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HETEROSUBSTITUTED 4-VINYLIMIDAZOLES – PREPARATION AND DIELS-ALDER REACTIONS

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Abstract – The Diels-Alder reactions of vinylimidazole derivatives provide an expedient stereocontrolled entry into polysubstituted tetrahydrobenzimidazole derivatives. Prior studies from our group have described methods for postcycloaddition functionalization of these adducts, however, in several cases we have been unable to achieve appropriate elaboration of cycloadducts and have sought alternatives. To circumvent this problem we have investigated pre-cycloaddition functionalization through the preparation of vinyl-substituted derivatives. Initial studies with vinyl halides or silyl enol ethers were compromised either by poor yields or postcycloaddition elimination. However, vinylsilanes and vinylstannanes participate in Diels-Alder reactions with retention of the heterosubstituent and provide a means for further elaboration, for example through Fleming-Tamao oxidation.

INTRODUCTION

The structural and architectural challenges presented by the oroidin alkaloids[1-6] have served as inspiration for the development of numerous synthetic methods that have not only proven useful in the applications for which they were designed,[7-9] but also in a broader context for use in synthesis.[10] In this vein, our lab has explored new methods for the elaboration and synthesis of functionalized imidazoles[11] as a means to provide entries to several members of the oroidin alkaloids.[12-15] In the context of approaches to spirocyclic members of these alkaloids, we have pursued a Diels-Alder/rearrangement strategy which efficiently delivers the core framework of these natural products (Figure 1).[16-24] It had been our plan to introduce the functionality at C17 in palau'amine (corresponding to C13 in axinellamine A and to C14 in massadine) through oxidation of the initial Diels-Alder adduct (for an example of this strategy see **62→63**

inset in Scheme 7); unfortunately in most intramolecular variants that we were using to obtain advanced intermediates, we were unable to arrest the reaction at the initial adduct stage as the higher temperatures required to effect the cycloaddition.[17,21,24] Furthermore, attempts to engage these cycloadducts in post-cycloaddition functionalization (i.e. Z = H → Z = Cl or OH) have not yet been successful (Figure 1).[25] Based on these observations, it was decided to revise our approach by the incorporation of a substituent into the cycloaddition precursor that could be elaborated into the required substituent.

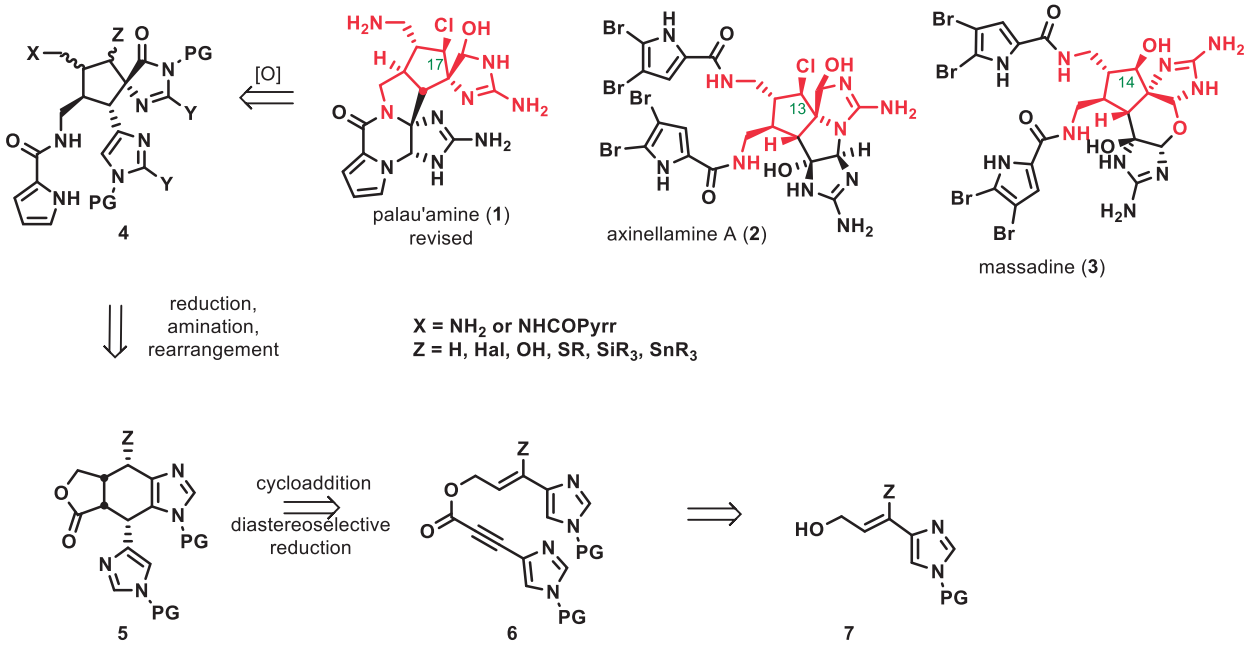
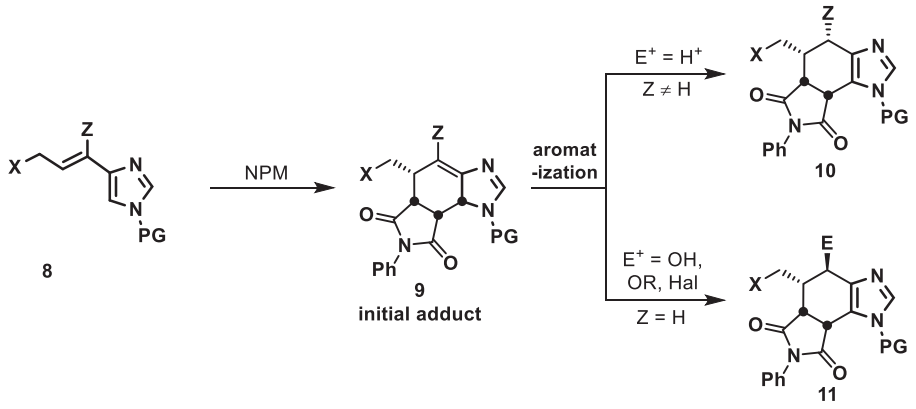


Figure 1. General overview of approach to the spirocyclic oroidin dimers

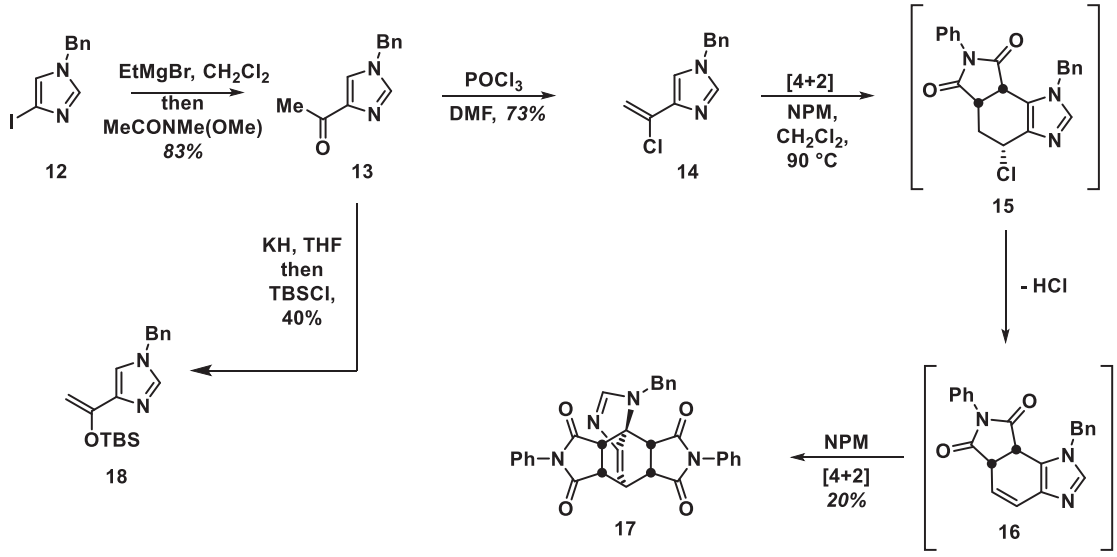
At the time that this effort was initiated, the stereochemistry of palau'amine at C17 had yet to be revised and thus the use of a chloro-substituted vinylimidazole **8** (Z = Cl or chloro surrogate) was attractive as it was anticipated that protonation would occur from the *exo*-face resulting in the desired configuration of the chloro-bearing stereocenter, i.e., **9**→**10** (Scheme 1). The prediction of stereocontrol was on the basis of all known reactions to date of the initial Diels-Alder adduct with addition of electrophiles (or enophiles) occurred from the *exo*-face, i.e., **9**→**11** (Z = H, Scheme 1) although we had not explicitly studied the rearomatization process in detail.[25,19,26] Rearomatization of the initial adduct presumably occurs via a deprotonation-reprotonation process, although the precise order of events is unknown and this may in fact depend upon the nature of the *N*-protecting group.



Scheme 1. Diels-Alder/aromatization reactions of vinylimidazoles

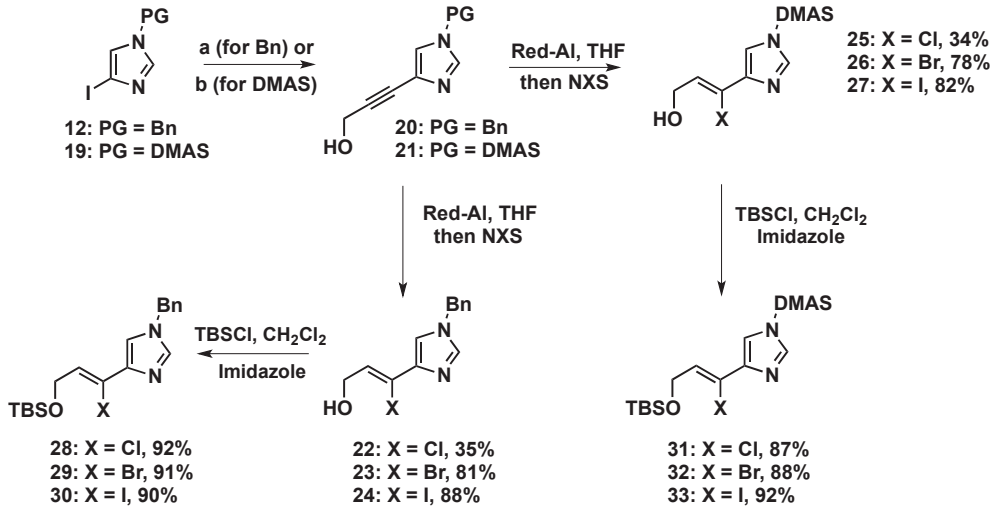
RESULTS AND DISCUSSION

An initial attempt was made with the parent vinyl chloride which could be prepared in good yield via a two-step sequence from **12**[18] involving iodine-magnesium exchange and trapping with the Weinreb amide affording methyl ketone **13** (Scheme 2).[27] Treatment of **13** with $POCl_3$ in DMF then delivered the vinyl chloride **14** in good yield.[28] An attempt to engage this substrate in a cycloaddition reaction with *N*-phenylmaleimide (NPM) occurred with mixed success. At temperatures which had been productive with the corresponding deschloro substrate (cf. **8**, Z = H) were not successful, simply returning mixtures of unreacted starting materials.[18,20] However, upon raising the reaction temperature to 90 °C a reaction occurred to deliver 2+1 cycloadduct **17**, a product that we had isolated previously via a reaction of the parent substrate under conditions where the reaction solvent had not been deoxygenated (Scheme 2).[18] The formation of this adduct **17**, which had been characterized previously through X-ray crystallography,[18] can be understood through cycloaddition to afford the 4-chloro derivative **15**. Dehydrochlorination produces a second vinylimidazole **16** which then undergoes a second Diels-Alder reaction to afford the observed product **17** in low, but unoptimized yield. The influence of the chloro substituent is interesting as the substrate lacking this moiety undergoes cycloaddition to afford the initial adduct at 45 °C in CH_2Cl_2 implying that the inductive effect of the chlorine atom deactivates the diene to cycloaddition. During the scouting phase of this chemistry, we also used the methyl ketone **13** to prepare the corresponding silyl enol ether **18** by treatment with KH and TBSCl (Scheme 2).[29-31] While it proved possible to purify and characterize this material, it was rather unstable and decomposed on standing and during attempted Diels-Alder reactions and thus was not pursued further.



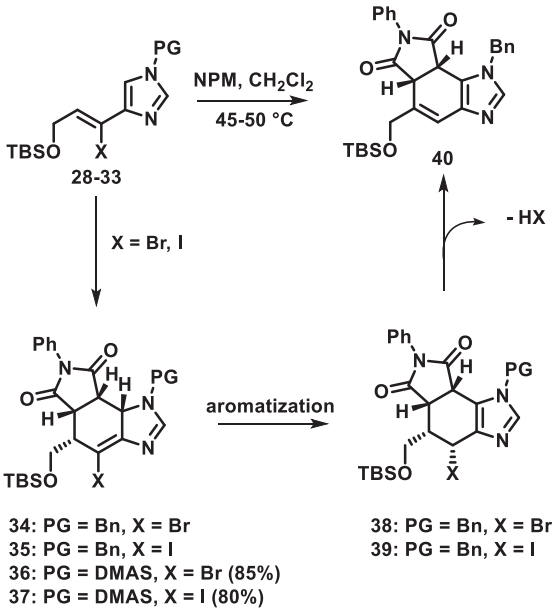
Scheme 2. Initial attempts using heterosubstituted vinylimidazoles

Although these initial results were somewhat disappointing, the isolation of the 2+1 adduct **17** demonstrated that a chloro substituted vinylimidazole was a competent diene. However, it was unclear whether using more highly substituted derivatives would offer any advantage and whether halogens could be tolerated at all in cycloaddition reactions. Further, it was not clear how other substituents used in place of chlorine might impact this chemistry and if such substrates could be employed in intramolecular variants akin to that outlined in Figure 1. Despite these concerns, we decided to continue to explore this pre-cycloaddition functionalization strategy through evaluating substrates that we might employ in total synthesis endeavors, specifically vinylimidazoles terminated with a silyl protected hydroxymethyl moiety. Studies towards the nagelamides in our lab had revealed that propargylic alcohols undergo facile *anti*-hydroalumination and trapping with tributyltin chloride as an electrophile;[12] use of *N*-halosuccinimides in place of the tin electrophile delivered the corresponding vinyl halides **22**-**27** for both the Bn- and DMAS protected series in modest to good yields (Scheme 3). The propargylic alcohols were readily accessible through Sonogashira cross-coupling between 4-iodoimidazoles and THP-protected propargyl alcohol for **20** (followed by deprotection) and freshly distilled propargyl alcohol for **21**.[12,32-33] Finally, the halovinyl alcohols were protected as the TBS-ethers **28**-**33** and then subjected to Diels-Alder reactions with *N*-phenylmaleimide (Scheme 4).



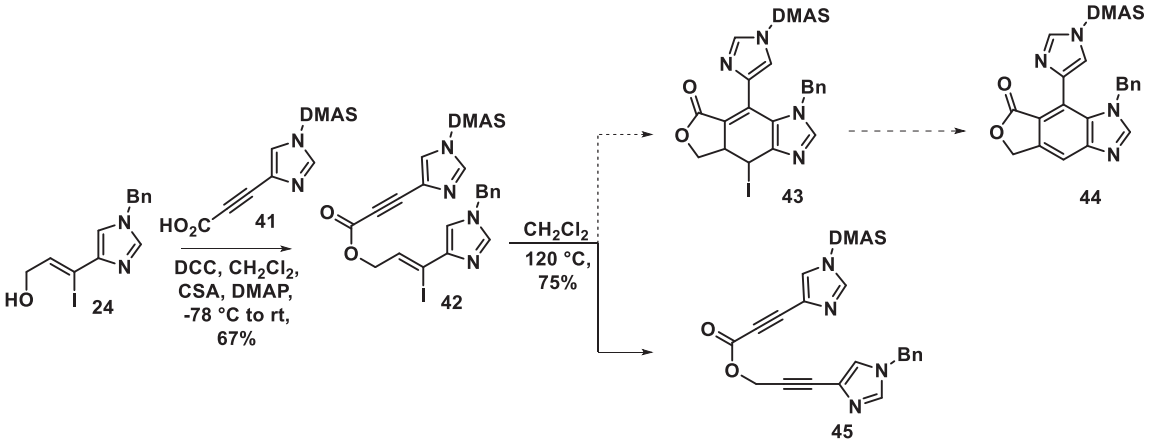
Scheme 3. Preparation of halo-substituted vinylimidazoles

The results from these cycloaddition reactions can be broadly divided into two groups depending upon the nitrogen protecting group. The three halovinyl imidazoles protected with a benzyl group **28-30** were either unreactive in the case of the chloro substituted system or resulted in the formation of the dehydrohalogenated adduct **40** in low to moderate yield (Scheme 4). This latter outcome was similar to what had been observed with **14**, but at the lower temperatures employed, the second addition did not occur. Presumably the presence of the benzyl group renders the tetrahydrobenzimidazole derivatives **38** and **39** sufficiently electron rich to facilitate ionization of the carbon-halogen bond followed be deprotonation.[25] In principle, the presence of the olefin in **40** presents the opportunity to incorporate functionality at C4 via electrophilic chemistry but unfortunately attempts to hydrate these materials either by hydroboration or oxymercuration were not successful. On the other hand, with the DMAS-protected series **31-33**, the bromo and iodo-substituted systems **32-33** underwent cycloaddition to deliver the initial adducts **36-37** as single stereoisomers which retained the halogen in excellent yields and stereoselectivity (Scheme 4). The electron withdrawing effect of the sulfamoyl moiety attenuates the propensity of the system to undergo rearomatization and is a consistent observation with other DMAS-substituted systems used in intermolecular Diels-Alder reactions.[34] The chloro-bearing system **31** was capricious, in most experiments we found that there was no reaction except on a single occasion where we were able to observe the formation of the initial adduct by ^{1}H NMR spectroscopy but isolation and purification of the cycloadduct was not achieved. Attempts to repeat the observation were not successful and based solely on circumstantial observations it appears that this particular transformation has a temperature sweet spot that we have been unable to reproduce. Below this temperature, reaction does not occur; above this temperature either decomposition or a retro Diels-Alder reaction occurs.



Scheme 4. Diels-Alder reactions of halo-substituted vinylimidazoles

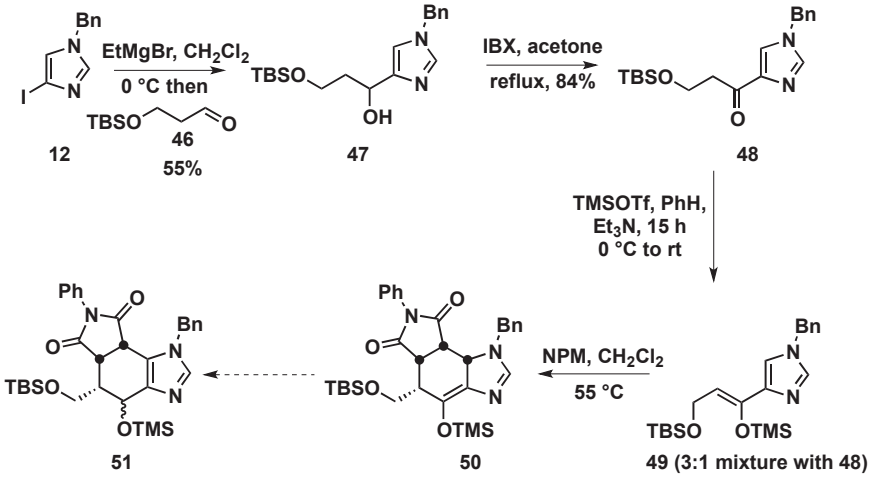
While these intermolecular experiments with halo-substituted dienes were in progress, their utility in intramolecular settings was briefly explored as it potentially offered rapid access to the complete carbon skeleton of several oroidin dimers. The iodo substituted allylic alcohol **24** was coupled with the propiolic acid derivative **41**[23] to provide the enyne **42** in good yield (Scheme 5). No reaction occurred until the reaction mixture reached 120 °C, the same temperature as the parent enynes.[23] However, rather than cycloaddition leading to **43** or potentially the benzimidazole **44**, only dehydroiodination was observed producing bis alkyne **45** in 75% yield.



Scheme 5. Attempted intramolecular variant

Overall, the results with these halo-substituted dienes were mixed demonstrating that they are competent dienes but the Bn-containing systems **28-30** did not retain the halide and to date only fairly electron rich tetrahydrobenzimidazoles have been shown to undergo the oxidative rearrangement chemistry.[19,22] As a

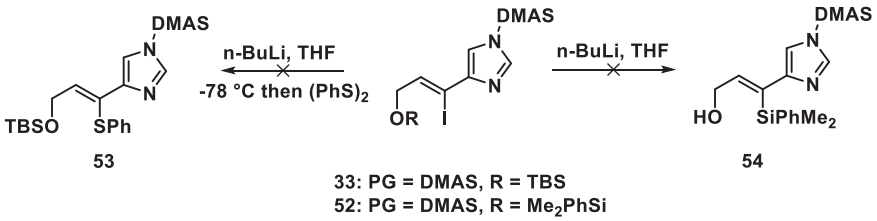
result our attention returned to functionalized vinylimidazoles which were unlikely to undergo post-cycloaddition elimination, in particular the preparation of enol ethers were revisited. This was driven in part by knowledge that protected C4-alcohols were known to engage in oxidative rearrangement,[19] further we suspected that as these dienes would be more electron rich, lower reaction temperatures might be possible and thereby circumventing the post cycloaddition elimination. To obtain the requisite substrate, the ketone was prepared from the 4-iodoimidazole derivative **12** by iodine-magnesium exchange followed by reaction with aldehyde **46** to produce alcohol **47** (Scheme 6); IBX oxidation then provided the corresponding ketone **48**. Treatment of **48** with TBSOTf in the presence of triethylamine delivered the expected silyl enol ether **49** as a 3:1 mixture with the unreacted ketone **48**. Attempted chromatographic purification of **49** was unsuccessful and thus the crude mixture was used in a Diels-Alder reaction with NPM. It was clear from analysis of the ^{1}H NMR spectrum of the crude reaction mixture that some cycloaddition occurred due to both the benzylic and the hydroxymethyl protons appearing as AB quartets – a diagnostic sign of cycloaddition in closely related substrates. However, we were unable to purify and isolate the cycloadduct **50** (or possibly **51**) to determine its precise identity. This is reminiscent of the initial Diels-Alder product derived from the parent substrate which we also were unable to isolate chromatographically but rather through crystallization. Unfortunately, we were unable to use this tactic to isolate **51**.[20,26] Similar results were obtained with the DMAS-protected derivative and thus our efforts were redirected towards evaluation of substrates with an oxygen surrogate.



Scheme 6. Synthesis and attempted Diels-Alder reaction of silyl enol ether **49**

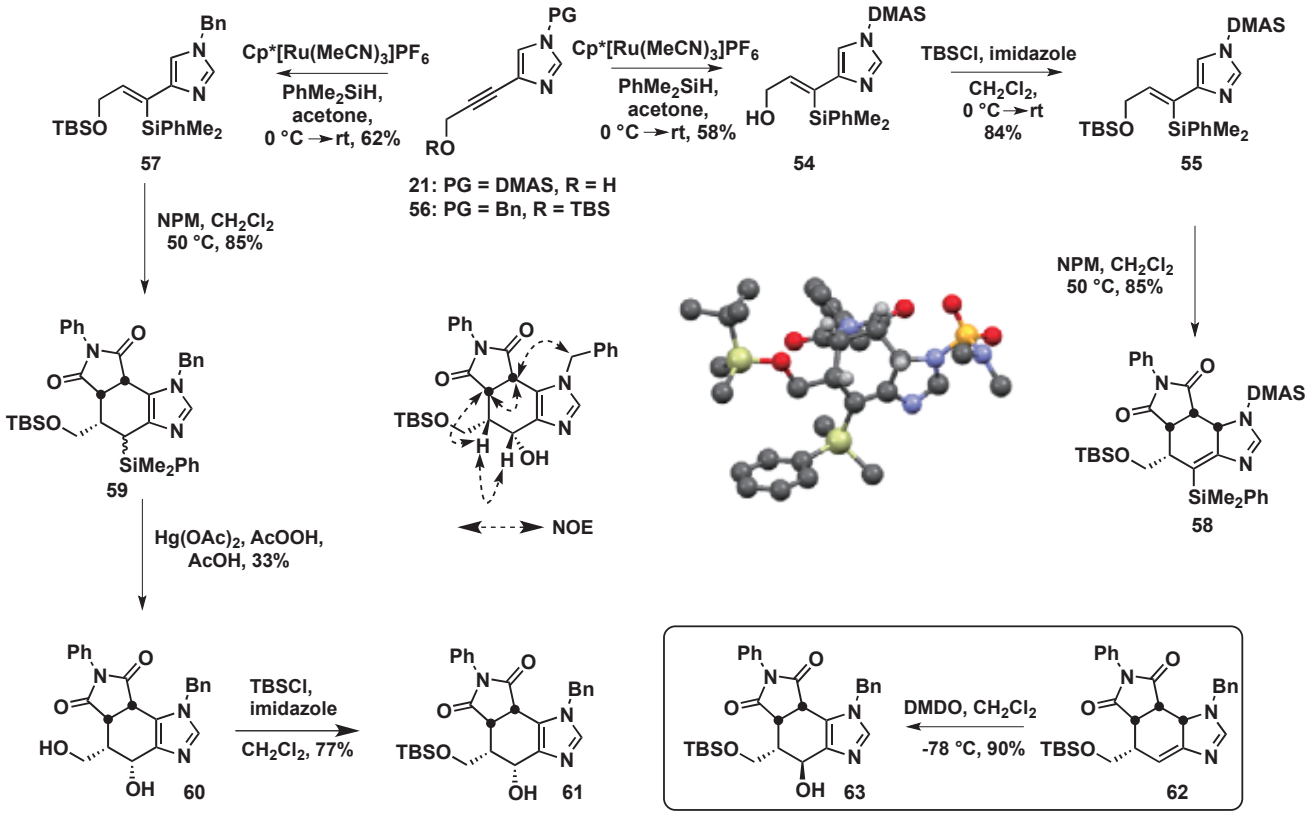
At this point, it was determined that a more robust substituent and synthetic approach was required. Two groups came to mind as possibilities, a vinyl sulfide[35-36] and a vinyl silane,[37-41] both of which can be viewed as oxygen surrogates.[42-47] Our initial plan was to trap the hydroalumination product derived from the propargyl alcohols with an appropriate silicon or sulfur source, but this proved unsuccessful. An

alternative approach, using the vinyliodides which had been prepared from the propargyl alcohols were identified as suitable starting materials. In the case of the sulfide we attempted metal-halogen exchange on **33** and then trapping of the putative vinyl anion with recrystallized phenyl disulfide but none of the desired product (Scheme 7), only the dehalogenated vinylimidazole was obtained. Vinylsilanes can be constructed through the rearrangement of iodoallyl alcohols via metalation of the corresponding silyl ethers.[48] Accordingly, the silyl ether **52** was prepared and then treated with *n*-butyllithium (Scheme 7); unfortunately, only iodine-lithium exchange occurred and the desired rearrangement was not observed.



Scheme 7. Attempted syntheses of vinylsulfide and vinylsilane

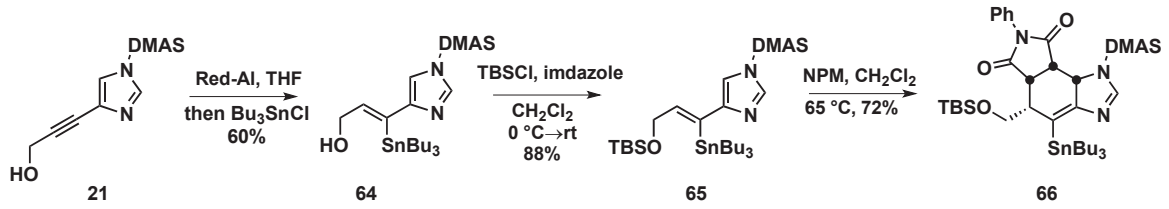
In order to overcome these problems, an alternative synthesis of the vinylsilane was sought, hydrosilylation of the propargyl alcohol was viewed as particularly attractive. The *anti*-hydrosilylation using $[Cp^*Ru(MeCN)_3]PF_6$ and silanes reported by Trost and Ball appeared to present the best approach for accessing the Z-vinylsilane.[49] Initially, the propargyl alcohols **20** and **21** were subjected to hydrosilylation and different results were obtained depending on the imidazole protecting group. In the case the DMAS-protected derivative two regioisomeric vinylsilanes (*ca.* 2:1) of which the required internal derivative **54** was isolated in 58% yield and then converted into the TBS-ether **55** (Scheme 8). In contrast, the Bn-protected derivative delivered a mixture of hydrosilylated and O-silylated products and thus this derivative was converted to the TBS-ether prior **56** to hydrosilylation. After protection the hydrosilylation produced a mixture of regioisomeric vinylsilanes from which the desired silane **57** was isolated in 62% yield (Scheme 8).



Scheme 8. Silyl substituted vinylimidazole in Diels-Alder reactions and X-ray crystal structure of adduct **58** (except for ring junctions, hydrogens omitted for clarity)

With these substituted vinylimidazoles in hand, they were subjected to Diels-Alder reactions with NPM in CH_2Cl_2 at 55-60 °C and in both examples cycloadducts were obtained (Scheme 8). In the case of the DMAS-protected derivative a single product was obtained that was shown to be the initial adduct **58**. This structural assignment was confirmed through an X-ray crystal structure which showed that the cycloaddition had occurred via an *endo* transition state, consistent with all of the other intermolecular Diels-Alder reactions reported to date.[20] On the other hand, the benzyl-protected derivative **57** delivered a mixture of two inseparable C4-epimeric silanes **59** which are formed by rearomatization of the initial cycloadduct. In a general sense this mirrored what we had observed in the parent system where aromatization was more facile with the benzyl group.[20] The stereochemistry at C4 is derived from the rearomatization step which is assumed to be protonation-deprotonation step (see Scheme 1). Unlike other electrophiles, this addition occurs non-selectively and this presumably reflects the fact that the cycloaddition reaction and therefore rearomatization occurs at higher temperature; in other examples these transformations are performed at rt or below. We have not been able to unequivocally assign the stereochemistry of the major diastereomer and sought to address this by conversion of the silyl group into an alcohol with the hope that separation would be possible at that stage. When the diastereomeric mixture

59 was subjected to oxidation[46] a single diol **60** was obtained in 33% yield (concomitant loss of TBS group).[45] We hypothesize the recovery of a single product is a function of the other diol undergoing elimination and forming the corresponding allylic alcohol and not due to any intrinsic selectivity issue as no silane remains after the reaction. Addition circumstantial evidence in support of the structure of the *endo*-alcohol was an attempt to obtain the bis-TBS ether was unsuccessful, whereas the corresponding *exo* derivative delivers the bis-silyl ether easily.[19] This attenuated reactivity is presumably a consequence of the hindered nature of the *endo* hydroxyl group. An NOE experiment was conducted on the alcohol obtained and these data were consistent with the *endo*-configured alcohol. We have prepared the corresponding *exo*-alcohol **63** as shown in Scheme 8 (inset) and in this case the spectroscopic data and the melting points were substantially different and in the case of **63** the relative stereochemistry was confirmed via X-ray crystallography.[19]



Scheme 9. Diels-Alder reaction of tin-substituted vinylimidazole **65**

One last derivative was prepared and evaluated in the Diels-Alder reaction, the vinylstannane **65** which had been prepared in connection with approaches to members of the nagelamide family of oroidin alkaloids from the corresponding propargylic alcohol **21** via hydrostannylation and *O*-silylation (Scheme 9).[50] This vinylimidazole resulted in the formation of the initial cycloadduct **66** similar in structure to the one obtained from the corresponding vinylsilane.

In summary, we have described the construction and evaluation of several heterosubstituted vinyl-imidazoles in intermolecular Diels-Alder reactions resulting in the formation of heterosubstituted cycloadducts in the majority of cases where cycloaddition occurred. These cycloadditions are highly stereoselective and provide the endo cycloadduct. In cases where rearomatization occurred, mixtures of stereoisomers were obtained. The results obtained in this study are guiding our current efforts towards the oroidin alkaloid where intramolecular variants are being pursued.

EXPERIMENTAL

General procedures: All reagents were purchased from commercial suppliers and were used as received unless otherwise noted. All reactions involving air- or water-sensitive compounds were conducted under an

atmosphere of dry nitrogen. All glassware was oven-dried overnight and cooled to rt in a desiccator containing Drierite. Anhydrous solvents were obtained from a Pure-Solv 400 solvent purification system from Innovative Technology Inc or distilled from sodium/benzophenone (THF). Flash chromatography was performed using silica gel (230-400 mesh) and thin layer chromatography (TLC) was performed on Sorbent Technologies Silica TLC aluminum backed plates. ^{1}H and ^{13}C NMR (δ in ppm) spectra were recorded in $CDCl_3$ (unless otherwise noted) at 500 and 125 MHz, respectively; using a JEOL Eclipse+ 500 spectrometer unless otherwise noted, using residual $CHCl_3$ as reference for (^{1}H NMR, δ = 7.26 ppm) and carbon absorption of $CDCl_3$ for (^{13}C NMR, δ = 77.1 ppm). In some cases spectra were recorded at 300 MHz (^{1}H NMR) or 75 MHz (^{13}C NMR) on a JEOL JNM-ECX 300 spectrometer. Infrared spectra were recorded either as neat films using a Bruker Alpha spectrometer (ATR spectroscopy). High resolution mass spectra (HR-MS) were obtained at the Shimazdu Center for Advanced Analytical Chemistry, University of Texas at Arlington.

4-Acetyl-1-benzylimidazole (13): A solution of EtMgBr in Et_2O (18.1 mL, 3.0 M, 1.10 equiv., 54.2 mmol) was added by syringe to a solution of 4-iodo-1-benzylimidazole **12** (14.0 g, 49.3 mmol) in dry CH_2Cl_2 (180 mL) at rt. The resulting suspension was stirred at rt for 1 h, then a solution of *N*-methoxy-*N*-methylacetamide (5.08 g, 49.3 mmol) in dry CH_2Cl_2 (15 mL) was added slowly. After stirring for a further 2 h, the mixture was quenched with saturated aqueous NH_4Cl (30 mL). The organic layer was dried ($MgSO_4$), and concentrated. Purification of the residue by chromatography (EtOAc → EtOAc/MeOH 10/1) afforded 7.90 g (80%) of ketone **13**. mp 65-66 ºC. ^{1}H NMR: δ = 7.56 (s, 1H), 7.54 (s, 1H), 7.40-7.34 (m, 3H), 7.19-7.17 (m, 2H), 5.13 (s, 2H), 2.54 (s, 3H); ^{13}C NMR: δ = 194.5, 142.9, 137.6, 134.9, 129.3, 128.9, 127.7, 123.4, 51.5, 26.6; MS (*m/z*): 200.3 (M^+, 100%), 185.2 (M^+-15, 95%); IR (KBr): 1720, 1667 cm^{-1}. Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 71.68; H, 5.97; N, 14.04.

1-Benzyl-4-(1-chloroethenyl)imidazole (14): To DMF (13.20 g, 0.18 mmol, 10.4 equiv) were added phosphorus oxychloride (1.78 mL, 19.1 mmol, 1.1 equiv) and methyl ketone **13** (3.50 g, 17.4 mmol) at –10 °C. Then the temperature was raised to and held at 35 °C for 1 h. Ice (6 g) and 7.4 g (0.185 mmol) of NaOH in 14 mL of water were added. The resulting suspension was heated until reflux was achieved, then it was allowed to cool to rt and extracted with EtOAc (2 x 100 mL). The organic phase was dried (Na_2SO_4) and concentrated. Purification of the residue by chromatography (EtOAc/hexanes 2/1) afforded 2.60 g (68%) of the desired product **14** as a colorless liquid. ^{1}H NMR: δ = 7.86 (s, 1H), 7.40-7.36 (m, 3H), 7.26-7.20 (m, 2H), 7.10 (s, 1H), 6.22 (d, *J* = 1.6 Hz, 1H), 5.38 (d, *J* = 1.6 Hz, 1H), 5.15 (s, 2H); ^{13}C

NMR: δ = 139.0, 137.9, 135.1, 130.6, 129.3, 128.8, 127.7, 118.7, 112.3, 51.6; MS (*m/z*): 218.2 (M^+, 100%), 220.2 (M^++2, 29%); IR (KBr): 1629 cm^{-1}.

1-Benzyl-4-(1-*tert*-butyldimethylsilyloxyethenyl)imidazole (18): Potassium hydride (1.32 g, 33.0 mmol) was added to a dry THF (25 mL) solution of methyl ketone **13** (1.60 g, 8.20 mmol) and TBSCl chloride (1.61 g, 10.7 mmol) at –78 °C. The stirred mixture was warmed slowly to 25 °C and stirred another 24 h. Although TLC analysis indicated that some ketone still remained, the reaction mixture was concentrated and the residue purified by chromatography (EtOAc/hexanes = 1:2) to afford the TBS enol ether **18** as a colorless liquid (1.0 g, 40%), which decomposes slowly at rt. ^{1}H NMR: δ = 7.41 (s, 1H), 7.33-7.30 (m, 3H), 7.12-7.10 (m, 2H), 6.91 (s, 1H), 5.12 (d, *J* = 1.1 Hz, 1H), 5.05 (s, 2H), 4.27 (d, *J* = 1.1 Hz, 1H), 0.93 (s, 9H), 0.18 (s, 6H); ^{13}C NMR: δ = 151.2, 141.5, 137.4, 136.2, 129.1, 128.3, 127.2, 116.7, 89.0, 50.9, 25.9, 18.3, -4.5; MS (*m/z*): 316 (M^++1, 24%), 273 (M^+-43, 93%), 257 (M^+-59, 100%); IR (KBr): 1671, 1539 cm^{-1}.

(*Z*)-3-(1-Benzyl-1*H*-imidazol-4-yl)-3-chloroprop-2-en-1-ol (22): In a round bottom flask compound **20** (250 mg, 1.17 mmol) was dissolved under N_2 atmosphere in anhydrous THF (20 mL). The reaction mixture was cooled to 0 °C and then to it Red-Al (65 wt% in toluene, 0.45 mL, 1.41 mmol) was added dropwise. After stirring the reaction mixture for 30 min, *N*-chlorosuccinimide (210 mg, 1.53 mmol), dissolved in anhydrous THF (2.5 mL), was added. Then the reaction mixture was stirred for another 1 h at rt. Finally the reaction was quenched with NH_4Cl (10 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%) providing **22** as a yellow thick liquid (102 mg, 35%). ^{1}H NMR (300 MHz): δ = 7.98 (s, 1H), 7.39-7.36 (m, 3H), 7.23 (dd, *J* = 7.4 , 2.1 Hz, 2H), 7.01 (s, 1H), 6.85 (t, *J* = 6.2 Hz, 1H), 5.17 (s, 2H), 4.44 (d, *J* = 6.2 Hz, 2H), 4.03 (br s, 1H); ^{13}C NMR (75 MHz): δ = 138.2, 137.5, 134.7, 129.3, 128.9, 127.9, 125.6, 124.1, 118.5, 59.6, 51.9; FT-IR (neat, cm^{-1}): 3230, 2948, 1610, 1512, 1415, 1331, 1140, 1080, 835, 712, 623; HRMS-ESI (*m/z*): calc for $[M+H]^+$ $C_{13}H_{14}ClN_2O$ 249.0797 found 249.0790.

(*Z*)-3-(1-Benzyl-1*H*-imidazol-4-yl)-3-bromoprop-2-en-1-ol (23): In a round bottom flask compound **20** (200 mg, 0.94 mmol) was dissolved under N_2 atmosphere in anhydrous THF (20 mL). The reaction mixture was cooled to 0 °C and then to it Red-Al (65 wt% in toluene, 0.35 mL, 1.13 mmol) was added dropwise. After stirring the reaction mixture for 30 min, *N*-bromosuccinimide (250 mg, 1.41 mmol) dissolved in anhydrous THF (2.5 mL) was added. Then the reaction mixture was stirred for another 1 h at

rt. Finally the reaction was quenched with NH_4Cl (10 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc/hexanes, 1:1) providing **23** as a yellow thick liquid (220 mg, 81%). ^{1}H NMR (300 MHz): δ = 7.52 (d, *J* = 1.4 Hz, 1H), 7.39-7.33 (m, 3H), 7.18 (dd, *J* = 7.4, 2.1 Hz, 2H), 7.10 (d, *J* = 1.0 Hz, 1H), 6.94 (t, *J* = 6.2 Hz, 1H), 5.08 (s, 2H), 4.43 (d, *J* = 6.2 Hz, 2H), 1.94 (br s, 1H); ^{13}C NMR (75 MHz): δ = 141.7, 137.9, 135.6, 129.2, 128.6, 127.4, 126.2, 119.2, 117.2, 62.4, 51.2; FT-IR (neat, cm^{-1}): 3246, 2935, 1640, 1537, 1454, 1231, 1160, 1043, 830, 711; HRMS-ESI (*m/z*): calc for $[M+H]^+$ $C_{13}H_{14}BrN_2O$ 293.0284 found 293.0281.

(*Z*)-3-(1-Benzyl-1*H*-imidazol-4-yl)-3-iodoprop-2-en-1-ol (24): In a round bottom flask compound **20** (1.2 g, 5.65 mmol) was dissolved under N_2 atmosphere in anhydrous THF (70 mL). The reaction mixture was cooled to 0 °C and then to it Red-Al (65 wt% in toluene, 2.10 mL, 6.78 mmol) was added dropwise. After stirring the reaction mixture for 30 min, *N*-iodosuccinimide (1.65 g, 7.35 mmol) dissolved in anhydrous THF (10 mL) was added. Then the reaction mixture was stirred for another 1 h at rt. Finally the reaction was quenched with NH_4Cl (10 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc/hexanes) providing **24** as a yellow solid (1.68 g, 88%). mp 84-86 °C. ^{1}H NMR (300 MHz): δ = 7.56 (d, *J* = 1.4 Hz, 1H), 7.37-7.32 (m, 3H), 7.18 (dd, *J* = 7.4, 2.1 Hz, 2H), 7.05 (d, *J* = 1.4 Hz, 1H), 6.83 (t, *J* = 6.2 Hz, 1H), 5.10 (s, 2H), 4.35 (d, *J* = 6.2 Hz, 2H), 2.95 (s, 1H); ^{13}C NMR (75 MHz): δ = 143.4, 137.9, 135.6, 133.4, 129.3, 128.6, 127.5, 121.2, 94.0, 67.3, 51.2; FT-IR (neat, cm^{-1}): 3192, 2850, 1633, 1493, 1457, 1355, 1156, 1041, 940, 840, 716; HRMS-ESI (*m/z*): calc for $[M+H]^+$ $C_{13}H_{14}IN_2O$ 341.0151 found 341.0146.

(*Z*)-4-(1-Chloro-3-hydroxyprop-1-enyl)-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide (25): In a round bottom flask compound **21** (300 mg, 1.31 mmol) was dissolved under N_2 atmosphere in anhydrous THF (25 mL). The reaction mixture was cooled to 0 °C and then to it Red-Al (65 wt% in toluene) (0.50 mL, 1.57 mmol) was added dropwise. After stirring the reaction mixture for 30 min, *N*-chlorosuccinimide (250 mg, 1.70 mmol) dissolved in anhydrous THF (5 mL) was added. Then the reaction mixture was stirred for another 1 h at rt. Finally the reaction was quenched with NH_4Cl (10 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc) providing **25** as a yellow solid (120 mg, 34%). ^{1}H NMR: δ = 7.85 (d, *J* = 1.4 Hz, 1H), 7.37 (d, *J* = 1.0 Hz, 1H), 6.84 (t, *J* = 6.2 Hz, 1H), 4.50 (d, *J* = 6.2 Hz, 2H), 2.90 (s, 6H); ^{13}C NMR

(75 MHz): δ = 141.3, 137.2, 125.9, 125.1, 115.6, 59.7, 38.3; FT-IR (neat, cm^{-1}): 3356, 2987, 1635, 1396, 1173, 1082, 968, 731, 599; HRMS-ESI (*m/z*): calc for $[M+H]^+$ $C_8H_{13}ClN_3O_3S$ 266.0361 found 266.0357.

(*Z*)-4-(1-Bromo-3-hydroxyprop-1-enyl)-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide (26): In a round bottom flask compound **21** (300 mg, 1.31 mmol) was dissolved under N_2 atmosphere in anhydrous THF (20 mL). The reaction mixture was cooled to 0 °C and then to it Red-Al (65 wt% in toluene, 0.5 mL, 1.57 mmol) was added dropwise. After stirring the reaction mixture for 30 min, *N*-bromosuccinimide (310 mg, 1.70 mmol) dissolved in anhydrous THF (5 mL) was added. Then the reaction mixture was stirred for another 1 h at rt. Finally the reaction was quenched with NH_4Cl (10 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 50 mL), the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc/hexanes, 1:1) providing **26** as a yellow solid (315 mg, 78%). mp 101-103 °C. ^{1}H NMR: δ = 7.88 (d, *J* = 1.4 Hz, 1H), 7.34 (s, 1H), 7.05 (t, *J* = 5.9 Hz, 1H), 4.43 (d, *J* = 5.5 Hz, 2H), 2.87 (s, 6H); ^{13}C NMR: δ = 142.1, 137.2, 129.9, 116.8, 114.9, 62.2, 38.3; FT-IR (neat, cm^{-1}): 2980, 2934, 1501, 1381, 1258, 1188, 1129, 839; HRMS-ESI (*m/z*): calc for $[M+H]^+$ $C_8H_{13}BrN_3O_3S$ 309.9861 found 309.9870.

(*Z*)-4-(3-Hydroxy-1-iodoprop-1-enyl)-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide (27): In a round bottom flask compound **21** (1.00 g, 4.36 mmol) was dissolved under N_2 atmosphere in anhydrous THF (50 mL). The reaction mixture was cooled to 0 °C and then to it Red-Al (65 wt% in toluene, 1.63 mL, 5.20 mmol) was added dropwise. After stirring the reaction mixture for 30 min, *N*-iodosuccinimide (1.27 g, 5.60 mmol) dissolved in anhydrous THF (4 mL) was added. Then the reaction mixture was stirred for another 1 h at rt. Finally the reaction was quenched with NH_4Cl (10 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc/hexanes, 1:1) providing **27** as a yellow solid (1.27 g, 82%). The proton and carbon contains residual acetone impurity. mp 94-96 °C. ^{1}H NMR (300 MHz): δ = 7.95 (d, *J* = 1.4 Hz, 1H), 7.34 (d, *J* = 1.4 Hz, 1H), 6.99 (t, *J* = 5.8 Hz, 1H), 4.39 (d, *J* = 6.2 Hz, 2H), 2.89 (s, 6H); ^{13}C NMR (75 MHz): δ = 144.2, 137.1, 136.2, 118.5, 91.1, 67.2, 38.3; FT-IR (neat, cm^{-1}): 3250, 1392, 1167, 1079, 962, 599, 508; HRMS-ESI (*m/z*): calc for $[M+H]^+$ $C_8H_{13}IN_3O_3S$ 357.9722 found 357.9723.

(*Z*)-1-Benzyl-4-(3-(*tert*-butyldimethylsilyloxy)-1-chloroprop-1-enyl)-1*H*-imidazole (28): In a round bottom flask compound **22** (100 mg, 0.40 mmol) was dissolved in CH_2Cl_2 (10 mL) under N_2 atmosphere. The solution was cooled to 0 °C and then to the reaction mixture imidazole (40 mg, 0.60 mmol) and TBSCl (78 mg, 0.52 mmol) was added. The reaction mixture was stirred for 8 h, then NH_4Cl (5 mL) was

added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%) providing **28** as a colorless solid (135 mg, 92%). mp 76-78 °C. ^{1}H NMR (300 MHz): δ = 7.54 (d, *J* = 1.4 Hz, 1H), 7.35-7.31 (m, 3H), 7.15 (dd, *J* = 7.4, 1.7 Hz, 2H), 7.03 (d, *J* = 1.0 Hz, 1H), 6.64 (t, *J* = 5.8 Hz, 1H), 5.06 (s, 2H), 4.49 (d, *J* = 5.8 Hz, 2H), 0.89 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75 MHz): δ = 140.3, 137.8, 135.6, 129.2, 128.6, 127.5, 124.6, 124.4, 118.0, 60.8, 51.2, 26.2, 18.4, -5.1; FT-IR (neat, cm^{-1}): 2934, 2858, 1590, 1475, 1384, 1167, 1082, 822, 740, 596; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{19}H_{27}ClN_2OSi$ 363.1659, found.

(*Z*)-1-Benzyl-4-(1-bromo-3-(*tert*-butyldimethylsilyloxy)prop-1-enyl)-1*H*-imidazole (29): In a round bottom flask compound **23** (170 mg, 0.58 mmol) was dissolved in CH_2Cl_2 (10 mL) under N_2 atmosphere. The solution was cooled to 0 °C and then to the reaction mixture imidazole (60 mg, 3.60 mmol) and TBSCl (110 mg, 0.75 mmol) was added. The reaction mixture was stirred for 8 h, then NH_4Cl (5 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc/hexanes, 1:4) providing **29** as a colorless thick liquid (210 mg, 91%). ^{1}H NMR (300 MHz): δ = 7.51 (d, *J* = 1.4 Hz, 1H), 7.37-7.34 (m, 3H), 7.16 (dd, *J* = 7.6, 1.4 Hz, 2H), 7.05 (d, *J* = 1.4 Hz, 1H), 6.83 (t, *J* = 5.5 Hz, 1H), 5.07 (s, 2H), 4.46 (d, *J* = 5.5 Hz, 2H), 0.90 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (75 MHz): δ = 141.5, 137.8, 135.7, 129.2, 128.6, 127.6, 127.4, 119.1, 115.3, 63.6, 51.2, 26.0, 18.4, -5.1; FT-IR (neat, cm^{-1}): 2943, 2840, 1604, 1495, 1457, 1255, 1115, 1065, 781, 704; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{19}H_{28}BrN_2OSi$ 407.1149 found 407.1136.

(*Z*)-1-Benzyl-4-(3-(*tert*-butyldimethylsilyloxy)-1-iodoprop-1-enyl)-1*H*-imidazole (30): In a round bottom flask compound **24** (0.77 g, 2.25 mmol) was dissolved in CH_2Cl_2 (25 mL) under N_2 atmosphere. The solution was cooled to 0 °C and then to the reaction mixture imidazole (240 mg, 3.60 mmol) and TBSCl (440 mg, 2.94 mmol) was added. The reaction mixture was stirred for another 8 h, then NH_4Cl (10 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc/hexanes, 1:4) providing **30** as a colorless thick liquid (920 mg, 90%). ^{1}H NMR (300 MHz): δ = 7.55 (d, *J* = 1.4 Hz, 1H), 7.40-7.33 (m, 3H), 7.16 (dd, *J* = 7.6, 1.4 Hz, 2H), 7.05 (*J* = 1.4 Hz, 1H), 6.73 (t, *J* = 5.5 Hz, 1H), 5.10 (s, 2H), 4.40 (d, *J* = 5.5 Hz, 2H), 0.92 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (75 MHz): δ = 143.6, 137.7, 134.0, 129.2, 128.5, 127.4, 120.3, 92.3, 77.8, 68.1, 50.9, 25.9, 18.4, 17.9, -5.1; FT-IR (neat, cm^{-1}): 2928, 2849, 1498, 1449, 1258, 1097, 1065, 842, 769, 707; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{19}H_{28}IN_2OSi$ 455.1010 found 455.1014.

(*Z*)-4-(3-(*tert*-Butyldimethylsilyloxy)-1-chloroprop-1-enyl)-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide (31): In a round bottom flask compound **25** (130 mg, 0.49 mmol) was dissolved in CH_2Cl_2 (10 mL) under N_2 atmosphere. The solution was cooled to 0 °C and then to the reaction mixture imidazole (50 mg, 0.73 mmol) and TBSCl (100 mg, 0.64 mmol) was added. The reaction mixture was stirred for 8 h, then NH_4Cl (5 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%) providing **31** as a colorless solid (161 mg, 87%). mp 88-90 °C. ^{1}H NMR (300 MHz): δ = 7.84 (s, 1H), 7.34 (s, 1H), 6.76 (t, *J* = 5.9 Hz, 1H), 4.52 (d, *J* = 5.9 Hz, 2H), 2.89 (s, 6H), 0.91 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (75 MHz): δ = 141.6, 137.1, 127.4, 123.2, 115.2, 60.7, 38.3, 26.0, 18.4, -5.1; FT-IR (neat, cm^{-1}): 2954, 2860, 1630, 1481, 1381, 1173, 1085, 827, 778, 754, 617; HRMS-ESI (*m/z*): calc for $[M+H]^+$ $C_{14}H_{26}ClN_3O_3SSi$ 380.1231 found 380.1231.

(*Z*)-4-(1-Bromo-3-(*tert*-butyldimethylsilyloxy)prop-1-enyl)-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide (32): In a round bottom flask compound **26** (280 mg, 0.90 mmol) was dissolved in CH_2Cl_2 (15 mL) under N_2 atmosphere. The solution was cooled to 0 °C and then to the reaction mixture imidazole (90 mg, 1.35 mmol) and TBSCl (177 mg, 1.17 mmol) was added. The reaction mixture was stirred for 8 h, then NH_4Cl (5 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc/hexanes, 1:4) providing **32** as a colorless solid (336 mg, 88%). mp 91-93 °C. ^{1}H NMR: δ = 7.86 (d, *J* = 1.4 Hz, 1H), 7.34 (d, *J* = 1.4 Hz, 1H), 6.97 (t, *J* = 5.5 Hz, 1H), 4.48 (d, *J* = 5.5 Hz, 2H), 2.88 (s, 6H), 0.92 (s, 9H), 0.10 (s, 6H); ^{13}C NMR: δ = 142.4, 137.0, 130.9, 116.3, 113.3, 63.4, 38.3, 26.0, 18.4, -5.1; FT-IR (neat, cm^{-1}): 2938, 2845, 1592, 1397, 1165, 1150, 1085, 987, 840, 717, 590; HR-MS (*m/z*): calc for $[M+Na]^+$ $C_{14}H_{26}BrN_3O_3SSiNa$ 446.0544 found 446.0528.

(*Z*)-4-(3-(*tert*-Butyldimethylsilyloxy)-1-iodoprop-1-enyl)-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide (33): In a round bottom flask compound **27** (400 mg, 1.12 mmol) was dissolved in CH_2Cl_2 (20 mL) under N_2 atmosphere. The solution was cooled to 0 °C and then to the reaction mixture imidazole (110 mg, 1.68 mmol) and TBSCl (220 mg, 1.45 mmol) were added. The reaction mixture was stirred for 8 h, then NH_4Cl (5 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc/hexanes, 1:4) providing **33** as a colorless solid (480 mg, 92%). mp 75-77 °C. ^{1}H NMR (300 MHz): δ = 7.88 (d, *J* = 1.0 Hz, 1H), 7.31 (d, *J*

= 1.4 Hz, 1H), 6.89 (t, *J* = 5.5 Hz, 1H), 4.39 (d, *J* = 5.5 Hz, 2H), 2.86 (s, 6H), 0.89 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75 MHz): δ = 144.3, 137.4, 136.9, 117.9, 89.4, 68.4, 38.3, 26.0, 18.4, -5.1; FT-IR (neat, cm^{-1}): 2934, 2852, 1703, 1592, 1396, 1173, 1148, 1079, 833, 731, 596; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{14}H_{27}IN_3O_3SSi$ 472.0582 found 472.0596.

(5aS*,5R*,8aS*,8bS*)-4-Bromo-5-*tert*-butyldimethylsilyloxymethyl-1,5,5a,6,7,8,8a,8b-octahydro-1-(*N*,*N*-dimethylsulfamoyl)-7-phenyl-6,8-dioxopyrrolo[3,4-*g*]benzimidazole (36): CH_2Cl_2 (0.75 mL) was placed in a resealable thick-walled tube and was purged with N_2 for 5 min, then compound **32** (25 mg g, 0.47 mmol) and *N*-phenylmaleimide (11 mg, 0.71 mmol) were added and again the reaction mixture was purged with N_2 for an additional 5 min. After sealing the tube with a Teflon screw cap, the reaction mixture was heated at 55-60 °C for 12 h. The reaction mixture was cooled to rt and the CH_2Cl_2 was evaporated under vacuum. The crude product was purified by chromatography (EtOAc/hexanes 1:3) to provide cycloadduct **36** (30 mg, 85%) as a yellow film. ^{1}H NMR: δ = 7.69 (s, 1H), 7.42 (d, *J* = 8.1 Hz, 2H), 7.37-7.35 (m, 1H), 7.07 (d, *J* = 7.5 Hz, 2H), 4.66 (dd, *J* = 6.9, 1.7 Hz, 1H), 4.41 (dd, *J* = 10.3, 9.2 Hz, 1H), 4.19 (dd, *J* = 10.7, 5.7 Hz, 1H), 4.12-4.07 (m, 1H), 3.77 (dd, *J* = 8.6, 6.9 Hz, 1H), 3.63, (dd, *J* = 8.0, 5.2 Hz, 1H), 3.05 (s, 6H), 2.70-2.66 (m, 1H), 0.94 (s, 9H), 0.16 (s, 3H), 0.150 (s, 3H); ^{13}C NMR: δ = 173.6, 172.4, 155.4, 149.4, 131.3, 129.4, 129.2, 126.7, 100.8, 74.3, 66.0, 62.2, 60.7, 44.9, 42.4, 38.1, 37.9, 26.0, 18.4, -5.2; FT-IR (neat, cm^{-1}): 2952, 2928, 2854, 1713, 1542, 1378, 1154, 1082, 968, 835, 773, 723, 692, 592; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{24}H_{34}BrN_4SSi$ 597.1197 found 597.1267.

(5aS*,5R*,8aS*,8bS*)-5-*tert*-Butyldimethylsilyloxymethyl-4-iodo-1,5,5a,6,7,8,8a,8b-octahydro-1-(*N*,*N*-dimethylsulfamoyl)-7-phenyl-6,8-dioxopyrrolo[3,4-*g*]benzimidazole (37): CH_2Cl_2 (2.1 mL) was placed in a resealable thick-walled tube and was purged with N_2 for 5 min, then compound **33** (0.10 g, 0.21 mmol) and *N*-phenylmaleimide (26 mg, 0.30 mmol) were added and again the reaction mixture was purged with N_2 for an additional 5 min. After sealing the tube with a Teflon screw cap, the reaction mixture was heated at 55-60 °C for 12 h. The reaction mixture was cooled to rt and the CH_2Cl_2 was evaporated under vacuum. The crude product was purified by chromatography (EtOAc/hexanes 1:3) to provide cycloadduct **37** (123 mg, 91%) as a thick red oil. ^{1}H NMR: δ = 7.68 (s, 1H), 7.42-7.39 (m, 2H), 7.37-7.35 (m, 1H), 7.09-7.07 (m, 2H), 4.68 (dd, *J* = 6.3, 1.8 Hz, 1H), 4.32 (dd, *J* = 9.8, 8.6 Hz, 1H), 4.08 (dd, *J* = 9.8, 6.3 Hz, 1H), 3.74 (dd, *J* = 8.6, 6.9 Hz, 1H), 3.64 (dd, *J* = 8.6, 5.2 Hz, 1H), 3.02 (s, 6H), 2.51-2.49 (m, 1H), 0.93 (s, 9H), 0.153 (s, 3H), 0.150 (s, 3H); ^{13}C NMR: δ = 173.7, 172.5, 155.5, 155.0, 131.3, 129.4, 129.1, 126.8, 74.4, 66.0, 60.7, 44.3, 42.4, 38.1, 37.8, 26.1, 18.4, -5.1; FT-IR (neat, cm^{-1}): 2952, 2928, 2856, 1705, 1499, 1378, 1155, 1096, 970, 908, 834, 778, 723, 691, 587; HR-MS (*m/z*): calc for $[M+Na]^+$ $C_{24}H_{33}N_4O_5SSiINa$ 667.0878 found 667.0898.

(5a*R,8a*S**)-1-Benzyl-5-((*tert*-butyldimethylsilyloxy)methyl)-7-phenyl-7,8a-dihydroimidazo[4,5-*e*]isoindole-6,8(1*H*,5a*H*)-dione (40):** CH_2Cl_2 (3 mL) was placed in a resealable thick-walled tube and was purged with N_2 for 5 min, then compound **29** (140 mg, 0.31 mmol) and *N*-phenylmaleimide (65 mg, 0.37 mmol) was added and again the reaction mixture was purged with N_2 for an additional 5 min. After sealing the tube with a Teflon screw cap, the reaction mixture was heated at 50 °C for 12 h. The reaction mixture was cooled to rt and the CH_2Cl_2 was evaporated under vacuum. The crude product was purified by chromatography (EtOAc/hexanes, 1:1) to provide **40** (69 mg, 45%) as a yellow solid. mp 202-204 °C. ^{1}H NMR: δ = 7.52 (s, 1H), 7.49-7.46 (m, 2H), 7.42-7.32 (m, 4H), 7.24 (d, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 7.3 Hz, 2H), 6.67 (s, 1H), 5.77 (d, *J* = 15.6 Hz, 1H), 5.28 (d, *J* = 15.6 Hz, 1H), 4.53 (s, 2H), 4.20 (d, *J* = 11.4 Hz, 1H), 4.09 (d, *J* = 11.4 Hz, 1H), 0.92 (s, 9H), 0.10 (s, 6H); ^{13}C NMR: δ = 175.3, 175.1, 139.6, 137.3, 135.9, 131.7, 129.3, 129.2, 129.0, 128.8, 128.3, 127.5, 126.5, 119.1, 118.9, 64.6, 50.0, 43.4, 39.8, 26.1, 18.5, -5.2; FT-IR (neat, cm^{-1}): 2934, 2858, 1721, 1498, 1375, 1194, 1123, 839; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{29}H_{34}N_3O_3Si$ 500.2364 found 500.2371.

(*Z*)-3-(1-Benzyl-1*H*-imidazol-4-yl)-3-iodoallyl 3-(1-(*N*,*N*-dimethylsulfamoyl)-1*H*-imidazol-4-yl)-propiolate (42): In a round bottom flask the alcohol **24** (200 mg, 0.58 mmol), acid **41** (210 mg, 0.88 mmol), DMAP (7 mg, 0.06 mmol) and camphorsulfonic acid (8 mg, 0.04 mmol) were dissolved in dry CH_2Cl_2 (15 mL) under N_2 atmosphere. The mixture was cooled to (-78 °C) and DCC (180 mg, 0.88 mmol) dissolved in dry CH_2Cl_2 (5 mL) was added dropwise. The reaction mixture was allowed to warm up to rt and stirred for 8 h. The mixture was filtered through Celite and the filter cake was washed with CH_2Cl_2. The filtrate was concentrated and the crude product was purified by chromatography (hexane/EtOAc, 2:18) affording **42** as a white solid (230 mg, 68%). mp 135-137 °C. ^{1}H NMR (300 MHz): δ = 7.86 (s, 1H), 7.61 (d, *J* = 0.9 Hz, 1H), 7.56 (s, 1H), 7.38-7.34 (m, 3H), 7.18 (d, *J* = 6.9 Hz, 2H), 7.11 (s, 1H), 6.83 (t, *J* = 15.6 Hz, 1H), 5.08 (s, 2H), 4.96 (d, *J* = 6.4 Hz, 2H), 2.90 (s, 6H); ^{13}C NMR (75 MHz): δ = 153.4, 140.9, 137.6, 137.2, 134.6, 129.9, 129.5, 129.2, 127.9, 124.9, 123.4, 122.1, 82.2, 79.2, 70.1, 52.1, 38.4; FT-IR (neat, cm^{-1}): 3138, 2849, 2219, 1703, 1453, 1386, 1333, 1212, 1167, 1086, 1048, 995, 850, 738, 617; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{21}H_{21}IN_5O_4S$ 566.0353 found 566.0352.

3-(1-Benzyl-1*H*-imidazol-4-yl)prop-2-ynyl 3-(1-(*N*,*N*-dimethylsulfamoyl)-1*H*-imidazol-4-yl)-propiolate (45): CH_2Cl_2 (10 mL) was placed in a thick-walled pressure tube and purged with N_2 for 10 min, then ester **42** (120 mg, 11.4 mmol) was added and again the reaction mixture was purged with N_2 for 5 min. After sealing the tube with a Teflon screw cap, the reaction mixture was heated to 120 °C for 12 h. The reaction mixture was cooled to rt, and then the reaction mixture was concentrated. The crude product was purified by chromatography (acetone/EtOAc, 7:3) to provide a yellow solid **45** (69 mg, 75%). mp

209-211 °C. ^{1}H NMR (300 MHz): δ = 8.14 (s, 1H), 8.00 (d, *J* = 0.9 Hz, 1H), 7.87 (s, 1H), 7.19-7.16 (m, 3H), 6.88 (d, *J* = 0.9 Hz, 1H), 6.58 (d, *J* = 6.9 Hz, 2H), 5.38 (s, 2H), 5.33 (s, 2H), 2.88 (s, 6H); ^{13}C NMR (75 MHz): δ = 170.0, 150.0, 149.2, 140.5, 135.8, 135.5, 133.4, 132.2, 128.9, 128.1, 125.3, 119.5, 118.5, 118.4, 113.7, 68.0, 50.7, 38.3; FT-IR (neat, cm^{-1}): 3101, 2927, 2241, 2219, 1759, 1501, 1456, 1390, 1264, 1167, 1077, 965, 734, 593; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{21}H_{20}N_5O_4S$ 438.1236 found 438.1241.

1-Benzyl-4-(3-(*tert*-butyldimethylsilyloxy)-1-hydroxypropanyl)-1*H*-imidazole (47): In a round bottom flask 4-iodoimidazole **12** (500 mg, 1.80 mmol) was dissolved in dry CH_2Cl_2 (50.0 mL) under N_2 atmosphere. The solution was cooled to 0 °C and to this reaction mixture 3M EtMgBr in Et_2O (0.90 mL, 2.70 mmol) was added dropwise and slowly allowed to warm up to rt. After stirring the reaction mixture for 30 min at the same temperature, compound **46** (509 mg, 2.70 mmol) was added dropwise and stirred for another 1 h. Finally, the reaction was quenched with NH_4Cl (25.0 mL) and the organic layer was separated. The aqueous layer was extracted with EtOAc (2 x 20 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and the solvent was removed by rotary evaporation. The crude product was purified by flash chromatography (EtOAc, 100%) providing **47** as a colorless wax (335 mg, 55%). mp 59-60 °C; ^{1}H NMR: δ = 7.48 (d, *J* = 1.2 Hz, 1H), 7.36-7.31 (m, 3H), 7.18-7.16 (m, 2H), 6.86 (s, 1H), 5.06 (s, 2H), 4.92 (dd, *J* = 8.0, 2.9 Hz, 1H), 3.88-3.85 (m, 2H), 2.09-2.08 (m, 1H), 2.03-2.01 (m, 1H), 0.88 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR: δ = 146.2, 136.8, 136.1, 129.1, 128.4, 127.5, 115.5, 69.2, 62.3, 51.0, 38.6, 26.0, 18.2, -5.5; FT-IR (neat, cm^{-1}): 3221, 2955, 2927, 2855, 1498, 1456, 1387, 1359, 1251, 1089, 1000, 945, 829, 771, 718, 638; HRMS-ESI (*m/z*): calc for $[M+H]^+$ $C_{19}H_{31}N_2O_2Si$ 347.2149 found 347.2145.

1-Benzyl-4-(3-(*tert*-butyldimethylsilyloxy)-1-propanonyl)-1*H*-imidazole (48): In a round bottom flask alcohol **47** (300 mg, 0.87 mmol) was dissolved in acetone (30.0 mL) at rt and IBX (487 mg, 1.74 mmol) was added to it in one portion. Then the reaction mixture was stirred for 1 h under reflux. After 1 h, the reaction was cooled to rt and acetone was evaporated. EtOAc was added to the residue (2 x 15 mL) and filtered. The solvent in the combined filtrate was concentrated by rotary evaporation. The crude product was then purified by flash chromatography (EtOAc/hexanes, 2:3) providing **48** as a thick colorless oil (251 mg, 84%). ^{1}H NMR: δ = 7.55 (d, *J* = 1.2 Hz, 1H), 7.52 (s, 1H), 7.38-7.34 (m, 3H), 7.17 (dd, *J* = 8.0, 2.3 Hz, 2H), 5.12 (s, 2H), 4.03 (t, *J* = 6.9 Hz, 2H), 3.17 (t, *J* = 6.9 Hz, 2H), 0.84 (s, 9H), 0.20 (s, 6H); ^{13}C NMR: δ = 198.9, 143.0, 137.6, 135.0, 129.3, 128.9, 127.7, 123.6, 59.2, 51.5, 42.2, 26.0, 18.4, -5.3; FT-IR (neat, cm^{-1}): 2952, 2928, 2883, 2855, 1668, 1535, 1471, 1386, 1251, 1167, 1095, 832, 776, 712; HRMS-ESI (*m/z*): calc for $[M+H]^+$ $C_{19}H_{29}N_2O_2Si$ 345.1993 found 345.1995.

1-Benzyl-4-(1-trimethylsilyloxy-3-(*tert*-butyldimethylsilyloxy)prop-1-enyl)-1*H*-imidazole (49): In a round bottom flask, ketone **48** (200 mg, 0.58 mmol) was dissolved in dry benzene (5.0 mL) under N_2 atmosphere. The solution was cooled to 0 °C and then to the reaction mixture Et_3N (0.20 mL, 2.32 mmol) was added slowly. After stirring the reaction mixture for 10 min at the same temperature, TMSOTf (0.32 mL, 1.74 mmol) was added dropwise and stirred for 15 h at rt. The reaction was quenched with brine (5.0 mL) and diluted with CH_2Cl_2 (15.0 mL). The aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4. The solvent was removed by rotary evaporation to provide mixture of silyl enol ether **49** and unreacted ketone **48** in 3.0:1.0 ratio (as determined by ^{1}H NMR spectroscopy). Characteristic peaks for **49** are reported here. ^{1}H NMR: δ = 7.44 (d, *J* = 1.7 Hz, 1H), 7.35-7.29 (m, 3H [1.29H from **48** overlapped], total 4.31H), 7.13-7.11 (m, 2H), 6.81 (d, *J* = 1.2 Hz, 1H), 5.71 (t, *J* = 6.9 Hz, 1H), 5.10 (s, 2H), 4.31 (d, *J* = 7.5 Hz, 1H), 0.88 (s, 9H), 0.14 (s, 9H), 0.06 (s, 6H); ^{13}C NMR: δ = 144.4, 141.6, 137.4, 136.1, 128.4, 127.3, 116.6, 107.9, 58.2, 51.0, 46.6, 26.1, 18.3, 8.7, 0.5, -5.0.

(*Z*)-4-(1-Dimethylphenylsilyl-3-hydroxyprop-1-enyl)-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide (54): Propargyl alcohol **21** (0.10 g, 0.44 mmol) was dissolved in dry acetone (1.0 mL) under N_2 atmosphere with cooling to 0 °C and dimethylphenylsilane (0.10 mL, 0.66 mmol) was added dropwise. Then Cp*[Ru(MeCN)$_3$]PF$_6$ (22.2 mg, 0.04 mmol) was added and stirred for 5 min at 0 °C. The cooling bath was removed and then the resulting mixture was stirred for 1 h at rt. The solvent was removed by rotary evaporator, then crude product was purified by flash chromatography (EtOAc/hexanes, 1:4) providing **54** as a colorless oil (92 mg, 58%) as the major product. ^{1}H NMR: δ = 7.90 (s, 1H), 7.56-7.55 (m, 2H), 7.38-7.36 (m, 3H), 7.21 (s, 1H), 6.63 (s, 1H), 5.69 (t, *J* = 7.5 Hz, 1H), 4.37 (d, *J* = 7.0 Hz, 2H), 2.90 (s, 6H), 0.46 (s, 6H); ^{13}C NMR: δ = 144.5, 141.0, 137.6, 136.6, 134.2, 130.0, 129.3, 128.0, 117.1, 60.2, 38.3, -3.1; FT-IR (neat, cm^{-1}): 3349, 3135, 3068, 2953, 2904, 1652, 1480, 1420, 1380, 1249, 1173, 1078, 957, 817, 723, 695; HRMS-ESI (*m/z*): calc for [M+Na]$^+$ $C_{16}H_{23}N_3O_3SSiNa$ 388.1122 found 388.1128.

(*Z*)-4-(1-Dimethylphenylsilyl-3-(*tert*-butyldimethylsilyloxy)prop-1-enyl)-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide (55): Vinylsilane **54** (79 mg, 0.22 mmol) was dissolved in CH_2Cl_2 (4.0 mL) under N_2 atmosphere. The solution was cooled to 0 °C and then imidazole (23 mg, 0.33 mmol) and TBSCl (44 mg, 0.29 mmol) were added to the reaction mixture. The resulting solution was stirred for 4 h at rt. Then NH_4Cl (1 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (2 x 5 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by flash chromatography (EtOAc/hexanes, 1:9)

providing **55** as a colorless oil (87 mg, 84%). ^{1}H NMR: δ = 7.79 (s, 1H), 7.57-7.55 (m, 2H), 7.34-7.32 (m, 3H), 6.85 (t, *J* = 6.3 Hz, 1H), 6.81 (d, *J* = 1.1 Hz, 1H), 4.16 (d, *J* = 5.7 Hz, 2H), 2.72 (s, 6H), 0.83 (s, 9H), 0.47 (s, 6H), -0.04 (s, 6H); ^{13}C NMR: δ = 148.3, 146.7, 138.9, 135.8, 133.9, 130.2, 129.2, 128.1, 112.9, 62.9, 38.2, 26.0, 18.4, -0.5, -5.2; FT-IR (neat, cm^{-1}): 3132, 2953, 2929, 2855, 1615, 1471, 1461, 1421, 1393, 1250, 1174, 1110, 1080, 1008, 964, 818, 773, 727, 701, 592; HR-MS (*m/z*): calc for $[M+Na]^+$ $C_{22}H_{37}N_3O_3SSi_2Na$ 502.1986 found 502.1977.

(*Z*)-1-Benzyl-4-(1-dimethylphenylsilyl-3-(*tert*-butyldimethylsilyloxy)prop-1-enyl)-1*H*-imidazole (57): TBS-protected propargyl alcohol **56**[12] (0.10 g, 0.31 mmol) was dissolved in dry acetone (1.0 mL) under N_2 atmosphere and was cooled to 0 °C and dimethylphenylsilane (0.08 mL, 0.47 mmol) was added dropwise. Cp*[Ru(MeCN)$_3$]PF$_6$ (15.6 mg, 0.03 mmol) was added and stirred for 5 min at 0 °C followed by additional stirring for 1 h at rt. The solvent was removed by rotary evaporation and the resulting crude product was purified by flash chromatography (EtOAc/hexanes, 1:9) providing **57** as a colorless oil (88 mg, 62%) as the major product. ^{1}H NMR: δ = 7.54 (d, *J* = 7.5 Hz, 2H), 7.35-7.30 (m, 6H), 7.1 (m, 2H), 6.76 (t, *J* = 6.3 Hz, 1H), 6.52 (s, 1H), 5.03 (s, 2H), 4.11 (d, *J* = 6.3 Hz, 2H), 0.81 (s, 9H), 0.45 (s, 6H), -0.08 (s, 6H); ^{13}C NMR: δ = 135.9, 134.0, 129.3, 128.8, 128.1, 126.7, 115.9, 62.9, 51.7, 26.0, 18.4, -0.5, -5.2 (13 peaks observed); FT-IR (neat, cm^{-1}): 3068, 2954, 2928, 2855, 1538, 1497, 1456, 1428, 1361, 1252, 1158, 1111, 1073, 1047, 831, 776, 699; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{27}H_{39}N_2OSi_2$ 463.2595 found 463.2602.

(5aS*,5R*,8aS*,8bS*)-5-*tert*-Butyldimethylsilyloxymethyl-1,5,5a,6,7,8,8a,8b-octahydro-1-(*N*,*N*-dimethylsulfamoyl)-4-dimethylphenylsilyl-7-phenyl-6,8-dioxopyrrolo[3,4-*g*]benzimidazole (58): CH_2Cl_2 (1.2 mL) was placed in a resealable thick-walled tube and was purged with N_2 for 5 min (bubbling N_2 through a sparge tube), then compound **55** (50 mg, 0.10 mmol) and *N*-phenylmaleimide (45 mg, 0.26 mmol) were added and again the reaction mixture was purged with N_2 for an additional 5 min. After sealing the tube with a Teflon screw cap, the reaction mixture was heated at 50 °C for 12 h. The reaction mixture was cooled to rt and the CH_2Cl_2 was evaporated under vacuum. The crude product was purified by chromatography (EtOAc/hexanes 1:11) to provide **58** (56 mg, 85%) as a light yellow film. ^{1}H NMR: δ = 7.64 (s, 1H), 7.51-7.50 (m, 2H), 7.44-7.41 (m, 2H), 7.38-7.29 (m, 4H), 7.06 (d, *J* = 7.5 Hz, 2H), 4.69 (d, *J* = 8.0 Hz, 1H), 4.20 (dd, *J* = 11.0, 9.8 Hz, 1H), 3.70-3.64 (m, 2H), 3.60 (dd, *J* = 9.2, 4.6 Hz, 1H), 3.06 (s, 6H), 2.38-2.36 (m, 1H), 0.82 (s, 9H), 0.57 (s, 3H), 0.40 (s, 3H), -0.06 (s, 3H), -0.08 (s, 3H); ^{13}C NMR: δ = 175.4, 173.4, 161.5, 154.3, 134.1, 129.3, 128.9, 127.9, 126.6, 62.3, 58.9, 47.5, 41.4, 38.0, 36.8, 26.0, 18.4, 0.9, -0.3, -5.4 (20 peaks observed); FT-IR (neat, cm^{-1}): 3068, 2953, 2854, 1709, 1598, 1499,

1379, 1146, 1094, 968, 833, 778, 723; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{32}H_{45}N_4O_4SSi_2$ 653.2644 found 653.2670.

(4R* and 4S*,5R*,5aS*,8aS*)-1-Benzyl-5-*tert*-butyldimethylsilyloxymethyl-1,4,5,5a,7,8,8a-octahydro-4-dimethylphenylsilyl-7-phenyl-6,8-dioxopyrrolo[3,4-*g*]benzimidazole (59): CH_2Cl_2 (1.2 mL) was placed in a resealable thick-walled tube and was purged with N_2 for 5 min, then compound **57** (50 mg, 0.104 mmol) and *N*-phenylmaleimide (45 mg, 0.26 mmol) were added and again the reaction mixture was purged with N_2 for an additional 5 min. After sealing the tube with a Teflon screw cap, the reaction mixture was heated at 50 °C for 12 h. The reaction mixture was cooled to rt and the CH_2Cl_2 was evaporated under vacuum. The crude product was purified by chromatography (EtOAc/hexanes 1:11) to provide 1.0:0.6 epimeric mixture of cycloadducts **59**[1] (56 mg, 85%) as a light yellow solid. ^{1}H NMR (corresponding peaks from the minor isomer are underlined): δ = 7.78 (s, 0.6H), 7.68 (d, *J* = 4.6 Hz, 1H), 7.53 (s, 1H), 7.45-7.30 (m, 17.8H), 7.16-7.09 (m, 5.4H), 5.91 (d, *J* = 16.1 Hz, 0.6H), 5.83 (d, *J* = 15.5 Hz, 1H), 5.36 (d, *J* = 15.5 Hz, 1H), 5.29 (d, *J* = 16.1 Hz, 0.6H), 4.09 (t, *J* = 10.3 Hz, 1H), 3.88 (d, *J* = 9.2 Hz, 1H), 3.69-3.63 (dd, *J* = 9.2, 5.2 Hz, + m, 2.2H), 3.51 (t, *J* = 11.3 Hz, 0.6H), 3.35 (dd, *J* = 10.3, 5.8 Hz, 1H), 3.20 (dd, *J* = 8.1, 4.0 Hz, 0.6H), 2.86 (d, *J* = 5.2 Hz, 1H + 0.6H), 2.63 (s, 0.6H), 2.53-2.49 (m, 1H), 0.78 (s, 9H), 0.56+0.58 (2 x s, total 9H), 0.50 (s, 3H), 0.19 (s, 3H), -0.10 (s, 3H), -0.13 (s, 3H), -0.43 (s, 1.8H), -0.60 (s, 1.8H); ^{3}C NMR (peaks from the minor isomer are underlined): δ = 176.3, 175.7, 175.0, 174.8, 138.1, 137.2, 134.4, 129.3, 129.2, 129.1, 128.7, 128.6, 128.4, 128.1, 127.5, 126.5, 118.7, 118.6, 64.2, 62.6, 50.2, 50.1, 45.2, 43.8, 42.1, 40.1, 39.0, 38.1, 28.8, 27.7, 26.1, 26.0, 18.6, 18.4, -0.4, -0.6, -2.1, -2.5, -5.3, -5.4; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{37}H_{46}N_3O_3Si_2$ 636.3072 found 636.3085.

(4R*,5R*,5aS*,8aS*)-1-Benzyl-1,4,5,5a,7,8,8a-octahydro-4-hydroxy-5-hydroxymethyl-7-phenyl-6,8-dioxopyrrolo[3,4-*g*]benzimidazole (60): Epimeric cycloadducts **59** (0.30 g, 0.47 mmol) were placed in peracetic acid solution (3.0 ml of a 32% solution in acetic acid 13.0 mmol) and mercuric acetate (0.28 g, 0.71 mmol) was added to the resulting mixture. The mixture was stirred for 3 h at rt and then diluted with water (100 ml) and extracted with EtOAc (250 mL). The organic layer was then washed with sodium thiosulfate, neutralized with sodium bicarbonate, finally washed with brine and dried over sodium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by flash chromatography (EtOAc/MeOH, 9:1) affording diol **60** as a light yellow solid (63 mg, 33%). mp 124-125 °C. ^{1}H NMR [DMSO-d_6]: δ = 7.65 (s, 1H), 7.44-7.41 (m, 2H), 7.38-7.33 (m, 3H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.14-7.12 (m, 4H), 5.53 (d, *J* = 15.5 Hz, 1H), 5.41 (d, *J* = 15.5 Hz, 1H), 5.13 (d, *J* = 3.0 Hz,

[1] There are other minor peaks in the ^{1}H NMR spectrum that may derive from a third cycloadduct – however, since we have been unable to purify the mixture we have not been able to assign its structure.

1H), 4.69 (t, *J* = 1.7 Hz, 1H), 4.47 (t, *J* = 4.6 Hz, 1H), 4.11 (d, *J* = 9.2 Hz, 1H), 3.96-3.92 (m, 2H), 3.48 (dd, *J* = 5.7, 3.0 Hz, 1H), 1.90-1.88 (m, 1H); ^{13}C NMR [DMSO-d_6]: δ = 177.0, 175.6, 142.7, 138.5, 137.6, 133.1, 129.4, 129.3, 128.8, 128.3, 127.6, 127.5, 121.6, 62.4, 60.3, 48.7, 47.1, 39.1, 38.4; FT-IR (neat, cm^{-1}): 3116, 2922, 1701, 1597, 1496, 1383, 1195, 1094, 709, 691, 646; HR-MS (*m/z*): calc for $[M+Na]^+$ $C_{23}H_{21}N_3O_4Na$ 426.1424 found 426.1417.

(4R*,5R*,5aS*,8aS*)-1-Benzyl-5-*tert*-butyldimethylsilyloxymethyl-1,4,5,5a,7,8,8a-octahydro-4-hydroxy-7-phenyl-6,8-dioxopyrrolo[3,4-*g*]benzimidazole (61): Diol **60** (60 mg, 0.15 mmol) was dissolved in CH_2Cl_2 (4.0 mL) under N_2 atmosphere. The solution was cooled to 0 °C and then imidazole (31 mg, 0.45 mmol) and TBSCl (68 mg, 0.45 mmol) were added to the reaction mixture. The resulting solution was stirred for 12 h at rt. Then NH_4Cl (1 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (2 x 10 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by flash chromatography (EtOAc/hexanes, 3:1) providing **61** as a waxy solid (59 mg, 77%). ^{1}H NMR: δ = 8.60 (br s, 1H), 7.38-7.34 (m, 5H), 7.31 (d, *J* = 7.5 Hz, 2H), 7.27 (s, 1H), 7.25 (s, 1H), 7.21 (t, *J* = 3.4 Hz, 2H), 5.74 (d, *J* = 15.0 Hz, 1H), 5.50 (d, *J* = 15.0 Hz, 1H), 5.15 (s, 1H), 4.40 (dd, *J* = 7.5, 3.0 Hz, 1H), 4.15 (t, *J* = 6.9 Hz, 1H), 4.00 (d, *J* = 8.8 Hz, 1H), 3.53 (dd, *J* = 5.7, 2.9 Hz, 1H), 2.21 (br s, 1H), 0.85 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H); ^{13}C NMR: δ = 175.0, 174.0, 136.6, 133.7, 131.7, 129.5, 129.2, 129.1, 129.0, 128.2, 126.8, 122.8, 61.4, 61.0, 51.3, 38.4, 26.1, 18.4, -5.2, -5.3 (20 observed); FT-IR (neat, cm^{-1}): 3241, 2952, 2928, 2882, 2855, 1710, 1598, 1497, 1457, 1384, 1250, 1197, 1081, 834, 778, 708; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{29}H_{36}N_3O_4Si$ 518.2470 found 518.2482.

(*Z*)-1-Hydroxy-3-tributylstannyl-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propene (64): In a round bottom flask compound **21** (5.00 g, 21.8 mmol) was dissolved under N_2 atmosphere in anhydrous THF (150 mL). The reaction mixture was cooled to 0 °C and then to it Red-Al (65 wt% in toluene, 7.90 mL, 26.2 mmol) was added dropwise. After stirring the reaction mixture for 30 min, Bu_3SnCl (8.80 mL, 32.7 mmol) was added. Then the reaction mixture was stirred overnight at rt. Finally the reaction was quenched with NH_4Cl (50 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAc, then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (hexanes/EtOAc, 60:40) providing **64** (6.80 g, 60%) as a pale yellow oil. ^{1}H NMR: δ = 7.79 (d, *J* = 1.1 Hz, 1H), 7.02 (d, *J* = 1.1 Hz, 1H), 6.87 (t, *J* = 6.4 Hz, $^3J_{Sn\text{-}H}$ = 110.4 Hz, 1H), 4.23 (t, *J* = 6.0 Hz, 2H), 2.84 (s, 6H), 1.61 (t, *J* = 5.8 Hz, 1H), 1.51-1.41 (m, 6H), 1.28 (sextet, *J* = 7.3 Hz, 6H), 1.05-0.95 (m, 6H), 0.86 (t, *J* = 7.3 Hz, 9H); ^{13}C NMR: δ = 148.5, 141.7, 138.3, 135.9, 111.7, 64.5, 38.2, 29.1, 27.3, 13.7, 11.7; IR (neat, cm^{-1}): 3323, 2954, 2870, 1459, 1391,

1269, 1173, 1080, 961, 829, 725; HRMS-ESI (*m/z*): Calcd. for $C_{20}H_{39}N_3O_3SSnNa$ $[M+Na]^+$ 544.1629, found 544.1642.

(*Z*)-1-*tert*-Butyldimethylsilyloxy-3-tributylstannyl-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propene (65): Alcohol **64** (4.00 g, 7.69 mmol) and imidazole (1.04 g, 15.38 mmol) were dissolved in dry CH_2Cl_2 (150 mL). The solution was cooled to 0 °C and TBSCl (1.51 g, 9.99 mmol) was added to it. The mixture was stirred at rt overnight. The reaction mixture was partitioned with water (45 mL), and the organic layer was washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by chromatography (hexanes/EtOAc, 75:25) to give **65** (4.29 g, 88%) as a thick colorless oil; ^{1}H NMR: δ = 7.77 (d, *J* = 1.1 Hz, 1H), 7.01 (d, *J* = 1.1 Hz, 1H), 6.76 (t, *J* = 6.4 Hz, $^3J_{Sn-H}$ = 114.5 Hz, 1H), 4.25 (d, *J* = 6.4 Hz, 2H), 2.83 (s, 6H), 1.51-1.42 (m, 6H), 1.29 (sextet, *J* = 7.3 Hz, 6H), 1.06-0.96 (m, 6H), 0.90 (s, 9H), 0.86 (t, *J* = 7.3 Hz, 9H), 0.09 (s, 6H); ^{13}C NMR: δ = 148.8, 143.1, 135.8, 135.7, 111.3, 65.2, 38.2, 29.1, 27.4, 26.0, 18.5, 13.7, 11.6, -5.0; IR (neat, cm^{-1}): 2953, 2925, 2854, 1461, 1391, 1250, 1174, 1066, 961, 833, 724; HRMS-ESI *(m/z)*: Calcd. for $C_{26}H_{53}N_3O_3SSiSnNa$ $[M+Na]^+$ 658.2494, found 658.2488.

(5aS*,5R*,8aS*,8bS*)-5-*tert*-Butyldimethylsilyloxymethyl-4-tributylstannyl-1,5,5a,6,7,8,8a,8b-octahydro-1-(*N*,*N*-dimethylsulfamoyl)-7-phenyl-6,8-dioxopyrrolo[3,4-*g*]benzimidazole (66): CH_2Cl_2 (6 mL) was placed in a thick-walled tube and was purged with N_2 for 6 min, then compound **65** (0.400 g, 0.63 mmol) and *N*-phenylmaleimide (0.131 g, 0.76 mmol) was added and again the reaction mixture was purged with N_2 for an additional 8 min. After sealing the tube with a Teflon screw cap, the reaction mixture was heated at 65 °C for 16 h. The reaction mixture was cooled to rt and the CH_2Cl_2 was evaporated under vacuum. The crude product was purified by chromatography (EtOAc/hexanes, 1:10) to provide **66** (0.365 g, 72%) as a colorless liquid. ^{1}H NMR: δ = 7.56 (s, 1H), 7.41-7.38 (m, 2H), 7.34-7.31 (m, 1H), 7.10-7.08 (m, 2H), 4.66 (dd, *J* = 10.0, 1.8 Hz, 1H), 4.42 (t, *J* = 9.8 Hz, 1H), 3.97 (q, *J* = 5.8 Hz, 1H), 3.70-3.67 (m, 1H), 3.58-3.54 (m, 1H), 3.04 (s, 6H), 2.47-2.43 (m, 1H), 1.44-1.40 (m, 6H), 1.30-1.22 (m, 6H), 1.04-0.96 (m, 6H), 0.94 (s, 9H), 0.83 (t, *J* = 7.5 Hz, 9H), 0.14 (s, 6H); ^{13}C NMR: δ = 175.3, 173.4, 159.7, 153.6, 131.6, 129.1, 128.7, 127.1, 126.6, 64.1, 58.3, 48.1, 41.9, 38.0, 37.4, 29.2, 27.5, 26.1, 18.5, 13.7, 12.0, -5.1, -5.2; FT-IR (neat, cm^{-1}): 2954, 2927, 2854, 1709, 1549, 1499, 1462, 1374, 1252, 1154, 1076, 969, 907, 727, 670, 592; HR-MS (*m/z*): calc for $[M+Na]^+$ $C_{36}H_{60}N_4O_5SiSSnNa$ 831.2973 found 831.2988.

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