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Schiff Bases from TRIS and Formylpyridines: Structure and Mechanistic Rationale Aided by DFT Calculations

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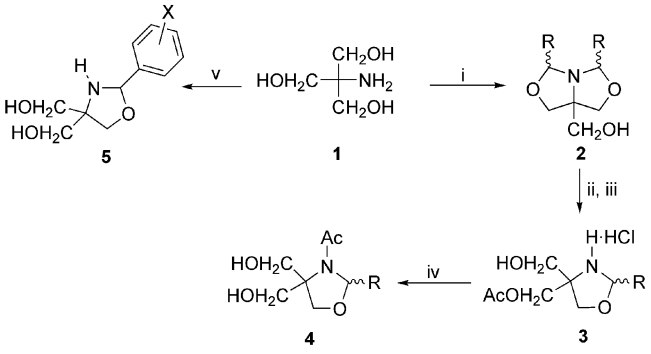
This paper describes the synthesis and structural elucidation of 1,3-oxazolidines derived from tris(hydroxymethyl)aminomethane (TRIS) and pyridine-based aldehydes. Divergent results were obtained with other formylpyridines, such as pyridoxal, in which intramolecular hydrogen-bonding largely stabilizes the iminic structure. The oxazolidines may undergo ring-opening under acetylating conditions to afford imines through different mechanistic pathways, which have also been evaluated by DFT calculations.

Introduction

Tris(hydroxymethyl)aminomethane (TRIS, **1**) is a versatile precursor of substituted 1,3-oxazolidines.[1] The usual synthetic strategy involves (Scheme 1, i–iv) the condensation of **1** with two moles of an aldehyde in benzene at reflux with azeotropic removal of water, which affords 1-aza-3,7-dioxabicyclo[3.3.0]octane derivatives **2**.[1,2] Acetylation with acetyl chloride followed by hydrolysis gives rise to the corresponding oxazolidine hydrochloride **3**. Neutralization with base ultimately causes acetyl migration to produce the *N*-acetyloxazolidine **4**.[3] This tedious protocol can significantly be abbreviated by an environmentally benign one-step synthesis, introduced recently by our group, that involves the direct condensation of **1** with aldehydes bearing electron-withdrawing substituents in an aqueous medium (Scheme 1, v).[4]

In an attempt to test the scope of this methodology in the case of heterocyclic aldehydes, we herein report the condensation of TRIS with formylpyridines and provide a full characterization by spectroscopic and crystallographic methods. In addition, the mechanism of this acetylation and ring closure has been interpreted with the aid of DFT calculations at the B3LYP/6-31G* level of theory.

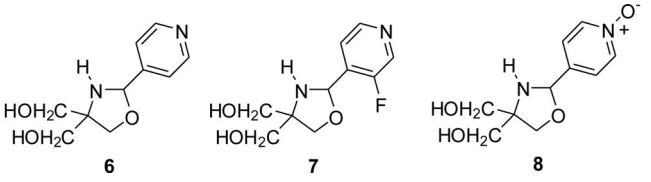


Scheme 1. Reagents and conditions: i) RCHO (2 mol), C_6H_6, Δ; ii) CH_3COCl; iii) H_2O; iv) NaOH (aq.) or $NaHCO_3$ (aq.); v) XC_6H_4CHO, H_2O.

Results and Discussion

Reaction of TRIS with Formyl Heterocycles

The condensation of **1** with formylpyridines, namely 4-formylpyridine, 3-fluoro-4-formylpyridine, and 4-formylpyridine *N*-oxide in aqueous medium did not produce the expected imine derivatives, but the alternative oxazolidines **6**–**8** instead (in yields of 51–91%).



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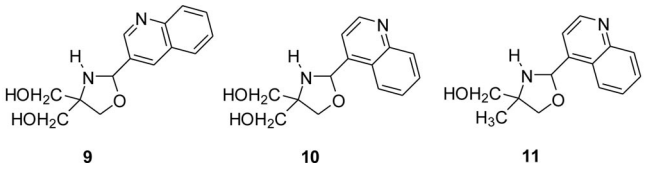
Extension of the reaction to 3-formyl- and 4-formylquinoline yielded the oxazolidines **9** (87%) and **10** (56%), respectively. Starting from a related amino alcohol, 2-amino-2-methyl-1,3-propanediol, and 4-formylquinoline, compound **11** was isolated in 27% yield.



9 **10** **11**

The structures attributed to **6**–**11** are consistent with their spectroscopic data and elemental analyses. Thus, their IR spectra show typical stretching bands for OH and NH bonds in the range 3500–3000 cm^{-1} and without any other bands above 1617 cm^{-1}, which could be attributed to the C=N bond, thereby ruling out an iminic structure. The presence of the oxazolidine ring is evidenced by NMR signals at around 5.5–6.0 ppm (2-H) and 85–90 ppm (C-2). Moreover, the structure of compound **6** was unequivocally established by single-crystal X-ray diffraction analysis (Figure 1 left).[5]

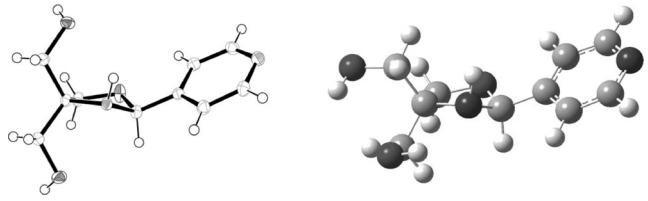


Figure 1. Crystal structure of **6** showing the conformation of the heterocyclic ring (left) and calculated geometry of **6** (right).

The geometry of **6** in the gas phase (Figure 1 right), computed with the hybrid functional B3LYP/6-31G*,[6,7] is almost coincidental with the solid-state structure, although the latter reveals a different orientation of the hydroxymethyl groups involved in intermolecular hydrogen-bonding.

The large coupling constant between the NH and 2-H protons in compounds **6**–**11** (ca. 11–12 Hz) points to an axial disposition of the N–H proton in solution, identical to that in the solid-state structure of **6**, which is inferred from the dihedral angle H–N–C–H (ca. 154°) and consistent with an E^1 conformation of the oxazolidine moiety (Figure 1).[8]

As in TRIS-based oxazolidines generated from aldehydes bearing electron-withdrawing groups, the above-mentioned arrangement reflects a strong anomeric effect. This is supported by a shorter N–C2 bond (1.473 Å) relative to the N–C4 length (1.491 Å) in compound **6**, both in the crystal and computationally-determined structures (Figure 2, Table S1 in the Supporting Information).

In addition, the stability associated with the n→σ* interaction was measured by NBO analysis of the optimized geometry of **6**. The strongest interaction involves the lone pair on the nitrogen atom (LPN) as donor and the σ^*_{C2-O1} orbital as acceptor fragment (Table 1).

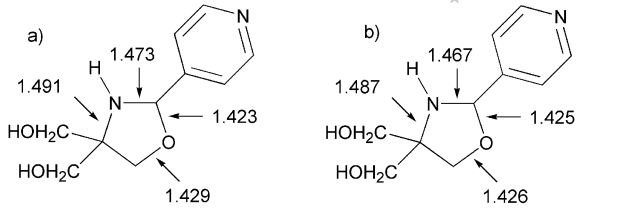


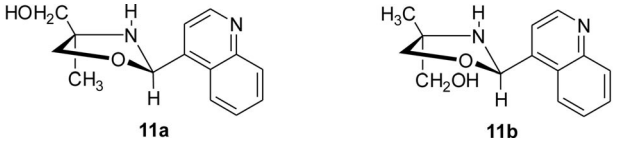
Figure 2. Bond lengths [Å] for compound **6** involved in the anomeric effect as determined by (a) X-ray crystallography and (b) DFT calculations.

Table 1. Second-order perturbational energies (E_2) in **6** from NBO analysis.

Donor NBO	Acceptor NBO	E_2[a] [kcal mol^{-1}]
LPN	σ^*_{C2-O1}	8.34
LPO1	σ^*_{C2-N}	1.57
LPO1	σ^*_{C2-N}	5.86

[a] Determined at the B3LYP/6-31G* level of theory.

Oxazolidine **11** was also observed as a diastereomeric mixture (ratio **11a**/**11b**, 54:46) as a result of the existence of two stereogenic centers.

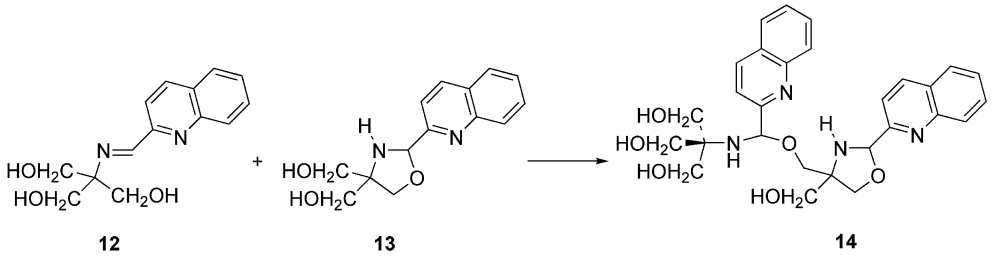


11a **11b**

When 2-formylquinoline was employed as the starting material, the expected oxazolidine **13** was not detected. Instead a substance identified as dimer **14** was isolated in 10% yield as a single diastereomer, for which crystals suitable for X-ray analysis could not be obtained.

Both **13** and **14** arise from the initial imine **12**, which may add a hydroxy group either intramolecularly giving rise to **13** or intermolecularly to another molecule of **12** to produce **14** (Scheme 2). The structure of the latter is also supported by its spectroscopic data. With the sole exception of the stretching bands for the hydroxy (3600–3000 cm^{-1}) and amino (3280–3250 cm^{-1}) groups, the IR spectrum does not show any signal above 1617 cm^{-1}. The ^1H and ^{13}C NMR spectra recorded in [D_6]DMSO show two signal sets in contrast to **13**. The presence of two protons at δ = 5.67 and 5.21 ppm along with their corresponding carbon resonances at δ = 94.12 and 94.71 ppm (Figure 3) is consistent with the typical shifts found for a hemiaminal ether, that is, combining an open fragment and a cyclic oxazolidine.

The oxazolidine moiety also manifests itself by the existence of three diastereotopic methylenes centered at δ = 4.14 (J_{gem} = 8.5 Hz), 4.07 (J_{gem} = 8.5 Hz), and 3.79 ppm (J_{gem} = 10.5 Hz), which correlate with carbon resonances at δ = 75.13, 72.82, and 65.56 ppm, respectively. The acyclic hydroxymethylene fragment shows a singlet signal at δ = 3.25 ppm (6 H) that correlates with the carbon signal at δ = 63.99 ppm (3 C). Furthermore, the mass spectrum (Figure S1) does not exhibit any line attributable to the molecular peak, although the fragmentation pattern supports the



Scheme 2.

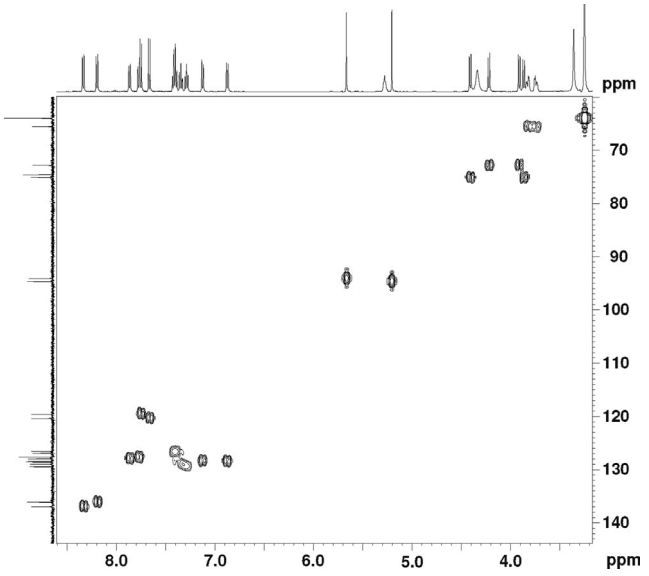
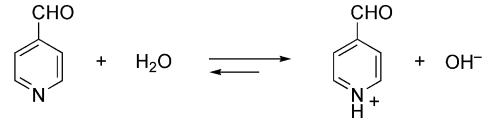


Figure 3. Heteronuclear multiple quantum correlation (HMQC) experiment in **14**.

proposed structure. The most important molecular subunits and their relative intensities are shown in Scheme S1 in the Supporting Information. The HRMS-CI analysis of the most abundant fragment (*m*/*z* = 400; 100%) is also in complete agreement with the proposed structure for **14**.

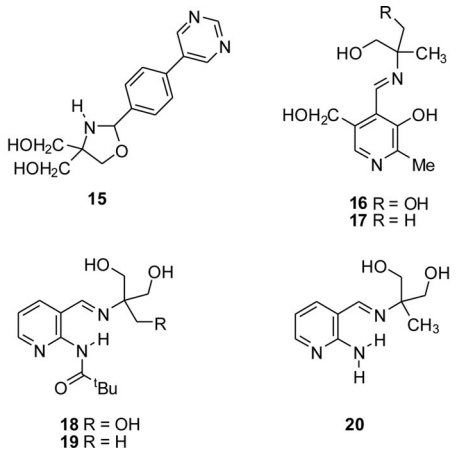
The facile formation of oxazolidines from formylpyridines or -quinolines should be ascribed to the π-deficient character and basicity of such heterocycles (pK_a ≈ 4.77 for 4-formylpyridine[9]).

In aqueous or hydro-alcoholic solution, these nitrogen-containing rings can be partially protonated, which enhances their reactivity in nucleophilic addition, and they behave as electron-withdrawing benzaldehydes (Schemes 3 and 4).[4] In a similar way, 4-formylpyridine *N*-oxide would act as a protonated 4-formylpyridine.



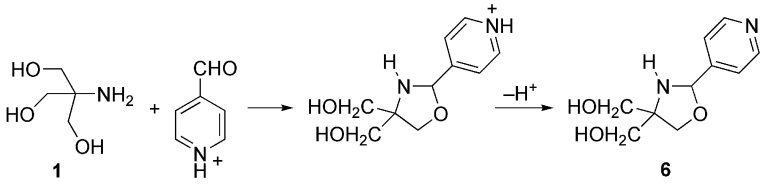
Scheme 3.

Accordingly, basic substituents susceptible to protonation play the role of an electron-withdrawing group capable of activating the aldehyde function. Thus, the condensation of **1** with 5-(4-formylphenyl)pyrimidine led to the corresponding oxazolidine **15** in almost quantitative yield (98%).



In stark contrast, the reactions of amino alcohols such as TRIS (**1**), 2-amino-2-methyl-1,3-propanediol, and 2-amino-2-methyl-1-propanol with pyridoxal, *N*-(3-formyl-2-pyridinyl)-2,2-dimethylpropanamide, and 2-amino-3-pyridinecarboxaldehyde afforded iminic structures **16**–**20** in yields of 32–84%.

Again, the proposed structures are supported by spectroscopic data. The imine function is evidenced by an IR absorption at around 1640 cm^{-1} (C=N), a singlet signal for



Scheme 4.

the iminic proton at around 8.8 ppm in compounds **16** and **17**, and at around 8.4 ppm in **18**–**20**; the iminic carbon resonates at around 161 ppm in all cases. The IR band at around 1680–1700 cm^{-1} along with a carbon signal at around 176 ppm also evidence the amide function in **18** and **19**. Finally, the existence of a downfield-shifted singlet at around 15 ppm in compounds **16** and **17** and at around 12 ppm in the cases of **18** and **19** suggests a strong intramolecular hydrogen bond involving the iminic nitrogen and a vicinal OH or NH group. The solid-state structures of **19** and **20** were determined by X-ray crystallographic analyses (Figures 4 and 5)[5] and are in agreement with those inferred from data in solution.

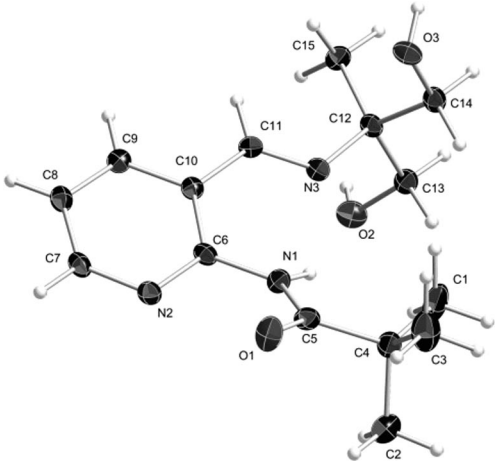


Figure 4. ORTEP diagram of imine **19** with ellipsoids drawn at the 50% probability level.

Thus, both **19** and **20** show in their crystal structures an intramolecular hydrogen bond between the NH group at C-2 of the pyridine ring and the iminic nitrogen. Moreover, there are additional inter- and intramolecular hydrogen bonds involving other atomic positions (Table 2, Figure 6). Clearly the presence of intramolecular hydrogen-bonding in

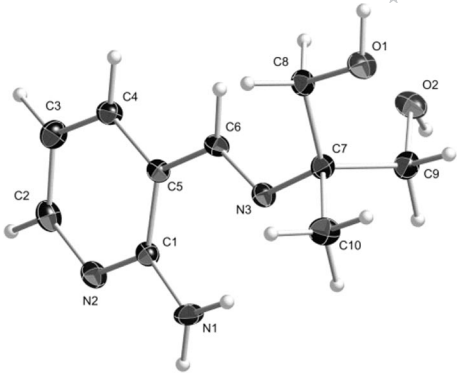


Figure 5. Thermal ellipsoid plot of imine **20** drawn at the 50% probability level.

compounds **16**–**20** contributes to the preservation of the iminic structure and avoids their further evolution to oxazolidines.

Table 2. Hydrogen bonds observed in the crystal structures of **19** and **20**.

	D–H···A	*d*(D–H) [Å]	*d*(H···A) [Å]	*d*(D···A) [Å]	∠(DHA) [°]
19	O2–H2···O3	0.84	1.92	2.74	162.7
	O3–H3···N2	0.84	1.95	2.77	164.2
	O3–H3···O1	0.84	2.55	3.07	121.0
	N1–H1···N3	0.88	2.16	2.75	124.5
20	N1–H1B···N3	0.91	2.02	2.72	132.4
	O1–H1O···O2	0.90	1.82	2.72	174.9
	O2–H2O···N2	0.92	1.80	2.72	175.0

Oxazolidine–Imine Equilibria

Oxazolidines **6**–**11** and **15** in [D_6]DMSO solution are in equilibrium with the corresponding imines **21**–**27**, the former cyclic structures being prevalent (>80%). Such equilibria can easily be monitored by NMR spectra, which show bands typical of imines (Table 3): A singlet signal for the iminic proton at around 8.50–9.00 ppm and the C=N resonance at around δ = 156–158 ppm.

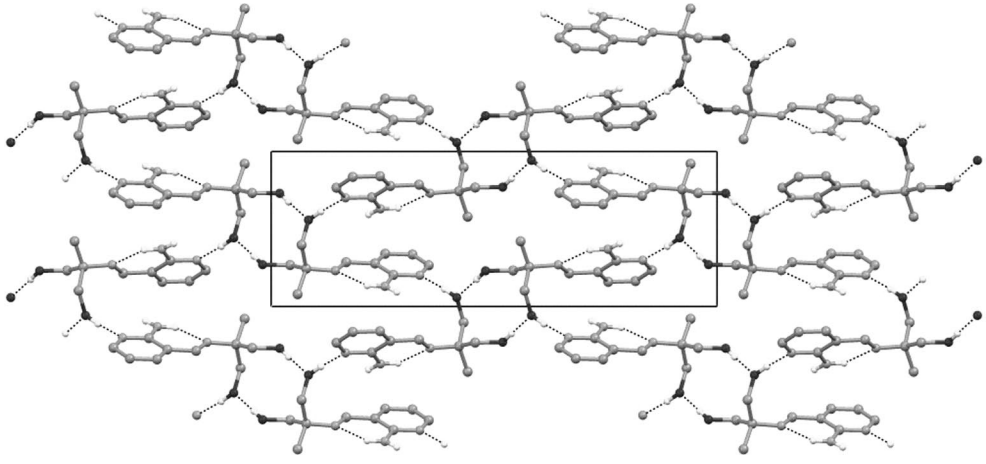
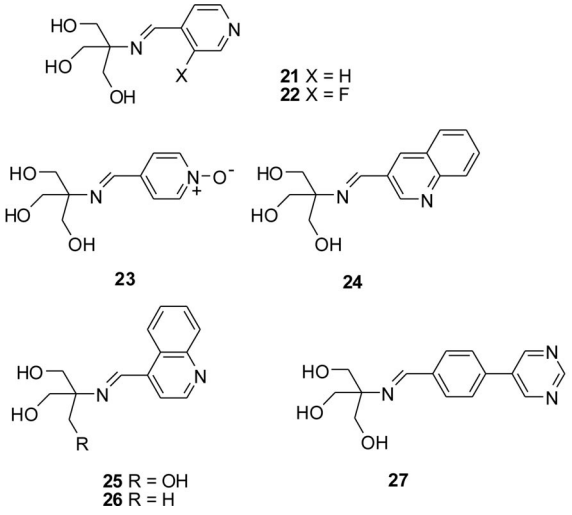


Figure 6. Extended hydrogen-bonding sheet in the *bc* plane for compound **20**.

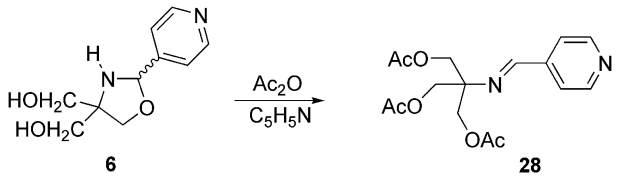
Table 3. Composition of the oxazolidine–imine equilibria and NMR spectroscopic data of imines **21**–**27**.

Equilibrium	Population	δ [ppm]	
		N=C*H* (mult.)	N=*C*H
6 ⇋ **21**	96:4	8.44 (s)	158.51
7 ⇋ **22**	97:3	8.29 (s)	158.48
8 ⇋ **23**	81:19	8.39 (s)	156.40
9 ⇋ **24**	89:11	8.67 (s)	157.86
10 ⇋ **25**	98:2	9.12 (s)	158.01
11 ⇋ **26**	85:15	9.02 (s)	156.93
15 ⇋ **27**	91:9	8.51 (s)	158.95



Acetylation of 4,4-Bis(hydroxymethyl)-2-(4-pyridyl)-oxazolidine

To compare the reactivity of the oxazolidines derived from formylpyridines against those of substituted benzaldehydes,[4] we scrutinized the acetylation of **6** with acetic anhydride in pyridine, which allowed us to isolate the per-*O*-acetylated imine **28** in 70% yield (Scheme 5). As usual, its analytical and spectroscopic data are consistent with this structure: The IR absorption at 1650 cm^{-1} (C=N stretching band) as well as the proton and carbon resonances at δ = 8.36 and 159.14 ppm are characteristic of the imine function. ^{1}H NMR monitoring of the reaction conducted with deuteriated reagents [C_5D_5N and $(CD_3CO)_2O$] is shown in Figure 7 and evidences the complete transformation of **6** into **28**.



Scheme 5.

The reaction leads quantitatively to **28** after 24 h via the di-*O*-acetyl derivative **29** (Scheme 6). The latter is formed rapidly as the process is essentially complete within 15 min. Only the resulting imine **28** could be detected at the end. This behavior appears to be general as ^{1}H NMR monitoring of the acetylation of **10** also evidences the formation of the diacetyl intermediate, which evolves to produce ultimately the corresponding imine (see Figure S2 in the Supporting Information).

Acetylation Mechanism: Theoretical Rationale

The acetylation protocol begins with the formation of diacetate **29** by acetylation of two hydroxymethyl groups. Three possible steps can then take place as depicted in Scheme 7: a) Attack of acetic anhydride on the endocyclic oxygen of **29** with concomitant ring-opening of the oxazolidine ring yielding iminium ion **30**, which, after deprotonation, releases the per-*O*-acetylated imine **28**, b) attack of the acetylating species on the nitrogen atom of the parent oxazolidine to give tetrahedral intermediate **31**, which leads to an *N*-acetyloxazolidine **32** by deprotonation, and c) at-

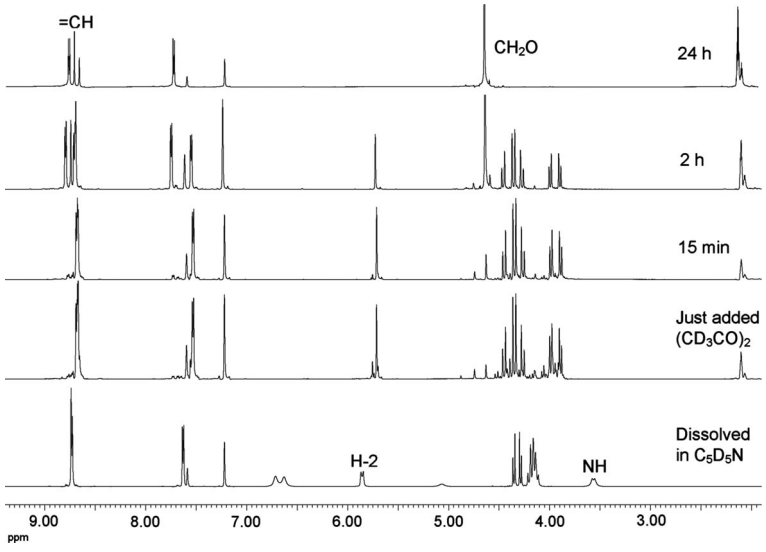
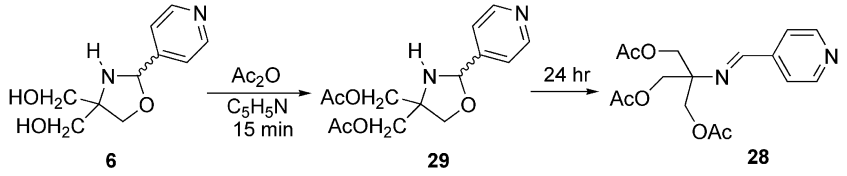
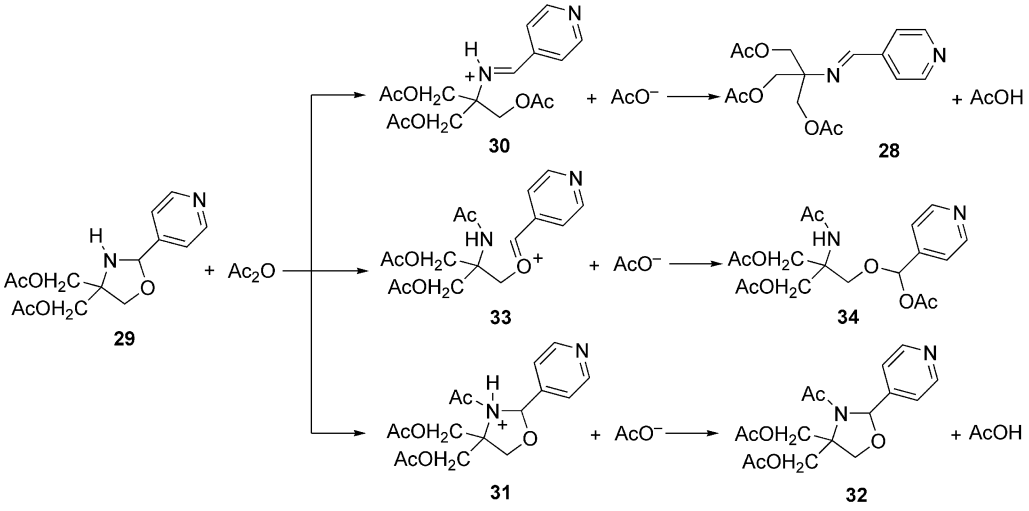


Figure 7. Evolution of the acetylation of **6** to **28**.



Scheme 6.



Scheme 7. Putative pathways for the acetylation of pyridine-substituted oxazolidines.

tack on the nitrogen atom with simultaneous ring-opening of the oxazolidine ring to afford oxonium ion **33**, which further adds acetate to give the acetal derivative **34**. Alternatively, **33** could also be generated by the ring-opening of **31**.

Table 4 presents the energies estimated for the above transformations in pyridine. Calculations with an SMD (B3LYP/6-31G*) SCRF model to take into account the solvent effect show that the formation of **28** should be the favored step because the intermediate **30**, which leads to **28**, is stabilized by around 16 kcal/mol relative to **31** and **33**, that is, the intermediates that yield the alternative products **32** and **34**, respectively. Figure 8 shows the energy profile estimated for these transformations.

Table 4. Energies calculated for the different mechanisms for the acetylation of **29**.[a]

	E_{rel} [kcal mol^{-1}]
29 + Ac_2O	0.00
30 + AcO^-	+28.63
28 + AcOH	–5.62
31 + AcO^-	+44.70
32 + AcOH	–9.76
33 + AcO^-	+48.57
34	–6.43

[a] Determined at the B3LYP/6-31G* level of theory.

The fact that both *N*-acetyloxazolidine **32** and acetal **34** are more stable species than **28** suggests that the latter should be the kinetically-controlled product. The differences observed between the reaction pathways can presumably be attributed to a stabilizing anomeric effect in the oxazolidines, a fact also accounting for the greater nucleophilicity of the oxygen atom relative to the alternative nitrogen.

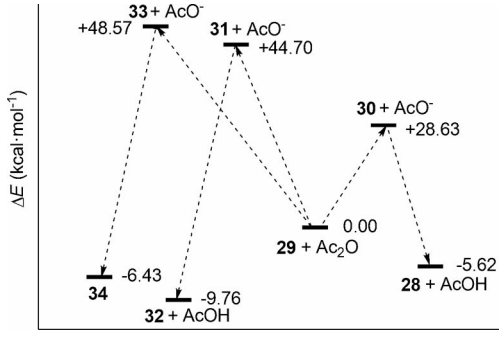


Figure 8. Schematic energy diagram for the acetylation of **29** in pyridine.

Conclusions

Formylpyridines and TRIS react under mild aqueous conditions to produce 1,3-oxazolidines in good yields. Spectroscopic and crystallographic data fully support the structures of such substances and reflect the existence of a stabilizing anomeric effect. The reaction can also be extended to formylquinolines, for which the anomalous dimer **14** has also been characterized. An evaluation of oxazolidine–imine equilibria in DMSO solution evidences the greater stability of the former. Oxazolidines undergo regiospecific

ring-opening under acetylating conditions leading to per-*O*-acetyl imines. A theoretical study in both the gas phase and in pyridine points to the intermediacy of an iminium ion as the preferential pathway, which also accounts for the greater nucleophilicity of the oxygen atom as the reaction site.

Experimental Section

General Methods: Melting points were determined with Gallenkamp and Electrothermal apparatuses. IR spectra were recorded in the range of 4000–600 cm^{-1} with a FT-IR THERMO spectrophotometer. Solid samples were recorded in KBr (Merck) pellets. NMR spectra were recorded with Bruker 400 and 500 AC/PC instruments in different solvent systems. Assignments were confirmed by homo- and hetero-nuclear double-resonance and DEPT (distortionless enhancement by polarization transfer) experiments. TMS was used as the internal standard (δ = 0.00 ppm) and all J values are given in Hz. Microanalyses were performed with a Leco 932 analyzer. High-resolution mass spectra (chemical ionization) were recorded with an Autospec-Q spectrometer by the Servicio de Espectrometría de Masas de la Universidad de Sevilla (Spain).

General Procedure for the Synthesis of 2-(Hetero)aryl-4,4-bis(hydroxymethyl)oxazolidines: A solution of the corresponding aldehyde (16.5 mmol) in a small volume of methanol was slowly added to a solution of α,α,α-tris(hydroxymethyl)methylamine (2.0 g, 16.5 mmol) in water (16 mL). The mixture was stirred at room temperature to yield a precipitate within a few minutes. When the mixture did not precipitate spontaneously, it was evaporated in vacuo to give a solid on standing or on cooling. The resulting product was collected by filtration, washed successively with cold water, ethanol, and diethyl ether, and recrystallized from ethanol or methanol.

4,4-Bis(hydroxymethyl)-2-(4-pyridyl)oxazolidine (6): Yield 3.16 g, 91%; m.p. 117–119 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3500–3100 (OH, NH), 1612, 1488 (arom.) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.57 (d, J = 4.0 Hz, 2 H, H-arom.), 7.42 (d, J = 4.8 Hz, 2 H, H-arom.), 5.43 (d, $J_{2\text{-H,NH}}$ = 10.8 Hz, 1 H, 2-H), 4.84 (br. s, 2 H, OH), 3.70 (d, J = 8.0 Hz, 1 H, CH_2, ring), 3.67 (d, J = 8.0 Hz, 1 H, CH_2, ring), 3.44 (s, 2 H, CH_2), 3.41 (d, J = 11.2 Hz, 1 H, CH_2), 3.32 (d, J = 11.2 Hz, 1 H, CH_2), 2.96 (d, $J_{NH,2\text{-H}}$ = 10.8 Hz, 1 H, NH) ppm. ^{13}C NMR: δ = (100 MHz, [D$_6$]DMSO): 149.6, 149.1, 121.2 (C-arom.), 90.0 (C-2), 69.1 (C-5), 67.3 (C-4), 62.7, 62.4 (2 C, CH_2) ppm. $C_{10}H_{14}N_2O_3$ (210.23): calcd. C 57.13, H 6.71, N 13.33; found C 57.12, H 6.70, N 13.22.

Spectroscopic Data for 21: ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.44 (s, 1 H, CH=N), 8.64 (d, J = 5.6 Hz, 2 H, H-arom.), 7.71 (d, J = 5.6 Hz, 2 H, H-arom.), 3.62 (s, 6 H, CH_2) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 158.5 (C=N), 150.5, 123.7, 122.3 (C-arom.), 68.8 (C-N), 62.0 (3 C, CH_2) ppm.

2-(3-Fluoropyridin-4-yl)-4,4-bis(hydroxymethyl)oxazolidine (7): Yield 3.38 g, 90%; m.p. 102–103 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3400–3000 (OH, NH), 1617, 1571 (arom.), 1078, 1057 (C–O) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.54 (d, J = 2.0 Hz, 1 H, H-arom.), 8.46 (dd, J = 0.8, J = 4.8 Hz, 1 H, H-arom.), 7.59 (t, J = 6.0 Hz, 1 H, H-arom.), 5.69 (s, 1 H, 2-H), 4.81 (t, J = 6.0 Hz, 1 H, OH), 4.80 (t, J = 6.0 Hz, 1 H, OH), 3.76 (d, J = 7.8 Hz, 1 H, CH_2, ring), 3.70 (d, J = 7.8 Hz, 1 H, CH_2, ring), 3.46 (d, $J_{CH2,OH}$ = 5.6 Hz, 2 H, CH_2), 3.43 (dd, $J_{CH2,OH}$ = 5.6, $J_{H,H}$ = 11.2 Hz, 1 H, CH_2), 3.36 (dd, $J_{CH2,OH}$ = 5.6, $J_{H,H}$ = 11.2 Hz, 1 H, CH_2), 3.08 (s, 1 H, NH) ppm. ^{13}C NMR: δ = (100 MHz, [D$_6$]DMSO): 157.5 (d, $J_{C\text{-F}}$ = 256.7 Hz), 146.6 (d, $J_{C\text{-F}}$ = 4.9 Hz), 138.3 (d, $J_{C\text{-F}}$ = 23.5 Hz), 136.4 (d, $J_{C\text{-F}}$ = 10.9 Hz), 122.4 (C-arom.), 85.8 (d, $J_{C2,F}$ = 1.3 Hz, C-2), 69.6 (C-5), 67.8 (C-4), 63.0, 62.9 (2 C, CH_2) ppm. $C_{10}H_{13}FN_2O_3$ (228.22): calcd. C 52.63, H 5.74, N 12.27; found C 52.69, H 5.66, N 12.22.

Spectroscopic Data for 22: ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.69 (d, J = 5.2 Hz, 1 H, H-arom.), 8.37 (d, J = 4.0 Hz, 1 H, H-arom.), 8.29 (s, 1 H, CH=N), 8.21 (s, 1 H, H-arom.), 3.62 (s, 6 H, CH_2) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 158.5 (C=N), 151.5, 146.2, 139.3, 130.4, 124.1 (C-arom.), 69.5 (C-N), 62.0 (3 C, CH_2) ppm.

4-[4,4-Bis(hydroxymethyl)oxazolidin-2-yl]pyridine *N*-Oxide (8): Yield 1.90 g, 51%; m.p. 109–110 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3400–3000 (OH, NH), 1617, 1491, 1446 (arom.), 1216, 1179 (N–O), 1077, 1052, 1021 (C–O, C–N), 871, 851 (py) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.19 (d, J = 6.4 Hz, 2 H, H-arom.), 7.40 (d, J = 6.4 Hz, 2 H, H-arom.), 5.43 (s, 1 H, 2-H), 4.80 (s, 2 H, OH), 3.69 (d, J = 8.0 Hz, 1 H, CH_2, ring), 3.64 (d, J = 8.0 Hz, 1 H, CH_2, ring), 3.43 (s, 2 H, CH_2), 3.40 (m, 1 H, CH_2), 3.31 (m, 1 H, CH_2), 3.00 (s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 139.0, 138.8, 124.7 (C-arom.), 89.8 (C-2), 69.7 (C-5), 67.8 (C-4), 63.1 (2 C, CH_2) ppm. $C_{10}H_{14}N_2O_4$ (226.23): calcd. C 53.09, H 6.24, N 12.38; found C 52.79, H 6.18, N 12.01.

Spectroscopic Data for 23: ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.39 (s, 1 H, CH=N), 8.24 (d, J = 5.2 Hz, 2 H, H-arom.), 7.77 (d, J = 5.2 Hz, 1 H, H-arom.), 3.60 (s, 6 H, CH_2) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 156.4 (C=N), 139.5, 133.7, 125.2 (C-arom.), 68.6 (C-N), 62.2 (3 C, CH_2) ppm.

4,4-Bis(hydroxymethyl)-2-(3-quinolinyl)oxazolidine (9): Yield 3.74 g, 87%; m.p. 157–158 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3268, 3190 (OH, NH), 1593, 1501, 1462 (arom.) cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 8.99 (s, 1 H, H-arom.), 8.39 (s, 1 H, H-arom.), 8.05 (d, J = 8.5 Hz, 1 H, H-arom.), 8.02 (d, J = 8.0 Hz, 1 H, H-arom.), 7.77 (t, J = 8.0 Hz, 1 H, H-arom.), 7.62 (t, J = 7.5 Hz, 1 H, H-arom.), 5.69 (d, $J_{2\text{-H,NH}}$ = 10.5 Hz, 1 H, 2-H), 4.87 (t, J = 5.5 Hz, 2 H, OH), 3.84 (d, J = 8.0 Hz, 1 H, CH_2, ring), 3.78 (d, J = 8.0 Hz, 1 H, CH_2, ring), 3.54 (d, $J_{CH2,OH}$ = 5.5 Hz, 2 H, CH_2), 3.52 (dd, $J_{CH2,OH}$ = 5.5, $J_{H,H}$ = 11.0 Hz, 1 H, CH_2), 3.44 (dd, $J_{CH2,OH}$ = 5.5, $J_{H,H}$ = 11.0 Hz, 1 H, CH_2), 3.12 (d, $J_{NH,2\text{-H}}$ = 10.5 Hz, 1 H, NH) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 150.0, 148.0, 133.8, 133.6, 130.1, 129.2, 128.8, 127.7, 127.3 (C-arom.), 90.4 (C-2), 69.8 (C-5), 68.0 (C-4), 63.4, 63.2 (2 C, CH_2) ppm. $C_{14}H_{16}N_2O_3$ (260.29): calcd. C 64.60, H 6.20, N 10.76; found C 64.48, H 6.34, N 10.70.

Spectroscopic Data for 24: ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 9.36 (d, J = 2.0 Hz, 1 H, H-arom.), 8.67 (s, 1 H, CH=N), 8.64 (d, J = 1.6 Hz, 1 H, H-arom.), 8.08 (m, 2 H, H-arom.), 7.83 (m, 1 H, H-arom.), 7.66 (m, 1 H, H-arom.), 4.54 (t, J = 5.6 Hz, 3 H, OH), 3.68 (d, J = 5.6 Hz, 6 H, CH_2) ppm. ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 157.9 (C=N), 148.7, 136.4, 130.9, 130.0, 129.3, 127.8 (C-arom.), 68.6 (C-N), 62.2 (3 C, CH_2) ppm.

4,4-Bis(hydroxymethyl)-2-(4-quinolinyl)oxazolidine (10): Yield 2.41 g, 56%; m.p. 149–150 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3512, 3453, 3291, 3136 (OH, NH), 1593, 1577, 1510, 1467, 1439, 768 (arom.), 1054, 1002 (C–O, C–N) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.93 (d, J = 4.4 Hz, 1 H, H-arom.), 8.35 (d, J = 8.4 Hz, 1 H, H-arom.), 8.05 (d, J = 8.4 Hz, 1 H, H-arom.), 7.77 (t, J = 8.0 Hz, 1 H, H-arom.), 7.71 (d, J = 4.4 Hz, 1 H, H-arom.), 7.63 (d, J = 8.0 Hz, 1 H, H-arom.), 6.08 (d, $J_{2\text{-H,NH}}$ = 11.2 Hz, 1 H, 2-H), 4.92 (t, J = 5.6 Hz, 1 H, OH), 4.85 (t, J = 5.6 Hz, 1 H, OH), 3.84 (s, 2 H, CH_2, ring), 3.58 (d, $J_{CH2,OH}$ = 5.6 Hz, 2 H, CH_2), 3.48 (dd, $J_{CH2,OH}$ = 6.0, $J_{H,H}$ = 11.2 Hz, 1 H, CH_2), 3.43 (dd, $J_{CH2,OH}$ = 5.6, $J_{H,H}$ =

11.2 Hz, 1 H, CH_2), 3.07 (d, $J_{NH,2-H}$ = 11.2 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 150.9, 148.2, 145.7, 129.7, 129.7, 126.8, 125.9, 125.7, 117.8 (C-arom.), 88.8 (C-2), 69.2 (C-5), 68.2 (C-4), 63.4, 62.7 (2 C, CH_2) ppm. $C_{14}H_{16}N_2O_3$ (260.29): calcd. C 64.60, H 6.20, N 10.76; found C 64.45, H 6.19, N 10.97.

Spectroscopic Data for 25: ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 9.12 (s, 1 H, CH=N), 9.01 (d, J = 4.4 Hz, 1 H, H-arom.), 8.85 (d, J = 8.4 Hz, 1 H, H-arom.), 8.10 (d, J = 8.4 Hz, 2 H, H-arom.), 3.74 (s, 6 H, CH_2) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 158.0 (C=N), 150.8, 148.9, 139.9, 129.9, 127.8, 125.2, 121.0 (C-arom.), 69.7 (C-N), 62.3 (3 C, CH_2) ppm.

4-Hydroxymethyl-4-methyl-2-(4-quinolinyl)oxazolidine (11): From 2-amino-2-methyl-1,3-propanediol and following the same procedure as used for **10**, compound **11** was isolated (1.09 g, 27%) as a mixture of diastereomers **11a** and **11b** (ratio 54:46; m.p. 102–103 °C). IR (KBr): $\tilde{\nu}_{max}$ = 3477, 3262, 3226 (OH, NH), 1597, 1569, 1509, 766 (arom.), 1111, 1057, 1006 (C–O, C–N) cm^{-1}. $C_{14}H_{16}N_2O_2$ (244.29): calcd. C 68.83, H 6.60, N 11.47; found C 68.66, H 6.65, N 11.24.

Spectroscopic Data for 11a: ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 8.91 (s, 1 H, H-arom.), 8.32 (t, J = 8.4 Hz, 1 H, H-arom.), 8.04 (dd, J = 4.4, J = 8.0 Hz, 1 H, H-arom.), 7.77 (dd, J = 7.3, J = 10.8 Hz, 1 H, H-arom.), 7.71 (d, J = 3.8 Hz, 1 H, H-arom.), 7.63 (dd, J = 6.6, J = 13.4 Hz, 1 H, H-arom.), 6.12 (d, $J_{2-H,NH}$ = 12.0 Hz, 1 H, 2-H), 4.93 (m, 1 H, OH), 3.91 (d, J = 7.2 Hz, 1 H, CH_2, ring), 3.52 (d, J = 5.6 Hz, 1 H, CH_2, ring), 3.30 (d, $J_{CH2,OH}$ = 4.4 Hz, 1 H, CH_2), 3.12 (d, $J_{NH,2-H}$ = 11.6 Hz, 1 H, NH), 1.25 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 150.9–117.5 (C-arom.), 88.4 (C-2), 72.9 (C-5), 65.5 (CH_2), 64.1 (C-4), 22.3 (CH_3) ppm.

Spectroscopic Data for 11b: ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 8.91 (s, 1 H, H-arom.), 8.32 (t, J = 8.4 Hz, 1 H, H-arom.), 8.04 (dd, J = 4.4, J = 8.0 Hz, 1 H, H-arom.), 7.77 (dd, J = 7.3, J = 10.8 Hz, 1 H, H-arom.), 7.71 (d, J = 3.8 Hz, 1 H, H-arom.), 7.63 (dd, J = 6.6, J = 13.4 Hz, 1 H, H-arom.), 6.09 (d, $J_{2-H,NH}$ = 12.0 Hz, 1 H, 2-H), 4.93 (m, 1 H, OH), 3.86 (d, J = 7.2 Hz, 1 H, CH_2, ring), 3.52 (d, J = 5.6 Hz, 1 H, CH_2, ring), 3.48 (dd, $J_{CH2,OH}$ = 7.2, $J_{H,H}$ = 14.4 Hz, 1 H, CH_2), 3.39 (dd, $J_{CH2,OH}$ = 5.6, 14.4 Hz, 1 H, CH_2), 3.26 (d, $J_{NH,2-H}$ = 11.2 Hz, 1 H, NH), 1.13 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 150.9–117.5 (C-arom.), 89.1 (C-2), 73.1 (C-5), 66.1 (CH_2), 64.1 (C-4), 22.3 (CH_3) ppm.

Spectroscopic Data for 26: ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 9.02 (s, 1 H, CH=N), 9.00 (d, J = 3.6 Hz, 1 H, H-arom.), 8.35–764 (m, 5 H, H-arom.), 3.54 (s, 6 H, CH_2) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 156.9 (C=N), 150.9–111.8 (C-arom.), 66.8 (C-N), 66.2 (3 C, CH_2) ppm.

4-[6′-Hydroxy-5′,5′-bis(hydroxymethyl)-3′-(2-quinolinyl)-4′-aza-2′-oxahexyl]-4-hydroxymethyl-2-(2-quinolinyl)oxazolidine (14): Yield 0.43 g, 10%; m.p. 164–165 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3594, 3453 (OH, NH), 1599, 1560, 1503, 1467 (arom.) cm^{-1}. ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 8.33 (d, J = 8.5 Hz, 1 H, H-arom.), 8.19 (d, J = 8.5 Hz, 1 H, H-arom.), 7.86 (d, J = 8.5 Hz, 1 H, H-arom.), 7.77 (d, J = 9.5 Hz, 1 H, H-arom.), 7.75 (d, J = 8.5 Hz, 1 H, H-arom.), 7.67 (d, J = 8.5 Hz, 1 H, H-arom.), 7.42 (d, J = 7.5 Hz, 1 H, H-arom.), 7.39 (d, J = 7.5 Hz, 1 H, H-arom.), 7.35 (t, J = 7.5 Hz, 1 H, H-arom.), 7.29 (t, J = 7.5 Hz, 1 H, H-arom.), 7.12 (d, J = 8.5 Hz, 1 H, H-arom.), 6.87 (d, J = 8.5 Hz, 1 H, H-arom.), 5.67 (s, 1 H, 2-H), 5.28 (br. s, 1 H, OH), 5.21 (s, 1 H, OCHN), 4.41 (d, J = 9.0 Hz, 1 H, CH_2), 4.34 (br. s, 3 H, OH), 4.22 (d, J = 8.5 Hz, 1 H, CH_2), 3.91 (d, J = 8.5 Hz, 1 H, CH_2), 3.87 (d, J = 8.5 Hz, 1 H, CH_2), 3.83 (dd, $J_{CH2,OH}$ = 4.0, $J_{H,H}$ = 10.5 Hz, 1 H, CH_2), 3.74 (dd, $J_{CH2,OH}$ = 4.0, $J_{H,H}$ = 10.5 Hz, 1 H, CH_2), 3.25 (s, 6 H, CH_2), 1.29 (br. s, 2 H, NH) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 159.6–119.6 (C-arom.), 94.7 (OCHN), 94.1 (C-2), 75.1 (CH_2), 74.6 (C-N), 72.8 (CH_2), 65.6 (CH_2), 64.0 (3 C, CH_2), 57.1 (C-N) ppm. HRMS (CI): calcd. for $C_{24}H_{22}N_3O_3^+$ 400.1661; found 400.1662.

4,4-Bis(hydroxymethyl)-2-[4-(pyrimidin-5-yl)phenyl]oxazolidine (15): Yield 4.50 g, 95%; m.p. 165–166 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3348, 3226 (OH, NH), 1574, 1552, 1490 (arom.) cm^{-1}. ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 9.20 (s, 1 H, H-arom.), 9.16 (s, 1 H, H-arom.), 7.82 (d, J = 8.5 Hz, 2 H, H-arom.), 7.60 (d, J = 8.0 Hz, 2 H, H-arom.), 5.45 (d, $J_{2-H,NH}$ = 11.0 Hz, 1 H, 2-H), 4.87 (t, J = 5.5 Hz, 1 H, OH), 4.76 (t, J = 5.5 Hz, 1 H, OH), 3.74 (d, J = 7.5 Hz, 1 H, CH_2, ring), 3.70 (d, J = 7.5 Hz, 1 H, CH_2, ring), 3.49 (dd, $J_{CH2,OH}$ = 6.0, $J_{H,H}$ = 11.0 Hz, 1 H, CH_2), 3.46 (d, $J_{CH2,OH}$ = 5.5 Hz, 2 H, CH_2), 3.43 (dd, $J_{CH2,OH}$ = 6.0, $J_{H,H}$ = 11.0 Hz, 1 H, CH_2), 2.83 (d, $J_{NH,2-H}$ = 11.0 Hz, 1 H, NH) ppm. ^{13}C NMR (125 MHz, [D$_6$]-DMSO): δ = 157.8, 155.2, 141.7, 134.2, 133.4, 127.7, 127.3 (C-arom.), 91.6 (C-2), 69.6 (C-5), 67.8 (C-4), 63.6, 62.9 (2 C, CH_2) ppm. $C_{15}H_{17}N_3O_3$ (287.31): calcd. C 62.71, H 5.96, N 14.63; found C 62.59, H 5.99, N 14.75.

Spectroscopic Data for 27: ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 9.25 (s, 1 H, H-arom.), 9.15 (s, 1 H, H-arom.), 8.51 (s, 1 H, CH=N), 8.07 (s, 1 H, H-arom.), 7.92 (d, J = 4.8 Hz, 4 H, H-arom.), 4.48 (t, J = 5.6 Hz, 3 H, OH), 3.63 (d, J = 5.6 Hz, 6 H, CH_2) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 159.0 (C=N), 157.9, 155.7, 137.8, 135.7, 130.7, 129.2 (C-arom.), 68.1 (C-N), 62.4 (3 C, CH_2) ppm.

2-Methyl-2-(pyridoxylideneamino)propane-1,3-diol (16): Starting from 2-amino-2-methyl-1,3-propanediol, diol **16** was obtained by following the general procedure; yield 3.10 g, 74%; m.p. 180–181 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3400–3100 (OH), 1643 (C=N), 1580, 1532 (arom.), 1061 (C–O) cm^{-1}. ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 15.31 (s, 1 H, OH-arom.), 8.83 (s, 1 H, CH=N), 7.76 (s, 1 H, H-arom.), 5.34 (s, 1 H, *H*O-CH_2-arom.), 4.95 (s, 2 H, OH), 4.63 (s, 2 H, CH_2-arom.), 3.52 (d, J = 3.2 Hz, 4 H, 2 CH_2), 2.35 (s, 3 H, CH_3-arom.), 1.22 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 161.4 (C=N), 157.6, 150.2, 135.8, 133.1, 118.5 (C-arom.), 65.7 (2 C, CH_2), 65.4 (C-N), 59.0 (CH_2-arom.), 19.3, 18.2 (2 C, CH_3) ppm. $C_{12}H_{18}N_2O_4$ (254.28): calcd. C 56.68, H 7.13, N 11.02; found C 56.47, H 7.10, N 10.80.

2-Methyl-2-(pyridoxylideneamino)propan-1-ol (17): Starting from 2-amino-2-methyl-1-propanol, propanol **17** was obtained by following the same procedure as used for **16**; yield 3.15 g, 80%; m.p. 178–179 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3368, 3077 (OH), 1633 (C=N), 1560, 1511 (arom.), 1073, 1036, 1016 (C–O, C–N) cm^{-1}. ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 15.26 (s, 1 H, OH-arom.), 8.81 (s, 1 H, CH=N), 7.80 (s, 1 H, H-arom.), 5.37 (s, 1 H, *H*O-CH_2-arom.), 5.06 (s, 1 H, OH), 4.65 (s, 2 H, CH_2-arom.), 3.40 (s, 2 H, CH_2), 2.35 (s, 3 H, CH_3-arom.), 1.27 (s, 6 H, 2 CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 160.4 (C=N), 156.8, 149.8, 136.4, 133.2, 118.8 (C-arom.), 69.4 (2 C, CH_2), 61.7 (C-N), 58.9 (CH_2-arom.), 23.9 (CH_3), 19.2 (2 C, CH_3) ppm. $C_{12}H_{18}N_2O_3$ (238.28): calcd. C 60.49, H 7.61, N 11.76; found C 60.46, H 7.40, N 11.49.

2-Hydroxymethyl-2-{2-[(2,2-dimethylpropanoyl)amino]-3-pyridylmethyleneamino}propane-1,3-diol (18): Yield 3.11 g, 61%; m.p. 183–184 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3447 (OH), 1680, 1580 (amide), 1644 (C=N), 1604, 1514, 1480, 1450 (arom.) cm^{-1}. ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 11.92 (s, 1 H, NH-arom.), 8.47 (s, 1 H, CH=N), 8.36 (dd, J = 1.6, J = 4.8 Hz, 1 H, H-arom.), 8.03 (dd, J = 2.0, J = 7.6 Hz, 1 H, H-arom.), 7.20 (dd, J = 4.8, J = 7.6 Hz, 1 H, H-arom.), 4.58 (t, J = 5.6 Hz, 3 H, 3 OH), 3.67 (d, J = 5.6 Hz, 6 H,

3 CH_2), 1.25 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, [D_6]-DMSO): δ = 176.2 (C=O), 161.8 (C=N), 151.4, 149.5, 141.4, 119.1 (C-arom.), 69.3 (C-N), 61.9 (CH_2), 40.4 (*C*-CO), 27.8 (CH_3) ppm. $C_{15}H_{23}N_3O_4$ (309.36): calcd. C 58.24, H 7.49, N 13.58; found C 57.96, H 7.58, N 13.59.

2-Methyl-2-{2-[(2,2-dimethylpropanoyl)amino]-3-pyridylmethylenamino}propane-1,3-diol (19): Starting from 2-amino-2-methyl-1-propanol, diol **19** was obtained by following the same procedure as used for **18**; yield 4.07 g, 84%; m.p. 173–174 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3400–3100 (OH), 1697, 1579 (amide), 1643 (C=N), 1602, 1509, 1479, 1446 (arom.) cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 11.92 (s, 1 H, NH-arom.), 8.39 (s, 1 H, CH=N), 8.36 (dd, *J* = 1.6, *J* = 4.8 Hz, 1 H, H-arom.), 8.06 (dd, *J* = 2.0, *J* = 7.6 Hz, 1 H, H-arom.), 7.20 (dd, *J* = 4.8, *J* = 7.6 Hz, 1 H, H-arom.), 4.69 (t, *J* = 5.6 Hz, 2 H, 2 OH), 3.57 (dd, *J* = 6.0, *J* = 10.8 Hz, 2 H, CH_2), 3.50 (dd, *J* = 5.6, *J* = 10.4 Hz, 2 H, CH_2), 1.26 (s, 9 H, 3 CH_3), 1.22 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 176.1 (C=O), 160.5 (C=N), 151.5, 149.5, 141.3, 119.1, 119.1 (C-arom.), 66.5 (C-N), 66.1 (CH_2), 40.4 (*C*-CO), 27.8, 18.7 (CH_3) ppm. $C_{15}H_{23}N_3O_3$ (293.36): calcd. C 61.41, H 7.90, N 14.32; found C 61.32, H 7.81, N 14.05.

2-(2-Amino-3-pyridylmethyleneamino)-2-methylpropane-1,3-diol (20): Starting from 2-amino-2-methyl-1-propanol, diol **20** was obtained by following the same procedure as used for **18**; yield 1.10 g, 32%; m.p. 118–119 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3466, 3337 (OH, NH), 1633 (C=N), 1597, 1577, 1556, 1450 (arom.) cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 8.38 (s, 1 H, CH=N), 7.98 (d, *J* = 4.8 Hz, 1 H, H-arom.), 7.81 (br. s, 2 H, NH_2), 7.64 (d, *J* = 7.2 Hz, 1 H, H-arom.), 6.60 (dd, *J* = 4.8, *J* = 7.8 Hz, 1 H, H-arom.), 4.63 (t, *J* = 5.6 Hz, 2 H, 2 OH), 3.51 (dd, *J* = 5.6, *J* = 10.8 Hz, 2 H, CH_2), 3.42 (dd, *J* = 5.6, *J* = 10.4 Hz, 2 H, CH_2), 1.15 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 160.5 (C=N), 158.4, 149.8, 141.6, 113.1, 111.7 (C-arom.), 66.5 (CH_2), 65.2 (C-N), 18.8 (CH_3) ppm. $C_{10}H_{15}N_3O_2$ (209.24): calcd. C 57.40, H 7.23, N 20.08; found C 57.16, H 7.31, N 19.99.

1,3-Diacetoxy-2-acetoxymethyl-2-(4-pyridylmethyleneamino)-propane (28): Acetic anhydride (6.5 mL) was added to a solution of the oxazolidine **6** (1.05 g, 5.0 mmol) in pyridine (6.7 mL). The reaction mixture was kept at 0 °C for 24 h and then it was poured into ice–water. The resulting product was extracted with chloroform (3 × 50 mL) and the organic layer was washed sequentially with 1 N HCl (2 × 50 mL), a saturated solution of $NaHCO_3$ (2 × 50 mL), and distilled water (2 × 50 mL). The organic layer was dried ($MgSO_4$) and evaporated to yield compound **28** as an oil (1.18 g, 70%). IR (NaCl): $\tilde{\nu}_{max}$ = 1742 (C=O), 1650 (C=N), 1600, 1560, 1466 (arom.) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.73 (d, *J* = 5.6 Hz, 2 H, H-arom.), 8.36 (s, 1 H, CH=N), 7.63 (d, *J* = 5.6 Hz, 2 H, H-arom.), 4.39 (s, 6 H, CH_2), 2.07 (s, 9 H, OAc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5 (C=O), 159.1 (C=N), 150.3, 142.7, 122.1 (C-arom.), 64.2 (C-N), 63.4 (CH_2), 20.8 (3 C, CH_3, OAc) ppm. HRMS-CI($C_{16}H_{21}N_2O_6$[M + H]$^+$): Calculated: 337.1400; found 337.1412.

Supporting Information (see also the footnote on the first page of this article): Figures S1 and S2, Scheme S1, Table S1, ^1H and ^{13}C NMR spectra, and computational data.

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