# A Lewis Acid Mediated Stereoselective Removal of an Anomeric Urea Substituent

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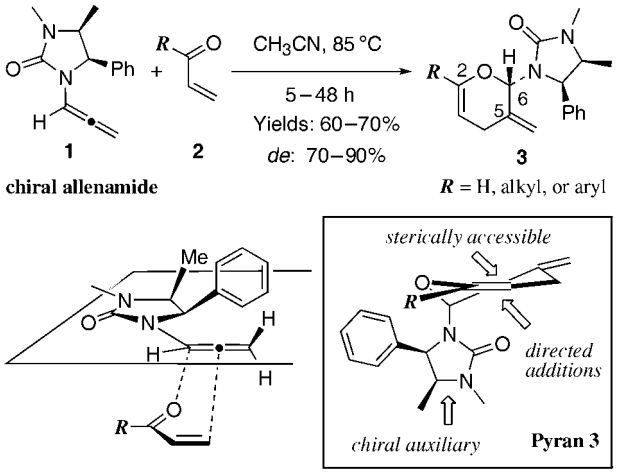
**Abstract:** The first Lewis acid mediated stereoselective removal of an anomeric chiral urea group or an electron deficient nitrogen substituent is described here. The ability to remove this urea group which had served as a chiral auxiliary, along with stereoselective hydroboration-oxidation of the endocyclic olefin renders the pyranyl cycloadduct from hetero [4+2] cycloadditions of chiral allenamides a useful chiral template. This represents a new approach to synthesis of complex pyranyl heterocycles or *C*-glycoside derivatives.

**Key words:** Lewis acid, [4+2] cycloaddition, *C*-glycoside derivatives

Allenamides, an electron-deficient variant of allenamines in which the nitrogen atom is substituted with an electron withdrawing acyl group, have emerged as useful synthons in organic synthesis.[2–6] The vastly improved stability and comparable reactivity of allenamides relative to allenamines have rendered them attractive in developing new stereoselective methodologies.[3,4] A while back we reported [4+2] cycloaddition reactions of the chiral allenamide **1** with hetero dienes such as vinyl ketones **2**, leading to pyranyl heterocycles **3** in a highly stereoselective manner (Scheme 1).[4a] This represents the first account of an inverse electron-demand hetero [4+2] cycloaddition involving a chiral enamide.[7,8] Mechanistically, it remains unclear as to the source of such high diastereoselectivities since the cycloaddition likely proceeds stepwise, although a model has been proposed based on the structural planarity of allenamides observed from modeling and crystal structure.[4a,5b,c,6b] Synthetically, this highly stereoselective cycloaddition led us to explore a new approach for constructing *C*-glycosides.[9,10]

The X-ray analysis and AM-1 minimization [Spartan™] of the pyran **3** reveal that the chiral imidazolidinone group at C6 is oriented pseudo-axially, situating beneath the two easily distinguishable olefins with one being electron-rich and endocyclic at C2/C3, and the other being exocyclic at C5 (Scheme 1). Such shielding of the bottom face supports the high stereoselectivity observed when these two olefins were hydrogenated sequentially.[4a] Based on this analysis, we envisioned that stereoselective transformation of these two well-differentiated olefins can occur either on the sterically less congested top face, or may be




**Scheme 1**

directed by the urea carbonyl group. Therefore, the pyran **3**, cycloadducts from hetero [4+2] cycloadditions of chiral allenamides, represents a unique chiral template with the imidazolidinone group at C6 being a chiral auxiliary for constructing highly functionalized *C*-glycosides or pyranyl heterocycles that can lead to relevant natural products. We report here our success in achieving a key Lewis acid mediated stereoselective removal of the chiral imidazolidinone at C6.

To render the pyran **3** a unique chiral template, two important concepts must be realized: 1) Stereoselective functionalization of the two olefins in **3** leading to **4**, and 2) a key removal of the chiral imidazolidinone at C6 in **4** that served as an auxiliary (Scheme 2). However, there is very few literature precedents describing useful removal of an electron deficient nitrogen substituent or an anomeric urea group.[11] Therefore, this second concept is a non-trivial task and became our primary focus. Our proposed approach for such a removal is shown in Scheme 2. A suitable Lewis acid could facilitate the departure of the C6 urea group in **4** via coordination to the carbonyl group to give an oxocarbenium ion **5**. An addition of a suitable nucleophile to **5** could lead to the pyran **6** stereoselectively.

To achieve this proposed sequence, a series of Lewis acids were screened carefully at various equivalents and different temperatures. These results are summarized in Table 1. Reactions were carried out using the pyran **8**[12] as a simplified model readily attainable from hydrogenation of **7**, and allyltrimethylsilane[9,13] was used as the nucleo-

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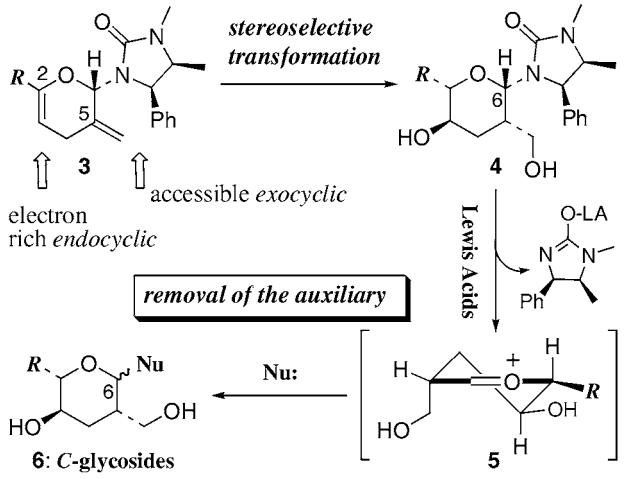
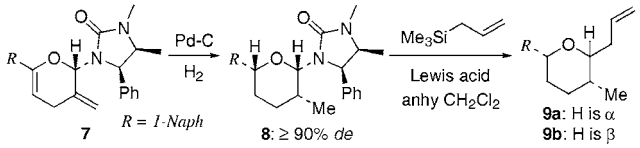



**Scheme 2**

phile. The most effective Lewis acid turned out to be $SnBr_4$,[14,15] and in the presence of 4.0 equivalents of allyltrimethylsilane, the allylation product **9**[16] was isolated in 49–77% yield with 60–66% de (entries 14 and 15). The amount of $SnBr_4$ appeared to be quite critical with the optimum being 1.0–1.5 equivalents (comparing entries 9–16). Although $BF_3{\cdot}OEt_2$ provided higher de (entries1–3), yields were inferior owing to hydrolysis or ring-opening of the pyran **8**.

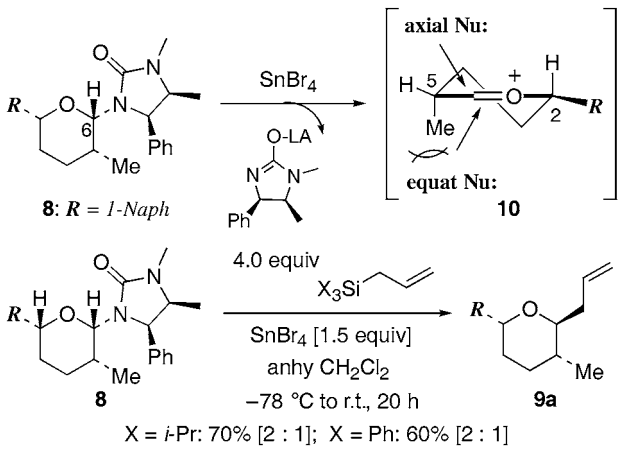
Isolation of the chiral imidazolidinone (the Close auxiliary)[17] suggests that the loss of the imidazolidinone had been facilitated via the usage of $SnBr_4$ where the oxocarbenium ion **10** was likely the intermediate (Scheme 3). The stereochemical assignment of the major isomer **9a** based on NOE implies that the allyltrimethylsilane had added in an anomerically favored axial trajectory to the oxocarbenium intermediate **10** where the bulky aromatic group at C2 predominates and assumes an equatorial position.[9,12–15,18]

**Table 1** Reaction Results with a Series of Lewis Acids at Various Equivalents and Different Temperatures



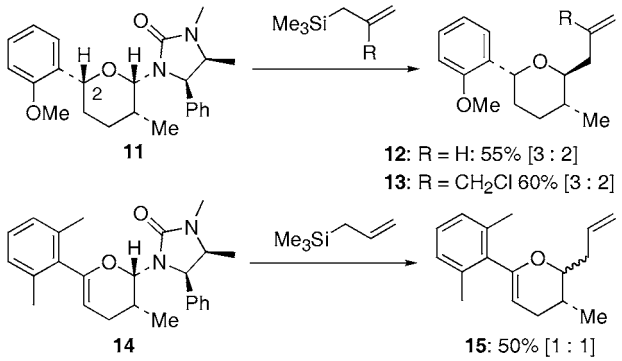

| Entry | Lewis acid (equiv) | Silane (equiv) | Temp | Time (h) | Yield[a] | Ratio (**9a**:**9b**)[b] |
|---|---|---|---|---|---|---|
| 1 | $BF_3{\cdot}OEt_2$ (2.5) | 4.0 | –78 °C to r.t. | 24 | 40% | 83:17 |
| 2 | $BF_3{\cdot}OEt_2$ (2.0) | 4.0 | –78 °C to r.t. | 5 | 33 | 84:16 |
| 3 | $BF_3{\cdot}OEt_2$ (1.5) | 4.0 | –78 °C to r.t. | 2 | 10 | 90:10 |
| 4 | $TiCl_4$ (1.2) | 4.0 | –78 °C to r.t. | 1 | decomp. | ND[c] |
| 5 | TMSOTf (2.4) | 4.0 | –78 °C to r.t. | 1 | decomp. | ND |
| 6 | $ZnCl_2$ (1.2) | 4.0 | –78 °C to r.t. | 18 | decomp. | ND |
| 7 | $InCl_3$ (1.5) | 4.0 | –78 °C to r.t. | 48 | 60 | 67:33 |
| 8 | $InCl_3$ (1.5) | 4.0 | r.t. | 72 | 10 | 51:49 |
| 9 | $SnBr_4$ (5.0) | 5.0 | 0 °C to r.t. | 5 | 30 | 75:25 |
| 10 | $SnBr_4$ (3.0) | 4.0 | –78 °C to r.t. | 18 | 65 | 53:47 |
| 11 | $SnBr_4$ (2.5) | 4.0 | –78 °C to r.t. | 18 | 67 | 67:33 |
| 12 | $SnBr_4$ (2.0) | 4.0 | –78 °C to r.t. | 18 | 67 | 75:25 |
| 13 | $SnBr_4$ (1.5) | 4.0 | –78 °C | 3 | 20 | ND |
| 14 | $SnBr_4$ (1.5) | 4.0 | –78 °C to r.t. | 12 | 77 | 80:20 |
| 15 | $SnBr_4$ (1.0) | 4.0 | –40 °C | 48 | 49 | 83:17 |
| 16 | $SnBr_4$ (0.5) | 4.0 | –78 °C | 60 | 60 | 67:33 |

[a] Isolated yields.
[b] Ratios determined by $^1H$ NMR.
[c] ND: Not determined.




**Scheme 3**

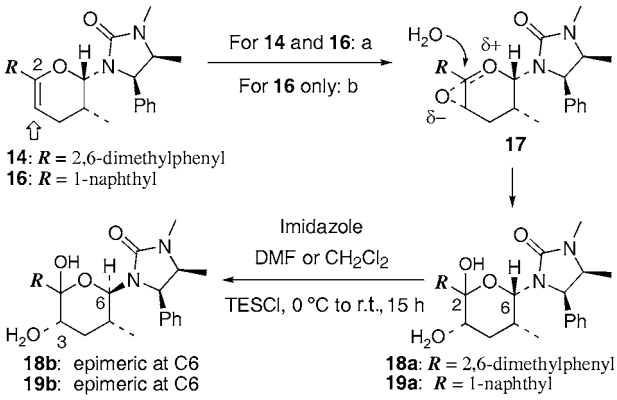
Based on this proposed conformation for **10**, the C5 pseudo axial methyl group could further disfavor the nucleophile to approach **10** from an equatorial trajectory. However, the addition of more bulky allyltri-*iso*-propyl- or allyltriphenylsilane did not improve the overall diastereoselectivity. Although the diastereoselectivity observed here is only modest for a simplified system, this is the first example of removal of an anomeric urea group.




**Scheme 4**

Having established the feasibility of $SnBr_4$-mediated removal of the chiral imidazolidinone at C6, its scope can be shown using pyrans with other aromatic substituents at C2 (see **11** and **14** in Scheme 4, and more examples are in the supplementary material). Other allyltrialkylsilanes could also be used to provide products such as **13**. Comparing with the diastereoselectivity observed for **9**, these examples provided lower diastereoselectivities suggesting that the substituent at C2 is likely more significant to the stereochemical outcome than the size of allyltrialkylsilanes. Particularly, by flattening out at C2/C3 as shown in **14**, any sense of diastereoselectivity was completely lost during the allylation presumably due to a more planar oxocarbenium intermediate.

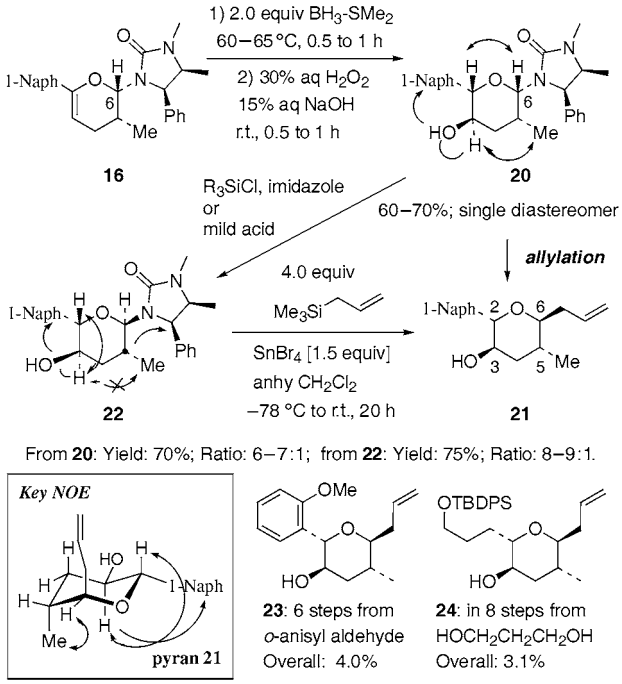
With this methodology in place, we began exploring stereoselective transformation involving the two olefins in the pyran **7**. The initial investigation was focusing on epoxidation of the endocyclic olefin at C2/C3 in **14** or **16** followed by addition of a hydride to the epoxy intermediate **17** (Scheme 5). The potential obstacle was that unlike 1,2-anhydro sugars (or glycosidic epoxides),[9] there are very few examples of stable epoxy intermediates such as **17**,[19] and isolated ones are extremely acid sensitive.[20] Most epoxides of this type would undergo rapid ring-opening to give an oxocarbenium intermediate that would lead to eventual scrambling of stereochemistry at the anomeric center.[9,20]




**Scheme 5** a) 2.0 Equiv MCPBA, $CH_2Cl_2$, phosphate buffer, –10 °C to r.t., 18 h. Ratio of **18a**:**18b**: 84:16 (60%); ratio of **19a**:**19b**: 80:20 (75%). b) 2.0 Equiv magnesium monoperoxyphthalate (MMPP), THF, $H_2O$, –10 °C to r.t., 17 h. Only **19b** (70%) as a single isomer.

As shown in Scheme 5, epoxidations of **14** and **16** using *m*-CPBA led to diols **18a** and **18b** (ratio 84:16), and **19a** and **19b** ([ratio 80:20), in 60% and 75% yield, respectively. This outcome implies that addition of hydride to C2 may not compete well with $H_2O$. NOE experiments unambiguously confirmed that MCPBA had actually added selectively from the more congested bottom face leading to a C3-α-OH in **18** and **19**. Although the stereochemistry at C2 could not be unambiguously assigned, stereochemistry of **18b** (or **19b**)] was also confirmed to be epimeric at C6 relative to **18a** (or **19a**)]. The diol **18a** (or **19a**) appeared to be prone to epimerization at C6 leading to **18b** (or **19b**). When the diol **18a** or **19a** was subjected to acylating or silylating conditions, **18b** or **19b** was isolated quantitatively, and MMPP epoxidation of **16** also led to only the epimer **19b**. While these results warrant further studies because it implies a potential urea-directed epoxidation, we shifted our attention because a successful hydroboration could be carried out using $BH_3{\cdot}SMe_2$ to achieve the equivalent task.

As shown in Scheme 6, a sequence of hydroboration–oxidation using **16** consisting of 2.0 equivalents $BH_3{\cdot}SMe_2$ and 30% aqueous $H_2O_2$ with 15% aqueous NaOH led to the alcohol **20** as a single diastereomer. The relative stereochemistry was assigned using NOE experiments, and no epimerization occurred at C6 during the hydroboration-oxidation. A subsequent allylation, without protecting the hydroxyl group, under the standard conditions of using 1.5 equivalents $SnBr_4$ led to the pyran **21** in 70% yield with an improved 72–76% de.




**Scheme 6**

The relative stereochemistry was assigned using NOE[21] (Scheme 6) with the allyl group again adding in an axial trajectory. The improved de suggests that additional substitutions on the pyranyl ring could lead to a conformationally more rigid oxocarbenium intermediate[14,18] leading to higher diastereoselectivity, although we are not certain if the C3 hydroxyl group played any role in directing the incoming silane.

Another interesting observation was that the pyran **20** did epimerize completely at C6 leading to **22** cleanly (see NOE arrows[21]) when attempts were made to silylate the C3 hydroxyl group. Allylation of **22** led to **21** in a comparable 75% yield but with a noticeable and consistently higher de in 78–80%. This observation led to the speculation that allylations of **20** and **22** could proceed through slightly different transition states with the latter having more of an oxocarbenium ion character.[9] This also suggests that the rate of departure of the urea group could depend upon whether it assumes an axial or equatorial position during the formation of the incipient oxocarbenium ion.[18b]

Finally, this protocol could be extended to other systems leading to successful preparations of pyrans or *C*-glycoside type derivatives such as **23** and **24** with an overall yield of 4.0% and 3.1%, respectively (unoptimized). The diastereoselectivity was found to be in the hydroboration–oxidation step (>15:1 in the case of **23** and 12:1 in the case of **23**) as well as the allylation step (2:1 for **23** and 2–3:1 for **24**). These relatively short sequences for the synthesis of **23** and **24** are also attractive because they are devoid of protection and deprotection steps during the functionalization of the pyran ring.

We have described here the first Lewis acid mediated stereoselective removal of an anomeric urea group (or an electron deficient nitrogen substituent). This methodology along with stereoselective hydroboration–oxidation of the endocyclic olefin renders pyranyl cycloadducts from hetero [4+2] cycloadditions of chiral allenamides with a useful chiral template leading to a new approach to constructing pyranyl heterocycles or *C*-glycosides.

## Acknowledgment

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(12) The X-ray structure of pyran **8** is available in supplementary materials (Figure 1).

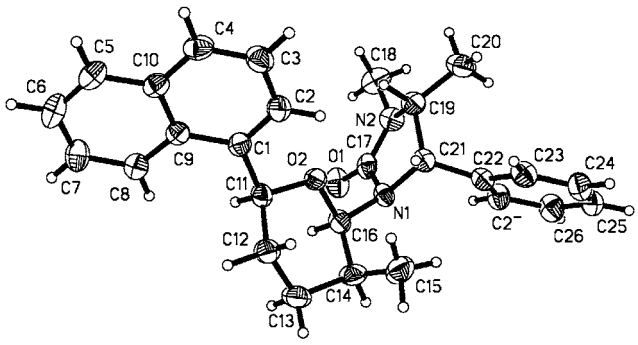


**Figure 1**

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(16) For selected experimental procedures and characterizations:
**General Procedure for Lewis Acid Mediated Allylations Using Pyran 8:** To a solution of 317.7 mg of pyran **8** in 65 mL of freshly distilled $CH_2Cl_2$ at –78 °C under $N_2$ were added 503.9 mg of $SnBr_4$ (1.5 equiv, 1.16 mmol) and 0.488 mL of allyltrimethylsilane (4 equiv, 3.06 mmol). The reaction was vigorously stirred for 12 h and allowed to slowly warm to r.t. The solvent was removed under reduced pressure and purification using silica gel column chromatography afforded 157.6 mg of **9a** and **9b** as a mixture in addition to recovery of the Close's auxiliary in 70–90% recovery range when attempted. The ratio of **9a**:**9b** was found to be 4:1 from the crude $^1$H NMR. Preparative thin layer chromatography (1% $Et_2O$ in hexanes) was useful to separate the major isomer **9a** from the minor isomer **9b**.
**9a** (major). $R_f$ = 0.30 (10% $Et_2O$ in hexanes). $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.06 (d, *J* = 7.0 Hz, 3 H), 1.70 (m, 1 H), 1.78 (m, 1 H), 2.03 (m, 2 H), 2.18 (m, 1 H), 2.47 (ddd, *J* = 1.0, 10.0, 18.0 Hz, 2 H) 3.43 (ddd, *J* = 6.0, 7.0, 7.0 Hz, 1 H), 4.96 (dd, *J* = 1.0, 10.0 Hz, 1 H), 5.04 (dd, *J* = 2.0, 15.0 Hz, 1 H), 5.52 (dd, *J* = 4.0, 8.0 Hz, 1 H), 5.74 (m, 1 H), 7.27–8.31 (m, 7 H). $^{13}$C NMR (125 MHz, $C_6D_5CD_3$): δ = 137.9, 135.8, 134.2, 128.8, 128.5, 127.8, 125.4, 125.2, 125.1, 124.8, 124.2, 115.6, 76.8, 69.6, 36.8, 32.2, 27.4, 27.3, 17.8. IR (thin film): 3052 (m), 2932 (m), 1641 (m) cm$^{-1}$. MS (EI): *m*/*e* (% relative intensity) = 266.2 (25) [M$^+$], 249.6 (100). Optical rotation was not pursued because samples of **9a** still contained some **9b**.
**9b** (minor). $R_f$ = 0.30 (10% $Et_2O$ in hexanes). $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.06 (d, *J* = 7.0 Hz, 3 H), 1.55 (m, 3 H), 1.74 (m, 1 H), 2.03 (m, 2 H), 2.65 (m, 1 H), 4.01 (dd, *J* = 4.0, 10.0 Hz, 1 H), 4.97 (d, *J* = 10.0 Hz, 1 H), 5.11 (d, *J* = 17.0 Hz, 1 H), 5.33 (dd, *J* = 1.0, 10.0 Hz, 1 H), 5.88 (m, 1 H), 7.07–8.25 (m, 7 H). $^{13}$C NMR (125 MHz, $C_6D_5CD_3$): δ = 136.0, 128.9, 128.8, 127.8, 127.5, 125.4, 123.8, 123.6, 115.7, 76.8, 68.1, 33.3, 32.6, 30.5, 27.6, 16.7 (3 signals are missing overlap with solvent). IR (thin film): 3064 (m), 2945 (m), 1635 (m)cm$^{-1}$. MS (EI): *m*/*e* (% relative intensity) = 284.2(50) [M + $NH_4$]$^+$, 264.1(10), 247.1(100); *m*/*e* calculated for $C_{19}H_{26}NO$: 284.2015. Found: 284.2015.
**General Procedure for Lewis Acid Mediated Allylations Using Pyran 20:** To a solution of pyran **20** (5.0 mg, 0.011

mmol) in 1.0 mL of anhyd $CH_2Cl_2$ at –78 °C were added 7.63 mg $SnBr_4$ (1.5 equiv, 0.0174 mmol) and 7.50 μL of allyltrimethylsilane (4 equiv. 0.0464 mmol). The mixture was warmed to r.t. and stirred at r.t. for 12 h before it was quenched with sat. aq $NH_4Cl$ (2 mL). The resultant mixture was extracted with $CH_2Cl_2$ (3 × 3 mL), and the combined extracts were dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. Silica gel flash chromatography (gradient eluent: 0–10% EtOAc in hexanes) of the crude gave 2.32 mg (combined yield 70%) of pyran **21a** and **22b** with a 7:1 diastereomeric ratio.

**Pyran 21a** (major): $R_f$ = 0.30 (10% EtOAc in hexanes). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.99 (d, *J* = 7.0 Hz, 3 H), 1.36 (ddd, *J* = 6.0, 12.0, 18.0 Hz, 1 H), 1.75 (dd, *J* = 12.0, 22.0 Hz, 1 H), 1.86 (m, 1 H), 2.27 (ddd, *J* = 6.5, 14.0, 15.0 Hz, 1 H), 2.42 (ddd, *J* = 4.5, 11.0, 16.5 Hz, 1 H), 2.71 (d, *J* = 1.5 Hz, 1 H), 3.68 (ddd, *J* = 4.5, 7.0, 15.5 Hz, 1 H), 4.46 (ddd, *J* = 3.5, 8.5, 15.5 Hz, 1 H), 5.13 (ddd, *J* = 9.5, 15.5, 17.5 Hz, 2 H), 5.84 (d, *J* = 2.0 Hz, 1 H), 5.94 (m, 1 H), 7.08–8.20 (m, 7 H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 134.9, 128.7, 127.5, 125.8, 125.4, 125.2, 122.8, 122.6, 116.7, 86.0, 80.6, 69.7, 39.0, 38.5, 33.5, 16.2 (missing 3 peaks). IR (thin film): 3432 (s), 3072 (w), 3063 (w), 2971 (s), 2962 (s), 2953 (s) $cm^{-1}$. MS (EI): *m*/*e* (% relative intensity) = 282.2 (15) [$M^+$], 125.1(100); *m*/*e* calcd for $C_{19}H_{22}O_2$: 282.1620. Found: 282.1618.

**Pyran 21b** (minor): $R_f$ = 0.32 (10% EtOAc in hexanes). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.98 (d, *J* = 7.0 Hz, 3 H), 1.33 (ddd, *J* = 11.0, 20.5, 22.5 Hz, 1 H), 1.64 (dd, *J* = 5.5, 15.5 Hz, 1 H), 2.28 (m, 3 H), 2.82 (s, 1 H), 4.05 (ddd, *J* = 10.0, 13.0, 22.5 Hz, 1 H), 4.36 (ddd, *J* = 5.5, 10.5, 16.0 Hz, 1 H), 5.22 (m, 2 H), 5.82 (d, *J* = 4.5 Hz, 1 H), 5.98 (m, 1 H), 7.30–8.20 (m, 7 H). MS (EI): *m*/*e* (% relative intensity) = 282.2(15) [$M^+$], 125.1(100); *m*/*e* calcd for $C_{19}H_{22}O_2$: 282.1620. Found: 282.1617.

**Hydroboration Reactions:** To a solution of 9.0 mg of pyran **16** (0.0218 mmol) in 2.0 mL of anhyd THF at r.t. was added 0.25 mL of $BH_3$·THF complex (2.5 equiv, 1 M solution in THF). The resultant mixture was stirred for 1 h and warmed to 55 °C for 1 h, and then, the mixture was cooled to r.t. and excess 30% aq $H_2O_2$ and 15% aq NaOH was added dropwise carefully. The resultant mixture was warmed to 60 °C for 10 min and vigorously stirred at r.t. for 1 h. The mixture was extracted with $Et_2O$ (2 × 5 mL) and EtOAc (2 × 5 mL). The combined extracts were dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. Silica gel flash chromatography (50% EtOAc in hexanes) of the crude provided 6.62 mg of the desired alcohol **20** (70% yield) as a colorless oil.

**Pyran 20:** $R_f$ = 0.35 (50% EtOAc in hexanes). $[\alpha]_D^{20}$ = –77.0 (*c* 0.35, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.68 (d, *J* = 7.0 Hz, 3 H), 0.94 (d, *J* = 6.5 Hz, 3 H), 2.01 (ddd, *J* = 3.5, 7.0, 10.0 Hz, 2 H), 2.25 (m, 1 H), 2.67 (s, 3 H), 3.72 (dq, *J* = 7.0, 8.5 Hz, 1 H), 4.02 (dd, *J* = 7.5, 16.0 Hz, 1 H), 4.84 (d, *J* = 8.0 Hz, 1 H), 5.04 (d, *J* = 9.0 Hz, 1 H), 5.63 (d, *J* = 2.0 Hz, 1 H), 7.20–8.41 (m, 12 H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 162.5, 139.0, 134.9, 133.8, 131.7, 128.8, 128.5, 128.2, 127.5, 126.1, 125.7, 125.3, 125.0, 124.4, 86.3, 82.4, 67.3, 58.9, 57.1, 40.2, 32.6, 28.6, 15.1, 13.9 (missing 3 signals). IR (thin film): 3391 (m), 3029 (w), 2980 (w), 2930 (m), 2878 (m), 1684 (s), 1435 (m) $cm^{-1}$. MS (EI): *m*/*e* (% relative intensity) = 430.3(5) [$M^+$], 273.2(100); *m*/*e* calcd for $C_{27}H_{30}N_2O_3$: 430.2256. Ffound: 430.2234.

**Pyran 22** [C6-epimer]: $R_f$ = 0.35 (50% EtOAc in hexanes). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.80 (d, *J* = 7.0 Hz, 3 H), 1.03 (d, *J* = 6.0 Hz, 3 H), 1.15 (ddd, *J* = 3.0, 5.0, 12.0 Hz, 1 H), 1.67 (dd, *J* = 12.0, 23.0 Hz, 1 H), 2.46 (m, 1 H), 2.81 (s, 3 H), 3.51 (ddd, *J* = 3.5, 5.0, 10.5 Hz, 1 H), 3.79 (dq, *J* = 6.5, 8.5 Hz, 1 H), 4.69 (d, *J* = 8.5 Hz, 1 H), 5.37 (d, *J* = 9.0 Hz, 1 H), 5.45 (d, *J* = 3.0 Hz, 1 H), 7.20–8.25 (m, 12 H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 167.6, 136.9, 134.9, 133.2, 128.6, 128.5, 128.3, 127.9, 127.8, 127.4, 125.6, 125.3, 125.1, 122.8, 90.9, 80.1, 68.4, 60.7, 55.7, 35.0, 32.2, 29.6, 28.5, 16.0, 14.5 (missing 2 peaks). MS (EI): *m*/*e* (% relative intensity) = 430.3 (5) [$M^+$], 273.2 (100); *m*/*e* calcd for $C_{27}H_{30}N_2O_3$: 430.2256. Found: 430.2232.

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(21) When substituents at C5 and C6 are *trans* in these pyranyl heterocycles, we observed strong NOE (see pyrans **21** and **22**) between protons at C2 and C3 presumably because these two protons are not necessarily locked in a diaxial relationship unlike those in **20**.