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Novel 2,5-Disubstituted 1,3-Dioxanes and Oxazolidines as Potential Chemoprevention Agents and Building Blocks for Organic Synthesis

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2,5-Disubstituted 1,3-dioxacycloalkanes have recently been found to be promising lead compounds that possess potent anti-inflammatory activity and therefore may act as chemoprevention agents. Encouraged by this we have designed and synthesized a new series of 5-amino-2-heteroaryl-1,3-dioxanes. Starting from *N*-protected 2-aminopropane-1,3-diol and the corresponding aromatic aldehydes, the products were isolated without isomeric inversion at the deprotection step. This is the first broadly applicable synthetic approach to the acetalization of heteroaromatic aldehydes to give 5-amino-1,3-dioxanes. Our route provides a mild access to both isomers of this kind of dioxane, that is, *cis* and *trans* products, as well as 4-(hydroxymethyl)-2-heteroaryloxazolidines, which are useful building blocks in organic synthesis.

Introduction

Cancer is a leading cause of death worldwide and in this context the development of chemoprevention agents,[1] used to prevent or inhibit the development of carcinogenesis,[2] is very important. Non-steroidal anti-inflammatory drugs (NSAIDS) appear to be useful in the prevention and suppression of colorectal, gastric as well as other types of cancer.[3,4] For example, celecoxib has been successfully used in the treatment of patients with familial adenomatous polyposis (FAP) because it reduces the numbers of colon and rectum polyps and it has also shown promising results in the prevention of lung cancer in a Phase IIb clinical trial.[5–7] However, the adverse effects, such as gastric bleeding, of some NSAIDS (e.g. aspirin) limit their long-term application as chemoprevention agents.[8] Hence there is strong demand for advanced pharmaceutics. Clearly, low toxicity and high activity at low dosage are also indispensable for novel drug candidates. In the field of chemoprevention a new substance class has emerged. Different research groups have described the great value of 1,3-dioxanes (**1**–**3**, Figure 1) in treating cancer, inflammation and reperfusion injury.[9–11]

In the last few years Zhao and co-workers have developed a series of new anti-inflammatory agents based on the dioxane scaffold **3**, which shows a comparable or higher anti-inflammatory activity than aspirin against xylene-induced ear edema in mice and does not prolong the tail bleeding time.[11] Because they reported 5-amino-2-(substituted phenyl)-1,3-dioxanes with electron-withdrawing groups on the phenyl ring to give the best results, we regarded the heterocyclic moiety **4** to have high potential in drug discovery programs.

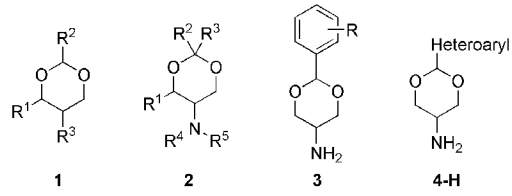

Figure 1. Potential chemoprevention agents with a 1,3-dioxane scaffold.[9–11]

Heteroaromatics are widely found in both pharmaceuticals and agrochemicals. Furthermore, the 4-(heteroaryl)cyclohexanamine moiety is present in several bioactive substances that might be effective as therapeutic agents for diabetes, benign prostatic hyperplasia and numerous other diseases. As an example, 11β-hydroxysteroid dehydrogenase (11β-HSD) inhibitor **5**, which has therapeutic potential, is shown in Figure 2.[12–17]

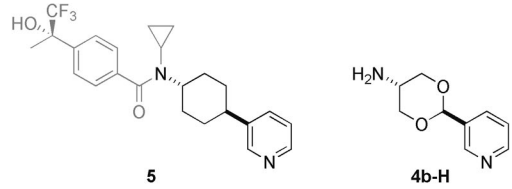

Figure 2. 11β-HSD inhibitor **5**[17] and building block **4b-H**.

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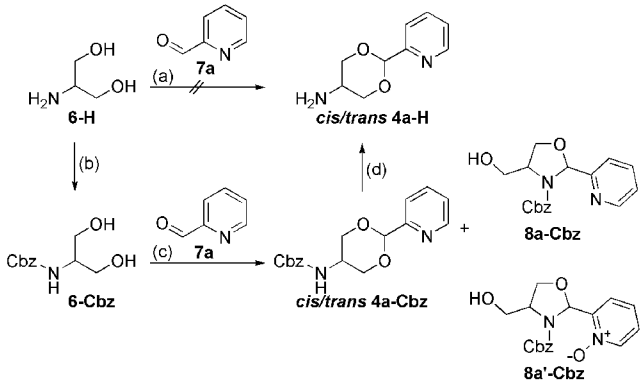
Because dioxanes are mimics of cyclohexanes, 5-amino-2-heteroaryl-1,3-dioxanes **4-H** are very adjuvant building blocks for the continuative development of future drugs (see Figure 2). The introduction of oxygen into the molecules alters the polarity and stability of the derivatives. This may be helpful for facilitating absorption into the body and transportation to the site of pharmacological action. Furthermore, the lability of acetals enables them to act as prodrugs.[18,19] As the pH in cell compartments varies and consequently the metabolism of acetals, dioxanes may have advantages over cyclohexanes as drugs. This encouraged us once more to find a widely applicable synthetic access to 5-amino-2-heteroaryl-1,3-dioxanes **4**, of which there is little reported in the literature.[20–29] Herein we describe a suitable route to these achiral 5-amino-1,3-dioxanes.

Results and Discussion

Preparation of *N*-Protected 5-Amino-1,3-dioxanes by Acetalization of Diol 6 and Heterocyclic Aldehydes 7

Starting from 2-amino-1,3-diol **6-H** we were able to find an appropriate protocol for the acetalization of heterocyclic aldehydes **7**, although it was not possible to convert diol **6-H** directly into acetal **4a-H** using conditions similar to those described in the literature for substituted benzaldehydes.[11] Therefore Cbz-protected aminodiol **6-Cbz** was used as the starting material for the cyclization step.[30] To develop a suitable procedure for the synthesis of heterocyclic acetals, pyridinecarbaldehyde **7a** (Scheme 1) was examined first. Aldehyde **7a** was treated with diol **6-Cbz** under Lewis and Brønsted acid catalysis with the addition of a suitable drying agent. In this way, both the *cis* and *trans* isomers of the desired acetal **4a-Cbz** were obtained although the ratio of isomers was slightly dependent on the reaction conditions.



Scheme 1. Acetalization of pyridine-2-carbaldehyde (**7a**). Reagents and conditions: a) *p*TsOH, Na_2SO_4, $CHCl_3$, THF, room temp.; b) Cbz-Cl, NEt_3, EtOH, 0 °C to room temp., 81%; c) NBS, $MgSO_4$, toluene, reflux, 52% (1.8:1 *cis*/*trans*) **4a-Cbz**, 15% **8a-Cbz**; d) H_2, Pd/C, MeOH, room temp., 88%.

Interestingly, we isolated oxazolidine **8a-Cbz** as a by-product, which means that monoprotection of the amine does not prevent nucleophilic attack of the nitrogen atom on the carbonyl. In addition to using dry reagents and solvents it was essential to work under an inert atmosphere because otherwise some oxidized product was obtained as well. The structure of this product, *N*-oxide **8a′-Cbz**, was elucidated by NMR and HRMS. We tried several methods for the acetalization in order to improve the ratio between the acetals and the side-products as well as the yield of the reaction.[11,31–35] The best results were achieved by using *p*TsOH, NBS and sulfamic acid as catalysts in toluene at reflux (Scheme 1). However, unfortunately it was not possible to suppress the formation of the oxazolidine completely and concurrently obtain acceptable yields of the required acetals **4a-Cbz**.

Because the condensation reaction with aminodiol **6-Cbz** is reversible and occurs largely under thermodynamic control under the conditions applied, more or less stable acetals and oxazolidines are in equilibrium.[36] Therefore we decided to use a different protecting group strategy to prevent formation of the oxazolidine. Because it was not possible to produce phthalimide **6-Phth** and nitro compound **9** in sufficient purity,[37,38] we examined the cyclization step using precursors **10** and **11**.[39,40] Both ketone **10** and hydroxymethyl derivative **11** can easily be converted into the corresponding amines. However, we were not able to acetalize pyridinecarbaldehyde **7a** with these diols (Figure 3).

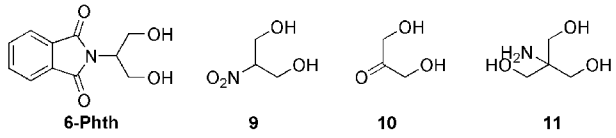
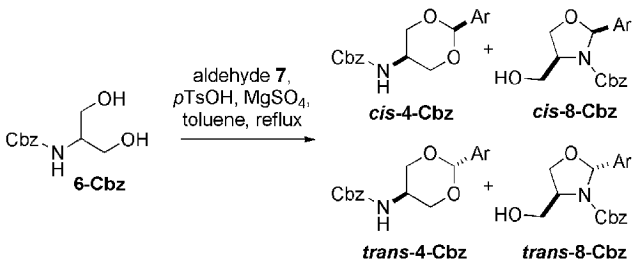


Figure 3. Precursors for the acetalization reaction with aldehydes.

With these results in hand we continued to use Cbz-protected aminodiol **6-Cbz** as the starting material for further acetalizations. To ensure that the developed procedure would work for different heterocycles, we used *p*TsOH, NBS and sulfamic acid as catalysts for the synthesis of pyridine acetals **4b** and **4c**. We achieved the best results for both aldehydes by using *p*TsOH (other results not shown here). Therefore we continued to use this catalyst for the synthesis of other heterocyclic acetals. It is quite clear that acetal formation is strongly dependent upon the substrate used in the reaction. Although pyrrolecarbaldehyde **7d** (Scheme 2, Table 1, Entry 4) underwent decomposition under the reaction conditions, even if the reaction was carried out at room temperature or in a different solvent, the other aldehydes could be transformed into acetals or oxazolidines, although thiophene acetal **4g-Cbz** was not that stable. Interestingly, the *cis* acetals were formed in preference to the *trans* products. This observation has been made previously for other 1,3-dioxanes. Eliel and co-workers reported a detailed study of the axial (*cis*) predominance of polar substituents at the 5-position of 1,3-dioxanes.[41] In particular, they discussed the presence of hydrogen-bonding between the ring and NH_3^+ substituents. The thermodynamic stability resulting from these hydrogen bonds is also shown by Zhao and co-workers for 5-amino-2-substi-

tuted-phenyl-1,3-dioxanes (energy-minimized structures by modelling).[11] In this study this finding is supported by the solid-state structures of pyridin-3-yl acetal **4b-H** (ammonium nitrate) and its protected surrogate **4b-Cbz**, which show hydrogen bridges between the NH and ring oxygen atoms with a distance of about 2.7 Å (see Figure 4).



Scheme 2. Acetalization of heteroaromatic aldehydes **7**.

Table 1. Acetalization of heteroaromatic aldehydes **7**.

Entry	Aldehyde	Acetal	Oxazolidine[c]
1[a]	**7a**	**4a-Cbz** 52 % *c*/*t* = 1.8/1	**8a-Cbz** 15 % *one isomer*
2	**7b**	**4b-Cbz** 56 % *c*/*t* = 10/1	**8b-Cbz** 0 %
3	**7c**	**4c-Cbz** 17 % *c*/*t* = 1.4/1	**8c'-Cbz** 25 % (*N*-oxide) *one isomer*
4[b]	**7d**	**4d-Cbz** 0 %	**8d-Cbz** 4 % *one isomer*
5	**7e**	**4e-Cbz** 33 % *c*/*t* = 2.6/1	**8e-Cbz** 21 % 1/3.4
6	**7f**	**4f-Cbz** 63 % *c*/*t* = 8/1	**8f-Cbz** 9 % 1/4
7	**7g**	**4g-Cbz** 46 % *c*/*t* = 3/1	**8g-Cbz** 21 % 1/7.5

[a] NBS used as catalyst. [b] Decomposition of aldehyde. [c] *cis*/*trans* configurations could not be elucidated.

In general we elucidated the configuration of the acetals by performing NOESY experiments. Unfortunately, this was not possible for oxazolidines **8-Cbz**. As there were strong cross-peaks between the hydrogen atoms at the 2- and 5-positions of the ring, the acetal was considered to be *cis*; the absence of these signals indicated a *trans* configuration. The results of these analyses are consistent with those obtained by X-ray crystallography of both *cis* and *trans* isomers of pyridin-3-yl acetals (see Figure 4 and Figure 5).

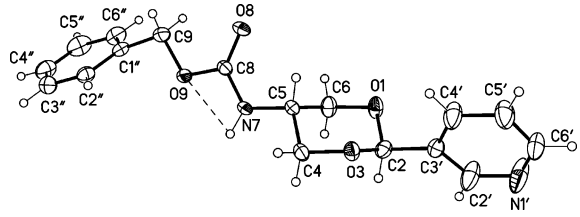


Figure 5. Molecular structure of *trans*-pyridin-3-yl acetal **4b-Cbz** showing the intramolecular NH–O hydrogen bond (displacement parameters are drawn at the 50% probability level).

In most cases it was possible to separate the *cis* and *trans* acetals as well as the oxazolidine by-products by simple column chromatography on silica gel. However, in most cases the chromatographic separation had to be performed twice, in particular, for analytical purposes. Only for the furan acetals **4e-Cbz** and **4f-Cbz** and the thiophene acetal **4g-Cbz** was it impossible to separate the *cis* and *trans* products. Although inseparable mixtures of the two isomers (*cis* and *trans*) of the oxazolidines **8e-Cbz**, **8f-Cbz** and **8g-Cbz** were obtained, the reactions of pyridinecarbaldehydes **7a** and **7c** as well as the pyrrolecarbaldehyde **7d** led to a single diastereomer in a stereoselective reaction (Scheme 2).

Although in general oxazolidines **8** were obtained as side-products in low yields the diastereomerically pure surrogates **8a-Cbz**, **8c′-Cbz** and **8d-Cbz** may have potential as building blocks in the synthesis of biologically active compounds. The application of oxazolidines is manifold. Some of them act as fungicides or show antimicrobial activity[42–44] and, in particular, they might be used for the

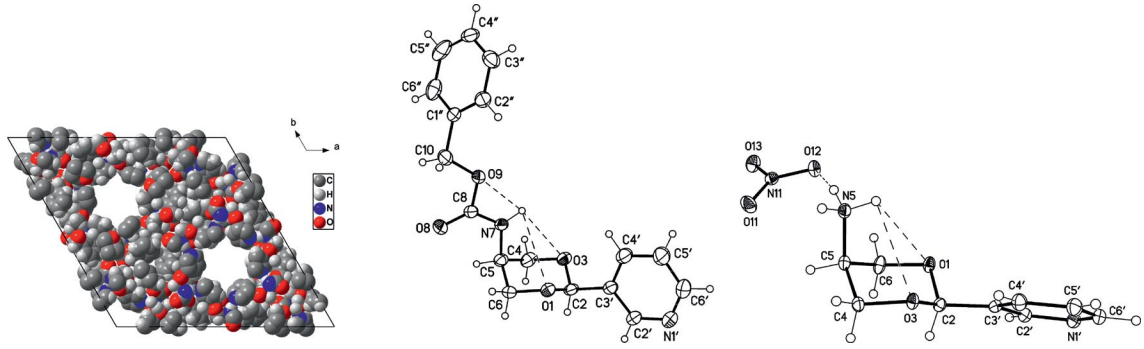


Figure 4. Crystal packing (space filling model) of *cis*-pyridine-3-yl acetal **4b-Cbz**, projection along the *a*/*b* plane (left). Molecular structure of *cis*-pyridin-3-yl acetal **4b-Cbz** (middle) and the cation of *cis*-**4b-H** (right) showing intramolecular NH–O hydrogen bonds (displacement parameters are drawn at the 50% probability level).

synthesis of various inhibitors of methyltransferase SMYD3, which plays a role in liver, colon and breast cancer.[45] Out of 150000 compounds, oxazolidine **12** was identified by molecular modelling as being capable of binding to this protein. The structural similarities exhibited by oxazolidines **8** and inhibitor **12** are illustrated in Figure 6.

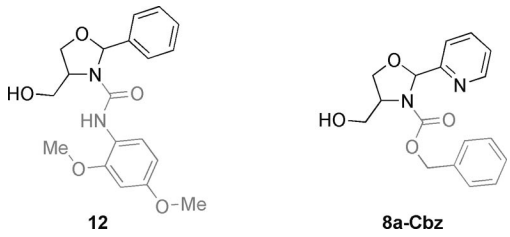


Figure 6. Inhibitor **12** of SMYD3 and building block **8a-Cbz**.

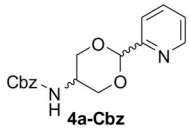
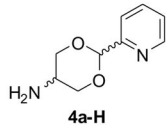
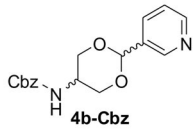
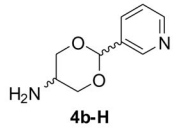
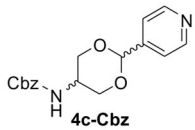
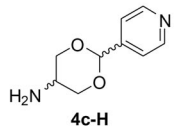
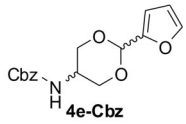
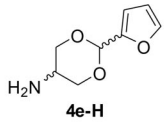
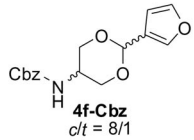
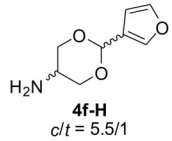
Deprotection of *N*-Protected 5-Amino-1,3-dioxanes 4-Cbz to Yield Acetals 4-H

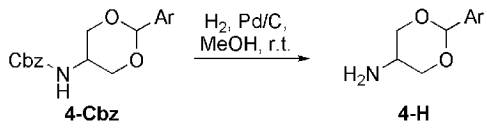
Further application of acetals **4** required deprotection of the amine functionality.[37] The use of Cbz as protecting group allowed the synthesis of free amino acetals **4-H** without isomeric inversion during the deprotection step. Not only was the configuration of the acetals retained, the deprotection proceeded in good-to-excellent yields for all acetals (see Table 2) with the exception of the free aminothiophene acetal **4g-H**, which could not be obtained due to the instability of its protected precursor **4g-Cbz**. Furthermore it was possible to separate the *cis* and *trans* acetal at this step of the synthesis if this had not been achieved before. Even if mixtures of isomers were employed, the *cis* to *trans* ratio was retained, except for the reaction with furan acetal **4f-Cbz** for which a small alteration was observed (Table 2, Entry 5). This was ascribed to a higher stability and/or reactivity of the *trans* isomer (Scheme 3).

In general, the acetals **4-Cbz** and **4-H** were relatively stable towards ring-opening, except for the thiophenes **4g-Cbz** and **8g-Cbz**, which underwent fast decomposition at room temperature if in contact with any solvent. Every other acetal **4-Cbz** and **4-H** was stable at room temperature in solvent-free conditions. Storage in slightly acidic media, for example, methanol or $CDCl_3$, for some days also did not lead to ring-opening or any other kind of decay of these acetals. To avoid ring-opening of the acetals **4** during column chromatography, silica gel enriched with 0.1% calcium ions (Fluka) may be used rather than basic additives like triethylamine because under these conditions the separation is not affected. Furthermore, in the case of the free amino acetals **4-H**, the use of this silica gel leads to nitrates. This facilitates crystallization and thus we were able to obtain crystals of acetal **4b-H** for X-ray analysis, but it was not indispensable to avoid decomposition.

Fortunately the heterocyclic moieties were stable under the deprotection conditions as well and even the furans **4e-H** and **4f-H** could be obtained without significant loss by hydrogenation.

Table 2. Deprotection of heteroaromatic acetals **4-Cbz**.

Entry	Starting material	Product	Yield
1	 **4a-Cbz**	 **4a-H**	90 %
2	 **4b-Cbz**	 **4b-H**	quant.
3	 **4c-Cbz**	 **4c-H**	98 %
4	 **4e-Cbz**	 **4e-H**	91 %
5	 **4f-Cbz** *c*/*t* = 8/1	 **4f-H** *c*/*t* = 5.5/1	72 %



Scheme 3. Deprotection of heteroaromatic acetals **4-Cbz**.

Conclusions

In this work we have developed a widely applicable synthetic approach to 5-amino-2-heteroaryl-1,3-dioxanes and 4-(hydroxymethyl)-2-heteroaryloxazolidines. Starting from inexpensive precursors, these products were synthesized in a short reaction sequence involving simple transformations. Owing to the uniqueness of their structural properties (including a high analogy to bioactive molecules) it would be worth investigating their use as drugs directly or as building blocks for the synthesis of pharmaceutics and agrochemicals.

Experimental Section

General: All reagents were used as purchased from Sigma–Aldrich, Thermo Fisher Scientific, ABCR and Alfa Aesar. Solvents were dried and purified by standard methods prior to use or purchased in suitable quality. Vials from Macherey–Nagel were used for all reactions above room temperature (sizes 20–20 and 20–10, in combination with N20 oA and N20 TB/oA-M septa). For TLC, aluminium foils layered with silica gel (silica gel 60 F_{254}) produced by Merck were used. Column chromatography was performed on silica gel enriched with 0.1% Ca (Fluka) or Geduran Si 60 (Merck) under flash conditions. NMR spectra were recorded with Bruker

AC 250, Avance 400, Avance DRX 500 and Avance 600 spectrometers. The ^{1}H and ^{13}C NMR chemical shifts are referenced relative to the residual proton signal and the central peak of the carbon multiplet of the deuterated solvent ($CDCl_3$ or $[D_4]$MeOH), respectively. IR spectra were recorded with an IFS 88 Bruker FTIR device neat or as a mixture with KBr (DRIFT). The absorption bands were measured in wavenumbers with units of cm^{-1}. The intensities of the bands are characterized as follows: vs = very strong 0–10% transmittance (T), s = strong 10–40% T, m = medium 40–70% T, w = weak 70–90% T, vw = very weak 90–100% T. EI-MS, FAB-MS, FAB-HRMS and HR-EIMS: spectra were measured with a Finnigan MAT 95 instrument. Elemental analyses were performed using an Elementar vario MICRO device.

Crystal Structure Determinations: All single-crystal X-ray diffraction studies were carried out with a Bruker–Nonius Kappa-CCD diffractometer at 123(2) K using Mo-K_α radiation (λ = 0.71073 Å). Direct methods (SHELXS-97) were used for structure solution and refinement was carried out by using SHELXL-97[46] (full-matrix least-squares on F^2). Non-hydrogen atoms were refined anisotropically; hydrogen atoms were localized by difference electron density determination and refined using a riding model [H(N) free].

***cis*-4b-H:** Colourless crystals, $(C_9H_{13}N_2O_2)^+\cdot(NO_3)^-$, M = 243.22, crystal size 0.40 × 0.20 × 0.10 mm, monoclinic, space group $P2_1/c$ (No. 14), a = 5.9353(4), b = 23.8424(22), c = 7.5294(6) Å, β = 90.100(6)°, V = 1065.50(15) Å^3, Z = 4, ρ(calcd.) = 1.516 Mg m^{-3}, F(000) = 512, μ = 0.125 mm^{-1}, 19555 reflections ($2\theta_{max}$ = 55°), 2442 unique (R_{int} = 0.026), 163 parameters, 9 restraints, $R1$ [$I > 2\sigma(I)$] = 0.032, $wR2$ (all data) = 0.087, S = 1.07, largest diff. peak and hole: 0.316 and –0.237 e Å^{-3}.

***cis*-4b-Cbz:** Colourless crystals, $C_{17}H_{18}N_2O_4$, M = 314.33, crystal size 0.30 × 0.12 × 0.08 mm, trigonal, space group R-3 (No. 148), a = b = 41.377(6), c = 5.263(1) Å, α = β = 90°, γ = 120°, V = 7803(2) Å^3, Z = 18, ρ(calcd.) = 1.204 Mg m^{-3}, F(000) = 2988, μ = 0.087 mm^{-1}, 28746 reflections ($2\theta_{max}$ = 55°), 3949 unique (R_{int} = 0.046), 211 parameters, 1 restraint, $R1$ [$I > 2\sigma(I)$] = 0.057, $wR2$ (all data) = 0.163, S = 1.03, largest diff. peak and hole: 0.561 and –0.286 e Å^{-3}.

The structure contains solvent-accessible voids of 1069.4 Å^3 in total. This void/cavity is approx. 13.7% of the unit cell volume (porosity).[47] There is no solvent inside the cavity. The packing index is 61.9.[48]

***trans*-4b-Cbz:** Colourless crystals, $C_{17}H_{18}N_2O_4$, M = 314.33, crystal size 0.40 × 0.20 × 0.08 mm, monoclinic, space group $P2_1/n$ (No. 14), a = 17.878(2), b = 4.882(1), c = 17.996(2) Å, β = 97.21(1)°, V = 1558.3(4) Å^3, Z = 4, ρ(calcd.) = 1.340 Mg m^{-3}, F(000) = 664, μ = 0.096 mm^{-1}, 23003 reflections ($2\theta_{max}$ = 55°), 3567 unique (R_{int} = 0.051), 211 parameters, 1 restraint, $R1$ [$I > 2\sigma(I)$] = 0.052, $wR2$ (all data) = 0.113, S = 1.03, largest diff. peak and hole: 0.320 and –0.322 e Å^{-3}.

CCDC-756389 (for ***cis*-4b-H**), -756391 (for ***cis*-4b-Cbz**) and -756390 (for ***trans*-4b-Cbz**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Benzyl 1,3-Dihydroxypropan-2-ylcarbamate (6-Cbz):[30] Triethylamine (3.07 mL, 2.23 g, 22.1 mmol) was added to a solution of 2-aminopropane-1,3-diol (**6-H**; 1.83 g, 20.1 mmol) in dry ethanol (15 mL) under argon. The solution was cooled to 0 °C and then Cbz-Cl (3.14 mL, 3.77 g, 22.1 mmol) was added slowly. The reaction mixture was stirred at room temp. for 2 h. After removing most of the solvent under reduced pressure the residue was partitioned between water (60 mL) and EtOAc (80 mL) and the aqueous layer was extracted with EtOAc (4 × 50 mL). The combined organic layers were dried with Na_2SO_4, filtered and the solvent was removed under reduced pressure. Column chromatography (silica gel, CH_2Cl_2/MeOH, 30:1–20:1, v/v) of the crude product yielded **6-Cbz** (3.66 g, 81%) as a white solid. R_f = 0.31 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (400 MHz, CD_3OD): δ = 3.57–3.63 [m, 4 H, CH-(CH_2)$_2$], 3.69 [m, 1 H, CH(CH$_2$)$_2$], 5.08 (s, 2 H, CH_2Ph), 7.25–7.38 (m, 5 H, Ar-H) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 56.0 [+, *C*H(CH$_2$)$_2$], 62.3 [–, CH(*C*H$_2$)$_2$], 67.5 (–, *C*H$_2$Ph), 128.9 (+, C-2,6$_{Ar}$), 129.0 (+, C-4$_{Ar}$), 129.5 (+, C-3,5$_{Ar}$), 138.3 (C$_{quat}$, C-1$_{Ar}$), 158.8 (C$_{quat}$, C=O) ppm. IR (DRIFT): $\tilde{\nu}$ = 3300 [s, ν(OH)], 3062 (m), 3030 [m, ν$_{Ar}$(C–H)], 2968 [m, ν(CH$_2$)], 2890 [m, ν(CH$_2$)], 1686 [s, ν(C=O)], 1542 [s, ν$_{Ar}$(C=C)], 1255 (s), 1042 [s, ν(C–O)], 695 (m) cm^{-1}. MS (70 eV, EI): m/z (%) = 225 (8) [M]$^+$, 194 (23) [M – C_2H_5O]$^+$, 150 (19), 108 (6), 91 (100) [C_7H_7]$^+$, 65 (7). HRMS ($C_{11}H_{15}NO_4$): calcd. 225.1001; found 225.0998. $C_{11}H_{15}NO_4$ (225): calcd. C 58.66, H 6.71, N 6.21; found C 58.65, H 6.76, N 6.21.

General Procedure for the Synthesis of Acetals and Oxazolidines (GP A): In a vial, $MgSO_4$ (0.5 g per mmol **6-Cbz**), benzyl 1,3-dihydroxypropan-2-ylcarbamate (**6-Cbz**; 1.00 equiv.) and a catalytic amount of *p*TsOH (0.05–0.10 equiv.) were suspended in dry toluene (3 mL per mmol **6**–**Cbz**) under argon and the corresponding aldehyde (1.10 equiv.) was added. The vial was sealed and the reaction mixture was stirred at 110 °C for 12–72 h. After cooling to room temp., the vial was opened and the suspension partitioned between water and EtOAc (50 mL per mmol **6-Cbz** each). The aqueous layer was extracted with EtOAc (2 × 50 mL per mmol **6-Cbz**) and the combined organic layers were dried with Na_2SO_4 and filtered. After removing the solvent under reduced pressure the crude products were purified by two-fold column chromatography (silica gel, CH_2Cl_2/MeOH, 100:1–30:1, v/v) to obtain the pure title compounds.

General Procedure for the Deprotection of Acetals (GP B): The corresponding acetal (1.00 equiv.) and palladium (10 wt.-% on activated carbon, 0.05–0.10 equiv.) were suspended in MeOH (10 mL per mmol acetal) and stirred under hydrogen. After filtration through a plug of Celite®, the solvent was removed under reduced pressure. The product was purified by column chromatography (silica gel, CH_2Cl_2/MeOH, 30:1–10:1, v/v) when necessary.

Benzyl 2-(Pyridin-2-yl)-1,3-dioxan-5-ylcarbamate (4a-Cbz): Prepared by slightly modified **GP A**, NBS was used as the catalyst; yield up to 52% (1.46 g). *cis*/*trans* = 1.8:1.

***cis*-4a-Cbz:** R_f = 0.30 (CH_2Cl_2/MeOH = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.78 (d, ^3J = 8.8 Hz, 1 H, 5-H), 4.20 (d, ^3J = 1.5 Hz, 4 H, 4,6-H), 5.15 (s, 2 H, CH_2Ph), 5.65 (s, 1 H, 2-H), 5.93 (d, ^3J = 8.8 Hz, 1 H, NH), 7.29–7.40 (m, 6 H, 5,2′–6′-H$_{Ar}$), 7.60 (d, ^3J = 7.7 Hz, 1 H, 3-H$_{Ar}$), 7.74 (ddd, ^4J = 1.6, ^3J = 7.7, ^3J = 7.7 Hz, 1 H, 4-H$_{Ar}$), 8.63 (d, ^3J = 4.7 Hz, 6-H$_{Ar}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.6 (+, C-5), 66.9 (–, *C*H$_2$Ph), 70.9 (–, C-4,6), 101.5 (+, C-2), 120.6 (+, C-5$_{Ar}$), 124.0 (+, C-3$_{Ar}$), 128.1 (+, C-2′,6′$_{Ar}$), 128.1 (+, C-4′$_{Ar}$), 128.5 (+, C-3′,5′$_{Ar}$), 136.3 (C$_{quat}$, C-1′$_{Ar}$), 136.9 (+, C-4$_{Ar}$), 149.1 (+, C-6$_{Ar}$), 155.8 (C$_{quat}$, C=O), 155.9 (C$_{quat}$, C-2$_{Ar}$) ppm. IR (DRIFT): $\tilde{\nu}$ = 3286 [m, ν(OH)], 3052 (m), 3002 (m), 2959 [m, ν(CH$_2$)], 2861 [m, ν(CH$_2$)], 1684 [s, ν(C=O)], 1540 [s, ν$_{Ar}$(C=C)], 1307 (s), 1182 [s, ν(C–O)], 1105 [s, ν(C–O)], 1080 [s, ν(C–O)], 1044 [s, ν(C–O)], 1001 (m), 780 (s), 745 (s) cm^{-1}. MS (FAB): m/z (%) = 337 [M + Na]$^+$, 315 (100) [M + H]$^+$, 271, 207 [M – C_7H_7O]$^+$, 181, 108, 91 [C_7H_7]$^+$. HRMS ($C_{17}H_{19}N_2O_4$): calcd. 315.1345; found 315.1342. $C_{17}H_{18}N_2O_4$ (314): calcd. C 64.96, H 5.77, N 8.91; found C 64.73, H 5.89, N 8.79.

***trans*-4a-Cbz:** R_f = 0.26 (CH_2Cl_2/MeOH = 20:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.61 (t, ^2J = 10.4 Hz, 2 H, 4,6-H), 4.13 (m_c, 1 H, 5-H), 4.38 (dd, ^3J = 3.6, ^2J = 9.9 Hz, 2 H, 4,6-H), 4.71 (m_c, 1 H, NH), 5.10 (s, 2 H, CH_2Ph), 5.48 (s, 1 H, 2-H), 7.27–7.39 (m, 6 H, 5,2′–6′-H_{Ar}), 7.59 (d, ^3J = 7.7 Hz, 1 H, 3-H_{Ar}), 7.74 (dd, ^3J = 7.7, ^3J = 7.7 Hz, 1 H, 4-H_{Ar}), 8.60 (d, ^3J = 4.7 Hz, 6-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.6 (+, C-5), 67.1 (–, CH_2Ph), 69.9 (–, C-4,6), 101.0 (+, C-2), 120.8 (+, C-5$_{Ar}$), 124.0 (+, C-3$_{Ar}$), 128.2 (+, C-2′,6′$_{Ar}$), 128.3 (+, C-4′$_{Ar}$), 128.6 (+, C-3′,5′$_{Ar}$), 136.0 (C_{quat}, C-1′$_{Ar}$), 137.0 (+, C-4$_{Ar}$), 149.0 (+, C-6$_{Ar}$), 155.6 (C_{quat}, C=O), 155.8 (C_{quat}, C-2$_{Ar}$) ppm. IR (DRIFT): $\tilde{\nu}$ = 3307 [m, ν(OH)], 3033 [m, ν_{Ar}(C–H)], 2958 [m, ν(CH_2)], 2874 [m, ν(CH_2)], 1686 [m, ν(C=O)], 1592 [m, ν_{Ar}(C=C)], 1541 [m, ν_{Ar}(C=C)], 1390 (m), 1311 (m), 1246 (m), 1161 [m, ν(C–O)], 1107 [m, ν(C–O)], 1047 [m, ν(C–O)], 1026 (m), 777 (m), 696 (m) cm^{-1}. MS (FAB): *m*/*z* (%) = 337 [M + Na]$^+$, 315 (100) [M + H]$^+$, 271, 217, 137, 108, 91 [C_7H_7]$^+$. HRMS ($C_{17}H_{19}N_2O_4$): calcd. 315.1345; found 315.1342. $C_{17}H_{18}N_2O_4$ (314): calcd. C 64.96, H 5.77, N 8.91; found C 64.85, H 6.06, N 8.78.

Benzyl 4-(Hydroxymethyl)-2-(pyridin-2-yl)oxazolidine-3-carboxylate (8a-Cbz): Prepared by slightly modified **GP A**, NBS used as the catalyst; yield up to 15% (104 mg). R_f = 0.18 (CH_2Cl_2/MeOH = 20:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.64–4.02 (m, 3.5 H, 4-H, CH_2, O*H*), 4.41 (m_c, 2 H, CH_2), 5.00 (m_c, 2 H, CH_2Ph), 6.13 (s, 1 H, 2-H), 6.86 (m_c, 1.5 H, Ar-H, OH), 7.11–7.47 (m, 6 H, Ar-H), 7.64 (m_c, 1 H, Ar-H), 8.57 (m_c, 1 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 59.3 (+, C-4), 64.1 (–, CH_2OH), 67.3 (–, C-5), 68.3 (CH_2Ph), 90.5 (+, C-2), 121.6 (+, C-3$_{Ar}$), 123.6 (+, C-5$_{Ar}$), 127.7 (+, C-2′,6′$_{Ar}$), 128.0 (+, C-4′$_{Ar}$), 128.3 (+, C-3′,5′$_{Ar}$), 135.6 (C_{quat}, C-1′$_{Ar}$), 136.6 (+, C-4$_{Ar}$), 149.4 (+, C-6$_{Ar}$), 154.3 (C_{quat}, C-2$_{Ar}$), 157.6 (C_{quat}, C=O) ppm. IR (neat): $\tilde{\nu}$ = 3435 [w, ν(OH)], 3064 [w, ν_{Ar}(C–H)], 2952 [w, ν(CH_2)], 2891 [w, ν(CH_2)], 1708 [m, ν(C=O)], 1592 [w, ν_{Ar}(C=C)], 1498 (w), 1414 (m), 1357 (m), 1304 (w), 1126 [w, ν(C–O)], 1080 [w, ν(C–O)], 1049 [w, ν(C–O)], 995 (w), 771 (w), 749 (w), 698 (w), 613 (w) cm^{-1}. MS (FAB): *m*/*z* (%) = 337 [M + Na]$^+$, 315 (100) [M + H]$^+$, 271, 207, 179, 108, 91 [C_7H_7]$^+$. HRMS ($C_{17}H_{19}N_2O_4$): calcd. 315.1345; found 315.1343.

2-[3-(Benzyloxycarbonyl)-4-(hydroxymethyl)oxazolidin-2-yl]pyridine 1-Oxide (8a′-Cbz): Prepared by slightly modified **GP A**, NBS used as the catalyst in acetonitrile; yield 4% (31.9 mg). R_f = 0.14 (CH_2Cl_2/MeOH = 20:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.70–3.92 (m, 3 H, CH_2), 4.13 (m_c, 1 H, 4-H), 4.56 (m_c, 2 H, CH_2, 2-H), 5.09 (s, 2 H, CH_2Ph), 5.87 (d, ^3J = 8.3 Hz, 1 H, NH), 7.27–7.35 (m, 5 H, 2′–6′-H_{Ar}), 7.49 (ddd, ^4J = 1.2, ^3J = 4.8, ^3J = 7.7 Hz, 1 H, 5-H_{Ar}), 7.85 (ddd, ^4J = 1.7, ^3J = 7.7, ^3J = 7.7 Hz, 1 H, 4-H_{Ar}), 8.11 (d, ^3J = 7.7 Hz, 1 H, 3-H_{Ar}), 8.70 (ddd, ^5J = 0.8, ^4J = 1.7, ^3J = 4.8 Hz, 1 H, 6-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.3 (+, C-4), 62.0 (–, CH_2OH), 65.5 (–, C-5), 66.9 (CH_2Ph), 77.2 (+, C-2), 125.4 (+, C-3$_{Ar}$), 127.3 (+, C-4$_{Ar}$), 128.1 (+, C-2′,6′$_{Ar}$), 128.1 (+, C-4′$_{Ar}$), 128.5 (+, C-3′,5′$_{Ar}$), 137.3 (+, C-5$_{Ar}$), 147.3 (C_{quat}, C-1′$_{Ar}$), 149.7 (+, C-6$_{Ar}$), 156.2 (C_{quat}, C-2$_{Ar}$), 165.0 (C_{quat}, C=O) ppm. IR (DRIFT): $\tilde{\nu}$ = 3223 [m, ν(OH)], 3056 [m, ν_{Ar}(C–H)], 2882 [m, ν(CH_2)], 2803 (m), 2632 (w), 2007 (w), 1976 (w), 1729 [m, ν(C=O)], 1711 [m, ν_{Ar}(C=C)], 1562 [m, ν_{Ar}(C=C)], 1470 (m), 1448 (m), 1250 (m), 1213 (m), 1168 [m, ν(C–O)], 1057 (m), 930 (m), 918 (m), 760 (m), 738 (m), 705 (m) cm^{-1}. MS (FAB): *m*/*z* (%) = 353 [M + Na]$^+$, 331 (100) [M + H]$^+$, 243, 136, 108, 91 [C_7H_7]$^+$. HRMS ($C_{17}H_{19}N_2O_5$): calcd. 331.1294; found 331.1292.

2-(Pyridin-2-yl)-1,3-dioxan-5-amine (4a-H): Prepared by **GP B**; yield 90% (76.8 mg). If a mixture of isomers was deprotected, the *cis*/*trans* ratio was preserved.

***cis*-4a-H:** R_f = 0.09 (CH_2Cl_2/MeOH = 10:1). ^1H NMR (400 MHz, CD_3OD): δ = 2.81 (m_c, 1 H, 5-H), 4.04 (d, ^2J = 11.8 Hz, 2 H, 4,6-H), 4.22 (d, ^2J = 11.8 Hz, 2 H, 4,6-H), 5.59 (s, 1 H, 2-H), 7.41 (m_c, 1 H, 5-H_{Ar}), 7.67 (d, ^3J = 7.8 Hz, 1 H, 3-H_{Ar}), 7.88 (ddd, ^4J = 1.6, ^3J = 7.7, ^3J = 7.8 Hz, 1 H, 4-H_{Ar}), 8.52 (d, ^3J = 4.8 Hz, 1 H, 6-H_{Ar}) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 46.7 (+, C-5), 73.4 (–, C-4,6), 102.7 (+, C-2), 122.8 (+, C-3$_{Ar}$), 125.8 (+, C-5$_{Ar}$), 139.1 (+, C-4$_{Ar}$), 149.5 (+, C-6$_{Ar}$), 157.5 (C_{quat}, C-2$_{Ar}$) ppm. IR (neat): $\tilde{\nu}$ = 3364 [w, ν(NH_2)], 3283 [w, ν(NH_2)], 2969 [w, ν(CH_2)], 2916 [w, ν(CH_2)], 2856 (m), 1593 (m), 1439 (m), 1387 (m), 1235 (w), 1150 [m, ν(C–O)], 1101 [m, ν(C–O)], 1066 [m, ν(C–O)], 1007 (m), 779 (m) cm^{-1}. MS (FAB): *m*/*z* (%) = 203 [M + Na]$^+$, 181 (100) [M + H]$^+$, 164, 150, 133, 108, 93. HRMS ($C_9H_{13}N_2O_2$): calcd. 181.0977; found 181.0975.

***trans*-4a-H:** R_f = 0.33 (CH_2Cl_2/MeOH = 10:1). ^1H NMR (400 MHz, CD_3OD): δ = 3.09 (m_c, 1 H, 5-H), 3.55 (td, ^3J = 1.4, ^2J = 11.2 Hz, 2 H, 4,6-H), 4.24 (m_c, 2 H, 4,6-H), 5.43 (s, 1 H, C-2), 7.39 (ddd, ^4J = 1.2, ^3J = 5.0, ^3J = 7.7 Hz, 1 H, 5-H_{Ar}), 7.61 (d, ^3J = 7.7 Hz, 1 H, 3-H_{Ar}), 7.85 (ddd, ^4J = 1.7, ^3J = 7.7, ^3J = 7.7 Hz, 1 H, 4-H_{Ar}), 8.50 (ddd, ^5J = 0.9, ^4J = 1.7, ^3J = 4.9 Hz, 1 H, 6-H_{Ar}) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 45.3 (+, CH-5), 74.1 (–, C-4,6), 102.0 (+, C-2), 122.6 (+, C-5$_{Ar}$), 125.8 (+, C-3$_{Ar}$), 139.1 (+, C-4$_{Ar}$), 149.6 (+, C-6$_{Ar}$), 157.7 (C_{quat}, C-2$_{Ar}$) ppm. IR (neat): $\tilde{\nu}$ = 3363 [w, ν(NH_2)]), 2966 [w, ν(CH_2)], 2917 [w, ν(CH_2)], 2846 (m), 1594 (m), 1385 (m), 1141 [m, ν(C–O)], 1088 [s, ν(C–O)], 1026 (m), 978 (m), 779 (m) cm^{-1}. MS (FAB): *m*/*z* (%) = 203 [M + Na]$^+$, 181 (100) [M + H]$^+$, 179, 164, 150, 124, 108, 93. HRMS ($C_9H_{12}NaN_2O_2$): calcd. 203.0796; found 203.0804.

Benzyl [2-(Pyridin-3-yl)-1,3-dioxan-5-yl]carbamate (4b-Cbz): Prepared by **GP A**; yield up to 56% (793 mg). *cis*/*trans* = 10:1.

***cis*-4b-Cbz:** R_f = 0.56 (CH_2Cl_2/MeOH = 10:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.77 (d, ^3J = 8.8 Hz, 1 H, 5-H), 4.6 (m_c, 4 H, 4,6-H), 5.12 (s, 2 H, CH_2Ph), 5.59 (s, 1 H, 2-H), 5.89 (m_c, 1 H, NH), 7.26–7.38 (m, 6 H, 5,2′–6′-H_{Ar}), 7.78 (d, ^3J = 7.9 Hz, 1 H, 4-H_{Ar}), 8.59 (d, ^3J = 4.7 Hz, 1 H, 6-H_{Ar}), 8.69 (d, ^4J = 1.2 Hz, 1 H, 2-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.4 (+, C-5), 66.9 (–, CH_2Ph), 70.7 (–, C-4,6), 99.8 (+, C-2), 123.1 (+, C-5$_{Ar}$), 128.1 (+, C-3′,5′$_{Ar}$), 128.2 (+, C-4′$_{Ar}$), 128.5 (+, C-2′,6′$_{Ar}$), 133.3 (C_{quat}, C-3$_{Ar}$), 133.5 (+, C-4$_{Ar}$), 136.2 (C_{quat}, C-1′$_{Ar}$), 147.8 (+, C-2$_{Ar}$), 150.2 (+, C-6$_{Ar}$), 155.8 (C_{quat}, C=O) ppm. IR (DRIFT): $\tilde{\nu}$ = 3260 [m, ν(OH)], 3036 [m, ν_{Ar}(C–H)], 2975 [m, ν(CH_2)], 2943 [m, ν(CH_2)], 2883 [m, ν(CH_2)], 1718 [s, ν(C=O)], 1535 [m, ν_{Ar}(C=C)], 1304 (m), 1275 (m), 1232 (m), 1172 [m, ν(C–O)], 1101 [m, ν(C–O)], 1072 [m, ν(C–O)], 1001 (s), 979 (m), 715 (m) cm^{-1}. MS (FAB): *m*/*z* (%) = 315 (100) [M + H]$^+$, 261, 217, 173, 120, 107 [C_7H_7O]$^+$, 91 [C_7H_7]$^+$. HRMS ($C_{17}H_{19}N_2O_4$): calcd. 315.1345; found 315.1348.

***trans*-4b-Cbz:** R_f = 0.51 (CH_2Cl_2/MeOH = 10:1). ^1H NMR (500 MHz, $CDCl_3$): δ = 3.60 (t, ^2J = 10.4 Hz, 2 H, 4,6-H), 4.08 (m_c, 1 H, 5-H), 4.36 (dd, ^3J = 4.2, ^2J = 10.4 Hz, 2 H, 4,6-H), 4.83 (d, ^3J = 7.9 Hz, 1 H, NH), 5.11 (s, 2 H, CH_2Ph), 5.46 (s, 1 H, 2-H), 7.28–7.39 (m, 6 H, 5,2′–6′-H_{Ar}), 7.81 (d, ^3J = 7.6 Hz, 1 H, 4-H_{Ar}), 8.60 (d, ^3J = 4.2 Hz, 1 H, 6-H_{Ar}), 8.69 (s, 1 H, 2-H_{Ar}) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 43.6 (+, C-5), 67.1 (–, CH_2Ph), 69.7 (–, C-4,6), 99.1 (+, C-2), 123.3 (+, C-5$_{Ar}$), 128.2 (+, C-3′,5′$_{Ar}$), 128.3 (+, C-4′$_{Ar}$), 128.6 (+, C-2′,6′$_{Ar}$), 133.1 (C_{quat}, C-3$_{Ar}$), 134.0 (+, C-4$_{Ar}$), 136.0 (C_{quat}, C-1′$_{Ar}$), 147.9 (+, C-2$_{Ar}$), 150.1 (+, C-6$_{Ar}$), 155.5 (C_{quat}, C=O) ppm. IR (DRIFT): $\tilde{\nu}$ = 3307 [m, ν(OH)], 3051 [w, ν_{Ar}(C–H)], 2981 [w, ν(CH_2)], 2958 [w, ν(CH_2)], 2857 [w, ν(CH_2)], 1679 [m, ν(C=O)], 1537 [m, ν_{Ar}(C=C)], 1392 (m), 1313 (m), 1250 (w), 1165 [m, ν(C–N)], 1129 [m, ν(C–O)], 1103 [m, ν(C–O)], 1049 [m, ν(C–O)], 700 (m) cm^{-1}. MS (FAB): *m*/*z* (%) = 315

(100) $[M + H]^+$, 261, 217, 176, 124, 107 $[C_7H_7O]^+$, 91 $[C_7H_7]^+$. HRMS ($C_{17}H_{19}N_2O_4$): calcd. 315.1345; found 315.1342.

2-(Pyridin-3-yl)-1,3-dioxan-5-amine (4b-H): Prepared by **GP B**; yield quantitative (236 mg). If a mixture of isomers was deprotected, the *cis*/*trans* ratio was preserved.

***cis*-4b-H·HNO$_3$:** R_f = 0.06 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (400 MHz, CD_3OD): δ = 3.43 (m_c, 1 H, 5-H), 4.25 (dd, ^2J = 13.0, ^3J = 1.1 Hz, 2 H, 4,6-H), 4.39 (dd, ^2J = 13.0, ^3J = 1.1 Hz, 2 H, 4,6-H), 5.80 (s, 1 H, 2-H), 7.47 (dd, ^3J = 5.0, ^3J = 7.9 Hz, 5-H$_{Ar}$), 8.01 (m_c, 1 H, 4-H$_{Ar}$), 8.54 (dd, ^4J = 1.5, ^3J = 5.0 Hz, 1 H, 6-H$_{Ar}$), 8.69 (d, ^4J = 1.5 Hz, 1 H, 2-H$_{Ar}$) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 47.0 (+, C-5), 69.2 (–, C-4,6), 101.3 (+, C-2), 125.0 (+, C-5$_{Ar}$), 135.5 (C_{quat}, C-3$_{Ar}$), 136.4 (+, C-4$_{Ar}$), 148.4 (+, C-2$_{Ar}$), 150.6 (+, C-6$_{Ar}$) ppm. IR (DRIFT): $\tilde{\nu}$ = 3009 (m), 1630 (m), 1602 [m, δ = (NH_2)], 1523 [m, ν_{Ar}(C=C)], 1386 (m), 1327 (m), 1186 [m, ν(C–O)], 1157 [m, ν(C-O)], 1137 [m, ν(C–O)], 1070 [m, ν(C–O)], 1012 (m) 802 (m), 712 (m) cm^{-1}. MS (FAB): *m*/*z* (%) = 181 (100) $[M + H]^+$, 165, 137 $[M – C_2H_5N]^+$, 115, 107, 102 $[M – C_4H_8NO_2]^+$, 89. HRMS ($C_9H_{13}N_2O_2$): calcd. 181.0977; found 181.0979.

***trans*-4b-H:** R_f = 0.20 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (500 MHz, CD_3OD): δ = 3.18 (m_c, 1 H, 5-H), 3.64 (t, ^2J = 11.0 Hz, 2 H, 4,6-H), 4.27 (dd, ^3J = 4.8, ^2J = 11.0 Hz, 2 H, 4,6-H), 5.56 (s, 1 H, 2-H), 7.44 (dd, ^3J = 4.9, ^3J = 7.9 Hz, 5-H$_{Ar}$), 7.91 (d, ^3J = 7.9 Hz, 1 H, 4-H$_{Ar}$), 8.51 (d, ^3J = 4.8 Hz, 1 H, 6-H$_{Ar}$), 8.60 (m_c, 1 H, 2-H$_{Ar}$) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 44.9 (+, C-5), 72.8 (–, C-4,6), 100.0 (+, C-2), 125.0 (+, C-5$_{Ar}$), 135.9 (C_{quat}, C-3$_{Ar}$), 136.3 (+, C-4$_{Ar}$), 148.2 (+, C-2$_{Ar}$), 150.3 (+, C-6$_{Ar}$) ppm. MS (FAB): *m*/*z* (%) = 181 (100) $[M + H]^+$, 164 $[M – NH_2]^+$, 137 $[M – C_2H_5N]^+$, 124, 108, 91. HRMS ($C_9H_{13}N_2O_2$): calcd. 181.0977; found 181.0979.

Benzyl [2-(Pyridin-4-yl)-1,3-dioxan-5-yl]carbamate (4c-Cbz): Prepared by **GP A**; yield up to 17% (242 mg). *cis*/*trans* = 1.4:1.

***cis*-4c-Cbz:** R_f = 0.58 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.78 (d, ^3J = 8.8 Hz, 1 H, 5-H), 4.17 (m_c, 4 H, 4,6-H), 5.12 (s, 2 H, C*H*$_2$Ph), 5.53 (s, 1 H, 2-H), 5.81 (d, ^3J = 8.8 Hz, 1 H, NH), 7.30–7.37 (m, 5 H, 2′–6′-H$_{Ar}$), 7.38 (d, ^3J = 5.8 Hz, 2 H, 3,5-H$_{Ar}$), 8.63 (d, ^3J = 5.8 Hz, 2 H, 2,6-H$_{Ar}$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 45.4 (+, C-5), 67.0 (–, *C*H$_2$Ph), 70.8 (–, C-4,6), 99.5 (+, C-2), 120.7 (+, C-3,5$_{Ar}$), 128.1 (+, C-3′,5′$_{Ar}$), 128.2 (+, C-4′$_{Ar}$), 128.5 (+, C-2′,6′$_{Ar}$), 136.2 (C_{quat}, C-1′$_{Ar}$), 146.0 (C_{quat}, C-4$_{Ar}$), 149.7 (+, C-2,6$_{Ar}$), 155.8 (C_{quat}, C=O) ppm. IR (DRIFT): $\tilde{\nu}$ = 3205 [m, ν(OH)], 3035 [m, ν_{Ar}(C–H)], 2950 [w, ν(CH_2)], 2882 [w, ν(CH_2)], 1955 (vw), 1716 [m, ν(C=O)], 1610 [m, ν_{Ar}(C=C)], 1552 [m, ν_{Ar}(C=C)], 1468 (w), 1418 (w), 1403 (w), 1345 (w), 1329 (w), 1302 (m), 1284 (m), 1250 (m), 1176 [m, ν(C–N)], 1113 [m, ν(C–O)], 1088 [m, ν(C–O)], 1070 [m, ν(C–O)], 1027 [m, ν(C–O)], 1009 (m), 988 (m), 947 (w), 917 (w), 859 (w), 842 (w), 817 (w), 753 (m), 721 (m), 698 (m), 657 (w), 598 (w), 578 (w), 553 (w), 539 (w), 519 (w) cm^{-1}. MS (FAB): *m*/*z* (%) = 315 (100) $[M + H]^+$, 270, 223, 207 $[M – C_7H_7O]^+$, 124, 108, 91 $[C_7H_7]^+$. HRMS ($C_{17}H_{19}N_2O_4$): calcd. 315.1345; found 315.1342.

***trans*-4c-Cbz:** R_f = 0.53 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.61 (t, ^2J = 10.2 Hz, 2 H, 4,6-H), 4.05 (m_c, 1 H, 5-H), 4.35 (dd, ^3J = 5.1, ^2J = 10.2 Hz, 2 H, 4,6-H), 4.80 (d, ^3J = 7.0 Hz, 1 H, NH), 5.10 (s, 2 H, C*H*$_2$Ph), 5.41 (s, 1 H, 2-H), 7.31–7.42 (m, 7 H, 3,5,2′–6′-H$_{Ar}$), 8.64 (s, 2 H, 2,6-H$_{Ar}$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 43.6 (+, C-5), 67.2 (-, *C*H$_2$Ph), 69.6 (–, C-4,6), 98.9 (+, C-2), 121.0 (+, C-3,5$_{Ar}$), 128.2 (+, C-3′,5′$_{Ar}$), 128.3 (+, C-4′$_{Ar}$), 128.6 (+, C-2′,6′$_{Ar}$), 136.0 (C_{quat}, C-1′$_{Ar}$), 145.6 (C_{quat}, C-4$_{Ar}$), 149.9 (+, C-2,6$_{Ar}$), 155.5 (C_{quat}, C=O) ppm. IR (DRIFT): $\tilde{\nu}$ = 3305 [w, ν(NH_2)], [w, ν_{Ar}(C–H)], 2978 [w, ν(CH_2)], 2879 [w, ν(CH_2)], 1963 (w), 1768 (w), 1728 [w, ν(C=O)], 1682 [w, ν_{Ar}(C=C)], 1606 [w, ν_{Ar}(C=C)], 1537 [w, ν_{Ar}(C=C)], 1454 (w), 1413 (w), 1279 (w), 1127 [w, ν(C–N)], 1047 [w, ν(C–O)], 983 (w), 851 (w), 812 (w), 756 (w), 700 (w), 631 (w), 591 (w), 558 (w), 493 (w), 478 (w) cm^{-1}. MS (FAB): *m*/*z* (%) = 315 (100) $[M + H]^+$, 215, 207 $[M – C_7H_7O]^+$, 124, 108, 91 $[C_7H_7]^+$. HRMS ($C_{17}H_{19}N_2O_4$): calcd. 315.1345; found 315.1346.

4-[3-(Benzyloxycarbonyl)-4-(hydroxymethyl)oxazolidin-2-yl]pyridine 1-Oxide (8c′-Cbz): Prepared by **GP A**; yield up to 25% (345 mg). R_f = 0.43 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.88 (s, 1 H, OH), 3.78 (m_c, 2 H, CH_2), 4.14 (s, 1 H, 4-H), 4.49 (m_c, 2 H, CH_2), 5.10 (m_c, 2 H, C*H*$_2$Ph), 5.40 (m_c, 1 H, 2-H), 7.29–7.36 (m, 5 H, 2′–6′-H$_{Ar}$), 7.80 (d, ^3J = 5.0 Hz, 2 H, 3,5-H$_{Ar}$), 8.75 (d, ^3J = 5.0 Hz, 2 H, 2,6-H$_{Ar}$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 51.5 (+, C-4), 61.6 (–, *C*H$_2$OH), 64.3 (–, C-5), 67.1 (–, *C*H$_2$Ph), 100.0 (+, C-2), 122.9 (+, C-3,5$_{Ar}$), 128.1 (+, C-2′,6′$_{Ar}$), 128.3 (+, C-4′$_{Ar}$), 128.5 (+, C-3′,5′$_{Ar}$), 136.1 (C_{quat}, C-1′$_{Ar}$), 136.9 (C_{quat}, C-4), 150.5 (+, C-2,6$_{Ar}$), 165.2 (C_{quat}, C=O) ppm. IR (DRIFT): $\tilde{\nu}$ = 3306 [m, ν(OH)], 3069 [m, νAr(C–H)], 2943 [m, ν(CH_2)], 2905 [m, ν(CH_2)], 1728 (m), 1694 [m, ν(C=O)], 1540 [m, ν_{Ar}(C=C)], 1415 (m), 1333 (m), 1295 (m), 1252 (m), 1139 [m, ν(C–O)], 1092 [m, ν(C–O)], 1029 [m, ν(C–O)], 687 (m) cm^{-1}. MS (FAB): *m*/*z* (%) = 353 [M + Na]$^+$, 331 (100) $[M + H]^+$, 315 $[M + H – O]^+$, 261, 241, 223 $[M – C_7H_7O]^+$, 214, 208, 165, 124, 107 $[C_7H_7O]^+$, 91 $[C_7H_7]^+$. HRMS ($C_{17}H_{19}N_2O_5$): calcd. 331.1294; found 331.1292. $C_{17}H_{18}N_2O_5$ (330): calcd. C 61.81, H 5.49, N 8.48; found C 62.04, H 5.40, N 8.72.

2-(Pyridin-4-yl)-1,3-dioxan-5-amine (4c-H): Prepared by **GP B**; yield 98% (37.6 mg). If a mixture of isomers was deprotected, the *cis*/*trans* ratio was preserved.

***cis*-4c-H:** R_f = 0.03 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (400 MHz, CD_3OD): δ = 2.89 (m_c, 1 H, 5-H), 4.06 (dd, ^2J = 11.9, ^3J = 1.3 Hz, 2 H, 4,6-H), 4.25 (m_c, 2 H, 4,6-H), 5.64 (s, 1 H, 2-H), 7.55 (m_c, 2 H, 3,5-H$_{Ar}$), 8.55 (m_c, 2 H, 2,6-H$_{Ar}$) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 49.6 (+, C-5), 72.9 (–, C-4,6), 100.6 (+, C-2), 122.7 (+, C-3,5$_{Ar}$), 149.1 (C_{quat}, C-4$_{Ar}$), 150.1 (+, C-2,6$_{Ar}$) ppm. IR (DRIFT): $\tilde{\nu}$ = 3431 [m, ν(NH_2)], 2878 [m, ν(CH_2)], 2577 (w), 2116 (vw), 1755 (vw), 1631 [w, ν_{Ar}(C=C)], 1536 [w, ν_{Ar}(C=C)], 1387 (m), 1276 (w), 1245 (w), 1157 [w, ν(C–N)], 1131 [w, ν(C–O)], 1095 [w, ν(C–O)], 1068 [w, ν(C–O)], 1016 [w, ν(C–O)], 986 (w), 968 (w), 941 (w), 819 (w), 802 (w), 785 (w), 738 (w), 655 (w), 592 (w), 525 (w), 497 (w), 446 (w), 432 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 180 (2) $[M]^+$, 163 (3), 123 (75) $[C_6H_5NO_2]^+$, 122 (84), 108 (49), 106 (11), 101 (5), 78 (8), 68 (4), 58 (32), 43 (100). HRMS ($C_9H_{13}N_2O_2$): calcd. 181.0977; found 181.0975.

***trans*-4c-H:** R_f = 0.11 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (250 MHz, CD_3OD): δ = 3.05 (m_c, 1 H, 5-H), 3.55 (m_c, 2 H, 4,6-H), 4.24 (dd, ^2J = 11.3, ^3J = 4.9 Hz, 2 H, 4,6-H), 5.46 (s, 1 H, 2-H), 7.50 (d, ^3J = 5.9 Hz, 2 H, 3,5-H$_{Ar}$), 8.54 (d, ^3J = 5.9 Hz, 2 H, 2,6-H$_{Ar}$) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 52.8 (+, C-5), 71.9 (–, C-4,6), 100.3 (+, C-2), 122.8 (+, C-3,5$_{Ar}$), 149.1 (C_{quat}, C-4$_{Ar}$), 150.2 (+, C-2,6$_{Ar}$) ppm. IR (DRIFT): $\tilde{\nu}$ = 3348 (w), 3288 [w, ν(NH_2)], 3037 [w, ν_{Ar}(C–H)], 2978 (w), 2929 [w, ν(CH_2)], 2851 [w, ν(CH_2)], 2771 (vw), 1948 (vw), 1875 (vw), 1755 (w), 1693 [w, ν_{Ar}(C=C)], 1605 [w, ν_{Ar}(C=C)], 1565 [w, ν_{Ar}(C=C)], 1462 (w), 1416 (w), 1393 (w), 1327 (w), 1288 (w), 1234 (w), 1138 [w, ν(C–N)], 1094 [w, ν(C–O)], 1067 [w, ν(C–O)], 1030 [w, ν(C–O)], 993 (w), 931 (w), 868 (w), 806 (w), 739 (w), 676 (w), 644 (w), 566 (w), 519 (vw), 480 (vw), 409 (vw) cm^{-1}. MS (EI): *m*/*z* (%) = 180 (2) $[M]^+$, 163 (2), 153 (6), 136 (3), 123 (98) $[C_6H_5NO_2]^+$, 122 (100), 108 (61), 106 (15), 89

(7) $[C_3H_7NO_2]^+$, 78 (10), 58 (6), 43 (80). HRMS ($C_9H_{13}N_2O_2$): calcd. 181.0977; found 181.0979.

Benzyl 4-(Hydroxymethyl)-2-(1*H*-pyrrol-2-yl)oxazolidine-3-carboxylate (8d-Cbz): Prepared by **GP A**; yield up to 4% (27.2 mg). R_f = 0.58 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.37 (br. s, 1 H, OH), 3.70 (m_c, 2 H, CH_2), 3.98 (m_c, 1 H, 4-H), 4.27 (m_c, 2 H, CH_2), 5.08 (s, 2 H, CH_2Ph), 5.40 (m_c, 1 H, 2-H), 7.28–7.37 (m, 7 H, 3,4,2′–6′-H_{Ar}), 8.04 (m_c, 1 H, 5-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.3 (+, C-4), 61.5 (–, CH_2OH), 62.4 (–, C-5), 67.0 (–, CH_2Ph), 77.2 (C-2), 128.1 (+, C-4,2′,6′$_{Ar}$), 128.2 (+, C-4′$_{Ar}$), 128.5 (+, C-2,3′,5′$_{Ar}$, C_{quat}), 136.0 (C_{quat}, C-1′$_{Ar}$), 156.2 (C_{quat}, C=O), 160.9 (+, C-3,5$_{Ar}$) ppm. MS (FAB): *m*/*z* (%) = 270, 254, 226, 217, 182, 176, 132, 107, 91, 77, 69, 57, 43. Due to strong fragmentation, the protonated molecular ion was not observed by FAB-MS.

Benzyl [2-(Furan-2-yl)-1,3-dioxan-5-yl]carbamate (4e-Cbz): Prepared by **GP A**; yield up to 33% (222 mg). Mixture of isomers: *cis*/*trans* = 2.6:1. R_f = 0.75/0.69 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.58 (m_c, 2 H, 4′,6′-H), 3.74 (m_c, 1 H, 5^c-H), 3.99–4.15 (m, 5 H, 5^t,4^c,6^c-H), 4.31 (dd, ^3J = 5.0, ^2J = 11.1 Hz, 2 H, 4′,6′-H), 4.88 (m_c, 1 H, NH^t), 5.10 (s, 2 H, CH_2Ph^t), 5.12 (s, 2 H, CH_2Ph^c), 5.53 (s, 1 H, 2^t-H), 5.61 (s, 1 H, 2^c-H), 5.89 (d, ^3J = 8.7 Hz, 1 H, NH^c), 6.37 (dd, ^3J = 1.8, ^3J = 3.3 Hz, 1 H, 4^{c,t}-H_{Ar}), 6.45 (d, ^3J = 3.3 Hz, 3^{c,t}-H_{Ar}), 7.30–7.39 (m, 5 H, 2′^{c,t}–6′^{c,t}-H_{Ar}), 7.41 (dd, ^4J = 0.9, ^3J = 1.8 Hz, 1 H, 5^{c,t}-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.7 (+, C-5^t), 45.5 (+, C-5^c), 63.5 (–, CH_2Ph^t), 66.9 (–, CH_2Ph^c), 69.0 (–, C-4′,6′), 70.6 (–, C-4^c,6^c), 95.2 (+, C-2^t), 96.3 (+, C-2^c), 107.7 (+, C-3$^c_{Ar}$), 108.1 (+, C-3$^t_{Ar}$), 110.2 (+, C-4$^c_{Ar}$), 110.3 (+, C-4$^t_{Ar}$), 128.1 (+, C-3′,5′$^c_{Ar}$), 128.1 (+, C-4′$^c_{Ar}$), 128.2 (+, C-3′,5′$^t_{Ar}$), 128.3 (+, C-4′$^t_{Ar}$), 128.5 (+, C-2′,6′$^c_{Ar}$), 128.5 (+, C-2′,6′$^t_{Ar}$), 136.0 (C_{quat}, C-1′$^t_{Ar}$), 136.2 (C_{quat}, C-1′$^c_{Ar}$), 142.7 (+, C-5$^c_{Ar}$), 142.7 (+, C-5$^t_{Ar}$), 149.8 (C_{quat}, C-2$^t_{Ar}$), 150.1 (C_{quat}, C-2$^c_{Ar}$), 155.5 (C_{quat}, C=O^t), 155.9 (C_{quat}, C=O^c) ppm. IR (DRIFT): $\tilde{\nu}$ = 3323 [m, ν(OH)], 3121 [w, ν_{Ar}(C–H)], 2947 [m, ν(CH_2)], 2865 [m, ν(CH_2)], 1717 [m, ν(C=O)], 1508 [m, ν_{Ar}(C=C)], 1307 (s), 1234 (m), 1175 [m, ν(C–O)], 1154 [m, ν(C–O)], 1108 [m, ν(C–O)], 1075 [m, ν(C–O)], 976 (m), 749 (m) cm^{-1}. MS (FAB): *m*/*z* (%) = 326 $[M + Na]^+$, 304 $[M + H]^+$, 261, 236, 208 $[M - C_5H_4O_2]^+$, 165, 123, 107 $[C_7H_7O]^+$, 97, 91 (100) $[C_7H_7]^+$. HRMS ($C_{16}H_{18}NO_5$): calcd. 304.1185; found 304.1182. $C_{16}H_{17}NO_5$ (303): calcd. C 63.36, H 5.65, N 4.62; found C 62.84, H 5.63, N 4.36.

Benzyl 2-(Furan-2-yl)-4-(hydroxymethyl)oxazolidine-3-carboxylate (8e-Cbz): Prepared by **GP A**; yield up to 21% (141 mg). Mixture of isomers: a/b = 1:3.4. R_f = 0.56 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.57–4.33 (m, 6 H, 4^{a,b}-H, 2 $CH_2^{a,b}$, OH^b), 5.09–5.16 (m, 2 H, CH_2Ph^{a,b}), 5.90 (d, ^3J = 8.7 Hz, 1 H, OH^a), 6.13 (s, 1 H, 2^a-H), 6.15 (s, 1 H, 2^b-H), 6.26–6.46 (m, 2 H, 3^{a,b},4^{a,b}-H), 7.06 (m_c, 1 H, 5^a-H_{Ar}), 7.12 (m_c, 1 H, 5^b-H_{Ar}), 7.26–7.42 (m, 5 H, 2′^{a,b}–6′^{a,b}-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.5 (+, C-5^a), 59.2 (+, C-5^b), 64.0 (–, CH_2^b), 66.9 (–, CH_2^a), 67.5 (–, CH_2^a), 67.7 (–, CH_2^b), 68.0 (–, CH_2^b), 70.6 (–, CH_2^a), 83.3 (+, C-2^a), 83.8 (+, C-2^b), 107.7 (+, C-3$^a_{Ar}$), 108.7 (+, C-4$^a_{Ar}$), 109.4 (+, C-3$^b_{Ar}$), 110.3 (+, C-4$^b_{Ar}$), 127.7–128.6 (+, m, 5 CH$^{a,b}_{Ar}$), 135.7 (C_{quat}, C-1′$^b_{Ar}$), 136.2 (C_{quat}, C-1′$^a_{Ar}$), 142.6 (+, C-5$^a_{Ar}$), 143.0 (+, C-5$^b_{Ar}$), 150.1 (C_{quat}, C-2$^a_{Ar}$), 151.0 (C_{quat}, C-2$^b_{Ar}$), 155.9 (C_{quat}, C=O^{a,b}) ppm. IR (neat): $\tilde{\nu}$ = 3440 [w, ν(OH)], 3034 [w, ν_{Ar}(C–H)], 2953 [w, ν(CH_2)], 2887 [w, ν(CH_2)], 1707 [s, ν(C=O)], 1499 [w, ν_{Ar}(C=C)], 1416 (s), 1357 (m), 1184 [w, ν(C–O)], 1127 [m, ν(C–O)], 1073 [m, ν(C–O)], 743 (m) cm^{-1}. MS (FAB): *m*/*z* (%) = 326 $[M + Na]^+$, 304 $[M + H]^+$, 260, 236, 208 $[M - C_5H_4O_2]^+$, 196, 168, 107 $[C_7H_7O]^+$, 102, 91 (100) $[C_7H_7]^+$. HRMS ($C_{16}H_{18}NO_5$): calcd. 304.1185; found 304.1189.

2-(Furan-2-yl)-1,3-dioxan-5-amine (4e-H): Prepared by **GP B**; yield 91% (136 mg). If a mixture of isomers was deprotected, the *cis*/*trans* ratio was preserved.

***trans*-4e-H:** R_f = 0.40 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (400 MHz, CD_3OD): δ = 3.11 (tt, ^3J = 4.7, ^3J = 9.9 Hz, 1 H, 5-H), 3.56 (dd, ^2J = 11.5, ^3J = 9.9 Hz, 2 H, 4,6-H), 4.20 (dd, ^2J = 11.5, ^3J = 4.7 Hz, 2 H, 4,6-H), 5.52 (s, 1 H, 2-H), 6.40 (dd, ^3J = 3.2, ^3J = 1.7 Hz, 4-H_{Ar}), 6.43 (m_c, 1 H, 3-H_{Ar}), 7.48 (dd, ^4J = 0.8, ^3J = 1.7 Hz, 1 H, 5-H_{Ar}) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 45.2 (+, C-5), 72.3 (–, C-4,6), 96.7 (+, C-2), 108.7 (+, C-3$_{Ar}$), 111.2 (+, C-4$_{Ar}$), 143.8 (+, C-5$_{Ar}$), 152.0 (C_{quat}, C-2$_{Ar}$) ppm. IR (DRIFT): $\tilde{\nu}$ = 3348 [w, ν(NH_2)], 2854 [w, ν(CH_2)], 1709 (w), 1658 [w, ν_{Ar}(C=C)], 1547 [w, ν_{Ar}(C=C)], 1368 (w), 1233 [w, ν(C–N)], 1080 [w, ν(C–O)], 883 (w), 823 (vw), 748 (vw), 600 (vw), 492 (vw) cm^{-1}. MS (FAB): *m*/*z* (%) = 170 (100) $[M + H]^+$, 158, 149, 132, 116, 107, 102 $[C_4H_8NO_2]^+$, 97, 95, 91. HRMS ($C_8H_{11}NO_3$): calcd. 170.0817; found 170.0814.

***cis*-4e-H·HNO$_3$:** R_f = 0.18 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (400 MHz, CD_3OD): δ = 3.40 (m_c, 1 H, 5-H), 4.19 (m_c, 2 H, 4,6-H), 4.32 (m_c, 2 H, 4,6-H), 5.73 (s, 1 H, 2-H), 6.42 (dd, ^3J = 3.3, ^3J = 1.8 Hz, 4-H_{Ar}), 6.54 (m_c, 1 H, 3-H_{Ar}), 7.50 (dd, ^4J = 0.8, ^3J = 1.8 Hz, 1 H, 5-H_{Ar}) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 47.0 (+, C-5), 68.8 (–, C-4,6), 97.8 (+, C-2), 109.1 (+, C-3$_{Ar}$), 111.3 (+, C-4$_{Ar}$), 143.9 (+, C-5$_{Ar}$), 151.6 (C_{quat}, C-2$_{Ar}$) ppm. IR (DRIFT): $\tilde{\nu}$ = 3439 [w, ν(NH_2)], 1640 [w, ν_{Ar}(C=C)], 1534 [w, ν_{Ar}(C=C)], 1356 (w), 1156 [vw, ν(C–N)], 1115 [vw, ν(C–O)], 1042 [w, ν(C–O)], 968 (vw), 931 (vw), 883 (vw), 823 (vw), 741 (vw) cm^{-1}. MS (FAB): *m*/*z* (%) = 233 $[M + H + HNO_3]^+$, 217, 189, 170 $[M + H]^+$, 149, 145, 133 (100), 115, 101. HRMS ($C_8H_{13}NO_3^+NO_3^-$): calcd. 233.0774; found 233.0776.

Benzyl [2-(Furan-3-yl)-1,3-dioxan-5-yl]carbamate (4f-Cbz): Prepared by **GP A**; yield up to 63% (423 mg). Mixture of isomers: *cis*/*trans* = 8:1. R_f = 0.48/0.41 (CH_2Cl_2/MeOH = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.53 (dd, ^3J = 10.3, ^2J = 10.5 Hz, 2 H, 4′,6′-H), 3.72 (m_c, 1 H, 5^c-H), 3.98–4.12 (m, 5 H, 5^t,4^c,6^c-H), 4.30 (dd, ^3J = 4.5, ^2J = 10.5 Hz, 2 H, 4′,6′-H), 4.69 (m_c, 1 H, NH^t), 5.10 (s, 2 H, CH_2Ph^t), 5.12 (s, 2 H, CH_2Ph^c), 5.46 (s, 1 H, 2^t-H), 5.56 (s, 1 H, 2^c-H), 5.83 (d, ^3J = 8.6 Hz, 1 H, NH^c), 6.45 (m_c, 1 H, 4^{c,t}-H_{Ar}), 7.31–7.40 (m, 6 H, 5^{c,t},2′^{c,t}–6′^{c,t}-H_{Ar}), 7.51 (m_c, 1 H, 2^{c,t}-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.7 (+, C-5^t), 45.5 (+, C-5^c), 66.9 (–, CH_2Ph^c), 67.1 (–, CH_2Ph^t), 69.3 (–, C-4^t,6^t), 70.5 (–, C-4^c,6^c), 96.4 (+, C-2^t), 97.4 (+, C-2^c), 108.0 (+, C-4$^c_{Ar}$), 108.3 (+, C-4$^t_{Ar}$), 123.4 (C_{quat}, C-3$^t_{Ar}$), 123.9 (C_{quat}, C-3$^c_{Ar}$), 128.2 (+, C-3′,5′$^c_{Ar}$), 128.2 (+, C-4′$^c_{Ar}$), 128.3 (+, C-3′,5′$^t_{Ar}$), 128.4 (+, C-4′$^t_{Ar}$), 128.6 (+, C-2′,6′$^c_{Ar}$), 128.6 (+, C-2′,6′$^t_{Ar}$), 136.0 (C_{quat}, C-1′$^t_{Ar}$), 136.3 (C_{quat}, C-1′$^c_{Ar}$), 140.4 (+, C-2$^c_{Ar}$), 140.5 (+, C-2$^t_{Ar}$), 143.3 (+, C-5$^c_{Ar}$), 143.3 (+, C-5$^t_{Ar}$), 155.5 (C_{quat}, C=O^t), 155.9 (C_{quat}, C=O^c) ppm. IR (DRIFT): $\tilde{\nu}$ = 3278 [s, ν(OH)], 3146 [m, ν_{Ar}(C–H)], 2964 [m, ν(CH_2)], 2868 [m, ν(CH_2)], 1703 [s, ν(C=O)], 1505 [m, ν_{Ar}(C=C)], 1459 (s), 1409 (s), 1344 [s, ν(C–N)], 1237 (m), 1154 [s, ν(C–O)], 1117 [s, ν(C–O)], 1089 [s, ν(C–O)], 1064 [s, ν(C–O)], 996 (s), 939 (s), 877 (m), 804 (s), 744 (m), 699 (s) cm^{-1}. MS (FAB): *m*/*z* (%) = 304 $[M + H]^+$, 255, 217, 208 $[M - C_5H_4O_2]^+$, 173, 123, 107 $[C_7H_7O]^+$, 97 (100), 91 $[C_7H_7]^+$. HRMS ($C_{16}H_{18}NO_5$): calcd. 304.1185; found 304.1182. $C_{16}H_{17}NO_5$ (303): calcd. C 63.36, H 5.65, N 4.62; found C 63.07, H 5.63, N 4.49.

Benzyl 2-(Furan-3-yl)-4-(hydroxymethyl)oxazolidine-3-carboxylate (8f-Cbz): Prepared by **GP A**; yield up to 9% (57.9 mg). Mixture of isomers: a/b = 1:4. R_f = 0.47 (CH_2Cl_2/MeOH = 10:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.62–3.78 (m, 2 H, $CH_2^{a,b}$), 3.84–3.99 (m, 1 H, 4^{a,b}-H), 4.07–4.25 (m, 2 H, $CH_2^{a,b}$), 5.03–5.20 (m, 2 H, CH_2Ph^{a,b}), 6.15 (s, 1 H, 2^b-H), 6.18 (s, 1 H, 2^a-H), 6.34 (s, 1 H, 4^a-

H_{Ar}), 6.40 (s, 4^b-H_{Ar}), 7.11–7.51 (m, 7 H, $2^{a,b}$,$5^{a,b}$,$2'^{a,b}$–$6'^{a,b}$-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.5 (+, C-5^b), 53.3 (+, C-5^a), 63.3 (–, $CH_2{}^a$), 66.9 (–, $CH_2{}^b$), 67.5 (–, $CH_2{}^a$), 67.8 (–, $CH_2{}^{a,b}$), 70.4 (–, $CH_2{}^{a,b}$), 84.5 (+, C-2^a), 97.3 (+, C-2^b), 108.0 (+, C-$4^a{}_{Ar}$), 108.6 (+, C-$4^a{}_{Ar}$), 123.9 (C_{quat}, C-$3^a{}_{Ar}$), 124.7 (C_{quat}, C-$3^b{}_{Ar}$), 128.0–128.5 (+, m, 5 C, $CH^{a,b}{}_{Ar}$), 135.6 (C_{quat}, C-$1'^b{}_{Ar}$), 136.2 (C_{quat}, C-$1'^a{}_{Ar}$), 140.3 (+, C-$2^a{}_{Ar}$), 141.0 (+, C-$2^b{}_{Ar}$), 143.2 (+, C-$5^b{}_{Ar}$), 143.5 (+, C-$5^a{}_{Ar}$), 151.3 (C_{quat}, C=O^a), 155.9 (C_{quat}, C=O^b) ppm. IR (neat): $\tilde{\nu}$ = 3434 [s, ν(OH)], 3065 [w ν_{Ar}(C–H)], 3034 (w), 2952 [m, $\nu(CH_2)$], 2884 [m, $\nu(CH_2)$], 1705 [s, ν(C=O)], 1603 [w, ν_{Ar}(C=C)], 1501 [m, ν_{Ar}(C=C)], 1419 (s), 1354 (s), 1306 (m), 1159 [m, ν(C–N)], 1127 [s, ν(C–O)], 1070 [s, ν(C–O)], 1020 [s, ν(C–O)], 978 (m), 875 (m), 777 (m), 699 (m), 602 (m) cm^{-1}. MS (FAB): *m*/*z* (%) = 304 $[M + H]^+$, 260, 236, 217, 208, 107 $[C_7H_7O]^+$, 102, 91 (100) $[C_7H_7]^+$, 69, 57, 43. HRMS ($C_{16}H_{18}NO_5$): calcd. 304.1185; found 304.1188.

2-(Furan-3-yl)-1,3-dioxan-5-amine (4f-H): Prepared by **GP B**; yield 72% (41.8 mg). The *cis*/*trans* ratio switched from 8:1 to 5.5:1 during the reaction.

***trans*-4f-H:** R_f = 0.21 (CH_2Cl_2/MeOH = 20:1). ^1H NMR (400 MHz, CD_3OD): δ = 3.01 (tt, ^3J = 4.9, ^3J = 10.2 Hz, 1 H, 5-H), 3.47 (m_c, 2 H, 4,6-H), 4.15 (ddd, ^2J = 10.0, ^3J = 4.9, ^4J = 1.4 Hz, 2 H, 4,6-H), 5.44 (s, 1 H, 2-H), 6.44 (dd, ^3J = 1.8, ^3J = 0.7 Hz, 4-H_{Ar}), 7.44 (t, ^3J = 1.7 Hz, 1 H, 5-H_{Ar}), 7.53 (m_c, 1 H, 2-H_{Ar}) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 45.2 (+, C-5), 73.7 (–, C-4,6), 97.8 (+, C-2), 109.6 (+, C-4_{Ar}), 125.7 (C_{quat}, C-3_{Ar}), 141.7 (+, C-2_{Ar}), 144.3 (+, C-5_{Ar}) ppm. IR (neat): $\tilde{\nu}$ = 3344 [w, $\nu(NH_2)$], 3142 [w, $\nu(NH_2)$], 2925 [w, $\nu(CH_2)$], 2853 [w, $\nu(CH_2)$], 2306 (vw), 1709 (w), 1657 [m, ν_{Ar}(C=C)], 1607 [m, ν_{Ar}(C=C)], 1502 (w), 1461 (w), 1409 (w), 1381 (w), 1287 (w), 1230 (w), 1201 [w, ν(C–N)], 1157 [w, ν(C–O)], 1097 [w, ν(C–O)], 1068 [w, ν(C–O)], 1021 [w, ν(C–O)], 875 (w), 793 (w), 744 (vw), 655 (vw), 602 (vw) cm^{-1}. MS (FAB): *m*/*z* (%) = 170 (100) $[M + H]^+$, 168, 149, 168, 111 $[C_6H_7O_2]^+$, 97, 95, 85. HRMS ($C_8H_{12}NO_3$): calcd. 170.0817; found 170.0820.

***cis*-4f-H:** R_f = 0.07 (CH_2Cl_2/MeOH = 20:1). ^1H NMR (400 MHz, CD_3OD): δ = 2.76 (m_c, 1 H, 5-H), 3.94 (m_c, 2 H, 4,6-H), 4.12 (ddd, ^2J = 12.1, ^3J = 3.2, ^4J = 1.4 Hz, 2 H, 4,6-H), 5.58 (s, 1 H, 2-H), 6.51 (dd, ^3J = 1.8, ^3J = 0.6 Hz, 4-H_{Ar}), 7.46 (t, ^3J = 1.7 Hz, 1 H, 5-H_{Ar}), 7.57 (m_c, 1 H, 2-H_{Ar}) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 46.7 (+, C-5), 72.7 (–, C-4,6), 98.5 (+, C-2), 109.5 (+, C-4_{Ar}), 126.0 (C_{quat}, C-3_{Ar}), 141.7 (+, C-2_{Ar}), 144.3 (+, C-5_{Ar}) ppm. IR (neat): $\tilde{\nu}$ = 3362 [m, $\nu(NH_2)$], 3148 [w, ν_{Ar}(C–H)], 2858 [w, $\nu(CH_2)$], 1709 (w), 1610 [w, ν_{Ar}(C=C)], 1547 [w, ν_{Ar}(C=C)], 1502 (w), 1450 (w), 1366 (m), 1280 (w), 1233 [w, ν(C–N)], 1150 [w, ν(C–O)], 1059 [w, ν(C–O)], 876 (w), 805 (w), 739 (w), 634 (w), 602 (w), 520 (vw) cm^{-1}. MS (EI): *m*/*z* (%) = 169 (7) $[M]^+$, 152 (5), 139 (2), 111 (20), 95 (12), 81 (4), 58 (20), 43 (100). HRMS ($C_8H_{11}NO_3$): calcd. 169.0739; found 169.0738.

Benzyl [2-(Thiophen-2-yl)-1,3-dioxan-5-yl]carbamate (4g-Cbz): Prepared by **GP A**; yield up to 46% (326 mg). Decomposition occurred after a short time. Mixture of isomers: *cis*/*trans* = 3:1. R_f = 0.57 (CH_2Cl_2/MeOH = 20:1). ^1H NMR (250 MHz, $CDCl_3$): δ = 3.59 (m_c, 2 H, 4^t,6^t-H), 3.75 (d, ^3J = 8.7 Hz, 1 H, 5^c-H), 3.99–4.16 (m, 5 H, 5^t,4^c,6^c-H), 4.34 (dd, ^3J = 4.4, ^2J = 10.9 Hz, 2 H, 4^t,6^t-H), 4.72 (m_c, 1 H, NH^t), 5.11 (s, 2 H, CH_2Ph^t), 5.13 (s, 2 H, CH_2Ph^c), 5.71 (s, 1 H, 2^t-H), 5.78 (s, 1 H, 2^c-H), 5.86 (d, ^3J = 8.7 Hz, 1 H, NH^c), 7.00 (m_c, 1 H, $5^{c,t}$-H_{Ar}), 7.14 (d, ^3J = 3.3 Hz, $4^{c,t}$-H_{Ar}), 7.28–7.41 (m, 6 H, $3^{c,t}$,$2'^{c,t}$–$6'^{c,t}$-H_{Ar}) ppm. MS (FAB): *m*/*z* (%) = 342 $[M + Na]^+$, 320 $[M + H]^+$, 236, 208, 165, 137, 113, 97, 91 (100) $[C_7H_7]^+$.

Benzyl 2-(Thiophen-2-yl)-4-(hydroxymethyl)oxazolidine-3-carboxylate (8g-Cbz): Prepared by **GP A**; yield up to 21% (149 mg). Decomposition occurred after a short time. Mixture of isomers: a/b = 1:7.5. R_f = 0.27 (CH_2Cl_2/MeOH = 20:1). ^1H NMR (250 MHz, $CDCl_3$): δ = 3.61–4.26 (m, 5 H, $4^{a,b}$-H, 2 $CH_2{}^{a,b}$), 4.93–5.16 (m, 2 H, $CH_2Ph^{a,b}$), 6.33 (s, 1 H, 2^b-H), 6.35 (s, 1 H, 2^a-H), 6.87–7.38 (m, 8 H, $3^{a,b}$–$5^{a,b}$,$2'^{a,b}$–$6'^{a,b}$-H_{Ar}) ppm. MS (FAB): *m*/*z* (%) = 342 $[M + Na]^+$, 320 $[M + H]^+$, 276, 236, 212, 208, 184, 113, 102, 91 (100) $[C_7H_7]^+$.

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