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# Chiral Pyridin-3-ones and Pyridines: Syntheses of Enantiopure 2,4-Disubstituted 6-Hydroxy-1,6-Dihydro-*2H*-Pyridin-3-ones, 2,3-Disubstituted 4-Iodopyridines, and Enantiopure 2,3-Disubstituted 4-Pyridinemethanols

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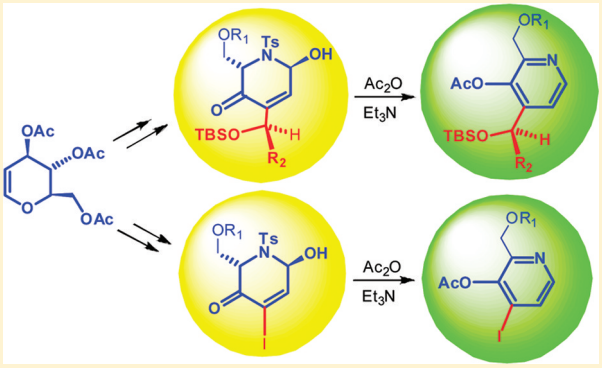
Supporting Information

**ABSTRACT:** The development of an innovative method to access enantiopure 2,4-disubstituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones starting from D-glucal via the aza-Achmatowicz transformation has been described. These highly functionalized pyridin-3-ones have been utilized for the synthesis of contiguously substituted pyridines through a rapid and efficient $Et_3N/Ac_2O$ promoted cyclo-elimination, aromatization cascade, allowing the facile assembly of important pyridine-based building blocks like 2-substituted 3-acetoxy-4-iodopyridines and enantiopure 2-substituted 3-acetoxy-4-pyridinemethanols possessing benzylic stereogenic centers, whose synthesis otherwise would be tedious. The utilization of commercially available sugars as starting materials, mild reaction conditions, catalytic transfer hydrogen (CTH) of $\alpha$-furfuryl azide derivatives, transfer of chiral aryl/alkyl methanols from enulosides to pyridin-3-ones and pyridines, high yields, and short reaction times are key features of this method. The utility of the method has been further exemplified by demonstrating the usage of the 2-substituted 3-acetoxy-4-iodopyridine for the construction of biologically significant molecules like 2,7-disubstituted furo[2,3-*c*]pyridines and 7,7′-disubstituted 2,2′-bifuro[2,3-*c*]pyridines.




## INTRODUCTION

Functionalized pyridines are biologically and synthetically important molecules. Their wide distribution in an array of important compounds ranging from natural products and pharmaceuticals[1−8] to catalysts[9−14] and polymers[15−17] is ample testimony of their significance. Among pyridines, chiral pyridines form a special subcategory (Figure 1). Not only are they present as structural elements in a plethora of important molecules like natural products,[4,5] but they also serve as chiral ligands[11,12] and important building blocks in organic synthesis.[18]

Though a large number of methods for synthesis of substituted pyridines are known, relatively fewer reports on preparation of substituted chiral pyridines are documented. Consequently construction of chiral pyridines with diverse substitution patterns remains a much sought after goal.[12,19−25] Likewise substituted 4-iodopyridines[26−29] are another important class of pyridine molecules widely employed as versatile building blocks for the synthesis of different types of molecules exhibiting potent biological activities[26,27] and natural products.[28,29] The increasing use of cross-coupling methodologies, Suzuki−Miyaura, Buchwald−Hartwig, Sonogashira reactions, etc., in organic synthesis have further widened the utility of these building blocks.[26−37] Regioselective synthesis of 4-iodopyridines is usually achieved by ortholithiation[26−28] or Sandmeyer reaction[38] by adopting reaction conditions that are not compatible with sensitive functional groups that may be present on the pyridine ring[37] Therefore, the search for a milder and more efficient method for the construction of substituted 4-iodopyridines remains an active research field for the chemical community.[37]

Aza-Achmatowicz transformation is a versatile synthetic strategy widely employed for the synthesis of biologically important chiral compounds and natural products.[39−45] The transformation of D-glucal-derived 2-furfurylamines into 2-substituted 1,6-dihydro-6-hydroxy-2*H*-pyridin-3-ones involving aza-Achmatowicz chemistry[43,45] becomes all the more relevant in the context of the increasing stress on the synthesis of organic molecules from renewable feedstock such as carbohydrate rather than steadily diminishing petroleum resources.[46,47]

However utility of this route is greatly restricted by its inability to provide access to 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones having substitution other than at position 2 of the pyridone ring.[44] Thus development of a new synthetic strategy that allows for the construction of highly functionalized

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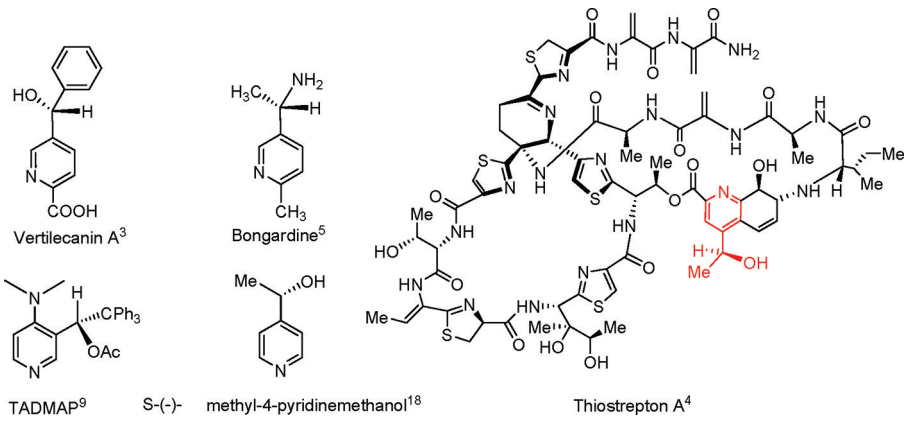


**Figure 1.** Structure of some chiral pyridine-based natural and synthetic compounds containing benzylic stereogenic centers.

6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones using the aza-Achmatowicz chemistry would significantly expand the utility of this approach.[48]

In the backdrop of the above discussion, we now report the development of a new method that allows for the construction of 2,4-disubstituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones from D-glucal, using the aza-Achmatowicz chemistry. This new method takes advantage of our earlier report on synthesis of enantiopure 2,3-disubstituted furans from D-glucal[49] to access novel 2,3-disubstituted furylamines, which on subjection to aza-Achmatowicz reaction furnished the desired 2,4-disubstituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones in good yields. These valuable pyridin-3-one moieties could serve as useful building blocks for the synthesis of highly functionalized enantiopure piperidines and pyridines based synthetic and natural products.[48]

To demonstrate the usefulness of these 2,4-disubstituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-one building blocks, we have developed a novel, mild, and facile $Et_3N/Ac_2O$ promoted conversion of these pyridine-3-ones into the corresponding 2,3,4-trisubstituted pyridines thus allowing easy access to important trisubstituted pyridine molecules, like 4-iodopyridines, and enantiopure 4-pyridinemethanols possessing benzylic stereogenic centers[4,50−54] whose synthesis otherwise would be tedious.[27,37,52] The utility of the 3-acetoxy-4-iodopyridines obtained by the method described herein has also been demonstrated by their facile transformation to biologically important molecules like furopyridines[31−34] and bifuropyridines.[35,36]

## RESULTS AND DISCUSSION

To achieve the synthesis of the target 2,4-disubstituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones, we believed that if suitable reaction conditions could be optimized to access simple 2-substituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones from unbranched 2,3-dideoxy-hex-2-enopyranosides, the same reaction conditions could be translated to obtain the desired 2,4-disubstituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones from C-3 branched 2,3-dideoxy-hex-2-enopyranosides (Figure 2).

We initiated our work with isoamyl-6-*O*-trimethylacetyl-2,3-dideoxy-hex-2-enopyranosid-4-ulose (**1**), which was converted into furan **3** by adopting our previously reported method.[49] A modified Mitsonubu reaction was employed to transform **3** into *α*-furfurylazide **4** in 74% yield in the presence of DPPA/DBU in dry toluene[45,55] followed by its hydrogenation over Pd−C/

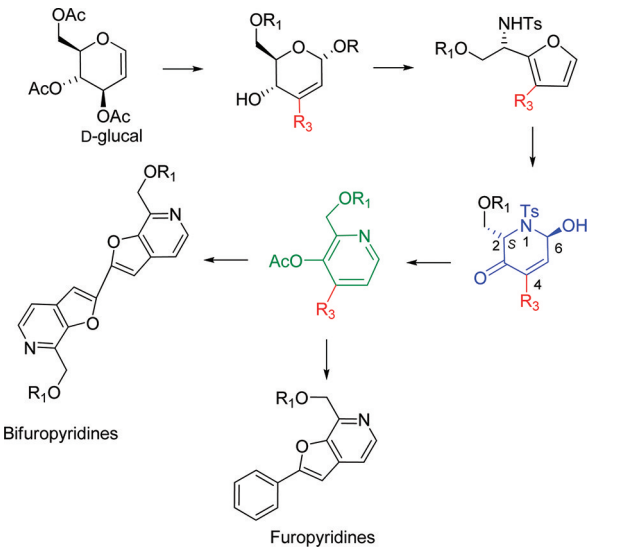


**Figure 2.** General synthetic approach for the synthesis of functionalized pyridin-3-ones and pyridines and their application.

$H_2$ to 2-furfurylamine, which was isolated as its tosyl-protected derivative **5** in 78% yield. It was then subjected to aza-Achmatowicz rearrangement in the presence of NBS/$NaOAc.3H_2O$ in $THF/H_2O$ (4:1) to obtain 1,6-dihydro-2*H*-pyridin-3-one **6** in 83% yield (Scheme 1).[56]

Once the strategy for the conversion of hex-2-enopyranosid-4-ulose **1** into 1,6-dihydro-2*H*-pyridin-3-one **6** had been worked out, we directed our attention to utilize this strategy for the construction of 2,4-disubstituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones **12** from stereochemically pure C-3 branched 2,3-dideoxy-hex-2-enopyranosid-4-uloses **7**, synthesized by using our earlier reported method.[57]

To achieve the synthesis of **12** successfully from **7** by adopting the above-described strategy to obtain **6** from the enuloside **1** via the key intermediate furan **5**, the protection of the secondary hydroxyl group at C-1′ of the hex-2-enopyranosid-4-uloses **7a−c** was necessary. First, the acetylation of C-1′ benzylic hydroxy group in **7a** was attempted, which however resulted in the formation of a mixture of diastereomers. To overcome this difficulty, we carried out TBS protection of the benzylic hydroxy group at C-1′ by using TBSOTf/2,6-lutidine in dry DCM, which furnished the TBS-protected derivative **8a** as a single isomer in 83% yield.[58] The TBS-protected derivative **8a** was transformed into the


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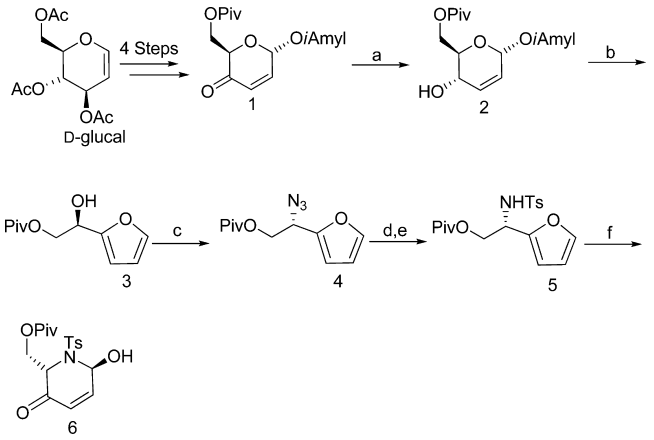
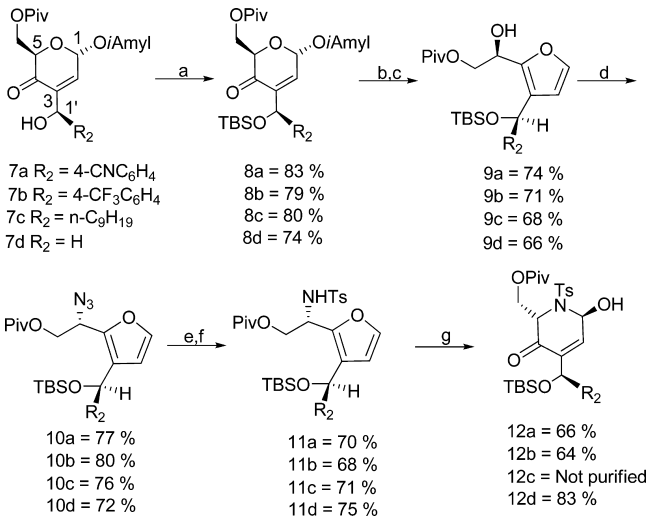
**Scheme 1**[a]




[a]Reagents and conditions: (a) $NaBH_4$, $CeCl_3{\cdot}7H_2O$, EtOH, 0 °C → 10 °C, 1 h, 84%; (b) $ZrCl_4$ (5 mol %), $ZnI_2$ (10 mol %), THF, RT, 35 min, 86%; (c) DPPA (1.19 equiv.), DBU (1.19 equiv.), dry toluene, 0 °C → RT, 24 h, 74%; (d) Pd−C/$H_2$, 45 min, RT; (e) TsCl (1.5 equiv.), $Et_3N$ (1.5 equiv.), DCM, 3 h, 78% over 2 steps; (f) NBS, NaOAc·$3H_2O$, THF/$H_2O$ (4:1), −5 °C → 0 °C, 3 h, 83%.

corresponding 2-furyl glycol **9a**[49] in 74% yield followed by its azidation with DPPA/DBU to obtain the enantiopure 2,3-disubstituted furylazide **10a** (Scheme 2). It was now subjected

**Scheme 2**[a]




[a]Reagents and conditions: (a) TBSOTf (1.5 equiv.), 2,6-lutidine (2 equiv.), DCM, 0 °C → RT, argon atm., 3 h; (b) $NaBH_4$, $CeCl_3{\cdot}7H_2O$, EtOH, 0 °C → 10 °C, 1−1.5 h; (c) $ZrCl_4$ (5 mol %), $ZnI_2$ (10 mol %), THF, 60 °C, 1.5−3 h; (d) DPPA (3 equiv.)/DBU (3 equiv.), dry toluene, 0 °C → RT, 24 h; (e) $Et_3SiH$ (2.5 equiv.), Pd−C (10%), argon atm., 1.5−2 h; (f) TsCl (1.5 equiv.), $Et_3N$ (1.5 equiv.), dry DCM, 3 h; (g) NBS, THF/$H_2O$ (4:1), −5 °C → RT, 3.5−4 h.

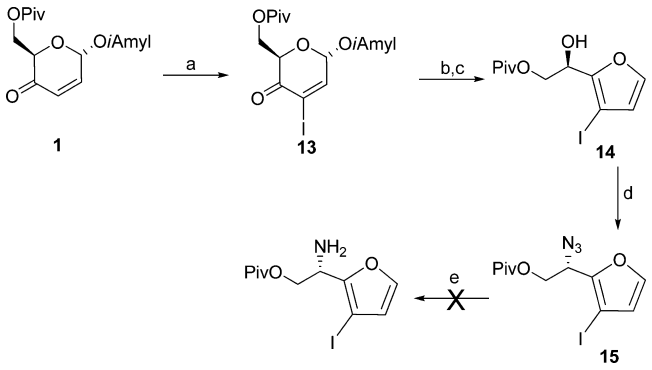
to hydrogenation over Pd−C to access the corresponding 2,3-disubstituted furylamine, which was isolated as its tosyl-protected derivative **11a** in 60% yield.

Moreover, its yield was improved to 70% when $Et_3SiH$/Pd−C mediated catalytic transfer hydrogenation (CTH) of **10a** was performed by adopting the protocol developed by McMurray and Mandal.[59] The resulting 2,3-disubstituted tosyl-protected furylamine **11a** was then subjected to undergo aza-Achmatowicz reaction in the presence of NBS/NaOAc·$3H_2O$ in THF/$H_2O$ (4:1) at −5 °C → 0 °C to obtain the desired 4-substituted 1,6-dihydro-2*H*-pyridin-3-one **12a**. To our surprise, the reaction did not proceed here even after stirring the reaction mixture for 5 h. Therefore, the temperature of the reaction mixture was raised to room temperature, but under this condition, the reaction proceeded very slowly. However, when the same reaction was carried out in presence of NBS alone at −5 °C → RT, the reaction progressed smoothly to completion in about 4 h to furnish 4-substituted 1,6-dihydro-2*H*-pyridin-3-one **12a** in 66% yield.[60] That the transformation of crowded 2,3-disubstituted furan **11a** to the pyridin-3-one **12a** in the presence of NBS/NaOAc·$3H_2O$ was unsuccessful could be attributed to the weaker reactivity of *in situ* generated brominating agent acetyl hypobromite ($CH_3COOBr$) from NBS and the buffer anion compared with that of NBS alone successfully utilized for the same transformation.[61]

The above optimized synthetic strategy was now successfully exploited to transform a series of C-3 branched 2,3-dideoxy-hex-2-enopyranosid-4-ulose **7b**, **7c**, and **7d**[62] into the corresponding 2,4-disubstituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones **12b−d** (Scheme 2). While compounds **12b** and **12d** were easily purified by column chromatography ($SiO_2$), the column purification of the pyridin-3-one **12c** led to its degradation, and that is why it was used as such without further purification for its next reaction.

Our next effort was to develop a synthetic route to 4-iodopyridones from enuloside **1**. Our attempt to synthesize 4-iodo-6-hydroxy-1,6-dihydro-2*H*-pyridin-3-one **16** from **1** using this strategy was futile because in this case the CTH of 3-iodo-α-furfurylazide **15** in the presence of $Et_3SiH$/Pd−C led to the reductive deiodination[63] instead of reduction of the azide group (Scheme 3).

**Scheme 3**[a]




[a]Reagents and conditions: (a) $I_2$, $CCl_4$, pyridine, −5 °C → 10 °C, 2 h, 88%; (b) $NaBH_4$, $CeCl_3{\cdot}7H_2O$, EtOH, 0 °C → 10 °C, 1.5 h; (c) $ZrCl_4$ (5 mol %), $ZnI_2$ (10 mol %), THF, 60 °C, 1.5 h; 73% over 2 steps; (d) DPPA (1.19 equiv.)/DBU (1.19 equiv.), dry toluene, 0 °C → RT, 24 h; 81%; (e) $Et_3SiH$ (2.5 equiv.), Pd−C (10%), argon atm., 3 h.

We, therefore, devised a different synthetic approach to achieve the synthesis of 2-substituted 4-iodo-6-hydroxy-1,6-dihydro-2*H*-pyridin-3-one **16**. Thus, when 2-substituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones **6** and **17**[45] were treated with $I_2$/pyridine in $CCl_4$, the corresponding 2-substituted 4-iodo-6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones **16** and **18** were obtained in good yields (Scheme 4).[64]

Once the route for the synthesis of enantiopure 2- and 2,4-difunctionalized 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones had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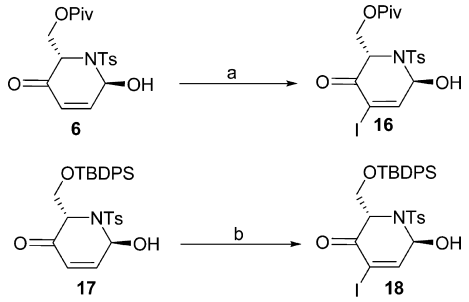
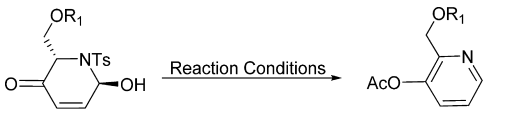
**Scheme 4**[a]




[a]Reagents and conditions: (a) $I_2$, $CCl_4$, pyridine, −5 °C → 0 °C, 2 h; (b) $I_2$, $CCl_4$, pyridine, −5 °C → 0 °C, 2 h, 81%.

been successfully established, we turned our attention to transform these pyridone-3-ones into the azasugars.[42,44] To achieve this goal successfully, the protection of the C-6 hydroxy group was essential prior to Luche's reduction of the C-3 carbonyl group. Thus, 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-one **6** was treated with $Ac_2O$/pyridine to obtain its 6-acetoxy derivative. The reaction proceeded smoothly with the formation of a single spot on TLC. However, to our surprise spectral analysis of the column purified product, which was isolated in 78% yield, revealed it to be a 2-trimethylacetoxymethyl-3-acetoxy-pyridine **19** instead of the expected acetyl derivative of **6** (Table 1). A literature survey revealed two

**Table 1. Optimization of Reaction Conditions for the Transformation of Pyridin-3-ones into Pyridines**




**6** $R_1$=Piv
**17** $R_1$=TBDPS

**19** $R_1$=Piv
**20** $R_1$=TBDPS

| entry | reagents | temp (°C) | time (min) | yield % (pyridine) |
|---|---|---|---|---|
| 1 | pyridine/$Ac_2O$ | 0 to RT | 30 | 78 (**19**) |
| 2 | DBU/DMF | 0 to RT | 30 | starting material degrades |
| 3 | pyridine | 0 to RT | 30 | no reaction |
| 4 | $Et_3N$ | 0 to RT | 30 | no reaction |
| 5 | $Et_3N$/$Ac_2O$ | 0 to RT | 30 | 76 (**19**) |
| 6 | pyridine/$Ac_2O$ | 0 | 90 | 66 (**19**) |
| 7 | $Et_3N$/$Ac_2O$ | 0 | 30 | 91 (**19**) |
| 8 | $Et_3N$/$Ac_2O$ | 0 | 30 | 94 (**20**) |

reports on transformation of 1,6-dihydro-2*H*-pyridin-3-one into 3-hydroxy pyridines. But both these reports are concerned with the conversion of simple 1,6-dihydro-2*H*-pyridin-3-one obtained by RCM of open chain precursors rather than that of 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones obtained by aza-Achmatowicz reaction as in our case.[65,66]

Since substituted pyridines are an important class of compounds possessing various biological properties, at this stage we turned our attention to optimizing the reaction conditions to obtain substituted pyridines from their respective 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones. Thus, a series of experiments was conducted to make this transformation more effective in terms of yield and reaction time. First, we tried a method developed by K. Yoshida et al. to transform 2-substituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-one **6** into its corresponding 2,3-disubstituted pyridine in the presence of DBU/DMF at 0 °C to RT (Table 1, entry 1).[65] Here the starting material was completely degraded within 30 min. Changing the base from DBU to pyridine or $Et_3N$ also did not make this transformation possible. In our next attempt, $Et_3N$ was used along with $Ac_2O$ at 0 °C → RT (Table 1, entry 5). In this case, the reaction proceeded smoothly to completion in about 30 min and the desired compound **19** was isolated in 76% yield. Now, it became clear from these experiments (Table 1, entry 1−5) that the use of $Ac_2O$ was essentially required for this reaction to take place. Performing this transformation in the presence of pyridine/$Ac_2O$ at 0 °C (Table 1, entry 6) afforded **19** in 66% yield in about 90 min. However, when the experiment was repeated with $Et_3N$ instead of pyridine at 0 °C, surprisingly there was a spike in yield (91%) and the reaction was completed in only 30 min (Table 1, entry 7).

To test the efficacy of above method (Table 1, entry 8), we conducted another experiment wherein 2-substituted pyridin-3-one **17** was treated with $Et_3N$/$Ac_2O$ at 0 °C leading to formation of the 2-substituted-3-acetoxy pyridine **20** in 94% yield in about 30 min.

At this juncture, we envisaged that if the strategy for the conversion of 2-substituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones into 2-substituted 3-acetoxy-pyridine could be successfully extended for the transformation of 2,4-disubstituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones into the 2,4-disubstituted 3-acetoxy-pyridines, it would enable easy access to important substituted pyridine scaffolds like 2,3-disubstituted 4-iodopyridines and enantiopure 2,3-disubstituted 4-pyridinemethanols, which are found in many biologically important molecules including natural products (Figure 1).

Consequently treatment of various enantiopure 2,4-disubstituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones **12a−d** with $Et_3N$/$Ac_2O$ at 0 °C led to the formation of the enantiopure 2,4-disubstituted-3-acetoxy pyridines **21a−d** in good to very good yields (Table 2). The efficacy of the present method was further demonstrated by its successful application for the construction of important substituted 4-iodopyridine scaffolds **22** and **23** from the 4-iodo-6-hydroxy-1,6-dihydro-2*H*-pyridin-3-one **16** and **18**, respectively (entry 5, Table 2).

Here, the plausible mechanistic pathway for the formation of functionalized pyridines is proposed to initiate by the acetylation of the C-6 hydroxyl group in pyridine-3-one **6** with $Et_3N^+COCH_3$ to generate species **I**. The concomitant cycloelimination of the N-tosyl group and the acetoxy group at C-6 position in **I** led to the formation of pyridone intermediate **II** and acetic 4-methylbenzenesulfonic anhydride **III**.[67] The enolization of C-3 carbonyl functionality of the intermediate **II** followed by acetyl protection of the resulting enol **IV** ultimately furnished the 3-acetoxy pyridine derivative. The stability of the pyridine moiety compared with the pyridone seems to be the driving force behind the proposed mechanistic pathway (Figure 3).

Further, to support our proposed mechanism that acid anhydride was essentially required to obtain the substituted pyridines from their respective 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-one, the treatment of 2-substituted 4-iodo-6-hydroxy-1,6-dihydro-2*H*-pyridin-3-one **18** with $Tf_2O$/$Et_3N$ in place of $Ac_2O$/$Et_3N$ led to the formation of 2-substituted 4-iodo-3-trifloxy-pyridine **24** in 84% yield (Scheme 5).

Having these results in our hand, we also became interested to explore the possibility of one-pot synthesis of 4-


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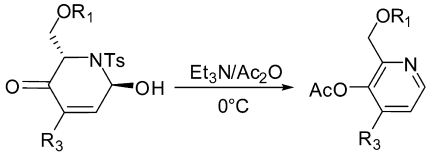
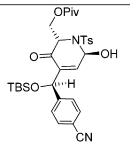
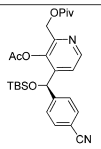
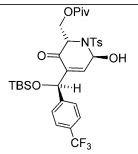
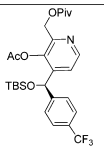
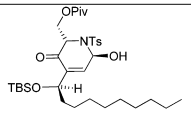
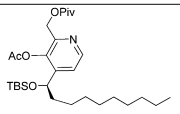
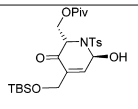
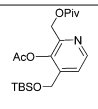
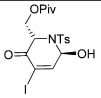
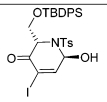
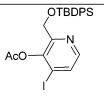
**Table 2. Transformation of Pyridin-3-ones 12a–d, 16, and 18 into Corresponding Pyridines 21a–d, 22, and 23**




$R_3$= protected ArCH(OH)/ alkylCH(OH)/ CH(OH) and iodo group

| Entry | Pyridin-3-one | Pyridine | Time (min) | Yield% |
|---|---|---|---|---|
| 1 |  **12a** |  **21a** | 30 | 84 |
| 2 |  **12b** |  **21b** | 30 | 82 |
| 3 |  **12c** |  **21c** | 30 | 70[a] |
| 4. |  **12d** |  **21d** | 30 | 86 |
| 5. |  **16** |  **22** | 30 | 89 |
| 6. |  **18** |  **23** | 30 | 93 |

[a]Yield calculated over two steps.

iodopyridines directly from 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones. Thus, when 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones **6** and **17** were treated with $I_2$ in pyridine/$CCl_4$ until the completion of $\alpha$-iodination (TLC) followed by stirring of the respective reaction mixture with $Ac_2O$ for 30 min, 4-iodopyridine derivatives **22** and **23** were obtained in 67% and 71% yields, respectively, in a sequential one-pot fashion (Scheme 6).

Further, we are also interested to show that the TBS- and TBDPS-protected pyridines **21a** and **23** were successfully deprotected with TBAF in THF to obtain their analogous hydroxy derivatives **25** and **26** in good yields (Scheme 7). The molecules of type **25** could be further utilized as synthetic intermediates for their transformation to medicinally important

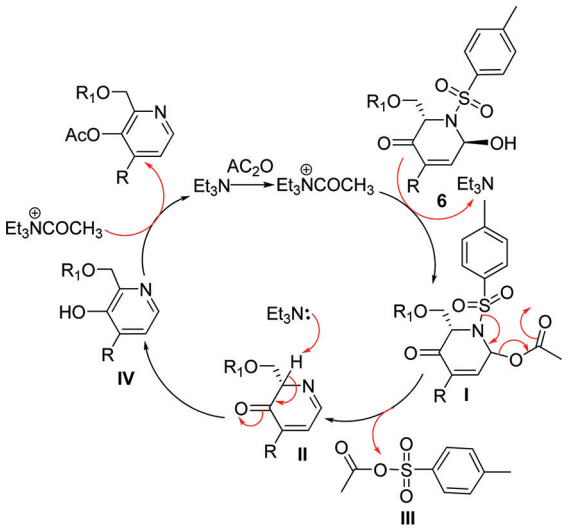
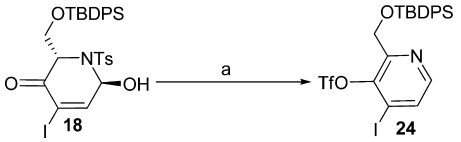


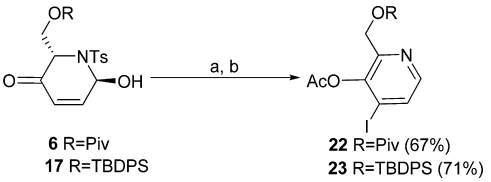

**Figure 3.** Plausible mechanism.

**Scheme 5**[a]



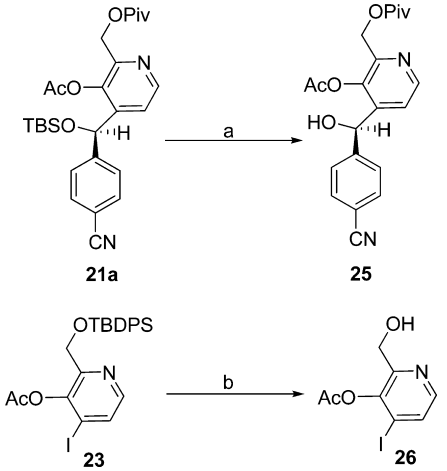

[a]Reagents and conditions: (a) $Tf_2O$, $Et_3N$, −78 °C → RT, 1.5 h, 84%.

**Scheme 6**[a]




[a]Reagents and conditions: (a) $I_2$, $CCl_4$, pyridine, −5 °C → 0 °C, 2 h; (b) $Ac_2O$, 0 °C, 30 min.

**Scheme 7**[a]




[a]Reagents and conditions: (a) TBAF, THF, 0 °C → RT, 1 h, 75%; (b) TBAF, THF, 0 °C → RT, 1 h, 70%.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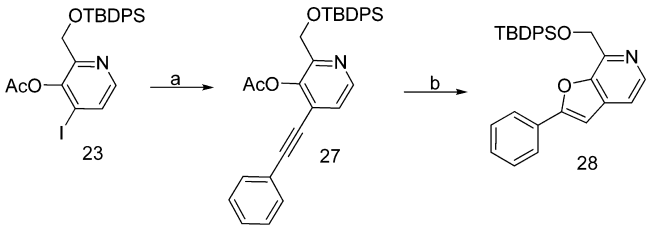
fused aromatic ring systems like highly substituted azafluorenes.[68,69]

**Synthesis of 2,7-Disubstituted Furo[2,3-*c*]pyridines.** Acetoxyhalopyridines[30,31] are widely used for the synthesis of medicinally important molecules like furopyridines[30,31] and naphthpyridines.[70] Herein, the synthetic potential of 3-acetoxy-4-iodopyridine **23** has been demonstrated by its chemical transformation to 2,7-disubstituted furo[2,3-*c*]pyridines **28** as illustrated in Scheme 8. Thus, Sonogashira reaction of 3-acetoxy-substituted 4-iodopyridine **23** gave alkynylpyridine **27**, which on cycloisomerization with $MeOH/Et_3N/H_2O$ furnished the furopyridine **28**.

**Scheme 8**[a]




[a]Reagents and conditions: (a) phenylacetylene, $Pd[(PPh_3)_2Cl_2]$, CuI, $Et_3N$, THF, RT, 2.5 h, 78%; (b) $MeOH/Et_3N/H_2O$ (4:1:1), RT, 12 h, 62%.

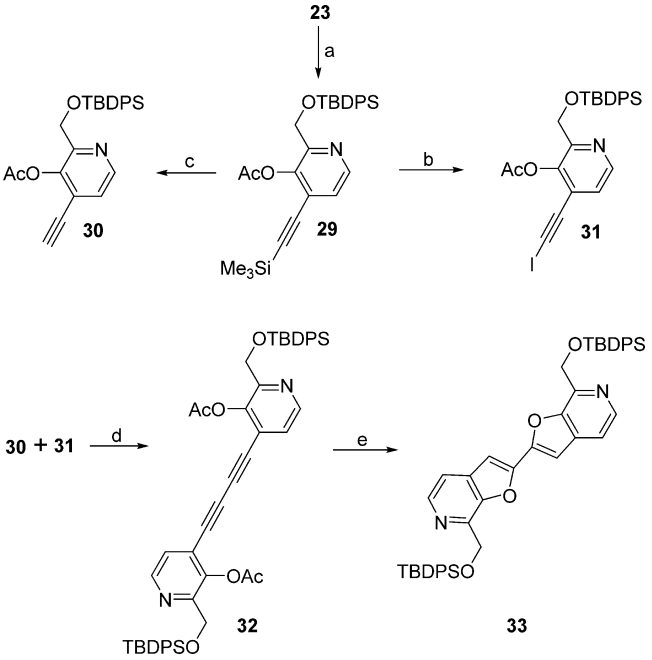
**Synthesis of 7,7′-Disubstituted 2,2′-Bifuro[2,3-*c*]-pyridines.** Bifuropyridines are another useful class of molecules, but unlike furopyridines there are only a few reports for their synthesis.[35,36] To further highlight the importance of our above method toward the synthesis of different types of highly substituted pyridine molecules, we have devised an efficient method for the synthesis of 7,7′-disubstituted 2,2′-bifuro[2,3-*c*]pyridine **33** from 2-substituted 3-acetoxy-4-iodopyridine **23**. The schematic representation for its synthesis is delineated in Scheme 9. Thus, heterocoupling of alkynylpyridines **30** and **31** led to bis-alkynylpyridines **32**, which on cycloisomerization gave bifuropyridine **33**.

It is worth mentioning here that 3-hydroxy-4-alkynylpyridines are unstable compounds that cyclize spontaneously to furo[2,3-*c*]pyridines and thus cannot be used as building blocks for further synthesis.[30] However, our method as discussed above for the synthesis of substituted pyridines allows direct access to 3-acetoxy-4-iodopyridine obviating the need for protection of 3-hydroxy-4-iodopyridine before proceeding with Sonogashira reaction to obtain the corresponding 4-alkynylpyridine derivatives.

## CONCLUSION

In summary, herein an innovative new method to access enantiopure 2,4-disubstituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones starting from D-glucal by utilizing aza-Achmatowicz chemistry has been described. These highly functionalized enantiopure 1,6-dihydro-2*H*-pyridin-3-ones would serve as useful building blocks for the synthesis of diverse types of important enantiopure nitrogen-containing synthetic and natural molecules. We have also disclosed a $Et_3N/Ac_2O$-mediated mild and novel method for the rapid transformation of 2-substituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones and 2,4-disubstituted 6-hydroxy-1,6-dihydro-2*H*-pyridin-3-ones into 2,3-disubstituted and 2,3,4-trisubstituted pyridines permitting facile access to key pyridine building blocks like 2-substituted 3-acetoxy-4-iodopyridines and enantiopure 2-substituted 3-acetoxy-4-pyridinemethanols possessing benzylic stereogenic centers.

**Scheme 9**[a]




[a]Reagents and conditions: (a) trimethylsilylacetylene, $Pd[(PPh_3)_2Cl_2]$, CuI, $Et_3N$, THF, RT, 2.5 h, 82%; (b) $NaHCO_3$, $I_2$, MeOH, RT, 24 h, 64%; (c) TBAF, THF, −20 °C, 20 min, 75%; (d) $Pd[(PPh_3)_2Cl_2]$, $Et_3N$, THF, RT, 2.5 h, 83%; (e) $MeOH/Et_3N/H_2O$ (4:1:1), RT, 18 h, 66%.

The utilization of commercially available sugars as starting materials, mild reaction conditions, catalytic transfer hydrogen-(CTH) of $\alpha$-furfuryl azide derivatives, transfer of chiral aryl/alkyl methanols from enulosides to pyridin-3-ones and pyridines, high yields, and short reaction times are the salient features of the present methodology to obtain various pyridones and pyridines that would find wide applications for the synthesis of biologically important molecules. The new methodology is also amenable to easy scale-up. Further work toward the synthesis of highly functionalized novel aza-sugars from 2,4,6-trisubstituted 1,6-dihydro-2*H*-pyridin-3-ones is presently underway.

## EXPERIMENTAL SECTION

**General Remarks.** Organic solvents were dried by standard methods. Analytical TLC was performed using 2.5 × 5 $cm^2$ plates coated with a 0.25 mm thickness of silica gel (60 F-254) to monitor all the reactions, and visualization was accomplished with $CeSO_4$ or 10% $H_2SO_4$/EtOH and subsequent charring over a hot plate. Silica gel (60−120), (100−200), and (230−400) were used for column chromatography. All the column-purified products were characterized by $^1H$ NMR, $^{13}C$ NMR, distortionless enhancement by polarization transfer (DEPT) pulse sequence, two-dimensional homonuclear correlation spectroscopy (COSY), heteronuclear single quantum correlation (HSQC), IR, HRMS (direct analysis in real time, DART), and HRMS (quadrupole time of flight, Q-TOF). All NMR spectra were recorded with spectrometers at 300 MHz ($^1H$) and 75 MHz ($^{13}C$). Experiments were recorded in $CDCl_3$. Chemical shifts are given on the $\delta$ scale. For $^{13}C$ NMR, reference $CDCl_3$ appeared at 77.40 ppm. Optical rotations were determined by using a 1 dm cell in chloroform or methanol as solvent at 25 °C unless otherwise stated;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concentrations mentioned are in g/100 mL. IR spectra were recorded on FT-IR spectrophotometer.

*Compound 4:* To a stirred solution of furfuryl alcohol **3** (300 mg, 1.4 mmol) and diphenylphosphoryl azide (DPPA) (0.36 mL, 1.68 mmol) in dry toluene (10 mL) at 0 °C was added DBU (0.25 mL, 1.68 mmol) dropwise over a period of 0.5 h. The reaction mixture was stirred for another 2.5 h at 0 °C and for an additional 21 h at room temperature. After completion of the reaction (TLC), the reaction mixture was washed with water (5 mL) and 1 N HCl (2 × 5 mL), and the organic layer was washed with brine, dried over $Na_2SO_4$, and concentrated under reduced pressure to yield the crude product mixture. The crude product was chromatographed to furnish the pure compound **4**: yield (250 mg, 74%); oil; $R_f$ = 0.50 (hexane/ethyl acetate, 90:10); eluent for column chromatography (hexane/ethyl acetate, 97:3); $[\alpha]^{30}_D$ = −118.47 (*c* 0.15, $CHCl_3$). IR (neat, $cm^{-1}$): 2923, 2357, 2109, 1593, 1734, 1645. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.43 (s, 1H), 6.37 (s, 2H), 4.77−4.71 (m, 1H), 4.40−4.37 (m, 2H), 1.20 (s, 9H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 178.3 (qC), 149.3 (qC), 143.6 (CH), 110.8 (CH), 109.2 (CH), 64.6 ($CH_2$), 57.6 (CH), 39.2 (qC), 27.4 (3 × $CH_3$). HRMS (DART): calcd for $C_{11}H_{16}N_3O_3$ $[M + H]^+$ 238.1191; found 238.1183.

*Compound 5:* To a solution of compound **4** (250 mg, 1.05 mmol) in $CH_3OH$ (6 mL) was added 10% Pd−C (40 mg) under $N_2$, and the resulting mixture was subjected to hydrogenation under 1 bar pressure for 45 min. The reaction mixture was filtered through a Celite bed and washed with $CH_3OH$ (3 × 3 mL). The solvents were removed under reduced pressure to obtain the crude product. It was dissolved in dry $CH_2Cl_2$ (5 mL), and $Et_3N$ (0.22 mL, 1.58 mmol) was added to it at 0 °C followed by dropwise addition of p-TsCl (300 mg, 1.58 mmol) dissolved in dry $CH_2Cl_2$ over a period of 0.5 h. The reaction mixture was now stirred at room temperature for an additional 2.5 h. On completion of the reaction (TLC), the reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with dichloromethane (2 × 5 mL). The combined organic layers were washed with brine, dried over $Na_2SO_4$, and concentrated under reduced pressure to yield the crude product mixture, which on subjection to flash column chromatography furnished the pure compound **5**: yield (330 mg, 78% over two steps); oil; $R_f$ = 0.44 (hexane/ethyl acetate, 80:20); eluent for column chromatography (hexane/ethyl acetate, 92:8); $[\alpha]^{29}_D$ = −98.51 (*c* 0.15, $CHCl_3$). IR (neat, $cm^{-1}$): 2965, 2359, 1723, 1647. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.67−7.62 (m, 2H), 7.23 (s, 1H), 7.19−7.17 (m, 2H), 6.15 (dd, 1H, *J* = 2.8, *J* = 4.9 Hz), 6.00 (d, 1H, *J* = 4.9 Hz), 5.17 (d, 1H, *J* = 12.5 Hz), 4.79−4.69 (m, 1H), 4.35 (dd, 1H, *J* = 9.4, *J* = 16.9 Hz), 4.17 (dd, 1H, *J* = 8.3, *J* = 16.9 Hz), 2.38 (s, 3H), 1.12 (s, 9H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 178.4 (qC), 150.4 (qC), 143.7 (qC), 142.7 (CH), 137.9 (qC), 129.9 (2 × CH), 127.3 (2 × CH), 110.5 (CH), 108.3 (CH), 64.8 ($CH_2$), 51.2 (CH), 39.1 (qC), 27.4 (3 × $CH_3$), 21.8 ($CH_3$). HRMS (DART): calcd for $C_{18}H_{24}N_1O_5S_1$ $[M + H]^+$ 366.1375; found 366.1380.

*Compound 6:* NBS (219 mg, 1.23 mmol) was added in small portions over 0.5 h to a stirred solution of *N*-furfurylsulfonamide **5** (300 mg, 1.82 mmol) and NaOAc·$3H_2O$ (145 mg, 1.06) in THF/$H_2O$ (10 mL, 4:1, v/v) at −5 °C, and the reaction mixture was allowed to warm to 0 °C. After completion of the reaction in about 3 h (TLC), the reaction mixture was diluted with ethyl acetate (10 mL) and washed successively with a saturated aqueous solution of KI, $Na_2S_2O_3$, and $NaHCO_3$. The organic layer was separated, washed with brine solution, dried over $Na_2SO_4$, and concentrated *in vacuo* at reduced temperature to furnish the crude product mixture, which was subjected to flash column chromatography to obtain the pure compound **6**: yield (260 mg, 83%); oil; $R_f$ = 0.37 (hexane/ethyl acetate, 70:30); eluent for column chromatography (hexane/ethyl acetate, 90:10); $[\alpha]^{27}_D$ = +10.53 (*c* 0.70, $CHCl_3$). IR (neat, $cm^{-1}$): 3406, 2372, 1696, 1348, 1161. $^1H$ NMR ($CDCl_3$, 300 M Hz): $\delta$ 7.64 (d, 2H, *J* = 8.3 Hz), 7.28 (d, 2H, *J* = 8.3), 6.86 (dd, 1H, *J* = 4.5 *J* = 10.3 Hz), 6.03 (dd, 1H, *J* = 1.0, *J* = 10.3 Hz), 5.87−5.84 (m, 1H), 4.63−4.60 (m, H), 4.51 (dd, 1H, *J* = 6.0, *J* = 6.2, *J* = 11.2 Hz), 4.39 (dd, 1H, *J* = 5.3, *J* = 11.2 Hz), 3.70 (d, OH, *J* = 5.5 Hz), 2.40 (s, 2H), 1.19 (s, 9H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 191.6 (C═O), 178.4 (qC), 144.8 (qC), 144.3 (CH), 136.6 (qC), 130.5 (2 × CH), 127.5 (CH), 127.0 (2 × CH), 73.4 (CH), 65.5 ($CH_2$), 59.7 (CH), 39.1 (qC), 27.4 (3 × $CH_3$), 21.9 ($CH_3$). HRMS (DART): calcd for $C_{18}H_{22}N_1O_5S_1$ $[M - OH]^+$ 364.1218; found 364.1232.

*Compound 7b:* To a stirred solution of TBAI (247 mg, 0.67 mmol) in dry DCM (25 mL) at −78 °C was added $TiCl_4$ (5 mmol, 0.55 mL) dropwise. After stirring for 5 min, a mixture containing 2,3-dideoxy-hex-2-enopyranosid-4-ulose **1** (1.0 g, 3.35 mmol) and 4-(trifluoromethyl)benzaldehyde (0.9 mL, 6.7 mmol) in dry DCM (15 mL) was added. The reaction mixture was allowed to warm to −30 °C and stirred for 5 h. The reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ and filtered through a Celite pad. The organic layer was separated from the filtrate, and the aqueous layer was extracted with dichloromethane (2 × 10 mL). The combined organic layers were washed with brine solution, dried over $Na_2SO_4$, and subjected to column chromatography to obtain the pure compound **7b**: yield (1.2 g, 76%); oil; $R_f$ = 0.42 (hexane/ethyl acetate, 12:5); eluent for column chromatography (hexane/ethyl acetate, 21:4); $[\alpha]^{29}_D$ = −21.28 (*c* 0.1, $CHCl_3$). IR (neat, $cm^{-1}$): 3458, 2962, 172, 1467, 1326. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.60 (d, 1H, *J* = 8.1 Hz), 7.4 (d, 1H, *J* = 8.1 Hz), 6.65−6.64 (m, 1H), 5.62 (s, 1H), 5.29−5.28 (m, 1H), 4.61 (dd, 1H, *J* = 2.7, *J* = 5.2), 4.49 (dd, 1H, *J* = 2.7, *J* = 11.9), 4.41 (dd, 1H, *J* = 5.3, *J* = 11.9), 3.87−3.80 (m, 1H), 3.61−3.53 (m, 1H), 1.69−1.63 (m, 1H), 1.51−1.48 (m, 2H), 1.12 (s, 9H), 0.90 (d, 6H, *J* = 6.6). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 195.0 (C═O), 178.4 (qC), 144.6 (qC), 140.4 (CH), 139.2 (qC), 130.8 (qC), 130.3 (qC), 127.4 (2 × CH), 126.2 (qC), 125.9−125.8 (2 × CH), 122.5 (qC), 93.7 (CH), 72.9 (CH), 71.1 (CH), 68.5 ($CH_2$), 62.9 ($CH_2$), 39.1 (qC), 38.6 ($CH_2$), 27.4 (3 × $CH_3$), 25.4 (CH), 23.0 ($CH_3$), 22.8 ($CH_3$). HRMS (DART): calcd for $C_{24}H_{30}F_3O_5$ $[M - OH]^+$ 455.2045; found 455.2042.

**General Procedure for the Synthesis of Compounds 8a−c from 7a−c.** *Compound 8a:* 2,6-Lutidine (1 mL, 9.32 mmol) was added at 0 °C to a solution of 2,3-dideoxy-hex-2-enopyranoside alcohol **7a** (2.0 g, 4.66 mmol) in dry $CH_2Cl_2$ (20 mL), followed by dropwise addition of TBSOTf (1.6 mL, 6.99 mmol) with a syringe, in argon atmosphere, and the mixture was stirred for 3 h. After completion of reaction (TLC), the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution (10 mL), and the aqueous layer was extracted with $CH_2Cl_2$ (2 × 10 mL). The combined organic extracts were dried over $Na_2SO_4$, concentrated under reduced pressure, and purified by flash column chromatography to furnish the pure compound **8a**: yield (2.1 g, 83%); oil; $R_f$ = 0.60 (hexane/ethyl acetate, 90:10); eluent for column chromatography (hexane/ethyl acetate, 97:3); $[\alpha]^{27}_D$ = −41.66 (*c* 0.1, $CHCl_3$). IR (neat, $cm^{-1}$): 3447, 2955, 2363, 2229, 1731, 1632, 1467. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.57 (d, 2H, *J* = 8.3 Hz), 7.50 (d, 2H, *J* = 8.3 Hz), 7.03−7.02 (m, 1H), 5.61 (s, 1H), 5.34−5.33 (m, 1H), 4.50−4.46 (m, 2H), 4.41−4.35 (m, 1H), 3.85−3.77 (m, 1H), 3.61−3.53 (m, 1H), 1.66−1.62 (m, 1H), 1.52−1.44 (m, 2H), 1.16 (s, 9H), 0.88 (d, 6H, *J* = 6.8), 0.85 (s, 9H), 0.02 (s, 3H), −0.10 (s, 3H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 193.1 (C═O), 178.3 (qC), 147.8 (qC), 140.6 (qC), 139.2 (CH), 132.4 (2 × CH), 127.9 (2 × CH), 119.1 (qC), 111.8 (CN), 93.9 (CH), 72.89 (CH), 69.6 (CH), 68.4 ($CH_2$), 62.8 ($CH_2$), 39.1 (qC), 38.6 ($CH_2$), 27.4 (3 × $CH_3$), 26.0 (3 × $CH_3$), 25.4 (CH), 23.0 ($CH_3$), 22.8 ($CH_3$), 18.5 (qC), −4.5 ($CH_3$), −4.6 ($CH_3$). HRMS (DART): calcd for $C_{30}H_{46}N_1O_6Si_1$ $[M + H]^+$ 544.3094; found 544.3107.

*Compound 8b:* Yield (980 mg, 79%); oil; $R_f$ = 0.50 (hexane/ethyl acetate, 95:5); eluent for column chromatography (hexane/ethyl acetate, 98.5:1.5); $[\alpha]^{32}_D$ = −108.21 (*c* 0.1, $CHCl_3$). IR (neat, $cm^{-1}$): 2958, 2363, 1735, 1468, 1325. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.55−7.48 (m, 4H), 7.03−7.02 (m, 1H), 5.65 (s, 1H), 5.35−5.34 (m, 1H), 4.51−4.47 (m, 2H), 4.42−4.36 (m, 1H), 3.86−3.78 (m, 1H), 3.62−3.54 (m, 1H) 1.69−1.63 (m, 1H), 1.51−1.48 0 (m, 2H), 1.17 (s, 9H), 0.89 (d, 6H, *J* = 6.8), 0.87 (s, 9H), 0.03 (s, 3H), −0.10 (s, 3H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 193.1 (C═O), 178.3 (qC), 146.4 (qC), 140.9 (qC), 138.9 (CH), 130.7 (qC), 130.2 (qC), 129.8 (qC), 129.4 (qC), 127.5 (2 × CH), 126.3 (qC), 125.5−125.4 (2 × CH), 122.7 (qC), 93.9 (CH), 72.8 (CH), 69.6 (CH), 68.3 ($CH_2$), 62.8 ($CH_2$), 39.1 (qC), 38.6 ($CH_2$), 27.4 (3 × $CH_3$), 26.0 (3 × $CH_3$), 25.4 (CH), 23.0 ($CH_3$), 22.8 ($CH_3$), 18.5 (qC), −4.5 ($CH_3$), −4.7 ($CH_3$). HRMS

(DART): calcd for $C_{25}H_{34}F_3O_5Si_1$ $[M - C_5H_{11}O]^+$ 499.2127; found 499.2121.

*Compound* ***8c:*** Yield (1.0 g, 80%); oil; $R_f$ = 0.55 (hexane/ethyl acetate, 96:4); eluent for column chromatography (hexane/ethyl acetate, 99:1); $[\alpha]^{26}_D$ = +87.76 (*c* 0.10, $CHCl_3$). IR (neat, $cm^{-1}$): 3022, 2930, 2361, 1724, 1521, 1467, 1216. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 6.85 (d, 1H, *J* = 2.6), 5.28 (d, 1H, *J* = 2.6), 4.60 (dd, 2H, *J* = 2.5, *J* = 5.4), 4.52 (dd, 1H, *J* = 2.6, *J* = 11.9), 4.43 (dd, 1H, *J* = 5.7, *J* = 11.9), 3.89−3.81 (m, 1H), 3.63−3.55 (m, 1H), 1.74−1.65 (m, 1H), 1.59−1.50 (m, 4H), 1.24 (s, 14H), 1.17 (s, 9H), 0.92−0.89 (m, 18H), 0.03 (s, 3H), −0.04 (s, 3H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 193.7 (C═O), 178.5 (qC) 141.9 (qC), 139.0 (CH), 94.1 (CH), 72.8 (CH), 68.2 ($CH_2$), 67.7 (CH), 63.1 ($CH_2$), 39.1 (qC), 38.7 ($CH_2$), 37.8 ($CH_2$), 32.2 ($CH_2$), 29.9−29.6 (4 × $CH_2$), 27.5 (3 × $CH_3$), 26.2 (3 × $CH_3$), 25.5 (CH), 25.3 (2 × $CH_2$), 23.0 ($CH_3$), 22.8 ($CH_3$), 18.8 (qC), 14.4 ($CH_3$), −4.2 ($CH_3$), −4.6 ($CH_3$). HRMS (DART): calcd for $C_{27}H_{49}O_5Si_1$ $[M - C_5H_{11}O]^+$ 481.3349; found 481.3355.

*Compound* ***8d:*** Imidazole (1.294 g, 18.92 mmol) was added at 0 °C to a solution of enone **7d** (4.0 g, 12.195 mmol) in dry $CH_2Cl_2$ (30 mL), followed by the addition of TBSCl (2.012 g, 13.41 mmol). The resulting mixture was stirred for an additional 2 h at room temperature. After completion of the reaction (TLC), the reaction mixture was quenched with saturated aqueous $NH_4Cl$ solution (15 mL) and extracted with $CH_2Cl_2$ (2 × 10 mL). The combined organic extracts were dried ($Na_2SO_4$), concentrated under reduced pressure, and purified by flash column chromatography to furnish the pure compound **8d**: yield (4.0 g, 74%); oil; $R_f$ = 0.57 (hexane/ethyl acetate, 95:5); eluent for column chromatography (hexane/ethyl acetate, 99:1); $[\alpha]^{31}_D$ = +13.52 (*c* 0.10, $CHCl_3$). IR (neat, $cm^{-1}$): 3427, 3021, 2361, 1725, 1216. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 6.84−6.81 (m, 1H), 5.28−5.27 (m, 1H), 4.60−4.57 (m, 1H), 4.54−4.49 (m, 1H), 4.41−4.33 (m, 3H), 3.87−3.82 (m, 1H), 3.62−3.57 (m, 1H), 1.74−1.68 (m, 1H), 1.54−1.48 (m, 2H), 1.18 (s, 9H), 0.94−0.92 (m, 15H), 0.09 (s, 6H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 193.9 (C═O), 178.4 (qC), 138.0 (qC), 137.8 (CH), 94.1 (CH), 72.9 (CH), 68.2 ($CH_2$), 63.2 ($CH_2$), 58.9 ($CH_2$), 39.1 (qC), 38.7 ($CH_2$), 27.4 (3 × $CH_3$), 26.2 (3 × $CH_3$), 25.4 (CH), 23.0−22.8 (2 × $CH_3$), 18.6 (qC), −5.1 (2 × $CH_3$). HRMS (DART): calcd for $C_{23}H_{43}O_6Si_1$ $[M + H]^+$ 443.2828; found 443.2832.

**General Procedure for the Synthesis of Compounds 9a−d from 8a−d.** *Compound* ***9a:*** To a stirred solution of **8a** (2.0 g, 3.68 mmol) in ethanol (15 mL) at −5 °C were added $CeCl_3·7H_2O$ (685 mg, 1.84 mmol) and $NaBH_4$ (68 mg, 1.84 mmol), and the reaction mixture was stirred for another 1.5 h at the same temperature. After completion of the reaction (TLC), excess $NaBH_4$ was neutralized with acetone, and the solvent was removed under reduced pressure to afford the crude product mixture, which was dissolved in ethyl acetate, filtered through silica gel, and concentrated under reduced pressure to give the crude product. To a stirred solution of the crude product mixture in dry THF (15 mL) were added $ZrCl_4$ (5 mol %) and $ZnI_2$ (10 mol %), and the resulting reaction mixture was stirred at 60 °C until completion of the reaction (TLC). The mixture was now quenched with water and extracted with ethyl acetate (4 × 10 mL). The combined organic layers were washed with brine, dried over $Na_2SO_4$, and concentrated under reduced pressure to afford the crude product. It was then chromatographed to afford pure compound **9a**: yield (1.245 g, 74%); oil; $R_f$ = 0.41 (hexane/ethyl acetate, 85:15); eluent for column chromatography (hexane/ethyl acetate, 95:5); $[\alpha]^{32}_D$ = +68.45 (*c* 0.1, $CHCl_3$). IR (neat, $cm^{-1}$): 3427, 2927, 2365, 2231, 1724, 1612, 1435. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.59 (d, 2H, *J* = 8.3 Hz), 7.53 (d, 2H, *J* = 8.3 Hz), 7.26 (d, 1H, *J* = 1.5 Hz), 6.24 (d, 1H, *J* = 1.7 Hz), 5.97 (s, 1H), 4.40 (dd, 1H, *J* = 7.4, *J* = 11.6 Hz), 4.33 (dd, 1H, *J* = 4.3, *J* = 11.6 Hz), 2.89 (s, OH), 1.19 (s, 9H), 0.90 (s, 9H), 0.04 (s, 3H), 0.01 (s, 3H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 179.0 (qC), 150.0 (qC)), 147.7 (qC), 142.5 (CH), 132.5 (2 × CH), 126.9 (2 × CH), 126.3, (qC), 119.2 (qC), 111.2 (CN), 110.4 (CH), 68.9 (CH), 66.9 ($CH_2$), 66.0 (CH), 39.2 (qC), 27.4 (3 × $CH_3$), 26.1 (3 × $CH_3$), 18.5 (qC), −4.4 ($CH_3$), −4.6 ($CH_3$). HRMS (DART): calcd for $C_{25}H_{35}N_1O_5Si_1$ $[M]^+$ 457.2284; found 457.2292.

*Compound* ***9b:*** Yield (575 mg, 71%); oil; $R_f$ = 0.46 (hexane/ethyl acetate, 90:10); eluent for column chromatography (hexane/ethyl acetate, 99:1); $[\alpha]^{31}_D$ = +93.90 (*c* 0.1, $CHCl_3$). IR (neat, $cm^{-1}$): 3448, 2364, 1724, 1325. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.58−7.55 (m, 4H), 7.25 (d, 1H, *J* = 1.5 Hz), 6.27 (d, 1H, *J* = 1.7 Hz), 5.98 (s, 1H), 5.10 (dd, 1H, *J* = 4.3, *J* = 6.6 Hz), 4.42 (dd, 1H, *J* = 7.7, *J* = 11.5 Hz), 4.33 (dd, 1H, *J* = 4.4, *J* = 11.5 Hz), 2.95 (s, OH), 1.19 (s, 9H), 0.92 (s, 9H), 0.04−0.03 (m, 6H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 179.0 (qC), 148.6 (qC), 147.7 (qC), 142.3 (CH), 130.3 (qC), 129.9 (qC), 129.5 (qC), 129.1 (qC), 126.7 (qC), 126.5 (2 × CH), 125.7−125.5 (2 × CH), 122.7 (qC), 110.6 (CH), 69.2 (CH), 66.8 (CH), 65.9 ($CH_2$), 39.1 (qC), 27.4 (3 × $CH_3$), 26.1 (3 × $CH_3$), 18.5 (qC), −4.4 ($CH_3$), −4.6 ($CH_3$). HRMS (DART): calcd for $C_{25}H_{34}F_3O_4Si_1$ $[M - OH]^+$ 483.2178; found 483.2195.

*Compound* ***9c:*** Yield (519 mg, 68%); oil; $R_f$ = 0.50 (hexane/ethyl acetate, 90:10); eluent for column chromatography (hexane/ethyl acetate, 98:2); $[\alpha]^{28}_D$ = +65.87 (*c* 0.10, $CHCl_3$). IR (neat, $cm^{-1}$): 3448, 2929, 2858, 2372, 1724, 1466. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.30−7.29 (m, 1H), 6.32−6.31 (m, 1H), 5.06 (s, 1H), 4.77−4.72 (m, 1H), 4.42 (dd, 1H, *J* = 7.9, *J* = 11.4 Hz), 4.34 (dd, 1H, *J* = 4.4, *J* = 11.4 Hz), 3.09 (d, OH, *J* = 5.3 Hz), 1.75−1.68 (m, 2H), 1.28 (s, 14H), 1.24 (s, 9H), 0.91 (s, 12H), 0.10 (s, 6H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 178.9 (qC), 147.6 (qC), 141.6 (CH), 127.1 (qC), 110.8 (CH), 68.7 (CH), 67.1 ($CH_2$), 66.0 (CH), 40.4 ($CH_2$), 39.1 (qC), 32.2 ($CH_2$), 30.0−29.6 (4 × $CH_2$), 27.5 (3 × $CH_3$), 26.2 (3 × $CH_3$), 25.9 ($CH_2$), 23.0 ($CH_2$), 18.5 (qC), 14.4 ($CH_3$), −4.2 ($CH_3$), −4.5 ($CH_3$). HRMS (DART): calcd for $C_{27}H_{51}O_5$ $Si_1[M + H]^+$ 483.3505; found 483.3506.

*Compound* ***9d:*** Yield (2.2 g, 66%); oil; $R_f$ = 0.37 (hexane/ethyl acetate, 88:12); eluent for column chromatography (hexane/ethyl acetate, 96:4); $[\alpha]^{29}_D$ = −4.44 (*c* 0.10, $CHCl_3$). IR (neat, $cm^{-1}$): 2950, 2361, 1723, 1473. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.25 (s, 1H), 6.26 (s, 1H), 4.97 (br s, 1H), 4.69−4.59 (m, 1H), 4.36 (dd, 1H, *J* = 7.4, *J* = 11.3 Hz), 4.29 (dd, 1H, *J* = 5.2, *J* = 11.3 Hz), 3.31 (br s, OH), 1.17 (s, 9H), 0.92 (s, 9H), 0.11 (s, 6H). $^{13}C$ NMR ($CDCl_3$+$CCl_4$, 75 MHz): $\delta$ 178.4 (qC), 149.8 (qC), 141.4 (CH), 122.1 (qC), 111.4 (CH), 66.7 ($CH_2$), 66.3 ($CH_2$), 58.1 (CH), 39.2 (qC), 27.6 (3 × $CH_3$), 26.4 (3 × $CH_3$), 18.8 (qC), −4.8 ($CH_3$), −4.9 ($CH_3$). HRMS (DART): calcd for $C_{18}H_{31}O_4Si_1$ $[M - OH]^+$ 339.1991; found 339.1982.

**General Procedure for the Synthesis of Compounds 10a−d from 9a−d.** *Compound* ***10a:*** To a stirred solution of alcohol **9a** (1.2 g, 2.62 mmol) and DPPA (1.69 mL, 7.87 mmol) in dry toluene (15 mL) at 0 °C was added DBU (1.17 mL, 7.87 mmol) dropwise with a syringe over a period of 0.5 h. The reaction mixture was stirred for another 2.5 h at 0 °C and for an additional 21 h at room temperature. Once the reaction was complete (TLC), the reaction mixture was quenched with water (10 mL) and washed with 1 N HCl (2 × 10 mL). The organic layer was separated, dried over $Na_2SO_4$, and concentrated under reduced pressure to afford the crude product mixture. The crude product was chromatographed to furnish the pure compound **10a**: yield (974 mg, 77%); oil; $R_f$ = 0.53 (hexane/ethyl acetate, 90:10); eluent for column chromatography (hexane/ethyl acetate, 98:2); $[\alpha]^{30}_D$ = −3.78 (*c* 0.1, $CHCl_3$). IR (neat, $cm^{-1}$): 2960, 2364, 2229, 2109, 1729, 1631. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.63 (d, 2H, *J* = 8.3 Hz), 7.49 (d, 2H, *J* = 8.2 Hz), 7.31 (d, 1H, *J* = 1.8 Hz), 6.24 (d, 1H, *J* = 1.8 Hz), 5.82 (s, 1H), 4.97 (dd, 1H *J* = 4.9, *J* = 8.7 Hz), 4.44 (dd, 1H *J* = 8.8, *J* = 11.5 Hz), 4.35 (dd, 1H *J* = 4.8, *J* = 11.5 Hz), 1.20 (s, 9H), 0.90 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 178.4 (qC)), 149.5 (qC), 144.3 (qC), 143.5 (CH), 132.8 (2 × CH), 127.4, (qC), 126.9 (2 × CH), 119.0 (CH), 111.7 (CN), 110.4 (CH), 69.6 (CH), 64.7 ($CH_2$), 56.2 (CH), 39.2 (qC), 27.4 (3 × $CH_3$), 26.1 (3 × $CH_3$), 18.5 (qC), −4.4 ($CH_3$), −4.5 ($CH_3$). HRMS (DART): calcd for $C_{25}H_{34}N_4O_4Si_1$ $[M]^+$ 482.234; found 482.2348.

*Compound* ***10b:*** Yield (462 mg, 80%); oil; $R_f$ = 0.56 (hexane/ethyl acetate, 95:5); eluent for column chromatography (hexane/ethyl acetate, 99.5: 0.5); $[\alpha]^{27}_D$ = −17.73 (*c* 0.1, $CHCl_3$). IR (neat, $cm^{-1}$): 3458, 2365, 2110, 1728, 1325. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.59 (d, 2H, *J* = 8.1 Hz), 7.50 (d, 2H, *J* = 8.1 Hz), 7.30 (d, 2H, *J* = 1.6 Hz), 6.26 (d, 1H, *J* = 1.6 Hz), 5.86−5.84 (m, 1H), 5.01−4.96 (m, 1H), 4.48−4.37 (m, 1H), 4.36−4.33 (m, 1H), 1.20 (s, 9H), 0.91 (s, 9H),

0.04 (s, 3H), 0.01 (s, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 178.4 (qC), 148.5 (qC), 144.1 (qC), 143.3 (CH), 130.3 (qC), 129.9 (qC), 129.7 (qC), 127.9 (qC), 126.6 (2 × CH), 125.9−125.8 (2 × CH), 121.8 (qC), 110.5 (CH), 69.8 (CH), 64.8 ($CH_2$), 56.3 (CH), 39.3 (qC), 27.4 (3 × $CH_3$), 26.1 (3 × $CH_3$), 18.7 (qC), −4.4 ($CH_3$), −4.5 ($CH_3$). HRMS (DART): calcd for $C_{19}H_{19}F_3N_3O_3$ [M − $C_5H_{13}O_1Si_1$]$^+$ 394.1378; found 394.1374.

*Compound* ***10c:*** Yield (400 mg, 76%); oil; $R_f$ = 0.58 (hexane/ethyl acetate, 98:2); eluent for column chromatography (hexane/ethyl acetate, 99:1); $[\alpha]^{27}_D$ = −13.27 (*c* 0.10, $CHCl_3$). IR (neat, cm$^{-1}$): 2927, 2363, 2110, 1731,1465, 1217. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.31 (d, 1H, *J* = 1.6 Hz), 6.31 (d, 1H, *J* = 1.7 Hz), 4.94 (dd, 1H, *J* = 4.4, *J* = 8.9 Hz), 4.69−4.65 (m, 1H), 4.48 (dd, 1H, *J* = 9.0, *J* = 11.5 Hz), 4.27 (dd, 1H, *J* = 4.6, *J* = 11.5 Hz), 1.69−1.60 (m, 2H), 1.25 (s, 14H), 1.22 (s, 9H), 0.88 (s, 12H), 0.60 (s, 3H) −0.05 (s, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 178.3 (qC), 143.7 (qC), 142.9 (CH), 128.9 (qC), 110.5 (CH), 68.1 (CH), 64.8 ($CH_2$), 56.3 (CH), 40.7 ($CH_2$), 39.2 (qC), 32.2 ($CH_2$), 29.9−29.6 (4 × $CH_2$), 27.4 (3 × $CH_3$), 26.2 (3 × $CH_3$), 25.6 ($CH_2$), 23.0 ($CH_2$), 18.5 (qC), 14.4 ($CH_3$), −4.2 ($CH_3$), −4.6 ($CH_3$). HRMS (DART): calcd for $C_{27}H_{50}N_1O_4Si_1$ [M − $N_2$]$^+$ 480.3509; found 480.3507.

*Compound* ***10d:*** Yield (1.618 g, 72%); oil; $R_f$ = 0.40 (hexane/ethyl acetate, 98:2); eluent for column chromatography (hexane/ethyl acetate, 99:1); $[\alpha]^{31}_D$ = −14.76 (*c* 0.10, $CHCl_3$). IR (neat, cm$^{-1}$): 3020, 2361, 2109, 1726, 1216. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.34 (d, 1H, *J* = 2.6 Hz), 6.30 (d, 1H, *J* = 2.6 Hz) 5.0 (dd, 1H, *J* = 8.5, *J* = 12.2 Hz), 4.63 (s, 2H), 4.43−4.30 (m, 2H), 1.19 (s, 9H), 0.92 (s, 9H), 0.11 (s, 6H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 177.9 (qC), 144.9 (qC), 142.9 (CH), 124.5 (qC), 111.1 (CH), 64.5 ($CH_2$), 57.7 ($CH_2$), 56.2 (CH), 39.2 (qC), 27.6 (3 × $CH_3$), 26.4 (3 × $CH_3$), 18.8 (qC), −4.8 (2 × $CH_3$). HRMS (DART): calcd for $C_{18}H_{32}N_3O_4Si_1$ [M + H]$^+$ 382.2162; found 382.2159.

**General Procedure for the Synthesis of Compounds 11a−d from 10a−d.** *Compound* ***11a:*** To a solution of compound **10a** (900 mg, 1.86 mmol) in $CH_3OH/CHCl_3$ (12 mL, 5:1, v/v) were added 10% Pd−C (150 mg) and $Et_3SiH$ (0.69 mL, 4.66 mmol) under argon, and the reaction mixture was stirred at room temperature for 2 h. It was filtered through a Celite bed and washed with $CH_3OH$. The solvents were removed under reduced pressure to obtain the crude product mixture, which was dissolved in dry $CH_2Cl_2$ (10 mL), and then $Et_3N$ (0.39 mL, 2.8 mmol) was added to it at 0 °C followed by dropwise addition of p-TsCl (532 mg, 2.8 mmol) dissolved in dry $CH_2Cl_2$ over a period of 0.5 h. The reaction mixture was now stirred at room temperature for an additional 2.5 h. On completion of the reaction (TLC), the reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with dichloromethane (2 × 5 mL). The combined organic layers were washed with brine, dried over $Na_2SO_4$, and concentrated under reduced pressure to yield the crude product mixture. Flash column chromatography gave the pure compound **11a**: yield (797 mg, 70%); oil; $R_f$ = 0.48 (hexane/ethyl acetate, 75:25); eluent for column chromatography (hexane/ethyl acetate, 98:2); $[\alpha]^{25}_D$ = +22.43 (*c* 0.5, MeOH). IR (neat, cm$^{-1}$): 2960, 2364, 2229, 2109, 1729, 1631. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.58 (d, 2H, *J* = 8.2 Hz), 7.54−7.45 (m, 4H), 7.13 (d, 1H, *J* = 9.0 Hz), 7.06 (d, 1H, *J* = 1.5 Hz), 6.22 (d, 1H, *J* = 1.6 Hz), 5.77 (s, 1H), 5.34 (d, 1H *J* = 8.6 Hz), 5.0−4.93 (m, 1H), 4.16 (dd, 1H *J* = 7.3, *J* = 11.3 Hz), 3.93 (dd, 1H *J* = 4.8, *J* = 11.3 Hz), 2.36 (s, 3H), 1.08 (s, 9H), 0.87 (s, 9H), 0.02 (s, 3H), −0.06 (s, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 178.3 (qC), 149.7 (qC), 144.9 (qC), 143.4 (qC), 142.5 (CH), 138.3 (qC), 132.6 (2 × CH), 129.7 (2 × CH), 127.2 (2 × CH), 126.8 (2 × CH), 125.6 (qC) 118.9 (qC), 111.5 (CN) 110.2 (CH), 69.9 (CH), 64.8 ($CH_2$), 49.8 (CH), 38.9 (qC), 27.2 (3 × $CH_3$), 26.0 (3 × $CH_3$), 21.7 ($CH_3$) 18.4 (qC), −4.5 (2 × $CH_3$). HRMS (DART): calcd for $C_{32}H_{42}N_2O_6S_1Si_1$ [M]$^+$ 610.2532; found 610.2522.

*Compound* ***11b:*** Yield (380 mg, 68%); oil; $R_f$ = 0.46 (hexane/ethyl acetate, 85:15); eluent for column chromatography (hexane/ethyl acetate, 95:5); $[\alpha]^{29}_D$ = −13.64 (*c* 0.1, $CHCl_3$). IR (neat, cm$^{-1}$): 3449, 2933, 1725, 1325. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.76−7.68 (m, 4H), 7.64 (d, 2H, *J* = 8.2 Hz), 7.32 (d, 2H, *J* = 8.0 Hz), 7.26 (d, 1H, *J* = 1.1 Hz), 6.43 (d, 2H, *J* = 1.4 Hz), 5.97 (s, 1H), 5.53 (d, 1H, *J* = 5.8 Hz), 5.20−5.13 (m, 1H), 4.38 (dd, 1H, *J* = 7.3, *J* = 11.2 Hz), 4.12 (dd, 1H, *J* = 4.9, *J* = 11.2 Hz), 2.54 (s, 3H), 1.27 (s, 9H), 1.08 (s, 9H), 0.23 (s, 3H), 0.13 (s, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 178.4 (qC), 148.5 (qC), 144.8 (qC), 143.4 (qC), 142.1 (CH), 138.3 (qC), 130.2 (qC), 129.7 (CH), 127.0 (CH), 126.9 (CH), 126.1 (CH), 125.9 (CH), 125.8 (CH), 122.6 (qC), 110.4 (CH), 70.2 (CH), 64.9 ($CH_2$), 49.9 (CH), 39.0 (qC), 27.3 (3 × $CH_3$), 26.1 (3 × $CH_3$), 21.7 ($CH_3$), 18.5 (qC), −4.4 ($CH_3$), −4.5 ($CH_3$). HRMS (DART): calcd for $C_{32}H_{42}F_3N_1O_6S_1Si_1$ [M]$^+$ 653.2454; found 653.2456.

*Compound* ***11c:*** Yield (311 mg, 71%); oil; $R_f$ = 0.40 (hexane/ethyl acetate, 96:4); eluent for column chromatography (hexane/ethyl acetate, 96:4); $[\alpha]^{30}_D$ = +17.50 (*c* 0.10, $CHCl_3$). IR (neat, cm$^{-1}$): 3274, 2858, 2368, 1724, 1266. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.62 (d, 2H, *J* = 8.2 Hz), 7.18 (d, 2H, *J* = 8.2 Hz), 7.09 (d, 1H, *J* = 1.6 Hz), 6.20 (d, 1H, *J* = 1.6 Hz), 5.23 (d, 1H, *J* = 8.2 Hz), 4.95 (d, 1H, *J* = 6.9, *J* = 13.0 Hz), 4.64−4.60 (m, 1H), 4.29 (dd, 1H, *J* = 7.0, *J* = 11.2 Hz), 4.07 (dd, 1H, *J* = 5.0, *J* = 11.2 Hz), 2.37 (s, 3H), 1.62−1.59 (m, 2H), 1.24 (s, 14H), 1.13 (s, 9H), 0.87 (s, 12H), 0.04 (s, 3H), −0.09 (s, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 178.5 (qC), 144.4 (qC), 143.4 (CH), 141.6 (CH), 138.4, 129.9 (qC), 129.8 (CH), 127.4, 127.1 (CH), 127.0 (qC), 126.9 (qC), 110.8 (CH), 68.0 (CH), 65.4 ($CH_2$), 49.9 (CH), 42.3 (qC), 40.4 ($CH_2$), 39.1 (qC), 32.2 ($CH_2$), 29.9.0−29.7 (4 × $CH_2$), 27.4 (3 × $CH_3$), 26.2 (2 × $CH_3$), 25.7 ($CH_2$), 23.0 ($CH_2$), 21.8 ($CH_3$), 14.5 ($CH_3$), −4.2 ($CH_3$) −4.6 ($CH_3$). HRMS (DART): calcd for $C_{34}H_{57}N_1O_6S_1Si_1$ [M]$^+$ 635.3675; found 635.3659.

*Compound* ***11d:*** Yield (1.6 g, 75%); oil; $R_f$ = 0.34 (hexane/ethyl acetate, 85:15); eluent for column chromatography (hexane/ethyl acetate, 90:10); $[\alpha]^{29}_D$ = −2.03 (*c* 0.10, $CHCl_3$). IR (neat, cm$^{-1}$): 3430, 3019, 2363, 1592, 1217. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.57 (d, 2H, *J* = 8.2 Hz), 7.13 (d, 2H, *J* = 8.0 Hz), 7.04 (d, 1H, *J* = 1.6 Hz), 6.03 (d, 1H, *J* = 1.59 Hz), 5.68 (d, 1H, *J* = 9.0 Hz), 4.91−4.83 (m, 1H), 4.45−4.41 (m, 1H), 4.34−4.27 (m, 1H), 4.20−4.15 (m, 1H), 2.34 (s, 3H), 1.12 (s, 9H), 0.92 (s, 9H), 0.11 (s, 6H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 178.4 (qC), 146.3 (qC), 143.3 (qC), 141.6 (CH), 138.0 (qC), 129.6 (2 × CH), 127.1 (2 × CH), 122.1 (qC), 110.8 (CH), 64.8 ($CH_2$), 57.9 ($CH_2$), 50.2 (CH), 39.1 (qC), 27.4 (3 × $CH_3$), 26.3 (3 × $CH_3$), 21.8 ($CH_3$), 18.7 (qC), −5.0 (2 × $CH_3$). HRMS (DART): calcd for $C_{25}H_{40}N_1O_6S_1Si_1$ [M + H]$^+$ 510.2345; found 510.2337.

**General Procedure for the Synthesis of Compounds 12a−d from 11a−d.** *Compound* ***12a:*** NBS (437 mg, 2.45 mmol) was added in small portions over 0.5 h to solution of *p*-toluenesulfonyl amine **11a** (750 mg, 1.22 mmol) in THF−$H_2O$ (10 mL, 4:1, v/v) cooled to −5 °C, and the reaction mixture was allowed to warm to room temperature. After completion of the reaction in about 3.5 h (TLC), the reaction mixture was diluted with ethyl acetate (10 mL) and washed successively with a saturated aqueous solution of KI, $Na_2S_2O_3$, and $NaHCO_3$. The organic layer was separated, washed with brine solution, dried over $Na_2SO_4$, and concentrated *in vacuo* at reduced temperature to furnish the crude mixture, which was subjected to flash column chromatography to give the pure compound **12a**: yield (507 mg, 66%); oil; $R_f$ = 0.33 (hexane/ethyl acetate, 80:20); eluent for column chromatography (hexane/ethyl acetate, 90:10); $[\alpha]^{31}_D$ = +5.79 (*c* 0.1, $CHCl_3$). IR (neat, cm$^{-1}$): 2923, 2357, 1728, 1596, 1216. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.64 (d, 2H, *J* = 8.2), 7.54 (d, 2H, *J* = 8.2), 7.43 (d, 2H, *J* = 8.2), 7.28−7.26 (m, 2H), 7.05 (d, 1H, *J* = 3.7), 5.98 (d, 1H, *J* = 3.6), 5.52 (s, 1H), 4.56−4.52 (m, 1H), 4.27 (dd, 1H *J* = 6.0, *J* = 11.3), 4.1 (dd, 1H *J* = 6.6, *J* = 11.3), 2.39 (s, 1H), 0.95 (s, 9H), 0.78 (s, 9H) −0.13 (s, 3H), −0.18 (s, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 190.7 (C═O), 177.9 (qC), 147.3 (qC), 144.7 (qC), 140.3 (qC), 139.1 (CH), 136.7 (qC), 132.5 (2 × CH), 130.5 (2 × CH), 127.6 (2 × CH), 127.0 (2 × CH), 118.9 (qC), 111.9 (CN), 73.9 (CH) 69.3 (CH), 64.8 ($CH_2$), 59.4 (CH), 38.9 (qC), 27.2 (3 × $CH_3$), 25.9 (3 × $CH_3$), 21.8 ($CH_3$), 18.3 (qC), −4.7 ($CH_3$), −4.9 ($CH_3$). HRMS (DART): calcd for $C_{32}H_{41}N_2O_6S_1Si_1$ [M − OH]$^+$ 609.2454; found 609.2463.

*Compound* ***12b:*** Yield (98 mg, 64%); oil; $R_f$ = 0.46 (hexane/ethyl acetate, 86:14); eluent for column chromatography (hexane/ethyl acetate, 95: 5); $[\alpha]^{29}_D$ = +7.86 (*c* 0.2, $CHCl_3$). IR (neat, cm$^{-1}$): 2921, 2363, 1732, 1218. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.76−7.70 (m,

4H), 7.64 (d, 2H, $J$ = 8.25), 7.32 (d, 2H, $J$ = 8.04), 7.26 (d, 1H, $J$ = 1.08), 6.43 (d, 2H, $J$ = 1.44) 5.97 (s, 1H), 5.53 (d, 2H, $J$ = 5.8), (dd, 1H, $J$ = 4.8, $J$ = 8.5), 4.38 (dd, 1H, $J$ = 7.2, $J$ = 10.11), 4.12 (dd, 1H, $J$ = 4.86, $J$ = 11.2) 1.27 (s, 9H), 1.08 (s, 9H), 0.23 (s, 6H) 0.13 (s, 6H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 190.6 (C═O), 177.9 (qC), 144.8 (qC)), 140.9 (qC), 138.7 (CH), 136.8 (CH), 130.5 (2 × CH), 127.2 (2 × CH), 127.1 (CH), 125.7 (CH), 125.6 (CH), 74.0 (CH), 69.4 (CH), 65.1 ($CH_2$), 59.4 (CH), 38.9 (qC), 27.3 (3 × $CH_3$), 27.1 (3 × $CH_3$), 21.7 ($CH_3$) 18.5 (qC), −4.6 ($CH_3$), −4.8 ($CH_3$). HRMS (DART): calcd for $C_{32}H_{41}F_3N_1O_6S_1Si_1$ [M − OH]$^+$ 652.2375; found 652.2387.

*Compound* ***12d:*** Yield (1.284 g, 83%); oil; $R_f$ = 0.33 (hexane/ethyl acetate, 85:15); eluent for column chromatography (hexane/ethyl acetate, 99:1); $[\alpha]^{30}_D$ = +9.48 ($c$ 0.10, $CHCl_3$). IR (neat, cm$^{-1}$): 3425, 2924, 2369, 1722, 1591, 1217. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.64 (d, 1H, $J$ = 8.3 Hz), 7.28−7.26 (m, 2H), 6.87−6.84 (m, 1H), 5.92 (br s, 1H), 4.59−4.46 (m, 1H), 4.49 (dd, 1H, $J$ = 5.8, $J$ = 11.2 Hz), 4.38 (dd, 1H, $J$ = 6.0, $J$ = 11.2 Hz), 4.24−4.23 (m, 2H), 3.65 (br s, OH), 2.39 (s, 3H), 1.16 (s, 9H), 0.88 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 191.4 (C═O) 178.2 (qC), 144.7 (qC), 137.8 (qC), 137.6 (CH), 136.8 (qC) 130.4 (2 × CH), 127.2 (2 × CH), 74.2 (CH), 65.8 ($CH_2$), 59.6 (CH), 59.2 (CH), 39.2 (qC), 27.4 (3 × $CH_3$), 26.1 (3 × $CH_3$), 21.9 ($CH_3$), 18.8 (qC), −5.1 ($CH_3$), −5.2 ($CH_3$). HRMS (DART): calcd for $C_{25}H_{38}N_1O_6S_1Si_1$ [M − OH]$^+$ 508.2189; found 508.2181.

*Compound* ***13:*** To a solution of 2,3-dideoxy-hex-2-enopyranosid-4-ulose **1** (600 mg, 2.0 mmol) in $CCl_4$/pyridine at −5 °C (1:1, 14 mL), a solution of iodine (2.147 g, 8.45 mmol) in $CCl_4$/pyridine (1:1, 14 mL) was added dropwise under argon. Subsequently, the reaction mixture was allowed to warm to 10 °C and stirred for 2 h. On completion of reaction (TLC), the reaction mixture was diluted with ether (30 mL) and washed successively with water (20 mL), HCl (1 N, 2 × 20 mL), water (20 mL), and saturated aqueous $Na_2S_2O_3$ solution (12 mL). The organic layer was separated, washed with brine solution, dried over $Na_2SO_4$, and evaporated *in vacuo* at room temperature to obtain the crude product. Column chromatographic purification of the crude product furnished the pure compound **13**: yield (750 mg, 88%); $R_f$ = 0.44 (hexane/ethyl acetate, 92:8); eluent for column chromatography (hexane/ethyl acetate, 96:4); $[\alpha]^{30}_D$ = +9.86 ($c$ 0.05, MeOH). IR (neat, cm$^{-1}$): 2926, 2362, 1728, 1596, 1219. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.59 (d, 1H, $J$ = 3.8 Hz), 5.11 (d, 1H, $J$ = 3.8 Hz), 4.85 (dd, 1H, $J$ = 2.7, $J$ = 5.4 Hz), 4.55 (dd, 1H, $J$ = 2.6, $J$ = 11.9 Hz), 4.46 (dd, 1H, $J$ = 5.5, $J$ = 11.9 Hz), 3.85−3.80 (m, 1H), 3.61−3.56 (m, 1H), 1.74−1.65 (m, 1H), 1.57−1.49 (m, 1H), 1.17 (s, 9H), 0.91(d, 6H, $J$ = 6.5 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 187.7 (C═O), 178.3 (qC), 153.2 (CH), 102.7 (qC), 95.3 (CH), 73.4 (CH), 68.4 ($CH_2$), 63.4 ($CH_2$), 39.1 (qC), 38.6 ($CH_2$) 27.5 (3 × $CH_3$), 25.3 (3 × CH), 22.9 ($CH_3$), 22.8 ($CH_3$). HRMS (DART): calcd for $C_{16}H_{26}I_1O_5$ [M + H]$^+$ 425.0824; found 425.0833.

**The Protocol Adopted for the Synthesis of 15 from 14 Was Similar to the Synthesis of 4 from 3.** *Compound* ***15:*** Yield (157 mg, 81%) oil; $R_f$ = 0.45 (hexane/ethyl acetate, 95:05); eluent for column chromatography (hexane/ethyl acetate, 99.5:0.5); $[\alpha]^{29}_D$ = +1.16 ($c$ 0.10, MeOH). IR (neat, cm$^{-1}$): 2357, 2106, 1642. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.43 (d, 1H, $J$ = 1.9 Hz), 6.49 (d, 1H, $J$ = 1.9 Hz), 4.89 (dd, 1H, $J$ = 6.3, $J$ = 7.6 Hz), 4.45 (dd, 1H, $J$ = 7.7, $J$ = 11.2 Hz), 4.33 (dd, 1H, $J$ = 6.2, $J$ = 11.2 Hz), 1.19 (s, 9H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 178.2 (qC), 150.1 (qC), 145.0 (CH), 118.3 (CH), 66.9 (qC), 63.9 ($CH_2$), 56.4 (CH), 39.2 (qC), 27.4 (3 × $CH_3$). HRMS (DART): calcd for $C_{11}H_{14}I_1O_3$ [M − $N_3$]$^+$ 320.9987; found 320.9983.

*Compound* ***16:*** To a stirred solution of pyridone **6** (400 mg, 1.04 mmol) in $CCl_4$/pyridine (1:1, 8 mL), dropwise addition of a solution of iodine (1.12 g, 4.41 mmol) in $CCl_4$/pyridine (1:1, 8 mL) was done under argon at −5 °C. Subsequently, the reaction mixture was allowed to warm to 0 °C and stirred for 2 h. On completion of the reaction (TLC), the reaction mixture was diluted with ether (20 mL) and washed successively with water (12 mL), HCl (1 N, 2 × 12 mL), water (12 mL), and saturated aqueous $Na_2S_2O_3$ solution (8 mL). The organic layer was separated, washed with brine solution, dried over $Na_2SO_4$, and evaporated *in vacuo* at room temperature to obtain the crude product. Its column chromatography furnished the pure compound **16**: yield (400 mg, 75%); oil; $R_f$ = 0.40 (hexane/ethyl acetate, 80:20); eluent for column chromatography (hexane/ethyl acetate, 90:10); $[\alpha]^{26}_D$ = −4.30 ($c$ 0.19 MeOH). IR (neat, cm$^{-1}$): 2961, 2376, 1716, 1589, 1346. $^1$H NMR ($CDCl_3$, 300 M Hz): $\delta$ 7.64 (d, 2H, $J$ = 8.3 Hz), 7.58 (d, 2H, $J$ = 4.8 Hz), 7.30 (d, 2H, $J$ = 8.0), 4.88−4.84 (m, 1H), 4.50 (dd, 1H, $J$ = 6.0, $J$ = 6.2, $J$ = 11.4 Hz), 4.39 (dd, 1H, $J$ = 5.4, $J$ = 11.4 Hz), 2.41 (s, 2H), 1.18 (s, 9H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 185.6 (C═O), 178.2 (qC), 152.7 (qC), 145.2 (CH), 136.2 (qC), 130.6 (2 × CH), 127.1 (CH), 102 (qC), 75.8 (CH), 65.6 ($CH_2$), 59.1 (CH), 39.1 (qC), 27.4 (3 × $CH_3$), 21.9 ($CH_3$). HRMS (DART): calcd for $C_{18}H_{21}I_1N_1O_5S_1$ [M − OH]$^+$ 490.0185; found 490.0192.

*Compound* ***18:*** A solution of iodine (399 mg, 1.6 mmol) in $CCl_4$/pyridine (1:1, 4 mL) was added dropwise under argon at −5 °C to a solution of **17** (200 mg, 0.4 mmol) in $CCl_4$/pyridine (1:1, 4 mL). Subsequently the reaction mixture was allowed to warm to 0 °C and stirred for 3 h, 30 min. On completion of reaction (TLC), the reaction mixture was diluted with ether (20 mL) and washed successively with water (10 mL), HCl (1 N, 2 × 10 mL), water (10 mL), and saturated sodium thiosulfate solution (10 mL). The worked-up product was dried over $Na_2SO_4$, evaporated at reduced pressure and temperature, and codistilled with toluene. Column chromatography furnished pure compound **18**: yield (200 mg, 81%); solid; mp 48−50 °C; $R_f$ = 0.50 (hexane/ethyl acetate, 80:20); eluent for column chromatography (hexane/ethyl acetate, 96:4); $[\alpha]^{21}_D$ = −22.62 ($c$ 0.30, MeOH). IR (KBr, cm$^{-1}$): 3365, 2931, 2363, 1695, 1354. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.79−7.75 (m, 2H), 7.46−7.38 (m, 6H), 7.43−7.35 (m, 6H), 5.98 (dd, 1H, $J$ = 5.3, $J$ = 11.9 Hz), 5.17 (d, 1H, $J$ = 11.9 Hz), 4.80 (s, 1H), 3.83 (dd, 1H, $J$ = 2.4, $J$ = 11.0 Hz), 3.52 (dd, 1H, $J$ = 1.8, $J$ = 11.0 Hz), 2.45 (s, 3H), 0.94 (s, 9H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 186.9 (C═O), 154.9 (CH), 144.6 (qC), 137.7 (qC), 136.1 (2 × CH), 135.6 (2 × CH), 131.3 (qC), 130.9 (qC), 130.6 (2 × CH), 130.3 (2 × CH), 128.4 (2 × CH), 128.3, (2 × CH), 127.8 (2 × CH), 104.0 (qC), 75.1 (CH), 65.4 ($CH_2$), 61.8 (CH), 27.1 (3 × $CH_3$), 22.0 ($CH_3$), 19.4 (qC). HRMS (DART): calcd for $C_{29}H_{31}I_1N_1O_4S_1Si_1$ [M − OH]$^+$ 644.0787; found 644.0806.

*Compound* ***19:*** To a solution of the pyridone **6** (100 mg, 0.26 mmol) in $Et_3N$ (5 mL) at 0 °C was added $Ac_2O$ (0.074 mL, 0.79 mmol), and the resulting mixture was allowed to stir for 0.5 h at the same temperature. $Et_3N$ and $Ac_2O$ were removed at reduced pressure, and the residue obtained was purified by column chromatography to furnish the pure compound **19**: yield (60 mg, 91%); oil; $R_f$ = 0.40 (hexane/ethyl acetate, 80:20); eluent for column chromatography (hexane/ethyl acetate, 92:8). IR (neat, cm$^{-1}$): 1731, 1645, 1200. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 8.09 (d, 1H, $J$ = 5.0 Hz), 7.76 (d, 1H, $J$ = 5.0 Hz), 7.26 (s, 1H), 5.17 (s, 2H), 2.38 (s, 3H), 1.20 (s, 9H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 178.4 (qC), 169.0 (qC), 148.5 (qC), 147.1 (CH), 131.0 (CH), 124.6 (CH), 63.3 ($CH_2$), 39.2 (qC), 27.5 (3 × $CH_3$), 21.2 ($CH_3$). HRMS (ESI): calcd for $C_{13}H_{18}N_1O_4$ [M + H]$^+$ 252.1236; found 252.1246.

**Similarly Compound 20 Was Synthesized from 17.** *Compound* ***20:*** Yield (1.494 g, 94%); oil; $R_f$ = 0.42 (hexane/ethyl acetate, 80:20); eluent for column chromatography (hexane/ethyl acetate, 92:8). IR (neat, cm$^{-1}$): 1768, 1638, 1214. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 8.47−8.46 (m, 1H), 7.73−7.71 (m, 4H), 7.47−7.37 (m, 7H), 7.31−7.28 (m, 1H), 4.86 (s, 2H), 2.19 (s, 3H), 1.07 (s, 9H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 169.0 (qC), 151.9 (qC), 146.7 (CH), 146.2 (qC), 136.0 (4 × CH), 133.7 (qC), 130.9 (CH), 130.0 (2 × CH), 128.0 (4 × CH), 123.8 (CH), 64.7 ($CH_2$), 27.1 (3 × $CH_3$), 21.2 ($CH_3$) 19.6 (qC). HRMS (DART): calcd for $C_{24}H_{28}N_1O_3Si_1$ [M + H]$^+$ 406.1838; found 406.1804.

**General Procedure for the Synthesis of Compounds 21a−d from 12a−d.** *Compound* ***21a:*** To a solution of the pyridone **12a** (150 mg, 0.239 mmol) in $Et_3N$ (2 mL) at 0 °C was added $Ac_2O$ (0.068 mL, 0.71 mmol), and the resulting mixture was allowed to stir for 0.5 h at the same temperature. $Et_3N$ and $Ac_2O$ were removed at reduced pressure, and the residue obtained was purified by column chromatography to furnish the pure compound **21a**: yield (88 mg,


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84%); oil; $R_f$ = 0.45 (hexane/ethyl acetate, 80:20); eluent for column chromatography (hexane/ethyl acetate, 93:7); $[\alpha]^{31}_D$ = +108.75 (*c* 0.1, $CHCl_3$). IR (neat, $cm^{-1}$): 2928, 2365, 2230, 1774, 1732, 1368. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.50 (d, 1H, *J* = 4.9), 7.61 (d, 2H, *J* = 8.2), 7.50 (d, H, *J* = 4.8), 7.41 (d, 2H, *J* = 8.2), 5.79 (s, 1H), 5.15 (d, 1H, *J* = 12.4), 5.09 (d, 1H, *J* = 12.3), 2.29 (s, 3H), 1.17 (s, 9H), 0.89 (s, 9H), −0.01 (s, 6H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 178.2 (qC), 168.3 (qC), 149.6 (qC), 147.7 (CH),145.8 (qC), 145.8 (qC), 143.0 (qC), 132.6 (2 × CH), 127.3 (2 × CH), 122.5 (CH), 118.8 (qC), 112.0 (CN), 70.5 (CH), 65.3 ($CH_2$), 39.1 (qC), 27.4 (3 × $CH_3$), 26.0 (3 × $CH_3$), 21.0 ($CH_3$), 18.5 (qC), −4.64 ($CH_3$), −4.7 ($CH_3$). HRMS (DART): calcd for $C_{27}H_{37}N_2O_5Si_1$ $[M + H]^+$ 497.2471; found 497.2473.

*Compound* ***21b:*** Yield (17 mg, 82%); oil; $R_f$ = 0.44 (hexane/ethyl acetate, 86:14); eluent for column chromatography (hexane/ethyl acetate, 94:6); $[\alpha]^{27}_D$ = +18.64 (*c* 0.1, $CHCl_3$). IR (neat, $cm^{-1}$): 2921, 1727, 1627,1218. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.50 (d, 1H, *J* = 4.9 Hz), 7.55 (d, 3H, *J* = 6.8 Hz), 7.40 (d, 2H, *J* = 8.04 Hz), 5.81 (s, 1H), 5.12 (d, 2H, *J* = 3.3 Hz), 2.28 (s, 3H), 1.18 (s, 9H), 0.85 (s, 9H), −0.002 (s, 3H), −0.01 (s, 3H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 178.3 (qC), 168.4 (qC), 149.5 (qC), 147.7 (CH), 146.5 (qC), 146.3 (qC), 143.1 (qC), 130.6 (2 × CH), 125.8 (CH), 125.7 (CH), 122.5 (CH), 70.7 (CH), 63.4 ($CH_2$), 39.1 (qC), 27.4 (3 × $CH_3$), 26.0 (3 × $CH_3$), 21.0 ($CH_3$), 18.5 (qC), −4.6 ($CH_3$), −4.7 ($CH_3$). HRMS (DART): calcd for $C_{27}H_{37}F_3N_1O_5Si_1$ $[M + 1]^+$ 540.2393; found 540.2394.

*Compound* ***21c:*** Yield (23 mg, 70% over two steps); oil; $R_f$ = 0.56 (hexane/ethyl acetate, 90:10); eluent for column chromatography (hexane/ethyl acetate, 97:3); $[\alpha]^{29}_D$ = +15.85 (*c* 0.20, MeOH). IR (neat, $cm^{-1}$): 2929, 2363, 1598, 1215. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.45 (d, 1H, *J* = 5.0 Hz), 7.46 (d, 1H, *J* = 5.0 Hz), 5.16 (s, 1H), 4.68 (dd, 1H, *J* = 4.7, *J* = 6.8 Hz), 2.32 (s, 3H), 1.62 (s, 2H), 1.24 (s, 14H), 1.19 (s, 9H), 0.87 (s, 12H), −0.02 (s, 3H), −0.15 (s, 3H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 178.4 (qC), 168.6 (qC), 148.7 (qC), 148.3 (qC), 147.3 (CH), 142.9 (qC), 122.7 (CH), 68.7 (CH), 63.6 ($CH_2$), 39.2 (qC), 39.0 ($CH_2$), 32.2 ($CH_2$), 29.9 ($CH_2$), 29.8−29.6 (3 × $CH_2$), 27.5 (3 × $CH_3$), 26.1 (3 × $CH_3$), 25.1 ($CH_2$), 23.0 ($CH_2$), 20.9 ($CH_3$), 18.4 (qC), 14.4 ($CH_3$), −4.4 ($CH_3$), −4.8 ($CH_3$). HRMS (DART): calcd for $C_{29}H_{52}N_1O_5Si_1$ $[M + H]^+$ 522.3614; found 522.3608.

*Compound* ***21d:*** Yield (45 mg, 85%); oil; $R_f$ = 0.55 (hexane/ethyl acetate, 85:15); eluent for column chromatography (hexane/ethyl acetate, 95:5). IR (neat, $cm^{-1}$): 2924, 2372, 1730, 1462, 1214, 761. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.48 (d, 1H, *J* = 4.8 Hz), 7.51 (d, 1H, *J* = 4.8 Hz), 5.17 (s, 2H), 4.61 (s, 2H), 2.32 (s, 3H), 1.19 (s, 9H), 0.94 (s, 9H), 0.09 (s, 6H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 178.7 (qC), 168.8 (qC), 148.2 (qC), 147.6 (CH) 144.3 (qC), 122.6 (CH), 63.4 ($CH_2$), 59.6 ($CH_2$), 39.2 (qC), 27.5 (3 × $CH_3$), 26.2 (3 × $CH_3$), 20.8 ($CH_3$) 18.7 (qC), −5.1 (2 × $CH_3$). HRMS (DART): calcd for $C_{20}H_{34}N_1O_5Si_1$ $[M + H]^+$ 396.2206; found 396.2196.

*Compound* ***22:*** To a solution of **16** (120 mg, 0.24 mmol) in $Et_3N$ (3 mL) at 0 °C was added $Ac_2O$ (0.067 mL, 0.71 mmol), and the resulting mixture was allowed to stir for 0.5 h at the same temperature. $Et_3N$ and $Ac_2O$ were removed at reduced pressure, and the residue obtained was purified by column chromatography to furnish the pure compound **22**: yield (79 mg, 89%); oil; $R_f$ = 0.35 (hexane/ethyl acetate, 85:15); eluent for column chromatography (hexane/ethyl acetate, 93:7). IR (neat, $cm^{-1}$): 2927, 2362, 1720, 1217. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.09 (d, 1H, *J* = 5.0 Hz), 7.75 (d, 1H, *J* = 5.0 Hz), 5.17 (s, 2H), 2.37 (s, 3H), 1.2 (s, 9H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 178.3 (qC), 167.9 (qC), 149.8 (qC), 147.6 (CH), 134.9 (CH), 104.0 (qC), 63.6 ($CH_2$), 39.2 (qC), 27.5 (3 × $CH_3$), 21.4 ($CH_3$). HRMS (DART): calcd for $C_{13}H_{17}I_1N_1O_4$ $[M + H]^+$ 378.0202; found 378.0196.

**Similarly Compound 23 Was Synthesized from 18.** *Compound* ***23:*** Yield (150 mg, 93%); oil; $R_f$ = 0.48 (hexane/ethyl acetate, 85:15); eluent for column chromatography (hexane/ethyl acetate, 97:3). IR (neat, $cm^{-1}$): 2927, 1774, 1557, 1215. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.06 (d, 1H, *J* = 5.0 Hz), 7.72−7.70 (m, 5H), 7.46−7.37 (m, 6H), 4.80 (s, 2H), 2.24 (s, 3H), 1.08 (s, 9H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 167.8 (qC), 153.1 (qC), 147.8 (qC), 147.2 (CH), 136.0 (4 × CH), 134.2 (CH), 133.5 (qC), 130.1 (2 × CH), 128.0 (4 × CH), 104.0 (qC), 65.2 ($CH_2$), 27.1 (3 × $CH_3$), 21.3 ($CH_3$), 19.6 (qC). HRMS (ESI): calcd for $C_{24}H_{27}I_1N_1O_3Si_1$ $[M + H]^+$ 532.0805; found 532.0769.

*Compound* ***24:*** $Et_3N$ (0.15 mL, 1.09 mmol) and $Tf_2O$ (0.14 mL, 0.82 mmol) were added dropwise under $N_2$ atmosphere to the solution of 4-iodopyridone **18** (180 mg, 0.27 mmol) in DCM (5 mL) cooled to −78 °C with continuous stirring, and the resulting mixture was allowed to reach room temperature. After 1.5 h, the reaction mixture was quenched with saturated aqueous $NH_4Cl$ and extracted with DCM (3 × 5 mL). The combined organic layers were washed with brine solution, dried over $Na_2SO_4$, and evaporated *in vacuo* to obtain the crude reaction mixture. Column chromatography of the crude mixture furnished the pure compound **24**: yield (142 mg, 84%); oil; $R_f$ = 0.50 (hexane/ethyl acetate, 90:10); eluent for column chromatography (hexane/ethyl acetate, 99:1). IR (neat, $cm^{-1}$): 2929, 1622, 1418, 1218. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.14 (d, 1H, *J* = 4.9 Hz), 7.73 (d, 1H, *J* = 4.9 Hz), 7.64 (d, 4H, *J* = 7.5 Hz), 7.42−7.33 (m, 6H), 4.98 (s, 2H), 1.07 (s, 9H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 154.4 (qC), 149.1 (CH), 145.4 (qC), 135.9 (4 × CH), 135.4 (CH), 133.2 (CH), 130.1 (2 × CH), 128.0 (4 × CH), 101.8 (qC), 64.2 ($CH_2$), 27.1 (3 × $CH_3$), 19.6 (qC). HRMS (DART): calcd for $C_{23}H_{24}F_3I_1N_1O_4S_1Si_1$ $[M + 1]^+$ 622.0192; found 622.0194.

*Compound* ***25:*** TBAF (0.2 mL, 0.2 mmol) was added at 0 °C to a solution of 4-pyridylalcohol **21a** (88 mg, 0.23 mmol) in THF (5 mL) with a syringe, and the resulting mixture was stirred for 1 h at room temperature. After completion of the reaction (TLC), the reaction mixture was quenched with saturated aqueous $NH_4Cl$ solution (4 mL), and it was extracted with EtOAc (2 × 5 mL). The combined extracts were dried over ($Na_2SO_4$), concentrated under reduced pressure, and purified by flash column chromatography to furnish the pure compound **25**: yield (50 mg, 75%); oil; $R_f$ = 0.42 (hexane/ethyl acetate, 60:40); eluent for column chromatography (hexane/ethyl acetate, 75:25); $[\alpha]^{30}_D$ = +26.12 (*c* 0.45, MeOH). IR (neat, $cm^{-1}$): 2926, 2360, 1742, 1427. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.88 (brs, OH), 8.20 (d, 2H, *J* = 4.8 Hz), 7.60 (d, 2H, *J* = 8.2 Hz), 7.52 (d, 1H, *J* = 8.2 Hz), 7.35 (d, 1H, *J* = 4.8 Hz), 7.16 (s, 1H), 5.25 (d, 1H, *J* = 12.1 Hz), 5.13 (d, 1H, *J* = 12.0 Hz), 2.17 (s, 3H), 1.17 (s, 9H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 182.6 (qC), 169.6 (qC), 149.6 (qC), 144.0 (qC), 142.5 (qC), 142.2 (CH), 137.1 (qC), 132.6 (2 × CH), 128.3 (2 × CH), 122.1 (CH), 118.8 (qC), 112.0 (CN), 70.8 (CH), 65.4 ($CH_2$), 39.4 (qC), 27.3 (3 × $CH_3$), 21.0 ($CH_3$). HRMS (ESI): calcd for $C_{21}H_{23}N_2O_5$ $[M + H]^+$ 383.1607; found 383.1576.

*Compound* ***26:*** Yield (160 mg, 70%); semisolid; $R_f$ = 0.41 (hexane/ethyl acetate, 60:40); eluent for column chromatography (hexane/ethyl acetate, 75:25). IR (KBr, $cm^{-1}$): 3375, 2363, 1656, 1588, 1111. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.79 (d, 1H, *J* = 4.9 Hz), 7.68 (d, 1H, *J* = 4.9 Hz), 5.26 (s, 1H), 2.13 (s, 3H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 174.3 (qC), 152.6 (qC), 142.3 (CH), 141.4 (qC), 135.6 (CH), 98.6 (qC), 65.3 ($CH_2$), 21.1 ($CH_3$). HRMS (ESI): calcd for $C_8H_9INO_3$ $[M + H]^+$ 293.9627; found 293.9643.

*Compound* ***27:*** To a mixture of compound **23** (350 mg, 0.659 mmol), phenyl acetylene (0.036 mL, 0.329 mmol), $Pd[Cl_2(PPh_3)_2]$, (46 mg, 0.065 mmol), and CuI (12 mg, 0.065 mmol) in 10 mL of THF under $N_2$ atmosphere was added $Et_3N$ (0.27 mL, 1.97 mmol), and resulting solution was stirred for 3 h at room temperature. The reaction was diluted with 20 mL of $CHCl_3$, washed with 1 N HCl (2 × 10 mL), and extracted with $CHCl_3$ (2 × 5 mL). The combined organic extracts were washed with brine, dried over $Na_2SO_4$, and evaporated *in vacuo* to obtain the crude compound, which was subjected to flash column chromatography to furnish the pure compound **27**: yield (250 mg, 78%); oil; $R_f$ = 0.45 (hexane/ethyl acetate, 84:16); eluent for column chromatography (hexane/ethyl acetate, 94:6). IR (neat, $cm^{-1}$): 2927, 2366 1772, 1645, 1216. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.43 (d, 1H, *J* = 4.9 Hz), 7.73−7.71 (m, 4H), 7.53−7.50 (m, 2H), 7.44−7.37 (m, 10H), 4.82 (s, 2H), 2.25 (s, 3H), 1.06 (s, 9H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 168.2 (qC), 152.8 (qC), 146.7 (qC), 146.6 (CH), 136.0 (4 × CH), 133.6 (qC), 132.1 (2 × CH), 130.0 (2 × CH), 129.8 (CH), 128.9 (2 × CH), 128.0 (4 × CH), 126.7 (qC), 126.1 (CH), 122.2 (qC), 98.6 (qC), 82.7 (qC), 64.8 ($CH_2$), 27.1 (3 ×


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$CH_3$), 20.9 ($CH_3$), 19.6 (qC). HRMS (ESI): calcd for $C_{32}H_{32}N_1O_3Si_1$ $[M + H]^+$ 506.2152; found 506.2128.

*Compound 28:* A solution of compound **27** (70 mg, 0.138 mmol) in MeOH−$Et_3N$−$H_2O$ (2 mL, 4:1:1), was allowed to stir at room temperature for 12 h. The reaction mixture was diluted with EtOAc (5 mL) and then extracted with EtOAc (2 × 2 mL). The combined extracts were washed with brine solution, dried over $Na_2SO_4$, and evaporated under reduced pressure to obtain the crude residue. Its flash chromatography furnished the pure compound **28**: yield (40 mg, 62%); oil; $R_f$ = 0.35 (hexane/ethyl acetate, 80:20); eluent for column chromatography (hexane/ethyl acetate, 93:7). IR (neat, $cm^{-1}$): 2361, 1648, 1544, 1216. $^1H$ NMR ($CDCl_3$, 300 M Hz): $\delta$ 8.35 (d, 1H, $J$ = 5.2 Hz), 7.784−7.78 (m, 4H), 7.45−7.43 (m, 4H), 7.40−7.35 (m, 6H), 7.01 (s, 1H), 5.20 (s, 2H), 1.09 (s, 9H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 159.0 (qC), 150.6 (qC), 144.0 (qC), 142.3 (CH), 136.5 (qC), 136.1 (4 × CH), 133.8 (qC), 130.1 (qC), 130.0 (2 × CH), 129.8 (CH), 129.2 (2 × CH), 128.0 (4 × CH), 126.1 (2 × CH), 115.6 (CH), 100.7 (CH), 64.9 ($CH_2$), 27.2 ($CH_3$), 19.7 (qC). HRMS (DART): calcd for $C_{30}H_{30}N_1O_2Si_1$ $[M + H]^+$ 464.2045; found 464.2063.

*Compound 29:* A mixture of **23** (400 mg, 0.75 mmol), (trimethylsilyl)acetylene (0.13 mL, 0.97 mmol), bis-(triphenylphosphine) palladium dichloride (52 mg, 0.08 mmol), and CuI (14 mg, 0.08 mmol) in 10 mL of THF under $N_2$ was treated with $Et_3N$ (0.3 mL, 2.25 mmol) and was stirred for 3 h at room temperature. The reaction was diluted with 20 mL of $CHCl_3$ and was washed with 2 × 10 mL of 1 N HCl. The combined aqueous layers were extracted with $CHCl_3$ (2 × 5 mL) and dried over $Na_2SO_4$; flash column chromatography furnished desired compound **29**: yield (310 mg, 82%); oil; $R_f$ = 0.51 (hexane/ethyl acetate, 88:12); eluent for column chromatography (hexane/ethyl acetate, 96:4). IR (neat, $cm^{-1}$): 2321, 1775, 1426, 1217. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.38 (d, 1H, $J$ = 4.9 Hz), 7.70−7.68 (m, 4H), 7.42−7.35 (m, 6H), 7.30 (d, 1H, $J$ = 4.9 Hz), 4.77 (s, 2H), 2.20 (s, 3H), 1.03 (s, 9H), 0.25 (s, 9H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 168.0 (qC), 152.7 (qC), 146.6 (CH), 136.0 (4 × CH), 133.6 (qC), 130.0 (2 × CH), 128.0 (4 × CH), 126.4 (qC), 126.3 (CH), 105.2 (qC), 97.6 (qC), 64.7 ($CH_2$), 27.1 (3 × $CH_3$), 20.9 ($CH_3$), 19.6 (qC), 0.0 (3 × $CH_3$). HRMS (ESI): calcd for $C_{29}H_{36}N_1O_3Si_2$ $[M + H]^+$ 502.2234; found 502.2202.

*Compound 30:* TBAF (0.33 mL, 0.33 mmol) was added at −30 °C to a solution of compound **29** (150 mg, 0.30 mmol) in THF (5 mL), and the reaction mixture was allowed to stir for 20 min. On completion of the reaction (TLC), the reaction mixture was quenched with saturated aqueous $NH_4Cl$ and extracted with DCM (3 × 5 mL). The organic layers were washed with brine solution, dried over $Na_2SO_4$, and concentrated under reduced pressure to afford the crude residue, which was purified by flash chromatography to furnish the compound **30**: yield (90 mg, 70%); solid; mp 70 °C; $R_f$ = 0.43 (hexane/ethyl acetate, 80:20); eluent for column chromatography (hexane/ethyl acetate, 96:4). IR (KBr, $cm^{-1}$): 2925, 2364, 1632, 1218. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.41 (d, 1H, $J$ = 4.9 Hz), 7.70−7.68 (m, 4H), 7.42−7.34 (m, 6H), 4.79 (s, 2H), 3.42 (s, 2H) 2.21 (s, 9H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 168.2 (qC), 153.0 (qC), 147.1 (qC), 146.6 (CH), 136.0 (4 × CH), 133.6 (qC), 130.0 (2 × CH), 128.0 (4 × CH), 126.8 (CH), 125.6 (qC), 86.3 (qC), 77.0 (qC), 64.7 ($CH_2$), 27.1 (3 × $CH_3$), 20.9 (CH), 19.6 (qC). HRMS (DART): calcd for $C_{26}H_{28}N_1O_3Si_1$ $[M + H]^+$ 430.1838; found 430.1836.

*Compound 31:* Iodine (456 mg, 1.80 mmol) and $NaHCO_3$ (150 mg, 1.80 mmol) were added at room temperature to a stirred solution of compound **29** (200 mg, 0.40 mmol) in MeOH (10 mL), and the resulting mixture was allowed to stir at the same temperature for 24 h. The reaction mixture was diluted with EtOAc (10 mL), washed successively with saturated aqueous $Na_2S_2O_3$ solution and brine, dried over $Na_2SO_4$, and concentrated under reduced pressure. The crude product was purified by flash chromatography to give compound **31**: yield (143 mg, 64%); solid; mp 110−112 °C; $R_f$ = 0.46 (hexane/ethyl acetate, 83:17); eluent for column chromatography (hexane/ethyl acetate, 95:5). IR (KBr, $cm^{-1}$): 2932, 2370, 1715, 1213. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.40 (d, 1H, $J$ = 4.9 Hz), 7.71−7.69 (m, 1H), 7.43−7.35 (m, 6H), 7.28 (d, 1H, $J$ = 4.9 Hz), 4.78 (s, 2H), 2.22 (s, 9H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 168.2 (qC), 152.9 (qC), 147.7 (qC), 146.5 (CH), 136.0 (4 × CH), 133.6 (qC), 130.0 (2 × CH), 128.0 (4 × CH), 126.7 (CH), 126.5 (qC), 87.7 (qC), 64.7 ($CH_2$), 27.1 (3 × $CH_3$), 20.9 ($CH_3$), 19.6 (qC), 18.5 (qC). HRMS (ESI): calcd for $C_{26}H_{27}I_1N_1O_3Si_1$ $[M + H]^+$ 556.0805; found 556.0774.

*Compound 32:* A mixture of **31** (75 mg, 0.135 mmol), 4-acetylenicpyridine **30** (75 mg, 0.175 mmol), bis(triphenylphosphine) palladium dichloride (9 mg, 0.013 mmol), and CuI (2.4 mg, 0.013 mmol) in 5 mL of THF under $N_2$ was treated with $Et_3N$ (0.024 mL, 0.175 mmol) and was stirred for 1 h at room temperature. The reaction was diluted with 5 mL of $CHCl_3$ and was washed with 2 × 2 mL of 1 N HCl. The combined aqueous layers were extracted with $CHCl_3$ (2 × 2 mL) and dried over $Na_2SO_4$; flash column chromatography furnished desired compound **32**: yield (96 mg, 83%); oil; $R_f$ = 0.40 (hexane/ethyl acetate, 80:20); eluent for column chromatography (hexane/ethyl acetate, 90:10). IR (Neat, $cm^{-1}$): 2925, 2341, 1777, 1592. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.44 (d, 2H, $J$ = 4.9 Hz), 7.70−7.67 (m, 9H), 7.43−7.36 (m, 15H), 4.80 (s, 4H), 2.24 (s, 6H), 1.05 (s, 18H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 168.2 (2 × qC), 153.3 (2 × qC), 147.4 (2 × qC), 146.7 (2 × CH), 136.0 (8 × CH), 133.5 (2 × qC), 130.1 (4 × CH), 128.0 (8 × CH), 126.7 (2 × CH), 124.8 (2 × qC), 80.9 (2 × qC), 77.1 (2 × qC), 64.7 (2 × $CH_2$), 27.1 (6 × $CH_3$), 20.9 (2 × $CH_3$), 19.6 (2 × qC). HRMS (ESI): calcd for $C_{52}H_{53}N_2O_6Si_2$ $[M + H]^+$ 857.3442; found 857.3411.

*Compound 33:* A solution of compound **32** (50 mg, 0.058 mmol) in MeOH−$Et_3N$−$H_2O$ (1.6 mL, 4:1:1) was allowed to stir at room temperature for 18 h. The reaction mixture was diluted with EtOAc (5 mL) and then extracted with EtOAc (2 × 2 mL). The combined extracts were washed with brine solution, dried over $Na_2SO_4$, and evaporated under reduced pressure to obtain the crude residue. Its flash chromatography furnished the pure **33**: yield (30 mg, 66%); oil; $R_f$ = 0.40 (hexane/ethyl acetate, 80:20); eluent for column chromatography (hexane/ethyl acetate, 90:10). IR (neat, $cm^{-1}$): 2931, 2368, 1626, 1369, 1218. $^1H$ NMR ($CDCl_3$, 300 M Hz): $\delta$ 8.39 (d, 2H, $J$ = 5.2 Hz), 7.80−7.77 (m, 8H), 7.47 (d, 2H, $J$ = 5.2 Hz), 7.41−7.34 (m, 12H), 6.96 (s, 2H), 5.23 (s, 4H), 1.12 (s, 18H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 150.9 (2 × qC), 149.5 (2 × qC), 144.8 (2 × qC), 142.6 (2 × CH), 136.1 (8 × CH), 135.6 (2 × qC), 133.8 (2 × qC), 130.1 (4 × CH), 128.1 (8 × CH), 116.2 (2 × CH), 104.8 (2 × CH), 77.6 (2 × qC), 65.2 (2 × $CH_2$), 27.2 (6 × $CH_3$), 19.8 (2 × qC). HRMS (ESI): calcd for $C_{48}H_{49}N_2O_4Si_2$ $[M + H]^+$ 773.3231; found 773.3214.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

$^1H$ and $^{13}C$ NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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