmol) was added, and the mixture was stirred at −78 °C for 30 min. Additional 1 M allyl magnesium bromide solution in ether (337.2 $\mu$L, 0.33 mmol) was added to it at −78 °C, and the reaction mixture was stirred for 2 h at −78 °C. The reaction mixture was slowly warmed to room temperature and stirred for an additional 15 h. The reaction mixture was quenched with aqueous $NH_4Cl$ and extracted with ethyl acetate (3 × 20 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude product was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 20% ethyl acetate/hexane as eluant to obtain the two diastereomers **10e** (19 mg) and **10f** (20 mg) in overall 86.7% yields as a colorless oil.

**10e.** MS ($ES^+$) *m*/*z* 671 (M + 1); mol. formula $C_{35}H_{50}N_2O_9Si$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.37 (m, 6H, Ph, CHC*H*═C−N), 6.97 (dd, 1H, *J* = 8.8 Hz and 2.5 Hz, C*H*CH═C−N), 6.82 (m, 1H, MEMOC−C*H*═C), 5.84 (m, 1H, $CHCH_2$-C*H*═$CH_2$), 5.25 (m, 4H, C$H_2$Ph, MEM), 5.10 (d, 2H, *J* = 16.3 Hz, $CH_2CH$═C$H_2$), 4.47 (m, 1H, NC*H*$CH_2$), 4.27 (m, 2H, $TMSCH_2CH_2O$), 4.22 (m, 1H, cbzN−C*H*), 3.86 (m, 1H, $CH_2CHOHCH_2$), 3.81 (m, 2H, MEM), 3.56 (m, 2H, MEM), 3.51 (m, 1H, C*H*O$CMe_2$), 3.39 (s, 3H, MEM), 2.28 (m, 2H, C$H_2$CH═$CH_2$), 1.73 (m, 2H, C$H_2$CHOH), 1.58 (brs, 3H, CC$H_3$), 1.27 (brs, 3H, CC$H_3$), 1.01 (m, 2H, $TMSCH_2CH_2O$), 0.01 (m, 9H, TMS); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 155.55, 155.42, 155.24, 136.22, 135.12 (2C), 129.03, 128.88 (3C), 128.74 (2C), 128.56, 117.91, 114.32, 111.89, 100.30, 94.06, 83.22, 71.89, 68.04, 67.29, 64.93, 60.07, 59.39, 55.31, 42.28, 41.86, 30.01, 26.39 (2C), 18.09, −1.25 (3C).

**10f.** MS ($ES^+$) *m*/*z* 671 (M + 1); mol. formula $C_{35}H_{50}N_2O_9Si$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.36 (m, 5H, Ph), 7.18 (m, 1H, CHC*H*═C−N), 6.95 (dd, 1H, *J* = 9.0 Hz and 3.2 Hz, C*H*CH═C−N), 6.84 (m, 1H, MEMOC−C*H*═C), 5.89 (m, 1H, $CHCH_2CH$═$CH_2$), 5.30−5.08 (m, 6H, C$H_2$Ph, MEM, $CH_2CH$═C$H_2$), 4.46 (m, 1H, NC*H*$CH_2$), 4.30 (m, 2H, $TMSCH_2CH_2O$), 4.25 (m, 1H, cbzN−C*H*), 3.87 (m, 1H, $CH_2CHOHCH_2$), 3.81 (m, 2H, MEM), 3.55 (m, 2H, MEM), 3.44 (m, 1H, C*H*O$CMe_2$), 3.38 (s, 3H, MEM), 2.36−2.28 (m, 1H, C*H*CH═$CH_2$), 2.28−2.20 (m, 1H, C*H*CH═$CH_2$), 1.70 (m, 2H, C$H_2$CHOH), 1.67 (brs, 3H, CC$H_3$), 1.58 (brs, 3H, CC$H_3$), 1.00 (m, 2H, $TMSCH_2CH_2O$), 0.004 (m, 9H, TMS); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 156.78, 155.84, 155.11, 136.21, 135.60, 134.10, 128.88 (2C), 128.70 (3C), 128.58, 128.33, 117.18, 114.22, 111.86, 100.29, 93.98, 83.60, 71.86, 68.13, 67.37, 65.32, 60.04, 59.34, 54.76, 43.11, 41.59, 30.01, 26.36 (2C), 17.89, −1.27 (3C).

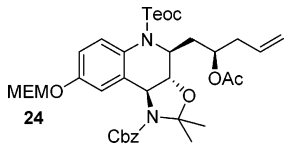
**Compound 21.**



**21**

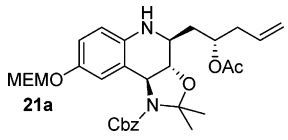
To a solution of alcohol (19 mg, 0.028 mmol) in 4 mL of dry $CH_2Cl_2$ at 0 °C was added dimethyl aminopyridine (3.7 mg, 0.031 mmol), and the mixture was stirred for 5 min. Then acetic anhydride (39.7 $\mu$L, 0.424 mmol) was added, and the reaction mixture was slowly warmed to room temperature and allowed to stir for 15 h. The reaction was quenched with aqueous $NaHCO_3$ solution and extracted with $CH_2Cl_2$ (3 × 15 mL). The combined organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude product was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 20% ethyl acetate/hexane as eluant to obtain title compound **21** (16 mg, 79.2%) as a colorless oil. MS ($ES^+$) *m*/*z* 713 (M + 1); mol. formula $C_{37}H_{52}N_2O_{10}Si$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.34 (m, 6H, Ph, CHC*H*═C−N), 6.97 (m, 1H, C*H*CH═C−N), 6.80 (m, 1H, MEMOC−C*H*═C), 5.72 (m, 1H, $CHCH_2CH$═$CH_2$), 5.25 (m, 2H, $CH_2Ph$), 5.19 (m, 2H, MEM), 5.08 (m, 2H, $CHCH_2CH$═C$H_2$), 4.95 (m, 1H, $CH_2CHOAcCH_2$), 4.43 (m, 1H, NC*H*$CH_2$), 4.27 (m, 2H, $TMSCH_2CH_2O$), 4.22 (m, 1H, CbzN−CH), 3.81 (m, 2H, MEM), 3.56 (m, 2H, MEM), 3.47 (m, 1H, C*H*O$CMe_2$), 3.39 (s, 3H, MEM), 2.39 (m, 2H, $CHCH_2CH$═$CH_2$), 2.20 (m, 1H, C*H*CHOAc$CH_2$), 1.90 (s, 3H, $COCH_3$), 1.70 (m, 4H, $CCH_3$, C*H*CHOAc$CH_2$), 1.59 (brs, 3H, $CCH_3$), 1.02 (m, 2H, $TMSCH_2CH_2O$), 0.01 (m, 9H, TMS); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 170.54, 155.62, 155.47, 155.17, 136.33, 133.49, 132.14, 129.09, 128.87 (3C), 128.73 (2C), 128.50, 118.44, 114.29, 111.89, 99.93, 94.04, 82.30, 71.88, 70.46, 68.00, 67.32, 64.78, 60.12, 59.34, 54.62, 39.20, 37.26, 26.26 (2C), 21.35, 17.97, −1.23 (3C).

**Compound 24.**



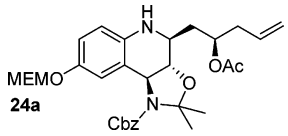

To a solution of alcohol (20 mg, 0.029 mmol) in 4 mL of dry $CH_2Cl_2$ at 0 °C was added dimethylaminopyridine (3.7 mg, 0.031 mmol), and the mixture was stirred for 5 min. Then acetic anhydride (40 $\mu$L, 0.424 mmol) was added, and the reaction mixture was slowly warmed to room temperature and allowed to stir for 15 h. The reaction was quenched with aqueous $NaHCO_3$ solution and extracted with $CH_2Cl_2$ (3 × 15 mL). The combined organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude product was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 20% ethyl acetate/hexane as eluant to obtain the title compound **24** (15 mg, 70.5%) as a colorless oil. MS ($ES^+$) *m*/*z* 713 (M + 1); mol. formula $C_{37}H_{52}N_2O_{10}Si$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.33 (m, 6H, Ph, CHC*H*═C−N), 6.97 (m, 1H, C*H*CH═C−N), 6.80 (m, 1H, MEMOC−C*H*═C), 5.79 (m, 1H, $CHCH_2CH$═$CH_2$), 5.25 (m, 2H, $CH_2Ph$), 5.19 (m, 2H, MEM), 5.13−5.09 (d, 2H, *J* = 17.3 Hz, $CHCH_2CH$═$CH_2$), 5.02 (m, 1H, $CH_2CHOAcCH_2$), 4.39 (m, 1H, $NCHCH_2$), 4.25 (m, 2H, $TMSCH_2CH_2O$), 4.18 (m, 1H, CbzN−CH), 3.81 (m, 2H, MEM), 3.57 (m, 2H, MEM), 3.48 (m, 1H, C*H*$OCMe_2$), 3.39 (s, 3H, MEM), 2.44 (m, 1H, $CHCHCH$═$CH_2$), 2.38 (m, 1H, $CHCHCH$═$CH_2$), 2.07 (m, 1H, C*H*$CHOAcCH_2$), 2.01 (s, 3H, $COCH_3$), 1.73 (brs, 3H, $CCH_3$), 1.58 (m, 4H, $CCH_3$, C*H*$CHOAcCH_2$), 1.00 (m, 2H, $TMSCH_2CH_2O$), 0.01 (m, 9H, TMS); $^{13}C$ NMR (400 MHz, $CDCl_3$) $\delta$ 170.80, 155.52, 155.45, 155.14, 136.30, 133.61 (2C), 129.05, 128.85 (3C), 128.68 (2C), 128.51, 118.29, 114.16, 111.79, 100.04, 93.98, 83.16, 71.89, 70.49, 67.98, 67.37, 64.79, 60.12, 59.35, 54.55, 38.84, 38.40, 26.38 (2C), 21.70, 17.99, −1.27 (3C).

**Compound 21a.**



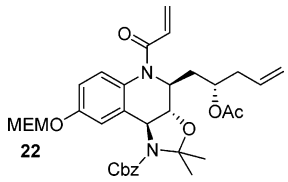

To a solution of *N*-Teoc-protected compound (16 mg, 0.022 mmol) in 4 mL of anhydrous THF was added a 1 M solution of tetrabutylammonium fluoride in THF (44.8 $\mu$L, 0.044 mmol), and the mixture was allowed to stir for 50 min at room temperature. The reaction mixture was quenched with aqueous $NH_4Cl$ solution, the aqueous layer was extracted with ethyl acetate (3 × 10 mL), the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude amine product was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 25% ethyl acetate/hexane as eluant to obtain title compound **21a** (12 mg, 94%) as a colorless oil. MS ($ES^+$) *m*/*z* 569 (M + 1); mol. formula $C_{31}H_{40}N_2O_8$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.38 (m, 5H, Ph), 6.87 (m, 1H, CHC*H*═C−N), 6.80 (dd, 1H, *J* = 8.3 Hz and 2.2 Hz, C*H*CH═C−N), 6.45 (d, 1H, *J* = 9 Hz, MEMOC−C*H*═C), 5.76 (m, 1H, $CHCH_2CH$═$CH_2$), 5.28 (m, 2H, $CH_2Ph$), 5.21 (m, 2H, MEM), 5.12 (m, 2H, $CHCH_2CH$═$CH_2$), 5.07 (m, 1H, $CH_2CHOAcCH_2$), 4.42 (m, 1H, $NCHCH_2$), 3.97 (m, 1H, CbzN−CH), 3.79 (m, 2H, MEM), 3.58 (m, 1H, C*H*$OCMe_2$), 3.55 (m, 2H, MEM), 3.38 (s, 3H, MEM), 2.39 (m, 2H, $CHCH_2CH$═$CH_2$), 2.09 (s, 3H, $COCH_3$), 2.04 (m, 1H, C*H*$CHOAcCH_2$), 1.70−1.60 (m, 4H, $CCH_3$, C*H*$CHOAcCH_2$), 1.55 (brs, 3H, $CCH_3$).

**Compound 24a.**




To a solution of *N*-Teoc-protected compound (15 mg, 0.021 mmol) in 4 mL of anhydrous THF was added a 1 M solution of tetrabutylammonium fluoride in THF (42 $\mu$L, 0.042 mmol), and the mixture was allowed to stir for 50 min at room temperature. The reaction mixture was quenched with aqueous $NH_4Cl$ solution, the aqueous layer was extracted with ethyl acetate (3 × 10 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude amine product was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 25% ethyl acetate/hexane as eluant to obtain title compound **24a** (11.5 mg, 96%) as a colorless oil. MS ($ES^+$) *m*/*z* 569 (M + 1); mol. formula $C_{31}H_{40}N_2O_8$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.37 (m, 5H, Ph), 6.86 (m, 1H, CHC*H*═C−N), 6.80 (dd, 1H, *J* = 8.5 Hz and 2.5 Hz, C*H*CH═C−N), 6.48 (d, 1H, *J* = 9 Hz, MEMOC−C*H*═C), 5.76 (m, 1H, $CHCH_2CH$═$CH_2$), 5.29 (m, 2H, $CH_2Ph$), 5.20 (m, 2H, MEM), 5.15 (m, 2H, $CHCH_2CH$═$CH_2$), 5.09 (m, 1H, $CH_2CHOAcCH_2$), 4.46 (m, 1H, $NCHCH_2$), 4.14 (m, 1H, CbzN−CH), 3.79 (m, 2H, MEM), 3.60 (m, 1H, C*H*$OCMe_2$), 3.55 (m, 2H, MEM), 3.38 (s, 3H, MEM), 2.40 (m, 2H, $CHCH_2CH$═$CH_2$), 2.10 (s, 3H, $COCH_3$), 2.06 (m, 1H, C*H*$CHOAcCH_2$), 1.75−1.60 (m, 4H, $CCH_3$, C*H*$CHOAcCH_2$), 1.58 (brs, 3H, $CCH_3$).

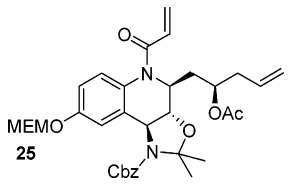
**Compound 22.**




To a solution of amine (12 mg, 0.021 mmol) in 5 mL of anhydrous $CH_2Cl_2$ at 0 °C was added triethyl amine (10.3 $\mu$L, 0.073 mmol), followed by acryloyl chloride (5.4 $\mu$L, 0.063 mmol). The reaction was allowed to stir at 0 °C for 1.5 h. The reaction was quenched with aqueous $NaHCO_3$, the aqueous layer was extracted with $CH_2Cl_2$ (3 × 10 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude amine product was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 25% ethyl acetate/hexane as eluant to obtain title compound **22** (9 mg, 68.5%) as a colorless oil. MS ($ES^+$) *m*/*z* 623 (M + 1); mol. formula $C_{34}H_{42}N_2O_9$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.46−7.30 (m, 5H, Ph),

7.04−7.00 (m, 2H, CHC*H*═C−N, C*H*CH═C−N), 6.85 (m, 1H, MEMOC−C*H*═C), 6.46 (dd, 1H, $J$ = 16.5 Hz and 3 Hz, COCH═C*H*), 6.38 (dd, 1H, $J$ = 16.5 Hz and 10 Hz, COC*H*═CH), 5.80−5.69 (m, 1H, $CHCH_2CH{=}CH_2$), 5.67 (dd, 1H, $J$ = 9.7 Hz and 2.5 Hz, COCH═C*H*), 5.25 (m, 2H, $CH_2Ph$), 5.19 (m, 2H, MEM), 5.11−5.03 (m, 2H, $CHCH_2$-$CH{=}CH_2$), 4.95−4.87 (m, 1H, $CH_2CHOAcCH_2$), 4.69 (m, 1H, $NCHCH_2$), 4.25 (m, 1H, CbzN−CH), 3.83 (m, 2H, MEM), 3.57 (m, 2H, MEM), 3.47−3.43 (dd, 1H, $J$ = 8.5 Hz and 1.5 Hz, $CHOCMe_2$), 3.40 (s, 3H, MEM), 2.43−2.40 (m, 2H, $CHCH_2CH{=}CH_2$), 2.29 (m, 1H, $CHCHOAcCH_2$), 1.93 (s, 3H, $COCH_3$), 1.71−1.61 (m, 3H, $CCH_3$), 1.59 (m, 1H, $CHCHOAcCH_2$), 1.57 (brs, 3H, $CCH_3$).

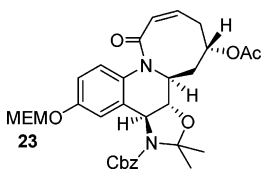
**Compound 25.**




**25**

To a solution of amine (12 mg, 0.021 mmol) in 5 mL of anhydrous $CH_2Cl_2$ at 0 °C was added triethyl amine (10.3 $\mu$L, 0.073 mmol), followed by acryloyl chloride (5.4 $\mu$L, 0.063 mmol). The reaction was allowed to stir at 0 °C for 1.5 h. The reaction was quenched with aqueous $NaHCO_3$, the aqueous layer was extracted with $CH_2Cl_2$ (3 × 10 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude amine product was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 25% ethyl acetate/hexane as eluant to obtain title compound **25** (8 mg, 61%) as colorless oil. MS ($ES^+$) $m/z$ 623 (M + 1); mol. formula $C_{34}H_{42}N_2O_9$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.47−7.29 (m, 5H, Ph), 6.96 (m, 2H, CHC*H*═C−N, C*H*CH═C−N), 6.85 (m, 1H, MEMOC−C*H*═C), 6.44 (dd, 1H, $J$ = 16.8 Hz and 2.7 Hz, COCH═C*H*), 6.36 (dd, 1H, $J$ = 17 Hz and 10 Hz, COC*H*═CH), 5.88−5.77 (m, 1H, $CHCH_2CH{=}CH_2$), 5.65 (dd, 1H, $J$ = 9.5 Hz and 2.7 Hz, COCH═C*H*), 5.26 (m, 2H, $CH_2Ph$), 5.20 (m, 2H, MEM), 5.16−5.07 (m, 2H, $CHCH_2CH{=}CH_2$), 5.05−4.97 (m, 1H, $CH_2CHOAcCH_2$), 4.60 (m, 1H, $NCHCH_2$), 4.25 (m, 1H, CbzN−CH), 3.84 (m, 2H, MEM), 3.58 (m, 2H, MEM), 3.54−3.49 (dd, 1H, $J$ = 8.5 Hz and 1.5 Hz, $CHOCMe_2$), 3.40 (s, 3H, MEM), 2.54−2.48 (m, 1H, $CHCHCH{=}CH_2$), 2.43−2.36 (m, 1H, $CHCHCH{=}CH_2$), 2.19 (m, 1H, $CHCHOAcCH_2$), 2.01 (s, 3H, $COCH_3$), 1.73−1.64 (m, 3H, $CCH_3$) 1.64−1.52 (m, 4H, $CHCHOAcCH_2$, $CCH_3$).

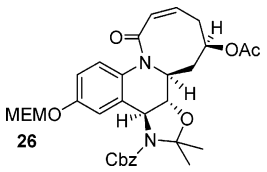
**Compound 23.**




**23**

To a solution of acryloylated compound (9 mg, 0.014 mmol) in 5 mL of anhydrous $CH_2Cl_2$ was added 10% mol of second-generation Grubbs' catalyst (1.5 mg, 0.0014 mmol), and the mixture was heated to 60 °C for 1 h. The reaction mixture was cooled and concentrated under vacuum. The crude product obtained was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 40% ethyl acetate/hexane as eluant to obtain title compound **23** (7 mg, 81.4%) as a colorless oil. MS ($ES^+$) $m/z$ 595 (M + 1); mol. formula $C_{32}H_{38}N_2O_9$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.41 (d, 1H, $J$ = 9.0 Hz, CHC*H*═C−N), 7.34 (m, 5H, Ph), 7.04 (dd, 1H, $J$ = 8.5 Hz and 3.0 Hz, C*H*CH═C−N), 6.82 (m, 1H, MEMO−C−C*H*═C), 6.12−6.03 (m, 2H, COC*H*═$CHCH_2$, COCH═C*H*$CH_2$), 5.29−5.08 (m, 5H, $CH_2Ph$, MEM, $CH_2$-$CHOAcCH_2$), 4.59 (m, 1H, $CONCHCH_2$), 4.25 (d, 1H, $J$ = 10.5 Hz, CbzN−C*H*), 3.80 (m, 2H, MEM), 3.56 (m, 2H, MEM), 3.39 (s, 3H, MEM), 3.32 (t, 1H, $J$ = 8 Hz, $CHOCMe_2$), 2.73−2.82 (m, 1H, CH═CH−C*H*CHOAc), 2.70−2.65 (dd, 1H, $J$ = 15.5 Hz and 6.5 Hz, CH═CH−C*H*CHOAc), 2.09 (s, 3H, $COCH_3$), 2.00 (m, 1H, CHC*H*-$CHOAcCH_2$), 1.87 (m, 1H, $CHCHCHOAcCH_2$), 1.72 (brs, 3H, $CCH_3$), 1.56 (brs, 3H, $CCH_3$); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 170.35, 167.90, 156.43, 154.25, 136.11, 134.32, 133.15, 129.17, 128.86 (3C), 128.57 (2C), 127.33, 125.68, 114.44, 112.12, 100.15, 93.92, 84.63, 71.85, 68.04, 67.87, 67.55, 59.49, 59.36, 54.17, 40.63, 33.00, 26.21 (2C), 21.43 (see Figures 5−8).

**Compound 26.**




**26**

To a solution of acryloylated compound (6 mg, 0.009 mmol) in 5 mL of anhydrous $CH_2Cl_2$ was added 10% mol of second-generation Grubbs' catalyst (1 mg, 0.0009 mmol), and the mixture was heated to 60 °C for 1 h. The reaction mixture was cooled and concentrated under vacuum. The crude product obtained was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 40% ethyl acetate/hexane as eluant to obtain title compound **26** (5 mg, 87%) as a colorless oil. MS ($ES^+$) $m/z$ 595 (M + 1); mol. formula $C_{32}H_{38}N_2O_9$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.39 (d, 1H, $J$ = 9.5 Hz, CHC*H*═C−N), 7.35 (m, 5H, Ph), 7.07 (dd, 1H, $J$ = 8.7 Hz and 2.7 Hz, C*H*CH═C−N), 6.83 (m, 1H, MEMO−C−C*H*═C), 6.24−6.15 (m, 1H, COC*H*═$CHCH_2$), 6.11 (d, 1H, $J$ = 11.3 Hz, COCH═C*H*$CH_2$), 5.29−5.11 (m, 4H, $CH_2Ph$, MEM), 4.94 (m, 1H, $CH_2CHOAcCH_2$), 4.38 (m, 1H, $CONCHCH_2$), 4.24 (d, 1H, $J$ = 10.7 Hz, CbzN−C*H*), 3.81 (m, 2H, MEM), 3.57 (m, 2H, MEM), 3.39 (s, 3H, MEM), 3.30 (t, 1H, $J$ = 8 Hz, $CHOCMe_2$), 2.89−2.80 (m, 1H, CH═CH−C*H*CHOAc), 2.52−2.47 (dd, 1H, $J$ = 14.3 Hz and 7.5 Hz, CH═CH−C*H*CHOAc), 2.25−2.17 (dd, 1H, $J$ = 15.0 Hz and 7.0 Hz, CHC*H*$CHOAcCH_2$), 2.06 (s, 3H, $COCH_3$), 1.71 (m, 4H, CHC*H*$CHOAcCH_2$, $CCH_3$), 1.56 (brs, 3H, $CCH_3$); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 170.35, 168.06, 156.52, 154.11, 136.13, 134.63, 131.94, 129.23, 128.89 (3C), 128.61 (2C), 127.45, 126.84, 114.42, 112.19, 100.04, 93.88, 84.65, 71.89, 68.40, 68.04, 67.58, 60.71, 59.43, 55.71, 39.75, 33.91, 26.34 (2C), 21.53 (see Figures 9 and 10).

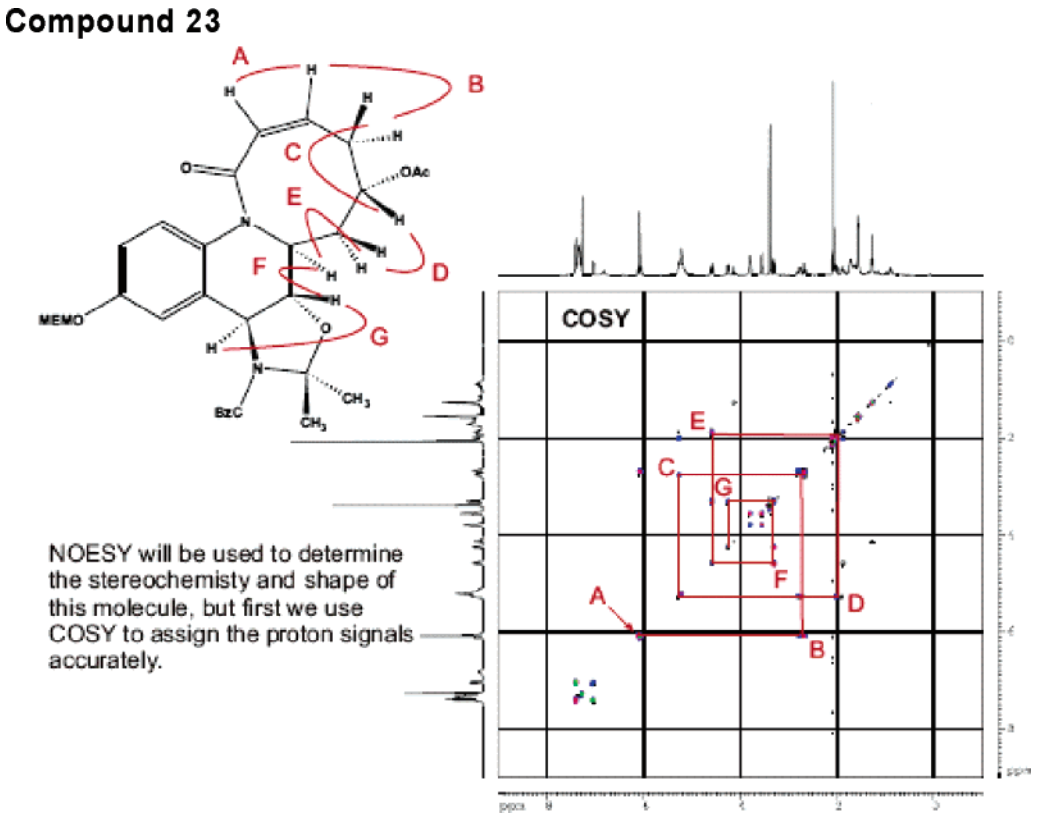



**Figure 5.**

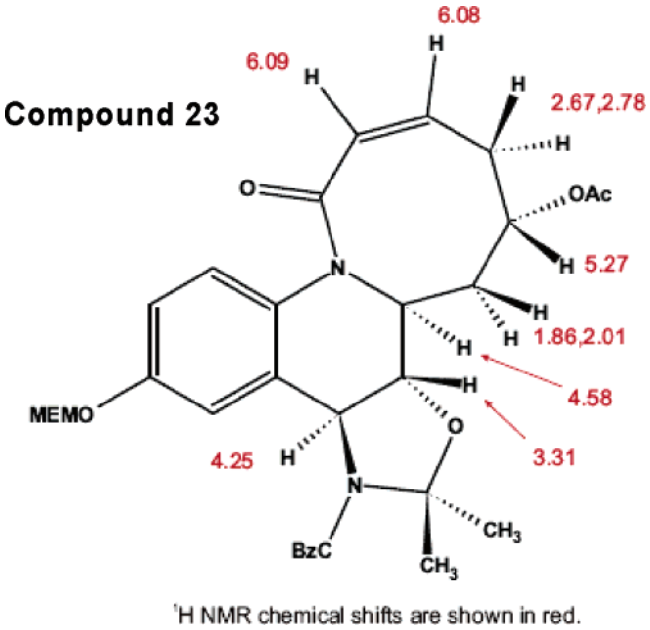
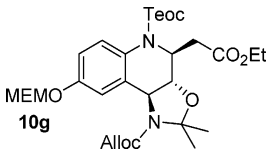


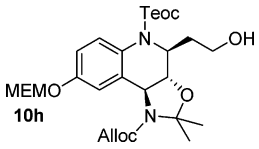

**Figure 6.**

**Compound 10g.**




To a solution of hydroxyl compound **10b** (1.0 g, 1.71 mmol) in 150 mL of anhydrous toluene was added 2-methoxyprop-1-ene (1.69 mL, 9.98 mmol) at room temperature, and the mixture was stirred for 15 min. Then pyridinium *p*-toluenesulfonate (21.5 mg, 0.08 mmol) and 4A molecular sieves was added to it, and the mixture was heated to 80 °C. The reaction was stirred at this temperature for 5 h. The reaction mixture was filtered and concentrated under vacuum and the crude product was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 25% ethyl acetate/hexane as eluant to obtain title compound **10g** (960 mg, 90.5%) as a colorless oil. MS ($ES^+$) *m*/*z* 623 (M + 1); mol. formula $C_{30}H_{46}N_2O_{10}Si$.

**Compound 10h.**




To a solution of ester (1.03 g, 1.65 mmol) in 150 mL of anhydrous THF was added a 2 M lithium borohydride solution in THF (1.24 mL, 2.48 mmol) at 0 °C, and the mixture was allowed to warm from 0 °C to RT and was stirred for 15 h. Then it was again cooled to 0 °C, and more 2 M lithium borohydride solution in THF (827 $\mu$L, 1.65 mmol) was added, and the mixture was stirred for another 20 h. The reaction mixture was quenched by reverse addition onto ice-cold saturated $NH_4Cl$ solution. The aqueous layer was extracted with ethyl acetate (3 × 50 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude product was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 25% ethyl acetate/hexane as eluant to obtain title compound **10h** (470 mg, 49%) as a colorless oil. MS ($ES^+$) *m*/*z* 581 (M + 1); mol. formula $C_{28}H_{44}N_2O_9Si$.

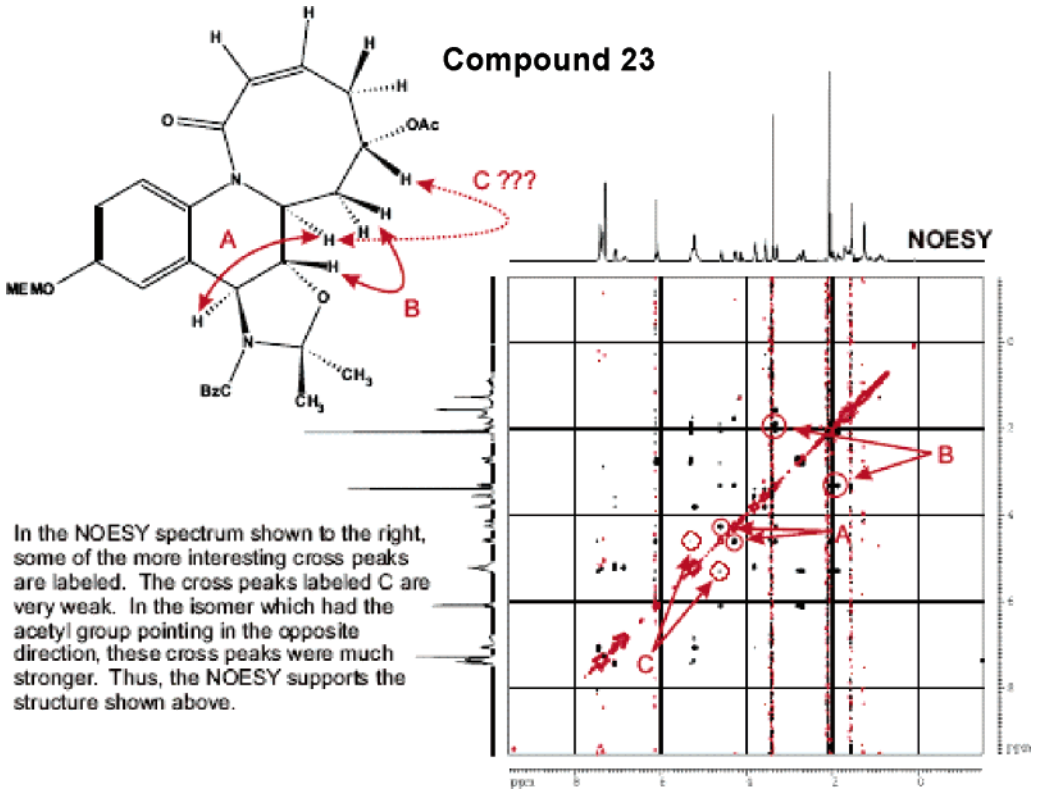



**Figure 7.**

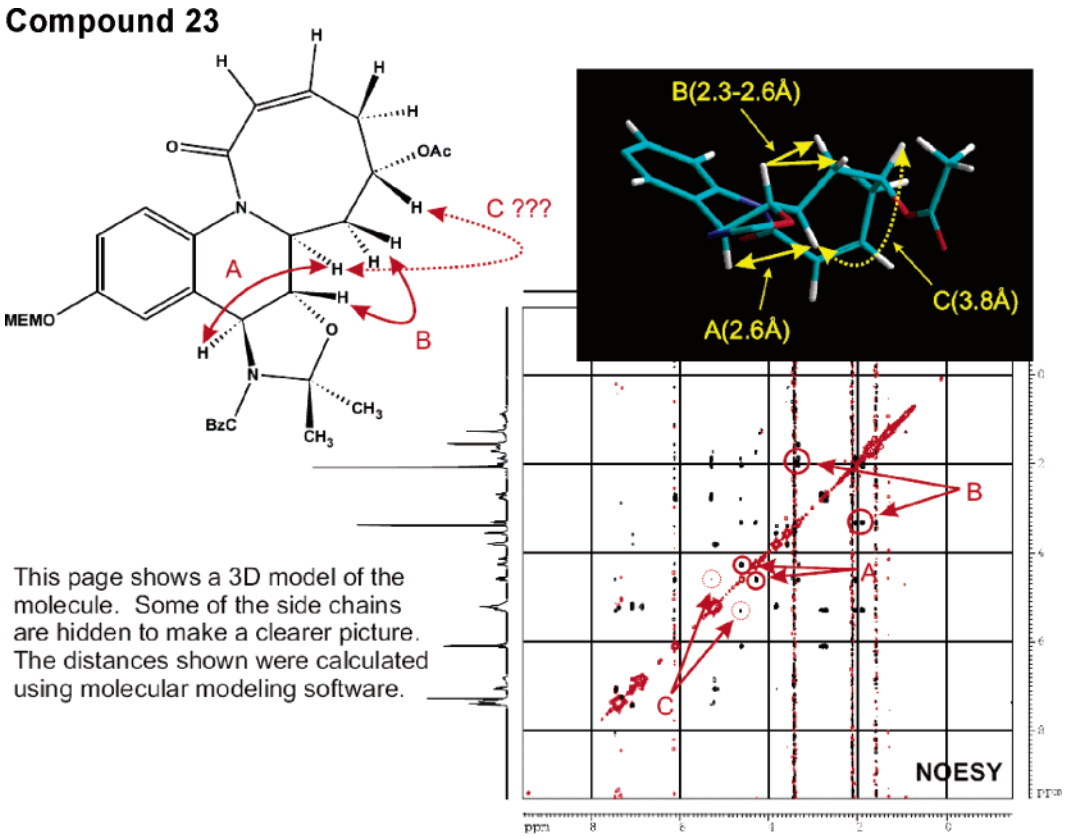



**Figure 8.**

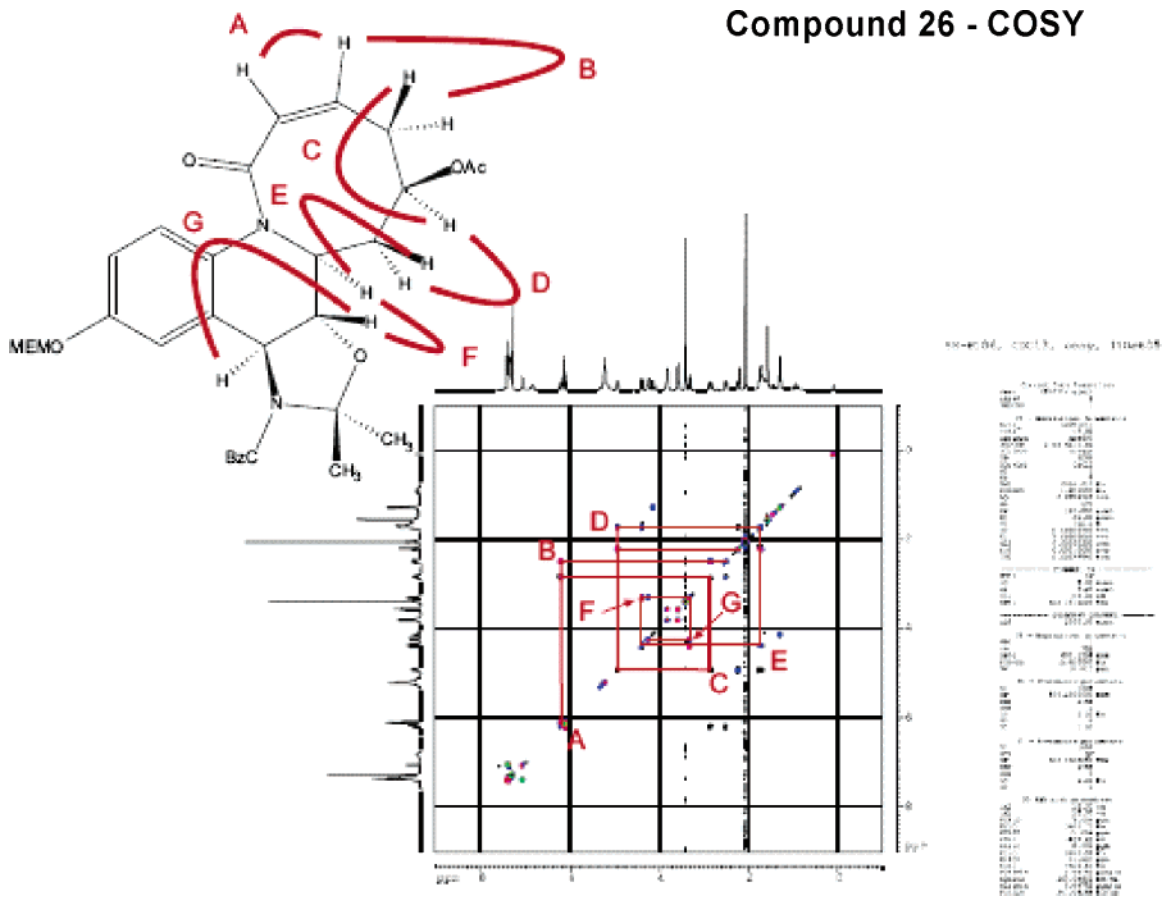
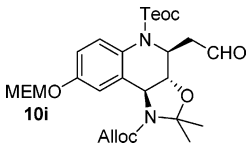


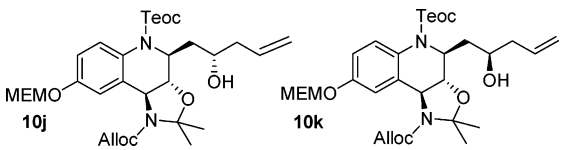

**Figure 9.**

**Compound 10i.**




To a solution of alcohol (608.0 mg, 1.04 mmol) in 100 mL of anhydrous $CH_2Cl_2$ was added Dess−Martin reagent (549.9 mg, 1.25 mmol) at room temperature, and the mixture was stirred for 2 h. Additional Dess−Martin reagent (183.3 mg, 0.41 mmol) was added, and the mixture was stirred at room temperature for an additional 1.5 h. Then 50 mL of a saturated solution of $NaHCO_3$ was added, the aqueous layer was extracted with $CH_2Cl_2$ (3 × 50 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude aldehyde **10i** (605 mg) was used for the next reaction without purification. MS ($ES^+$) *m*/*z* 579 (M + 1).

**Compound 10j and 10k.**




The crude aldehyde (605 mg, 1.04 mmol) was dissolved in 150 mL of anhydrous THF and cooled to −78 °C. Then 1 M $ZnCl_2$ solution in ether (4.18 mL, 4.18 mmol) was added, and the mixture was stirred at −78 °C for 30 min. Additional 1 M allyl magnesium bromide solution in ether (4.18 mL, 4.18 mmol) was added to it at −78 °C, and the reaction mixture was stirred for 2 h at −78 °C. The reaction mixture was slowly warmed to room temperature and stirred for an additional 15 h. The reaction mixture was quenched with aqueous $NH_4Cl$ and extracted with ethyl acetate (3 × 50 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude product was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 20% ethyl acetate/hexane as eluant to obtain two diastereomers **10j** (195 mg) and **10k** (200 mg) in overall 61% yield as a colorless oil.

**10j.** MS ($ES^+$) *m*/*z* 621 (M + 1); mol. formula $C_{31}H_{48}N_2O_9Si$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.27−7.16 (m, 1H, CHC*H*=C−N), 6.95 (dd, 1H, *J* = 8.7 Hz and 2.3 Hz, C*H*CH=C−N), 6.83 (m, 1H, MEMOC−C*H*=C), 6.04−5.89 (m, 1H, $OCH_2CH$=$CH_2$), 5.88−5.76 (m, 1H, $CHOHCH_2CH$=$CH_2$), 5.37−5.16 (m, 4H, MEM, $OCH_2CH$=$CH_2$), 5.15−5.04 (m, 2H, $CHOHCH_2CH$=$CH_2$), 4.77−4.59 (br d, 2H, *J* = 5.0 Hz, $OCH_2CH$=$CH_2$), 4.51−4.40 (m, 1H, NC*H*$CH_2$), 4.36−4.09 (m, 3H, $TMSCH_2CH_2O$, AllocNHC*H*), 3.93−3.83 (m, 1H, $CH_2CHOHCH_2$), 3.82 (t, 2H, *J* = 5.0 Hz, MEM), 3.57 (t, 2H, *J* = 5.0 Hz, MEM), 3.54−3.46 (m, 1H, C*H*OC$(CH_3)_2$), 3.39 (s, 3H, MEM), 2.27 (t, 2H, *J* = 6.5 Hz, $CHOHCH_2CH$=$CH_2$), 1.78−1.69 (br s, 3H, $CCH_3$), 1.68−

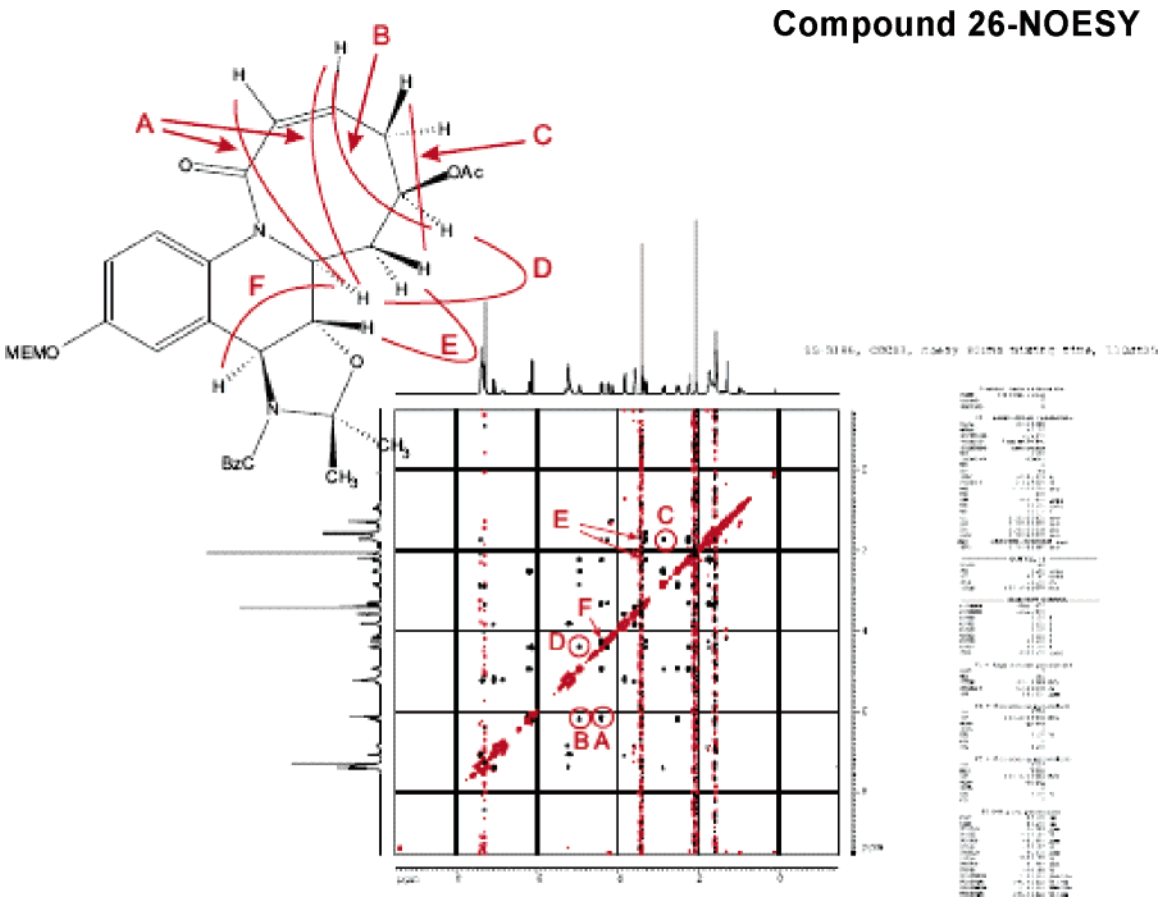
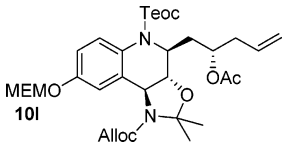



**Figure 10.**

1.60 (m, 2H, C$H_2$CHOHCH$_2$CH=CH$_2$), 1.60−1.55 (br s, 3H, CC$H_3$), 1.12−0.93 (m, 2H, TMSC$H_2$CH$_2$O), 0.10 to −0.09 (m, 9H, TMS); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 155.58, 155.52, 155.42, 135.12, 133.63, 132.64, 127.92, 127.78, 118.77, 117.89, 114.44, 111.67, 100.05, 94.06, 83.22, 71.79, 68.58, 68.03, 66.61, 64.92, 60.10, 59.37, 55.55, 42.28, 41.90, 26.41 (2C), 18.12, −1.23 (3C).

**10k.** MS (ES$^+$) *m*/*z* 621 (M + 1); mol. formula $C_{31}H_{48}N_2O_9$Si; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.15 (m, 1H, CHC*H*=C−N), 6.95 (dd, 1H, *J* = 8.5 Hz and 3.5 Hz, C*H*CH=C−N), 6.84 (m, 1H, MEMOC−C*H*=C), 6.03−5.82 (m, 2H, OCH$_2$C*H*=CH$_2$, CHOHCH$_2$C*H*=CH$_2$), 5.35−5.16 (m, 4H, MEM, OCH$_2$CH=C*H*$_2$), 5.14−5.02 (m, 2H, CHOHCH$_2$-CH=C*H*$_2$), 4.76−4.62 (br d, 2H, *J* = 5.2 Hz, OC*H*$_2$CH=CH$_2$), 4.53−4.42 (m, 1H, NC*H*CH$_2$), 4.34−4.10 (m, 4H, TMSCH$_2$C*H*$_2$O, CH$_2$CHO*H*CH$_2$, Alloc-NHC*H*), 3.88−3.77 (m, 1H, CH$_2$C*H*OHCH$_2$), 3.83 (t, 2H, *J* = 5.2 Hz, MEM), 3.57 (t, 2H, *J* = 5.2 Hz, MEM), 3.46−3.33 (m, 1H, C*H*OC(CH$_3$)$_2$), 3.39 (s, 3H, MEM), 2.37−2.27 (m, 1H, CHOHC*H*$_2$-CH=CH$_2$), 2.27−2.17 (m, 1H, CHOHC*H*$_2$CH=CH$_2$), 1.76−1.65 (br s, 3H, CC*H*$_3$), 1.65−1.60 (m, 1H, C*H*$_2$CHOHCH$_2$-CH=CH$_2$), 1.59−1.52 (m, 4H, 3H from CC*H*$_3$ and 1H from C*H*$_2$CHOHCH2CH=CH$_2$), 1.05−0.92 (m, 2H, TMSC*H*$_2$-CH$_2$O), 0.09 to −0.12 (m, 9H, TMS); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 156.83, 156.69, 155.90, 135.60, 134.20, 132.65, 128.63, 128.35, 118.74, 117.21, 114.38, 111.85, 100.05, 94.04, 83.62, 71.91, 68.07, 67.38, 66.58, 65.31, 60.05, 59.37, 54.81, 43.10, 41.63, 26.40 (2C), 17.92, −1.23 (3C).

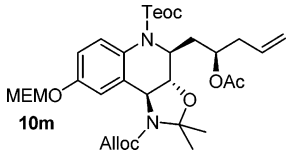
**Compound 10l.**




To a solution of alcohol (181 mg, 0.29 mmol) in 30 mL of dry $CH_2Cl_2$ at 0 °C was added dimethyl aminopyridine (38.9 mg, 0.32 mmol), and the mixture was stirred for 5 min. Then acetic anhydride (412.2 $\mu$L, 4.3 mmol) was added, and the reaction mixture was slowly warmed to room temperature and allowed to stir for 15 h. The reaction was quenched with aqueous $NaHCO_3$ solution and extracted with $CH_2Cl_2$ (3 × 25 mL). The combined organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude product was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 15% ethyl acetate/hexane as eluant to obtain title compound **10l** (192 mg, 99%) as a colorless oil. MS (ES$^+$) *m*/*z* 663 (M + 1); mol. formula $C_{33}H_{50}N_2O_{10}$Si; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.25 (m, 1H, CHC*H*=C−N), 6.95 (m, 1H, C*H*CH=C−N), 6.82 (m, 1H, MEMOC−C*H*=C), 6.02−5.86 (m, 1H, OCH$_2$C*H*=CH$_2$), 5.79−5.66 (m, 1H, CHOAcCH$_2$C*H*=CH$_2$), 5.35−5.13 (m, 4H, MEM, OCH$_2$CH=C*H*$_2$), 5.10−5.01 (m, 2H, CHOAcCH$_2$CH=C*H*$_2$), 4.98−4.86 (m, 1H, C*H*OAcCH$_2$-CH=CH$_2$), 4.74−4.59 (br d, 2H, *J* = 5.0 Hz, OC*H*$_2$CH=CH$_2$), 4.48−4.35 (m, 1H, NC*H*CH$_2$), 4.33−4.13 (m, 3H, TMSCH$_2$C*H*$_2$O, AllocNHC*H*), 3.82 (m, 2H, MEM), 3.56 (m,

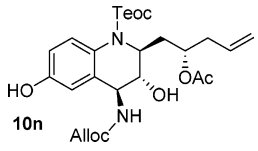
2H, MEM), 3.50−3.41 (m, 1H, C*H*OC $(CH_3)_2$), 3.38 (s, 3H, MEM), 2.42−2.35 (m, 2H, CHOAcC$H_2$CH═$CH_2$), 2.24−2.13 (m 1H, C$H_2$CHOAcCH$_2$CH═$CH_2$), 1.90 (s, 3H, COC$H_3$), 1.77−1.61 (m, 4H, 1H from C$H_2$CHOAcCH$_2$CH═$CH_2$, CC$H_3$), 1.55 (br s, 3H, CC$H_3$), 1.13−0.93 (m, 2H, TMSC$H_2$-CH$_2$O), 0.11 to −0.07 (m, 9H, TMS); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 170.52, 155.51, 155.46, 155.19, 133.66, 133.46, 132.70, 129.11, 127.84, 118.68, 118.44, 114.38, 111.63, 99.89, 94.06, 82.34, 71.86, 70.49, 68.01, 66.52, 64.80, 60.16, 59.37, 54.73, 39.22, 37.26, 26.33 (2C), 21.35, 18.05, −1.21 (3C).

**Compound 10m.**



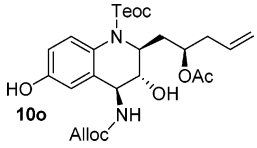

To a solution of alcohol (180 mg, 0.28 mmol) in 30 mL of dry $CH_2Cl_2$ at 0 °C was added dimethyl aminopyridine (39 mg, 0.31 mmol), and the mixture was stirred for 5 min. Then acetic anhydride (410.9 $\mu$L, 4.34 mmol) was added, and the reaction mixture was slowly warmed to room temperature and allowed to stir for 15 h. The reaction was quenched with aqueous $NaHCO_3$ solution and extracted with $CH_2Cl_2$ (3 × 25 mL). The combined organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude product was chromatographed over 9:1 hexane/triethylamine-neutralized silica using 15% ethyl acetate/hexane as eluant to obtain title compound **10m** (186 mg, 97%) as a colorless oil. MS ($ES^+$) *m*/*z* 663 (M + 1); mol. formula $C_{33}H_{50}N_2O_{10}Si$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.23−7.11 (m, 1H, CHC*H*═C−N), 6.94 (m, 1H, C*H*CH═C−N), 6.82 (m, 1H, MEMOC−C*H*═C), 6.04−5.85 (m, 1H, OCH$_2$C*H*═CH$_2$), 5.85−5.72 (m, 1H, CHOAcCH$_2$C*H*═CH$_2$), 5.40−5.15 (m, 4H, MEM, OCH$_2$CH═C$H_2$), 5.14−5.05 (m, 2H, CHOAcCH$_2$CH═C$H_2$), 5.04−4.98 (m, 1H, C*H*OAcCH$_2$-CH═CH$_2$), 4.75−4.60 (br d, 2H, $J$ = 5.1 Hz, OC$H_2$CH═CH$_2$), 4.44−4.31 (m, 1H, NC*H*CH$_2$), 4.31−4.12 (m, 3H, TMSCH$_2$C$H_2$O, AllocNHC*H*), 3.82 (m, 2H, MEM), 3.57 (m, 2H, MEM), 3.51−3.41 (m, 1H, C*H*OC $(CH_3)_2$), 3.39 (s, 3H, MEM), 2.50−2.40 (m, 1H, CHOAcC$H_2$CH═CH$_2$), 2.40−2.31 (m, 1H, CHOAcC$H_2$CH═CH$_2$), 2.11−2.03 (m 1H, C$H_2$-CHOAcCH$_2$CH═CH$_2$), 2.00 (s, 3H, COCH$_3$), 1.83−1.74 (m, 1H, C$H_2$CHOAcCH$_2$CH═CH$_2$), 1.73−1.66 (br s, 3H, CC$H_3$), 1.60−1.54 (br s, 3H, CC$H_3$), 1.11−0.89 (m, 2H, TMSC$H_2$-CH$_2$O), 0.12 to −0.09 (m, 9H, TMS); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 170.81, 155.58, 155.38, 155.15, 133.71, 133.61, 132.69, 128.93, 127.96, 118.69, 118.33, 114.40, 111.86, 99.80, 94.00, 83.11, 71.87, 70.51, 67.99, 66.52, 64.85, 60.13, 59.30, 54.64, 38.76, 38.40, 26.38 (2C), 21.67, 18.00, −1.25 (3C).

**Compound 10n.**



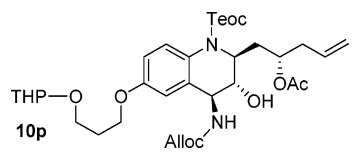

To a solution of *O*-MEM-protected compound (192 mg, 0.29 mmol) in 10 mL of anhydrous $CH_2Cl_2$/ethanol (9:1) solution was added *p*-toluenesulfonic acid monohydrate (56.2 mg, 0.29 mmol), and the mixture was heated at 50 °C for 28 h. The reaction was monitored by HPLC−MS. The reaction mixture was cooled and concentrated under vacuum. The residue was dissolved in $CH_2Cl_2$ and washed with water (2 × 10 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration,, it was concentrated under vacuum and used for the next step as crude material **10n** (130 mg). MS ($ES^+$) *m*/*z* 535 (M + 1); mol. formula $C_{26}H_{38}N_2O_8Si$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.21 (m, 1H, CHC*H*═C−N), 6.70 (m, 2H, C*H*CH═C−N, HOC−C*H*═C), 6.00−5.83 (m, 1H, OCH$_2$C*H*═CH$_2$), 5.77−5.62 (m, 1H, CHOAcCH$_2$C*H*═CH$_2$), 5.40−5.19 (m, 3H, CHO*H*, OCH$_2$CH═C$H_2$), 5.16−4.96 (m, 3H, CHOAcCH$_2$CH═C$H_2$, C*H*OAcCH$_2$CH═CH$_2$), 4.68−4.51 (m, 4H, OC$H_2$CH═CH$_2$, TMSCH$_2$C$H_2$O), 4.40 (m, 1H, NC*H*CH$_2$), 4.27−4.22 (m, 1H, AllocNHC*H*), 3.53 (m, 1H, C*H*OH), 2.43−2.26 (m, 2H, CHOAcC$H_2$CH═CH$_2$), 1.98 (s, 3H, COC$H_3$), 1.71−1.57 (m 2H, C$H_2$CHOAcCH$_2$-CH═CH$_2$), 1.11−0.98 (m, 2H, TMSC$H_2$CH$_2$O), 0.11 to −0.08 (m, 9H, TMS).

**Compound 10o.**




To a solution of *O*-MEM-protected compound (186 mg, 0.28 mmol) in 10 mL of anhydrous $CH_2Cl_2$/ethanol (9:1) solution was added *p*-toluenesulfonic acid monohydrate (53.4 mg, 0.28 mmol) and heated at 50 °C for 28 h. The reaction was monitored by HPLC/MS. The reaction mixture was cooled and concentrated under vacuum. The residue was dissolved in $CH_2Cl_2$ and washed with water (2 × 10 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration, it was concentrated under vacuum and used for the next step as crude material **10o** (143 mg). MS ($ES^+$) *m*/*z* 535 (M + 1); mol. formula $C_{26}H_{38}N_2O_8Si$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.24−7.14 (m, 1H, CHC*H*═C−N), 6.77−6.59 (m, 2H, C*H*CH═C−N, HOC−C*H*═C), 5.99−5.78 (m, 1H, OCH$_2$C*H*═CH$_2$), 5.75−5.60 (m, 1H, CHOAcCH$_2$C*H*═CH$_2$), 5.52 (m, 1H, CHO*H*), 5.36−5.14 (m, 2H, OCH$_2$CH═C$H_2$), 5.10−4.97 (m, 2H, CHOAcCH$_2$CH═C$H_2$), 4.97−4.88 (m, 1H, C*H*OAcCH$_2$CH═CH$_2$), 4.67−4.47 (m, 4H, OC$H_2$-CH═CH$_2$, TMSCH$_2$C$H_2$O), 4.40 (m, 1H, NC*H*CH$_2$), 4.31−4.14 (m, 1H, AllocNHC*H*), 3.61 (m, 1H, C*H*OH), 2.51−2.21 (m, 2H, CHOAcC$H_2$CH═CH$_2$), 2.03 (s, 3H, COC$H_3$), 1.77−1.57 (m 2H, C$H_2$CHOAcCH$_2$CH═CH$_2$), 1.08−0.96 (m, 2H, TMSC$H_2$CH$_2$O), 0.06 to −0.09 (m, 9H, TMS).

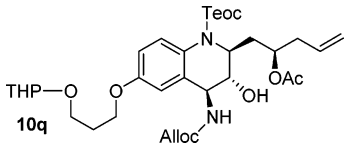
**Compound 10p.**




To a solution of hydroxyl compound (124 mg, 0.23 mmol) in 5 mL of anhydrous DMF was added baked $Cs_2CO_3$ (113.4

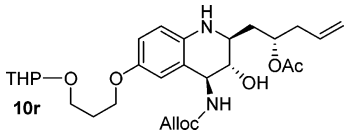
mg, 0.34 mmol), followed by 3-(tetrahydro-2*H*-pyran-2-yloxy)propyl 4-methylbenzene sulfonate (109.3 mg, 0.34 mmol) and, the mixture was allowed to stir for 24 h at room temperature. Then again, baked $Cs_2CO_3$ (37.8 mg, 0.11 mmol), followed by 3-(tetrahydro-2*H*-pyran-2-yloxy)propyl 4-methylbenzenesulfonate (36.4 mg, 0.11 mmol), was added and, the mixture was stirred for an additional 24 h. DMF was evaporated under vacuum, and the residue was dissolved in ethyl acetate. The organic layer was washed with water (2 × 15 mL) and brine (1 × 15 mL) and dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude product was chromatographed using 30% ethyl acetate/hexane as eluant to obtain the title compound **10p** (77 mg, 49%) as a colorless oil. MS ($ES^+$) *m*/*z* 677 (M + 1); mol. formula $C_{34}H_{52}N_2O_{10}Si$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.36−7.23 (m, 1H, CHC*H*═C−N), 6.84−6.73 (m, 2H, C*H*CH═C−N, $CH_2CH_2OC-CH$═C), 6.00−5.84 (m, 1H, $OCH_2CH$═$CH_2$), 5.76−5.61 (m, 1H, $CHOAcCH_2CH$═$CH_2$), 5.47−5.29 (br d, 1H, $J$ = 17.0 Hz, $OCH_2CH$═$CH_2$), 5.28−5.18 (br d, 1H, $J$ = 10.8 Hz, $OCH_2CH$═$CH_2$), 5.09−5.00 (m, 2H, $CHOAcCH_2CH$═$CH_2$), 5.00−4.93 (m, 1H, C*H*O$AcCH_2CH$═$CH_2$), 4.65−4.61 (br d, 2H, $J$ = 5.2 Hz, O$CH_2CH$═$CH_2$), 4.60−4.54 (m, 2H, $TMSCH_2CH_2O$), 4.46−4.35 (m, 1H, OC*H*O), 4.29−4.13 (m, 2H, NC*H*$CH_2$, AllocNHC*H*), 4.10−4.00 (t, 2H, $J$ = 6.5 Hz, $CH_2OAr$), 3.94−3.88 (m, 1H, $CH_2OCH$), 3.88−3.79 (m, 1H, $CH_2OCH$), 3.60−3.52 (m, 1H, $CH_2OTHP$), 3.52−3.44 (m, 2H, C*H*OH and 1H from $CH_2OTHP$), 2.41−2.26 (m, 2H, $CHOAcCH_2$-CH═$CH_2$), 2.10−2.00 (m, 2H, $OCH_2CH_2CH_2O$), 1.95 (s, 3H, $COCH_3$), 1.90−1.76 (m, 2H, 1H from $CH_2CH_2CHOO$ and 1H from $CH_2CHOAcCH_2CH$═$CH_2$), 1.74−1.61 (m 2H, 1H from $CH_2CHOAcCH_2CH$═$CH_2$ and 1H from $CH_2CH_2$-CHOO), 1.60−1.44 (m, 4H, 1H from $CH_2CH_2CHOO$, 1H from $CH_2CH_2CHOO$ and $CH_2CH_2OCHO$), 1.06−0.96 (m, 2H, $TMSCH_2CH_2O$), 0.09 to −0.08 (m, 9H, TMS); $^{13}C$ NMR (400 MHz, $CDCl_3$) $\delta$ 171.41, 157.02, 156.90, 155.09, 133.43, 132.85, 128.67, 127.44, 118.37, 113.46, 113.29, 110.41, 99.25, 70.89, 66.37, 65.46, 65.42, 64.69, 64.23, 62.72, 62.67, 57.22, 54.60, 38.95, 37.56, 30.92, 29.92, 25.68, 21.39, 19.98, 17.93, −1.28 (3C).

**Compound 10q.**




To a solution of hydroxyl compound (123 mg, 0.23 mmol) in 5 mL of anhydrous DMF was added baked $Cs_2CO_3$ (112.5 mg, 0.34 mmol), followed by 3-(tetrahydro-2*H*-pyran-2-yloxy)propyl 4-methyl benzenesulfonate (108.4 mg, 0.34 mmol), and the mixture was allowed to stir for 24 h at room temperature. Then again, baked $Cs_2CO_3$ (37.5 mg, 0.11 mmol), followed by 3-(tetrahydro-2*H*-pyran-2-yloxy)propyl 4-methylbenzenesulfonate (36.1 mg, 0.11 mmol), was added, and the mixture was stirred for an additional 24 h. DMF was evaporated under vacuum, and the residue was dissolved in ethyl acetate. The organic layer was washed with water (2 × 15 mL) and brine (1 × 15 mL) and dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude product was chromatographed using 30% ethyl acetate/hexane as eluant to obtain the title compound **10q** (60 mg, 39%) as a colorless oil. MS ($ES^+$) *m*/*z* 677 (M + 1); mol. formula $C_{34}H_{52}N_2O_{10}Si$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.37−7.28 (m, 1H, CHC*H*═C−N), 6.86−6.76 (m, 2H, C*H*CH═C−N, $CH_2CH_2OC-CH$═C), 6.02−5.89 (m, 1H, $OCH_2CH$═$CH_2$), 5.75−5.60 (m, 1H, $CHOAcCH_2CH$═$CH_2$), 5.40−5.34 (br d, 1H, $J$ = 17.2 Hz, $OCH_2CH$═$CH_2$), 5.27−5.22 (br d, 1H, $J$ = 16 Hz, $OCH_2CH$═$CH_2$), 5.15−5.07 (m, 1H, CHOH), 5.06−4.97 (m, 2H, $CHOAcCH_2CH$═$CH_2$), 4.97−4.87 (m, 1H, C*H*O$AcCH_2CH$═$CH_2$), 4.69−4.63 (br d, 2H, $J$ = 5.0 Hz, O$CH_2CH$═$CH_2$), 4.62−4.51 (m, 3H, OC*H*O, $TMSCH_2CH_2O$), 4.31−4.20 (m, 1H, NC*H*$CH_2$), 4.20−4.11 (m, 1H, AllocNHC*H*), 4.10−4.03 (t, 2H, $J$ = 6.0 Hz, $CH_2OAr$), 3.96−3.89 (m, 1H, $CH_2OCH$), 3.89−3.80 (m, 1H, $CH_2OCH$), 3.67−3.54 (m, 2H, $CH_2OTHP$), 3.54−3.46 (m, 1H, C*H*OH), 2.43−2.33 (m, 1H, $CHOAcCH_2CH$═$CH_2$), 2.33−2.24 (m, 1H, $CHOAcCH_2CH$═$CH_2$), 2.11−2.00 (m, 2H, $OCH_2CH_2CH_2O$), 2.04 (s, 3H, $COCH_3$), 1.87−1.77 (m, 1H, $CH_2CH_2CHOO$), 1.77−1.66 (m 3H, $CH_2CHOAcCH_2$-CH═$CH_2$ and 1H from $CH_2CH_2CHOO$), 1.63−1.46 (m, 4H, 1H from $CH_2CH_2CHOO$, 1H from $CH_2CH_2CHOO$ and $CH_2$-$CH_2OCHO$), 1.08−0.95 (m, 2H, $TMSCH_2CH_2O$), 0.07 to −0.05 (m, 9H, TMS); $^{13}C$ NMR (400 MHz, $CDCl_3$) $\delta$ 171.07, 157.02, 156.08, 155.46, 133.45, 132.80, 128.65, 127.70, 118.54, 118.37, 113.96, 111.17, 99.35, 70.20, 66.50, 65.56, 65.48, 64.84, 64.26, 62.79, 62.75, 55.90, 54.45, 38.66, 36.68, 31.00, 29.98, 25.71, 21.63, 19.96, 17.99, −1.22 (3C).

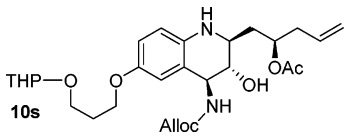
**Compound 10r.**




To a solution of *N*-Teoc-protected compound (77 mg, 0.12 mmol) in 10 mL of anhydrous THF was added a 1 M solution of tetrabutylammonium fluoride in THF (257.2 $\mu$L, 0.25 mmol), and the mixture was allowed to stir for 75 min at room temperature. The reaction mixture was quenched with aqueous $NH_4Cl$ solution, the aqueous layer was extracted with ethyl acetate (3 × 15 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude amine product was chromatographed using 35% ethyl acetate/hexane as eluant to obtain title compound **10r** (48 mg, 79.3%) as a colorless oil. MS ($ES^+$) *m*/*z* 533 (M + 1); mol. formula $C_{28}H_{40}N_2O_8$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 6.73 (m, 1H, CHC*H*═C−N), 6.67 (dd, 1H, $J$ = 8.8 Hz and 2.5 Hz, C*H*CH═C−N), 6.43 (d, 1H, $J$ = 8.5 Hz, $CH_2CH_2OC-CH$═C), 6.00−5.88 (m, 1H, $OCH_2CH$═$CH_2$), 5.83−5.70 (m, 1H, $CHOAcCH_2CH$═$CH_2$), 5.34 (dd, 1H, $J$ = 17.3 Hz and 1.5 Hz, $OCH_2CH$═$CH_2$), 5.24 (d, 1H, $J$ = 10.2 Hz, $OCH_2CH$═$CH_2$), 5.19 (br d, 1H, CHOH), 5.13−5.05 (m, 3H, $CHOAcCH_2CH$═$CH_2$, C*H*O$AcCH_2CH$═$CH_2$), 4.82 (t, 1H, $J$ = 8 Hz, OC*H*O), 4.65−4.60 (br d, 2H, $J$ = 5.2 Hz, O$CH_2CH$═$CH_2$), 4.60−4.56 (m, 1H, AllocNHC*H*), 4.00−3.93 (t, 2H, $J$ = 6.2 Hz, $CH_2OAr$), 3.92−3.78 (m, 3H, NC*H*$CH_2$, $CH_2OCHO$), 3.59−3.45 (m, 3H, $CH_2OTHP$, C*H*OH), 3.20 (t, 1H, $J$ = 8 Hz, $NHCHCH_2$-

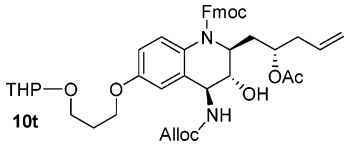
CHOAc), 2.47−2.27 (m, 3H, CHOAcC$H_2$CH═$CH_2$ and 1H from NHCHC$H_2$CHOAc), 2.07 (s, 3H, COC$H_3$), 2.03−1.96 (m, 2H, OC$H_2$C$H_2$C$H_2$O), 1.85−1.75 (m, 1H, C$H_2$C$H_2$-CHOO), 1.74−1.63 (m 1H, C$H_2$C$H_2$CHOO), 1.62−1.47 (m, 4H, 1H from C$H_2$C$H_2$CHOO, 1H from C$H_2$C$H_2$CHOO and C$H_2$C$H_2$OCHO); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 170.93, 158.66, 152.18, 138.81, 133.40, 132.64, 121.06, 118.57, 116.10, 115.67, 113.96, 99.12, 75.76, 73.47, 66.54, 60.08, 64.31, 62.54, 60.64, 56.89, 56.16, 39.47, 36.11, 30.95, 30.04, 25.67, 21.61, 19.87.

**Compound 10s.**



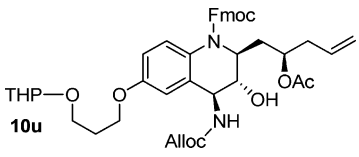

To a solution of *N*-Teoc-protected compound (54 mg, 0.079 mmol) in 4 mL of anhydrous THF was added a 1 M solution of tetrabutylammonium fluoride in THF (159.6 $\mu$L, 0.15 mmol), and the mixture was allowed to stir for 75 min at room temperature. The reaction mixture was quenched with aqueous $NH_4Cl$ solution, the aqueous layer was extracted with ethyl acetate (3 × 10 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude amine product was chromatographed using 35% ethyl acetate/hexane as eluant to obtain title compound **10s** (34 mg, 80.9%) as a colorless oil. MS ($ES^+$) *m*/*z* 533 (M + 1); mol. formula $C_{28}H_{40}N_2O_8$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.75 (m, 1H, CHC*H*═C−N), 6.71 (dd, 1H, *J* = 9 Hz and 2.5 Hz, C*H*CH═C−N), 6.55 (d, 1H, *J* = 9 Hz, $CH_2CH_2OC-CH$═C), 6.01−5.91 (m, 1H, $OCH_2CH$═$CH_2$), 5.81−5.71 (m, 1H, $CHOAcCH_2CH$═$CH_2$), 5.35 (dd, 1H, *J* = 17.0 Hz and 1.5 Hz, $OCH_2CH$═C$H_2$), 5.26 (dd, 1H, *J* = 10 Hz and 1 Hz, $OCH_2CH$═C$H_2$), 5.21−5.15 (m, 1H, CHOH), 5.15−5.08 (m, 3H, $CHOAcCH_2CH$═C$H_2$, C*H*O$AcCH_2CH$═$CH_2$), 4.84 (t, 1H, *J* = 12.5 Hz, OC*H*O), 4.70−4.62 (m, 2H, OC$H_2$CH═$CH_2$), 4.62−4.56 (m, 1H, AllocNHC*H*), 4.36−4.21 (br s, 1H, NH), 4.02−3.95 (t, 2H, *J* = 6.0 Hz, C$H_2$OAr), 3.94−3.87 (m, 1H, NC*H*$CH_2$), 3.87−3.81 (m, 2H, C$H_2$OCHO), 3.61−3.54 (m, 2H, C$H_2$OTHP), 3.54−3.46 (m, 1H, C*H*OH), 3.10 (t, 1H, *J* = 10 Hz, NHCHC$H_2$CHOAc), 2.42−2.35 (m, 2H, $CHOAcCH_2CH$═$CH_2$), 2.31 (t, 1H, *J* = 12 Hz, NHCHC$H_2$CHOAc), 2.05 (s, 3H, COC$H_3$), 2.07−2.00 (m, 2H, $OCH_2CH_2CH_2O$), 1.86−1.77 (m, 1H, $CH_2CH_2CHOO$), 1.76−1.62 (m 1H, C$H_2$C$H_2$-CHOO), 1.62−1.48 (m, 4H, 1H from $CH_2CH_2CHOO$, 1H from C$H_2$C$H_2$CHOO and C$H_2$C$H_2$OCHO); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 171.72, 158.71, 152.48, 138.99, 133.49, 132.58, 120.85, 118.62, 118.53, 116.57, 116.27, 113,76, 99.16, 76.39, 69.80, 69.68, 66.01, 64.30, 62.65, 56.79, 53.55, 39.68, 36.81, 30.94, 30.09, 35.75, 21.41, 19.88.

**Compound 10t.**




To a solution of amine (48 mg, 0.09 mmol) in 5 mL of ethyl acetate at room temperature was added 5% mol $NaHCO_3$ solution in water (3 mL), followed by FmocCl (36 mg, 0.13 mmol), and the mixture was allowed to stir at room temperature for 24 h. The two layers were separated, the aqueous layer was extracted with ethyl acetate (3 × 10 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude amine product was chromatographed using 35% ethyl acetate/hexane as eluant to obtain title compound **10t** (48 mg, 70.5%) as a colorless oil. MS ($ES^+$) *m*/*z* 755 (M + 1); mol. formula $C_{43}H_{50}N_2O_{10}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.79−7.70 (br s, 2H, Ph), 7.63−7.43 (m, 2H, Ph), 7.42−7.35 (br q, 2H, *J* = 7.0 Hz, Ph), 7.33−7.23 (m, 2H, Ph), 7.13−6.86 (m, 1H, CHC*H*═C−N), 6.85−6.77 (m, 1H, C*H*CH═C−N), 6.76−6.65 (m, 1H, $CH_2CH_2OC-CH$═C), 6.02−5.86 (m, 1H, $OCH_2CH$═$CH_2$), 5.74−5.58 (m, 1H, $CHOAcCH_2CH$═$CH_2$), 5.35 (d, 1H, *J* = Hz, $OCH_2CH$═C$H_2$), 5.25 (d, 1H, *J* = Hz, $OCH_2CH$═C$H_2$), 5.21−5.09 (m, 1H, OC*H*O), 5.02 (d, 2H, *J* = 11.7 Hz, $CHOAcCH_2CH$═C$H_2$), 4.97−4.86 (m, 1H, C*H*O$AcCH_2CH$═$CH_2$), 4.64 (br d, 2H, *J* = 5.0 Hz, OC$H_2$-CH═$CH_2$), 4.62−4.55 (m, 3H, COOC$H_2$CH, AllocNHC*H*), 4.54−4.47 (m, 1H, NC*H*$CH_2$), 4.46−4.29 (br s, 1H, NH), 4.26−4.15 (m, 1H, $COOCH_2CH$), 4.10−4.02 (br t, 2H, *J* = 5.5 Hz, C$H_2$OAr), 3.98−3.90 (m, 1H, C$H_2$OCHO), 3.90−3.82 (m, 1H, C$H_2$OCHO), 3.64−3.55 (m, 1H, C$H_2$OTHP), 3.55−3.43 (m, 2H, 1H from C$H_2$OTHP and C*H*OH), 2.39−2.19 (m, 2H, $CHOAcCH_2CH$═$CH_2$), 2.13−2.01 (m, 3H, 1H from NHCHC$H_2$CHOAc and $OCH_2CH_2CH_2O$), 1.92 (br s, 3H, COC$H_3$), 1.88−1.77 (m, 2H, 1H from $CH_2CH_2CHOO$ and 1H from NHCHC$H_2$CHOAc), 1.77−1.67 (m 1H, C$H_2$-$CH_2CHOO$), 1.64−1.47 (m, 4H, 1H from $CH_2CH_2CHOO$, 1H from C$H_2$C$H_2$CHOO and C$H_2$C$H_2$OCHO); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 171.46, 157.21, 156.86, 154.79, 143.99, 141.62, 141.58, 133.35, 132.83, 128.25 (2C), 127.99, 127.44, 127.38 (2C), 125.37 (2C), 125.27, 120.22 (3C), 118.54 (2C), 118.46, 113.40, 110.53, 99.39, 70.74, 67.81, 66.44, 65.51, 64.25, 62.76, 62.73, 57.39, 54.50, 47.52, 38.91, 37.86, 30.98, 29.98, 25.69, 21.44, 19.96.

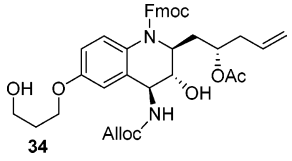
**Compound 10u.**




To a solution of amine (11 mg, 0.02 mmol) in 3 mL of ethyl acetate at room temperature was added 5% mol $NaHCO_3$ solution in water (2 mL), followed by FmocCl (8.2 mg, 0.03 mmol), and the mixture was allowed to stir at room temperature for 24 h. The two layers were separated, the aqueous layer was extracted with ethyl acetate (3 × 5 mL), and the organic layer was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the crude amine product was chromatographed using 35% ethyl acetate/hexane as eluant to obtain title compound **10u** (12 mg, %) as a colorless oil. MS ($ES^+$) *m*/*z* 755 (M + 1); mol. formula $C_{43}H_{50}N_2O_{10}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.75 (t, 2H, *J*

= 6.8 Hz, Ph), 7.54−7.41 (m, 2H, Ph), 7.40−7.33 (q, 2H, *J* = 7.0 Hz, Ph), 7.32−7.21 (m, 2H, Ph), 7.13−6.86 (m, 1H, CHC*H*═C−N), 6.83−6.76 (m, 1H, C*H*CH═C−N), 6.74−6.66 (m, 1H, $CH_2CH_2OC-CH$═C), 6.03−5.88 (m, 1H, $OCH_2CH$═$CH_2$), 5.69−5.56 (m, 1H, $CHOAcCH_2CH$═$CH_2$), 5.36 (d, 1H, *J* = 16.8 Hz, $OCH_2CH$═$CH_2$), 5.27 (d, 1H, *J* = 12 Hz, $OCH_2CH$═$CH_2$), 5.12−5.03 (m, 1H, OC*H*O), 5.03−4.95 (m, 2H, $CHOAcCH_2CH$═$CH_2$), 4.90−4.80 (m, 1H, C*H*O$AcCH_2CH$═$CH_2$), 4.65 (br d, 2H, *J* = 5.7 Hz, $OCH_2CH$═$CH_2$), 4.63−4.59 (m, 1H, $COOCH_2CH$), 4.58−4.52 (m, 1H, AllocNHC*H*), 4.51−4.40 (m, 2H, 1H from $COOCH_2CH$ and NC*H*$CH_2$), 4.22−4.14 (m, 1H, $COOCH_2$-C*H*), 4.07 (t, 2H, *J* = 6.5 Hz, C$H_2$OAr), 3.98−3.90 (m, 1H, C$H_2$OCHO), 3.90−3.81 (m, 1H, C$H_2$OCHO), 3.66−3.56 (m, 2H, C$H_2$OTHP), 3.55−3.47 (m, 1H, C*H*OH), 2.72−2.44 (m, 1H, NHCHC$H_2$CHOAc), 2.36−2.13 (m, 2H, $CHOAcCH_2$-$CH$═$CH_2$), 2.13−2.04 (m, 2H, $OCH_2CH_2CH_2O$), 1.99 (br s, 3H, $COCH_3$), 1.88−1.79 (m, 1H, $CH_2CH_2CHOO$), 1.78−1.67 (m 2H, 1H from $CH_2CH_2CHOO$ and 1H from NHCHC$H_2$CHOAc), 1.61−1.48 (m, 4H, 1H from $CH_2CH_2$-CHOO, 1H from $CH_2CH_2CHOO$ and $CH_2CH_2OCHO$); $^{13}$C NMR (400 MHz, $CDCl_3$) *δ* 171.13, 157.21, 156.79, 155.17, 144.09, 141.68, 141.63, 133.43, 132.77, 128.21, 127.98 (2C), 127.50 (2C), 127.38, 125.46 (2C), 125.27, 120.21 (3C), 118.57 (2C), 118.38, 113.81, 111.20, 99.49, 70.12, 67.81, 66.56, 65.59, 64.28, 62.87, 56.22, 54.46, 47.57, 38.65, 36.61, 31.05, 29.98, 25.75, 21.59, 20.04.

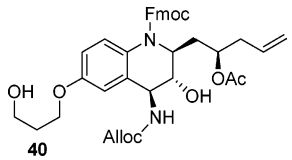
**Compound 34.**




**34**

To a stirred solution of THP-protected alcohol (48 mg, 0.063 mmol) in 5 mL of ethanol was added pyridinium-*p*-toluenesulfonate (16.3 mg, 0.063 mmol), and the mixture was heated to 50 °C for 7 h. The reaction mixture was cooled and evaporated under reduced pressure. The crude alcohol product was chromatographed using 50% ethyl acetate/hexane as eluant to obtain title compound **34** (38 mg, 89%) as a colorless oil. MS ($ES^+$) *m*/*z* 671 (M + 1); mol. formula $C_{38}H_{42}N_2O_9$; $^1$H NMR (400 MHz, $CDCl_3$) *δ* 7.80−7.70 (m, 2H, Ph), 7.64−7.44 (m, 2H, Ph), 7.43−7.35 (br q, 2H, Ph), 7.33−7.20 (m, 2H, Ph), 7.12−6.87 (m, 1H, CHC*H*═C−N), 6.85−6.77 (m, 1H, C*H*CH═C−N), 6.76−6.63 (m, 1H, $CH_2$-$CH_2OC-CH$═C), 6.01−5.84 (m, 1H, $OCH_2CH$═$CH_2$), 5.73−5.54 (m, 1H, $CHOAcCH_2CH$═$CH_2$), 5.34 (d, 1H, *J* = 17.5 Hz, $OCH_2CH$═$CH_2$), 5.30−5.19 (m, 1H, $CH_2OH$), 5.24 (d, 1H, *J* = 11.2 Hz, $OCH_2CH$═$CH_2$), 5.02 (d, 2H, *J* = 12 Hz, $CHOAcCH_2CH$═$CH_2$), 4.94−4.86 (m, 1H, C*H*O$AcCH_2CH$═$CH_2$), 4.67−4.60 (br d, 2H, *J* = 5.5 Hz, $OCH_2CH$═$CH_2$), 4.60−4.54 (br t, 2H, *J* = 8.5 Hz, $COOCH_2$-CH), 4.53−4.47 (m, 1H, AllocNHC*H*), 4.44−4.29 (m, 1H, NC*H*$CH_2$), 4.26−4.15 (m, 1H, $COOCH_2CH$), 4.13−4.06 (m, 2H, C$H_2$OAr), 3.89−3.79 (br t, 2H, *J* = 5.5 Hz, C$H_2$OH), 3.54−3.43 (m, 1H, C*H*OH), 2.38−2.17 (m, 2H, $CHOAcCH_2$-$CH$═$CH_2$), 2.12−1.98 (m, 3H, $OCH_2CH_2CH_2O$ and 1H from NHCHC$H_2$CHOAc), 1.97−1.87 (br s, 3H, $COCH_3$), 1.85−1.75 (m, 1H, NHCHC$H_2$CHOAc); $^{13}$C NMR (400 MHz, $CDCl_3$) *δ* 171.45, 157.04, 156.92, 154.81, 143.98, 141.62, 141.58, 133.35, 132.77, 128.49, 128.00 (2C), 127.98, 127.43, 127.36, 125.41 (2C), 125.25, 120.24 (3C), 118.53, 118.47 (2C), 113.40, 110.53, 70.74, 67.88, 66.44, 66.07, 60.42, 57.36, 54.52, 47.53, 38.91, 37.26, 32.19, 21.42.

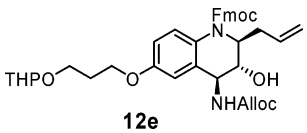
**Compound 40.**




**40**

To a stirred solution of THP-protected alcohol (10 mg, 0.013 mmol) in 5 mL of ethanol was added pyridinium-*p*-toluenesulfonate (3.3 mg, 0.013 mmol), and the mixture was heated to 50 °C for 7 h. The reaction mixture was cooled and evaporated under reduced pressure. The crude alcohol product was chromatographed using 50% ethyl acetate/hexane as eluant to obtain title compound **40** (7 mg, %) as a colorless oil. MS ($ES^+$) *m*/*z* 671 (M + 1); mol. formula $C_{38}H_{42}N_2O_9$; $^1$H NMR (400 MHz, $CDCl_3$) *δ* 7.74 (t, 2H, *J* = 6.2 Hz, Ph), 7.58−7.42 (m, 2H, Ph), 7.38 (q, 2H, *J* = 7.0 Hz, Ph), 7.32−7.21 (m, 2H, Ph), 7.10−6.84 (m, 1H, CHC*H*═C−N), 6.80 (m, 1H, C*H*CH═C−N), 6.75−6.65 (m, 1H, $CH_2CH_2OC-CH$═C), 6.02−5.88 (m, 1H, $OCH_2CH$═$CH_2$), 5.69−5.57 (m, 1H, $CHOAcCH_2CH$═$CH_2$), 5.36 (d, 1H, *J* = 17.0 Hz, $OCH_2CH$═$CH_2$), 5.26 (d, 1H, *J* = 10 Hz, $OCH_2$-$CH$═$CH_2$), 5.15 (d, 1H, *J* = 8.5 Hz, $CH_2OH$), 5.04−4.95 (m, 2H, $CHOAcCH_2CH$═$CH_2$), 4.89−4.80 (m, 1H, C*H*O$Ac$-$CH_2CH$═$CH_2$), 4.70−4.59 (m, 1H, $COOCH_2CH$), 4.64 (br d, 2H, *J* = 5.8 Hz, $OCH_2CH$═$CH_2$), 4.59−4.52 (m, 1H, AllocNHC*H*), 4.52−4.39 (m, 2H, 1H from $COOCH_2CH$ and NC*H*$CH_2$), 4.22−4.15 (m, 1H, $COOCH_2CH$), 4.13−4.08 (m, 2H, C$H_2$OAr), 3.90−3.82 (br t, 2H, *J* = 4.5 Hz, C$H_2$OH), 3.65−3.54 (m, 1H, C*H*OH), 2.95−2.64 (m, 1H, NHCHC$H_2$-CHOAc), 2.35−2.16 (m, 2H, $CHOAcCH_2CH$═$CH_2$), 2.10−2.02 (m, 2H, $OCH_2CH_2CH_2O$), 1.96 (br s, 3H, $COCH_3$), 1.93−1.82 (m, 1H, NHCHC$H_2$CHOAc); $^{13}$C NMR (400 MHz, $CDCl_3$) *δ* 170.84, 156.61, 156.51, 154.84, 143.73, 141.33, 141.29, 133.09, 132.44, 128.10, 127.68 (2C), 127.63, 127.19, 127.05, 125.12 (2C), 124.88, 119.87 (3C), 118.23, 118.07 (2C), 113.57, 110.78, 69.80, 67.46, 66.21, 65.87, 60.21, 55.82, 54.10, 47.21, 38.27, 36.27, 31.89, 21.25.

**Compound 12e.**



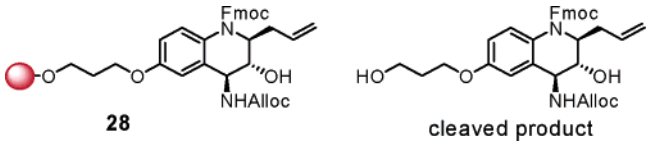

**12e**

To a solution of compound **12a** (100 mg, 0.153 mmol) in 20 mL EtOH was added *p*-TsOH (58 mg, 0.306 mmol) at 0 °C, and the mixture was stirred at 50 °C for 5 h. The reaction

mixture was quenched with $NaHCO_3$, extracted with EtOAc (3 × 30 mL), and concentrated to obtain a yellowish oil. The crude product was dissolved in 10 mL of DMF, and 1.4 equiv of $CsCO_3$ (70 mg, 0.214 mmol) was added to the solution at 0 °C. To this mixture was added toluene-4-sulfonic acid 3-(tetrahydropyran-2-yloxy)-propyl ester (62.4 mg, 0.198 mmol) in DMF (5 mL), and it was then stirred at room temperature overnight. The reaction was quenched with saturated $NH_4Cl$ solution, extracted with EtOAc (3 × 30 mL), and dried over anhydrous $MgSO_4$. The solvent was evaporated on a rotovap, and the residue was dried over a high vacuum pump overnight to obtain a yellowish oil. The crude product was dissolved in THF and to the following solution was added TBAF (0.3 mL, 0.3 mmol) at 0 °C. The reaction mixture was stirred at the same temperature for 30 min. The reaction mixture was quenched with $NaHCO_3$ and extracted with EtOAc (3 × 30 mL), the solvent was evaporated on a rotovap, and the crude product was dried over a high vacuum pump overnight. The crude product was then dissolved in 10 mL of EtOAc and 2 mL of 10% $NaHCO_3$ in water was added. The resulting mixture was stirred vigorously. To the reaction mixture was added FmocCl (79 mg, 0.306 mmol), and it was then stirred for 5 h at room temperature. The reaction mixture was extracted with EtOAc (3 × 30 mL), the combined was dried over anhydrous $MgSO_4$, and the solvent was evaporated on a rotovap. The crude product was purified by flash column chromatography using 20% EtOAc in hexane to obtain Fmoc-protected derivative **12e** (72 mg, 70% over four steps). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.78−6.82 (m, 12H), 5.84 (m, 2H), 5.50 (m, 1H), 5.28 (m, 4H), 4.96 (bs, 1H), 4.86 (bs, 1H), 4.54 (bs, 1H), 4.20 (bs, 1H), 4.15 (m, 4H), 3.89 (m, 2H), 3.79 (m, 4H), 3.60 (m, 1H), 2.72 (bs, 1H), 2.20 (bs, 1H), 2.06 (m, 4H), 1.29 (m, 4H); MS (EI) *m*/*z* (rel. intensity) 532 (M + 1).

**Compound 27.** To a solution of **12e** (500 mg, 0.748 mmol) in 100 mL of EtOH was added PPTS (18 mg, 10 mol %), and the mixture was stirred vigorously for 3 h at 50 °C. The solvent was evaporated on a rotovap, and the crude product was purified by flash column chromatography using 1% MeOH in $CH_2Cl_2$ to obtain diol **27** (349 mg, 80%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.92−6.85 (m, 12H), 5.85 (m, 2H), 5.28 (m, 4H), 4.97 (bs, 1H), 4.88 (bs, 1H), 4.54 (bs, 1H), 4. 20 (bs, 1H), 4.17 (m, 4H), 3.86 (m, 3H), 3.82 (m, 2H), 3.60 (m, 1H), 2.72 (bs, 1H), 2.20 (bs, 1H), 2.07 (m, 2H); MS (EI) *m*/*z* (rel. intensity) 585 (M + 1).

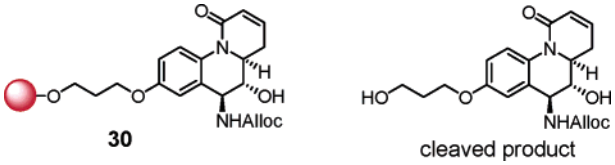
**Solid-Phase Synthesis. Loading of Compound 27.**




The alkylsilyl macrobeads (116 mg, 0.149mmol, 1.29 mmol/g, ICCB batch MX-19) were swollen in $CH_2Cl_2$ (1.0 mL) in a BioRad plastic container under argon for 30 min. The solvent was then drained under positive argon pressure. A solution of trifluoromethanesulfonic acid in $CH_2Cl_2$ (4%, 1.7 mL, 0.89 mmol) was added by syringe, and the resin turned orange. The resin was then left to sit for 20 min under argon with occasional swirling. The solvent was then drained under positive argon pressure. The activated resin was treated with 2,6-lutidine (0.17 mL, 1.49 mmol) for 30 min, followed by addition of a solution of diol **27** (180 mg, 0.308 mmol) in $CH_2Cl_2$ (0.4 mL). The resin was tumbled in the BioRad plastic container overnight. The resin was washed with $CH_2Cl_2$ (3×), THF (3×), and $CH_2Cl_2$ (3×). The beads were then dried on the lyophilizer overnight (168 mg, 90% loading). The cleaved product showed MS (EI) *m*/*z* (rel. intensity) 585 (M + 1).

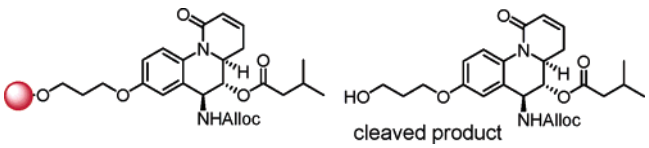
***N*-Fmoc Removal.** To a loaded resin (180 mg, 0.126 mmol) in a 20-mL BioRad plastic reaction vessel was added 2.0 mL of $CH_2Cl_2$. The beads were suspended for 30 min. To this solution, 20% piperidine in $CH_2Cl_2$ (5 mL) was added, and the mixture was tumbled for 12 h. The resin was washed with $CH_2Cl_2$ (3 × 5 mL), DMF (3 × 5 mL), and THF (3 × 5 mL) and then freeze-dried for 24 h. The cleaved product showed MS (EI) *m*/*z* (rel. intensity) 363 (M + 1). HPLC yield >98%.

**Acryloylation and Ring Closing Metathesis Reaction on Solid Phase.**




The beads (150 mg, 0.126 mmol) were transferred to a 20.0-mL round-bottom flask containing 5 mL of $CH_2Cl_2$. To this solution, $Et_3N$ (0.18 mL, 1.26 mmol) was added at −45 °C and acryloyl chloride (51 $\mu$L, 0.63 mmol) in 2 mL of $CH_2Cl_2$ at −10 °C. The reaction mixture was stirred for 4 h at −10 °C. The resin was washed with $CH_2Cl_2$ (3 × 5 mL), DMF (3× 5 mL), and THF (3 × 5 mL) and freeze-dried for 12 h. The resin was transferred to a 20.0-mL round-bottom flask containing 5.0 mL of $CH_2Cl_2$. To this solution, a second-generation Grubbs' catalyst (30 mol %) was added, and then the mixture was refluxed for 24 h. The resin was washed with $CH_2Cl_2$ (3 × 5 mL), DMF (3 × 5 mL), and THF (3 × 5 mL) and freeze-dried for 24 h. MS (EI) *m*/*z* (rel. intensity) 389 (M + 1). HPLC yield >98%.

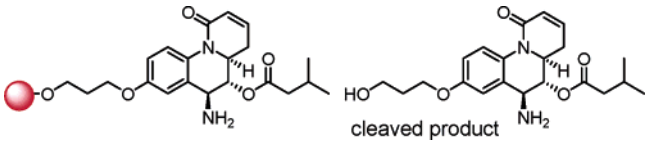
**Acylation of Secondary Alcohol (Test of First Diversity).**




The beads (20 mg, 0.0174 mmol) were transferred to a 20.0-mL BioRad plastic reaction vessel containing 5.0 mL of THF. To this solution, NaHMDS (0.17 mL, 0.17mmol) was added

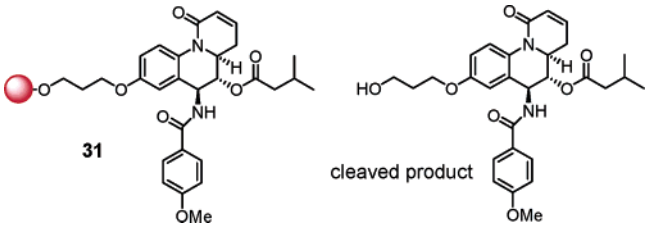
at −78 °C. To this solution was added valeryl chloride (10 μL, 0.087 mmol) at the same temperature, then the mixture was warmed to room temperature and tumbled for an additional 12 h. The resin was washed with THF (3 × 5 mL), $CH_2Cl_2$ (3 × 5 mL), and DMF (3 × 5 mL) and freeze-dried for 24 h. The cleaved product showed MS (EI) *m/z* (rel. intensity) 473 (M + 1). HPLC yield >98%.

***N*-Alloc Removal.**



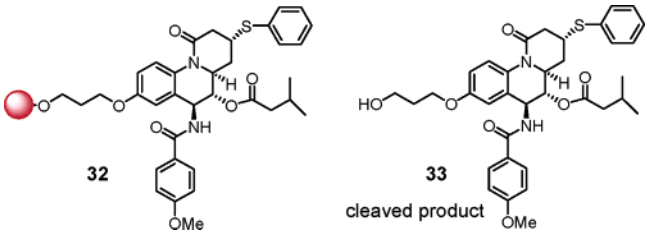

The loaded resin (20 mg, 0.0162 mmo) was transferred to a 20.0-mL BioRad plastic reaction vessel covered with aluminum foil containing 5.0 mL of $CH_2Cl_2$. To this solution, $Pd(PPh_3)_4$ (1.8 mg, 0.0015 mmol) and piperidine (6.4 mL, 0.064 mmol) were added at 0 °C. The reaction vessel was tumbled for 6 h at room temperature. The resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and DMF (3 × 5 mL) and freeze-dried for 24 h. The cleaved product showed MS (EI) *m/z* (rel. intensity) 389 (M + 1). HPLC yield >98%.

**Amide Formation − Compound 31 (Test of Second Diversity).**



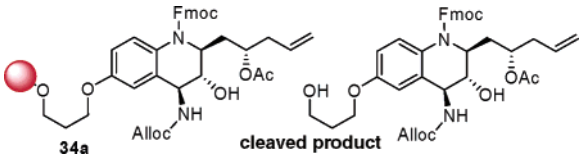

The loaded resin (20 mg, 0.0174 mmol) was transferred to a 20.0-mL BioRad plastic reaction vessel containing 5.0 mL of $CH_2Cl_2$. To this solution were added $Et_3N$ (24 mL, 0.172 mmol) and *p*-methoxybenzoyl chloride (14.8 mg, 0.087 mmol) at −45 °C. The reaction mixture was warmed to room temperature and then tumbled at room temperature for 24 h. The resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and DMF (3 × 5 mL) and then freeze-dried for 24 h. The cleaved product showed MS (EI) *m/z* (rel. intensity) 523 (M + 1). HPLC yield >98%.

**Compounds 32 and 33.**



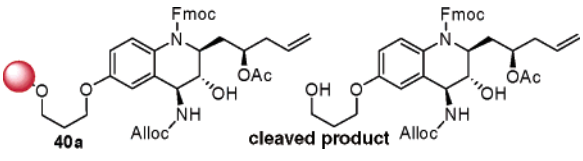

The resin (20 mg, 0.0156 mmol) was transferrd to a 20.0-mL BioRad plastic reaction vessel containing 5.0 mL of $CH_2Cl_2$. To this solution were added $Et_3N$ (27 μL, 0.155 mmol) and benzenethiol (8 μL, 0.0778) at 0 °C, and then the mixture was tumbled at room temperature for 48 h. The resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and DMF (3 × 5 mL) and then freeze-dried for 24 h. The cleaved product was purified over silica gel using 30% EtOAc in hexane. $^1$H NMR δ 7.81−6.97 (m, 7H), 7.02−6.03 (m, 5H), 5.36 (t, 1H, *J* = ), 5.23 (dd, 1H, *J* = 6.8 Hz), 5.17 (d, 1H, *J* = 6.8 Hz), 4.22 (t, 1H, *J* = 7.9 Hz), 3.78 (t, 2H, *J* = 4.6 Hz), 3.50 (m, 2H), 3.34 (s, 3H), 2.74 (m, 1H), 2.52 (m, 5H), 1.74 (m, 4H), 0.87 (s, 6H); MS (EI) *m/z* (rel. intensity) 633 (M + 1). HPLC yield >95%.

**Loading of 34.**




The resin (33.8 mg, 0.046 mmol) and compound **34** (62 mg, 0.092 mmol) were dried on a freeze dryer for 24 h. The beads were placed in a vial, and 1.0 mL of anhydrous $CH_2Cl_2$ was added at room temperature to allow the beads' swelling. The solution containing the beads was gently shaken for 30 min. The $CH_2Cl_2$ was then removed, and a 0.45 M trifluoromethanesulfonate solution (0.62 mL, 0.277 mmol) was added to the resin and kept for 20 min (shaking gently in between). The beads and the solution became orange-red. The trifluoromethanesulfonate solution was removed completely, and the resin was washed with anhydrous $CH_2Cl_2$ (3 mL). Then 1 mL of anhydrous $CH_2Cl_2$ was added to the resin, followed by the 2, 6-lutidine (43.3 μL, 0.37 mmol). The beads became colorless and were allowed to stand for 10 min. The compound was dissolved in a minimum of solvent (0.5 mL of anhydrous $CH_2Cl_2$) and added to the resin. The resulting mixture was shaken gently for 1 h, then the vial was capped and kept on the tumble shaker for 12 h. The vial was removed from the tumble shaker and washed with DCM (5 mL) 3 times, with THF 3 times, and with again with DCM for 3 times. Finally, the resin was dried on vacuum pump for 6 h and in the freeze dryer for 12 h (43.7 mg, 72%). LRMS: MS ($ES^+$) *m/z* = 671 (M + 1); mol. formula $C_{38}H_{42}N_2O_9$; HPLC: 10.776 min.

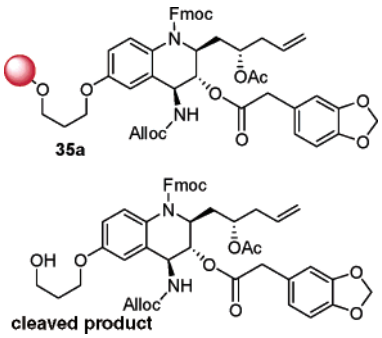
**Loading of 40.**




The resin (21.3 mg, 0.029 mmol) and compound **40** (39 mg, 0.058 mmol) were dried on a freeze dryer for 24 h. The beads were placed in a vial, and 1 mL of anhydrous $CH_2Cl_2$ was added at room temperature to allow the beads' swelling. The solution containing the beads was gently shaken for 30 min. The $CH_2Cl_2$ was then removed, and a 0.45 M trifluoromethanesulfonate solution (0.39 mL, 0.175 mmol) was

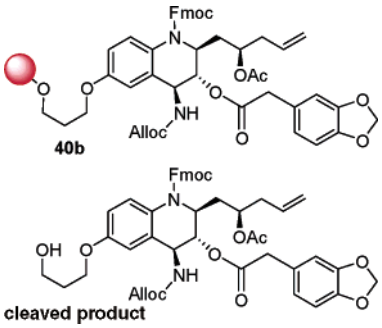
added to the resin and kept for 20 min (shaking gently between). The beads and the solution became orange-red. The trifluoromethanesulfonate solution was removed completely, and the resin was washed with anhydrous $CH_2Cl_2$ (3 mL). Then 1 mL of anhydrous $CH_2Cl_2$ was added to the resin, followed by the 2,6-lutidine (27.3 $\mu$L, 0.232 mmol). The beads became colorless and were allowed to stand for 10 min. The compound was dissolved in a minimum of solvent (0.5 mL of anhydrous $CH_2Cl_2$) and added to the resin. The resulting mixture was shaken gently for 1 h, then the vial was capped and kept on a tumble shaker for 12 h. The vial was removed from the tumble shaker and washed with DCM (5 mL) 3 times, with THF 3 times, and with again DCM 3 times. Finally, the resin was dried on a vacuum pump for 6 h and in the freeze dryer for 12 h (27.5 mg, 71%). LRMS: MS ($ES^+$) $m/z$ = 671 (M + 1); mol. formula $C_{38}H_{42}N_2O_9$; HPLC: 10.739 min.

**Acylation of Secondary Alcohol (35a).**



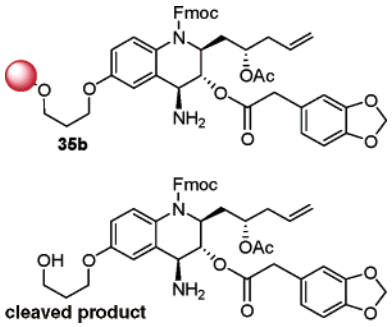

The resin (compound loaded onto the resin, 43.7 mg, 0.043 mmol) was swollen in 3 mL of anhydrous $CH_2Cl_2$ for 30 min. The solvent was removed and replaced with 1 mL of anhydrous $CH_2Cl_2$. To the beads were added 1,3-diisopropylcarbodiimide (13.6 $\mu$L, 0.086 mmol), 3,4-methylenedioxyphenylacetic acid (11.7 mg, 0.064 mmol), and 4-(dimethylamino)-pyridine (0.5 mg, 0.004 mmol) at once and at room temperature. The mixture was shaken with a tumble shaker for 23 h. The mixture was filtered, and the resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and $CH_2Cl_2$ (3 × 5 mL) and dried under vacuum overnight. Compound obtained after cleavage of three beads: LRMS, MS ($ES^+$) $m/z$ = 833 (M + 1); mol. formula $C_{47}H_{48}N_2O_{12}$; HPLC, 12.143 min.

**Acylation of Secondary Alcohol (40b).**



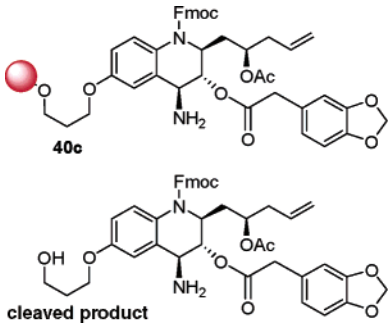

The resin (compound loaded onto the resin, 27.5 mg, 0.026 mmol) was swollen in 3 mL of anhydrous $CH_2Cl_2$ for 30 min. The solvent was removed and replaced with 1 mL of anhydrous $CH_2Cl_2$. To the beads were added 1,3-diisopropylcarbodiimide (8.4 $\mu$L, 0.053 mmol), 3,4-methylenedioxyphenylacetic acid (7.3 mg, 0.039 mmol), and 4-(dimethylamino)-pyridine (0.3 mg, 0.002 mmol) at once and at room temperature. The mixture was shaken with a tumble shaker for 23 h. The mixture was filtered, and the resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and $CH_2Cl_2$ (3 × 5 mL) and dried under vacuum overnight. Compound obtained after cleavage of three beads: LRMS, MS ($ES^+$) $m/z$ = 833 (M + 1); mol. formula $C_{47}H_{48}N_2O_{12}$; HPLC, 12.014 min.

**N-Alloc Removal (35b).**




The resin (compound loaded onto the resin, 0.043 mmol) was swollen in 3 mL of anhydrous THF for 30 min. The solvent was removed and replaced with 1 mL of a mixture of anhydrous $CH_2Cl_2$ (5 mL), 4-methylmorpholine (0.32 mL), and acetic acid (0.66 mL). To the beads were added triphenylphosphine (149.5 mg, 0.549 mmol) and tetrakis-(triphenylphosphine)palladium (133.8 mg, 0.114 mmol) at room temperature. The mixture was shaken with a tumble shaker for 17 h. The mixture was filtered, and the resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and $CH_2Cl_2$ (3 × 5 mL) and dried under vacuum overnight. Compound obtained after cleavage of three beads: LRMS, MS ($ES^+$) $m/z$ = 749 (M + 1); mol. formula $C_{43}H_{44}N_2O_{10}$; HPLC, 10.757 min.

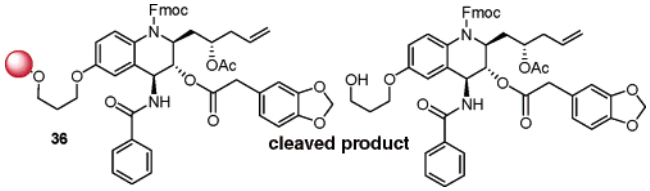
**N-Alloc Removal (40c).**




The resin (compound loaded onto the resin, 0.026 mmol) was swollen in 3 mL of anhydrous THF for 30 min. The solvent was removed and replaced with 1 mL of a mixture of anhydrous $CH_2Cl_2$ (5 mL), 4-methylmorpholine (0.32 mL),

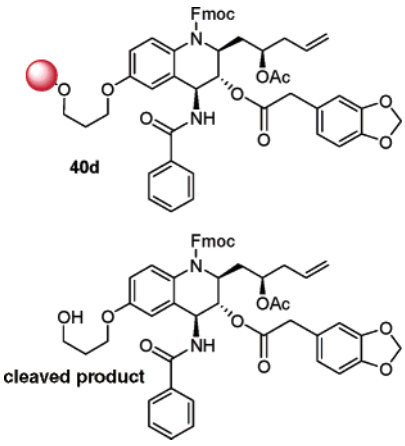
and acetic acid (0.66 mL). To the beads were added triphenylphosphine (89.8 mg, 0.339 mmol) and tetrakis-(triphenylphosphine)palladium (82.6 mg, 0.070 mmol) at room temperature. The mixture was shaken with a tumble shaker for 17 h. The mixture was filtered, and the resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and $CH_2Cl_2$ (3 × 5 mL) and dried under vacuum overnight. Compound obtained after cleavage of three beads: LRMS, MS ($ES^+$) $m/z$ = 749 (M + 1); mol. formula $C_{43}H_{44}N_2O_{10}$; HPLC, 10.720 min.

**Amide Formation (36).**



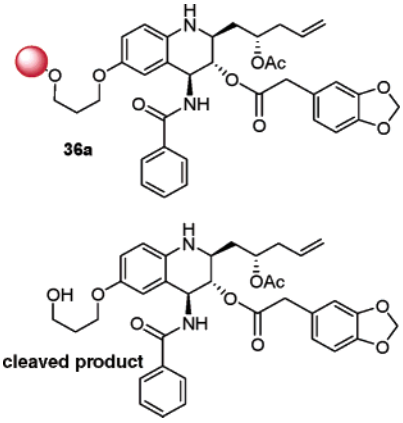

The resin (compound loaded onto the resin, 0.043 mmol) was swollen in 3 mL of anhydrous $CH_2Cl_2$ for 30 min. The solvent was removed and replaced with 1 mL of anhydrous $CH_2Cl_2$. To the beads were added 2,4,6-collidine (57.5 $\mu$L, 0.431 mmol) and benzoyl chloride (25.2 $\mu$L, 0.215 mmol) at room temperature. The mixture was shaken with a tumble shaker for 17 h. The mixture was filtered, and the resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and $CH_2Cl_2$ (3 × 5 mL) and dried under vacuum. After cleavage of three beads, it was observed that 40−50% of the starting material still remained, so a second cycle was run using the same quantities of the reagents as in the first cycle for 20 h. Compound obtained after cleavage of three beads: LRMS, MS ($ES^+$) $m/z$ = 853 (M + 1); mol. formula $C_{50}H_{48}N_2O_{11}$; HPLC, 12.088 min.

**Amide Formation (40d).**



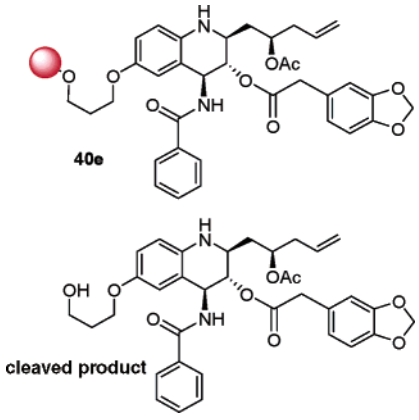

The resin (compound loaded onto the resin, 0.026 mmol) was swollen in 3 mL of anhydrous $CH_2Cl_2$ for 30 min. The solvent was removed and replaced with 1 mL of anhydrous $CH_2Cl_2$. To the beads were added 2,4,6-collidine (35.5 $\mu$L, 0.266 mmol) and benzoyl chloride (15.6 $\mu$L, 0.133 mmol) at room temperature. The mixture was shaken with a tumble shaker for 17 h. The mixture was filtered, and the resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and $CH_2Cl_2$ (3 × 5 mL) and dried under vacuum. After cleavage of three beads it was observed that 40−50% of the starting material still remained, so a second cycle was run using the same quantities of the reagents as in the first cycle for 20 h.. Compound obtained after cleavage of three beads: LRMS, MS ($ES^+$) $m/z$ = 853 (M + 1); mol. formula $C_{50}H_{48}N_2O_{11}$; HPLC, 11.977 min.

***N*-Fmoc Removal (36a).**




The resin (0.043 mmol) was swollen in 3 mL of anhydrous DMF for 30 min. The solvent was removed and replaced with 1 mL of anhydrous DMF. To the beads was added morpholine (1.0 mL) at room temperature. The mixture was shaken with a tumble shaker for 17 h. The mixture was filtered, and the resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and $CH_2Cl_2$ (3 × 5 mL) and dried under vacuum overnight. Compound obtained after cleavage of three beads: LRMS, MS ($ES^+$) $m/z$ = 631 (M + 1); mol. formula $C_{35}H_{38}N_2O_9$; HPLC, 10.240 min.

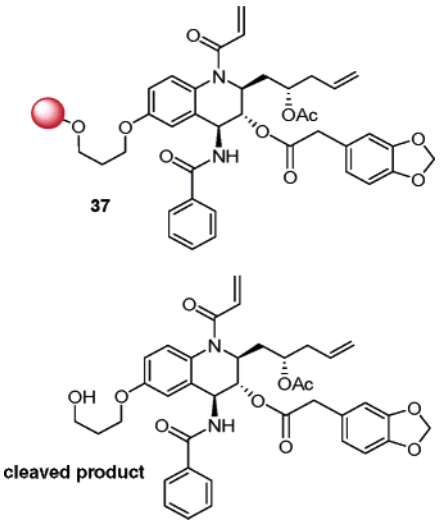
***N*-Fmoc Removal (40e).**




The resin (compound loaded onto the resin, 0.026 mmol) was swollen in 3 mL of anhydrous DMF for 30 min. The solvent was removed and replaced with 1.0 mL of anhydrous DMF. To the beads was added morpholine (1.0 mL) at room temperature. The mixture was shaken with a tumble shaker for 17 h. The mixture was filtered, and the resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and $CH_2Cl_2$ (3 × 5 mL) and dried under vacuum overnight. Compound obtained after cleavage of three beads: LRMS, MS ($ES^+$)

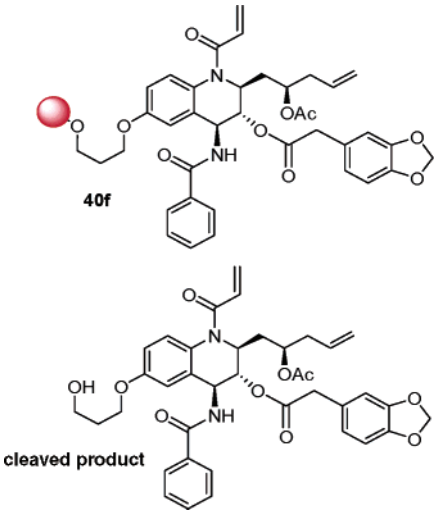
*m/z* = 631 (M + 1); mol. formula $C_{35}H_{38}N_2O_9$; HPLC, 10.295 min.

***N*-Acryloylation (37).**



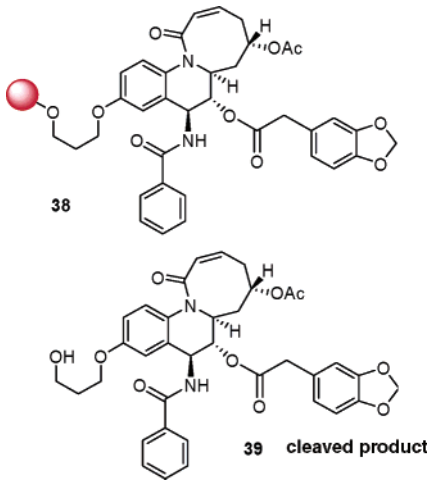

The resin (compound loaded onto the resin, 0.043 mmol) was swollen in 4.0 mL of anhydrous $CH_2Cl_2$ for 30 min in an RBF with a magnetic stirring bar. The RBF was stirred and cooled to 0 to −10 °C and then to the beads was added 2,4,6-collidine (57.5 μL, 0.431 mmol), followed by acryloyl chloride (18.2 μL, 0.215 mmol) dissolved in anhydrous $CH_2Cl_2$ (0.5 mL), dropwise at the same temperature. The mixture was stirred at 0 °C for 2 h and then at room temperature for 16 h. The mixture was filtered, the resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and $CH_2Cl_2$ (3 × 5 mL) and dried under vacuum overnight. Compound obtained after cleavage of two beads: LRMS, MS ($ES^+$) *m/z* = 685 (M + 1); mol. formula $C_{38}H_{40}N_2O_{10}$; HPLC, 10.184 min.

***N*-Acryloylation (40f).**



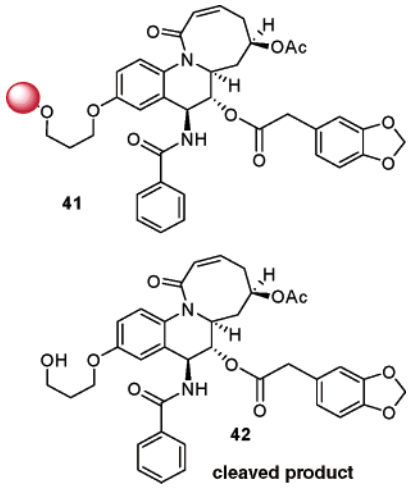

The resin (compound loaded onto the resin, 0.026 mmol) was swollen in 4 mL of anhydrous $CH_2Cl_2$ for 30 min in an RBF with a magnetic stirring bar. The RBF was stirred and cooled to 0 to −10 °C and then to the beads was added 2,4,6-collidine (35.5 μL, 0.266 mmol), followed by acryloyl chloride (11.3 μL, 0.133 mmol) dissolved in anhydrous $CH_2Cl_2$ (0.5 mL), dropwise at the same temperature. The mixture was stirred at 0 °C for 2 h and then at room temperature for 16 h. The mixture was filtered, and the resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and $CH_2Cl_2$ (3 × 5 mL) and dried under vacuum overnight. Compound obtained after cleavage of two beads: LRMS, MS ($ES^+$) *m/z* = 685 (M + 1); mol. formula $C_{38}H_{40}N_2O_{10}$; HPLC, 10.129 min.

**Ring Closing Metathesis Reaction on Solid Phase (38 and 39).**




The resin (compound loaded onto the resin, 0.043 mmol) was swollen in 2.0 mL of anhydrous $CH_2Cl_2$ for 30 min in an RBF. To the beads was added second-generation Grubbs' catalyst (7.3 mg, 0.008 mmol) at room temperature. The mixture was heated to reflux for 19 h. After cooling, the mixture was filtered, and the resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and $CH_2Cl_2$ (3 × 5 mL) and dried under vacuum overnight. Compound obtained after cleavage of three beads: LRMS, MS ($ES^+$) *m/z* = 657 (M + 1); HPLC, 9.334 min. After cleavage of all the above resin, the crude product was purified to give the title compound **39** (>85% HPLC yield). White solid, $R_f$ = 0.2 (1:20, methanol/dichloromethane). LRMS: MS ($ES^+$) *m/z* = 657 (M + 1); mol. formula $C_{36}H_{36}N_2O_{10}$.

**Ring Closing Metathesis Reaction on Solid Phase (41 and 42).**




The resin (0.026 mmol) was swollen in 2.0 mL of anhydrous

$CH_2Cl_2$ for 30 min in an RBF. To the beads was added second generation Grubbs' catalyst (4.5 mg, 0.005 mmol) at room temperature. The mixture was heated to reflux for 19 h. After cooling, the mixture was filtered, and the resin was washed with $CH_2Cl_2$ (3 × 5 mL), THF (3 × 5 mL), and $CH_2Cl_2$ (3 × 5 mL) and dried under vacuum overnight. Compound obtained after cleavage of three beads: LRMS, MS ($ES^+$) $m/z = 657$ (M + 1); HPLC, 9.278 min. After cleavage of all the above resin, the crude product was purified to give the title compound **42** (>85% HPLC yield). White solid, $R_f = 0.2$ (1:20, methanol/dichloromethane). LRMS: MS ($ES^+$) $m/z = 657$ (M + 1); mol. formula, $C_{36}H_{36}N_2O_{10}$.

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**Supporting Information Available.** Additional information as noted in test. This material is available free of charge via the Internet at http://pubs.acs.org.

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