Neighboring-Group Participation in Nitrile-Forming Beckmann Fragmentation Reactions: Synthesis of Enantiopure (*E*)-2,3-Di-*O*-substituted-5-methoxypent-4-enenitriles and Their Conversion into Pyranosylamines

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The selective Beckmann fragmentations of multifunctionalised ketoximes have been proven to proceed effectively to give the corresponding nitriles. The chiral (*E*)-1,3,4-tri-*O*-substituted-6-methoxy-hex-5-en-2-one oxime derivatives, available from glycals and glycosyl glycals, gave enantiopure (*E*)-2,3-di-*O*-substituted-5-methoxypent-4-enenitriles by treatment with mesyl chloride and triethylamine. The C1–C2 heterolytic fragmentation was completely controlled and directed by the adjacent C1 ether oxygen, which generates a carbonium-oxonium ion as an active electrofugal group. Unexpectedly, the C3 heteroatom did not assist the cleavage reaction and products derived from C2–C3 fragmentation were never detected. The excellent regio- and stereospecificity of the fragmentation reaction, based on the stereochemical outcome, are discussed. A simple synthetic approach to some pyranosylamines is also described.

Introduction

Heterolytic fragmentations are a widespread class of organic reactions that involve the regulated cleavage of molecules whose structures contain combinations of atoms, such as carbon, oxygen, nitrogen, sulfur, silicon, and halogens.[1] The Beckmann fragmentation can be included in this class of reaction when ketoximes are cleaved into nitriles and a second fragment. In particular, nitrile-forming fragmentation reactions have been observed to occur in ketoximes with α-substituents, such as heteroatoms, which can stabilize the intermediary carbocations. Since the formation of nitriles is an important aspect of this fragmentation, these reactions can be utilized both for degradation and structure elucidation and for preparative purposes.[2−4]

During recent years, cyclic ketoximes have been widely studied and utilized in organic synthesis. Thus, the Beckmann fragmentation has proven to be particularly useful for cyclic ketoximes with quaternary centers adjacent to the oxime carbon.[2−4] Recently, Hu and co-workers developed a novel and practical procedure for heterolytic fragmentation of steroid 17-oximes.[5] This protocol represents the best method with which to obtain 13,17-*seco*-alkenenitrile products, which can then easily be converted into biologically important 18-nor-17-ketosteroids.[6−11]

Furthermore, cyclic ketoximes that contain functional groups that direct the fate of the cationic intermediates have been utilized preparatively.[2−4] Nishiyama et al. found that the Beckmann fragmentation of cyclic β-trimethylsilyl ketoximes is completely controlled and directed by a trimethylsilyl group to give regio- and stereospecific unsaturated nitriles.[12] More recently, Fleming et al.[13] reported a silicon-directed Beckmann fragmentation of a suitable cyclic ketoxime acetate with a dimethylphenylsilyl group as the active electrofugal group in the β-position,[1] in which a high level of stereocontrol in the open-chain unsaturated nitrile, the key intermediate in the synthesis of phytol, was achieved.

However, a significant drawback of this approach is that the fragmentation produces two or more products when the oxime is acyclic: a nitrile and the product or products derived from the cation. Hence, the reaction is preparatively useful only when the nitrile is the desired product.[2−4,14]

To the best of our knowledge, the synthetic utility of the Beckmann fragmentation has never been studied with differentially and densely functionalised ketoximes, particularly acyclic and unsymmetrically substituted ketoximes.

Some years ago, we described the synthesis of acyclic multifunctional compounds, such as (*E*)-1,3,4-tri-*O*-substituted-6-methoxyhex-5-en-2-ol derivatives **1**, that are readily available by a one-pot procedure from *O*-benzyl derivatives of glycals and glycosyl glycals by reaction with the

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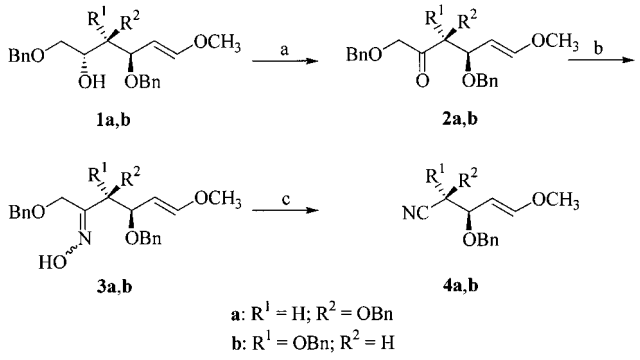
$Tl(NO_3)_3/NaBH_4$ reagent combination.[15,16] These compounds have been utilized as precursors in the synthesis of some biologically active products, such as natural and unnatural sphingosines.[17]

Prompted by these findings, we became interested in exploiting the reactivity of ketoximes derived from **1** in heterolytic fragmentation reactions. These acyclic molecules, with two *O*-protected hydroxy groups, C1 and C3, both located adjacent to the oxime C2 atom, contain a suitable combination (scaffold or frame) of groups and heteroatoms with which to study the regio- and stereocontrol of neighboring-group participation in nitrile-forming Beckmann fragmentation reactions.

Here we describe some of our results in the development of a method in which regio- and stereocontrolled bond fragmentation of densely functionalised ketoximes occurs to give enantiopure functionalised pentanenitrile derivatives, which are valuable as precursors in the synthesis of biologically active compounds, such as glycosylamines,[18] 1-β-amino-1-deoxynojirimycins[19,20] and D-glucoamidines.[21−23]

Results and Discussion

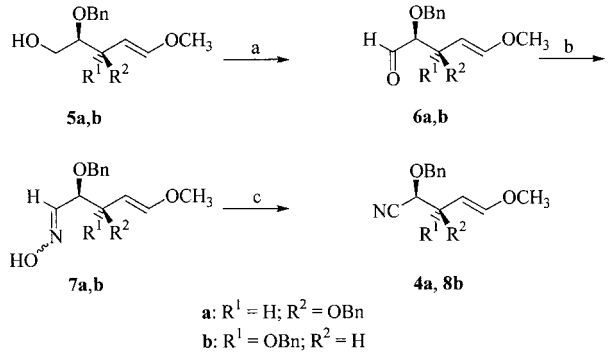
All the starting materials were prepared in one step from *O*-benzyl derivatives of glycals and glycosyl glycals according to our previously reported procedure by reaction with $Tl(NO_3)_3/NaBH_4$ reagent combination in methanol.[15,16,24] The C2 free hydroxy groups of **1a**,**b** (available from *O*-benzyl derivatives of D-glucal and D-galactal, respectively) were easily oxidized to the corresponding ketones **2a**,**b** in high yield (90−95%) by reaction with PDC in acetonitrile (Scheme 1). The reaction of compounds **2a**,**b** with three equivalents of hydroxylamine, prepared from hydroxylamine hydrochloride and triethylamine in a 1:1 EtOH/THF solution, gave ketoximes **3a**,**b** as *E*/*Z* stereoisomeric mixtures (75−80%). Since the mechanism of the Beckmann fragmentation requires reagents with dehydrating properties,[5,6,11] the ketoximes **3a**,**b** were treated with mesyl chloride and triethylamine in dichloromethane at room temp., a reagent combination previously utilized for this purpose.[24]



Scheme 1. Reagents and conditions: a) PDC, CH_3CN, 4-Å molecular sieves, room temp. (90−95%); b) $NH_2OH{\cdot}HCl$, NEt_3, EtOH/THF 1:1, 40 °C, (75−80%); c) CH_3SO_2Cl, NEt_3, CH_2Cl_2, room temp. (60−70%)

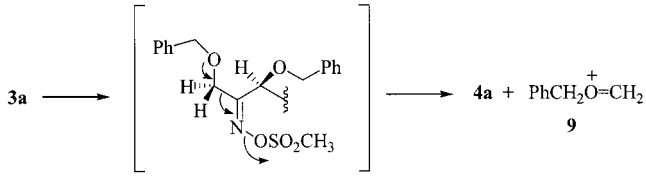
Surprisingly, we observed a very fast reaction (15 min) leading directly to the regioselective formation of (*E*,2*R*,3*R*)-2,3-bis(benzyloxy)-5-methoxypent-4-enenitrile (**4a**) and (*E*,2*S*,3*R*)-2,3-bis(benzyloxy)-5-methoxypent-4-enenitrile (**4b**) as the only reaction products and in acceptable yields (60−70%). The structures of **4a** and **4b** were determined by HRMS analysis and from the spectroscopic data: **4a**, ^{13}C NMR: δ = 116.6 (CN), 72.5, 69.8 (CH_2Ph) ppm; **4b**, ^{13}C NMR: δ = 116.8 (CN), 72.3, 69.7 (CH_2Ph) ppm. Neither compound showed a CN absorption in their IR spectra, like other nitriles described in this work, and similarly to what has been previously observed for α-alkoxynitriles.[25,26]

The structures of compounds **4a**,**b** were confirmed by correlation with products obtained by known methods (Scheme 2). Starting from **5a**, available from the *O*-benzyl derivative of D-xylal[15,16] and in accordance with the reaction sequence depicted in Scheme 2, a compound identical to **4a**, already prepared from **1a** (see Scheme 1), was obtained. Then **5b**, available from the *O*-benzyl derivative of D-arabinal,[15,16] was converted by the same reaction sequence into (*E*,2*R*,3*S*)-2,3-bis(benzyloxy)-5-methoxypent-4-enenitrile (**8b**), the enantiomer of **4b**.



Scheme 2. Reagents and conditions: a) PDC, CH_3CN, 4-Å molecular sieves, room temp. (80%); b) $NH_2OH{\cdot}HCl$, NEt_3, EtOH/THF 1:1, 40 °C, (90%); c) CH_3SO_2Cl, NEt_3, CH_2Cl_2, room temp. (90%)

In general, the heterolytic fragmentation is stereospecific and carbon−carbon cleavage occurs when an active electrofugal group is *anti* to a nucleofugal group on the nitrogen, as shown in Scheme 3.[2−4,12,13]



Scheme 3

Both the mildness of the experimental conditions and the fast reaction times can be explained by a stereocontrolled donation of electrons by the oxygen atom of the C1 benzyloxy group to the fragmenting carbon, which favours the formation of a more accessible and less crowded transition

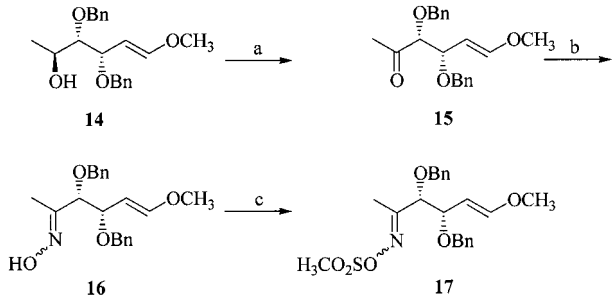
state (Scheme 3). Unexpectedly, the C3 heteroatom did not assist the cleavage reaction and products derived from C2−C3 fragmentation were never detected. Note that in a previous study of a series of (*E*)- and (*Z*)-ketoximes the same fragmentation products were observed, the reactions varying only in their rate constants for fragmentation and in their yields.[27]

In order to study the role of the benzyl(methylene)-oxonium ion **9**, the stabilized electrofugal group, in controlling and directing the regiochemistry of the fragmentation reaction, we examined the reactivity of (*E*,2*R*,3*R*,4R)-1,3-di-*O*-substituted-4-benzyloxy-6-methoxyhex-5-en-2-ol derivatives, such as **10a**−**e**, with differently protected C1 and C3 hydroxy groups, such as a sugar moiety either at C1 or C3. These compounds are readily available from *O*-benzyl derivatives of cellobial,[15,16] maltal (see Expt. Sect.), lactal,[15,16] melibial[15,16] and gentiobial[24] (see Expt. Sect.) respectively.

Compounds **12a**,**b**,**c**, prepared from **10a**,**b**,**c** by the reaction sequence shown in Scheme 4, reacted similarly to **3a**,**b** as described above, undergoing regioselective C1−C2 fragmentation to give (*E*,2*R*,3*R*)-2-*O*-substituted-3-benzyloxy-5-methoxypent-4-enenitriles **13** with a sugar moiety at C2, such as 2′,3′,4′,6′-tetra-*O*-benzyl-β-D-glucopyranosyl (**13a**), 2′,3′,4′,6′-tetra-*O*-benzyl-α-D-glucopyranosyl (**13b**) and 2′,3′,4′,6′-tetra-*O*-benzyl-β-D-galactopyranosyl (**13c**), in the same yields as reported before (60−70%) (Scheme 4). The outcome of the reaction clearly indicates that the presence of a sugar derivative adjacent to the ketoxime moiety in **12a**,**b**,**c** does not influence the Beckmann fragmentation or its regiochemistry.

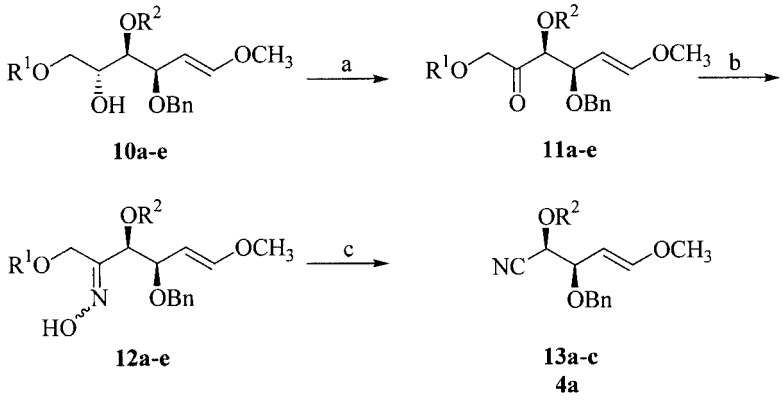
Interestingly, the ketoximes **12d**,**e**, prepared from **10d**,**e** and with a sugar derivative located at C1, underwent the regioselective heterolytic cleavage reaction with the unusual pyranoside-oxonium ion as the electrofugal group to give **4a** as the only detectable reaction product (Scheme 4). The yields were modest (30−40%), probably because the pyranoside-oxonium ion is an inefficient cationic leaving group. We were unable to detect any other products from the fragmentation reaction or the starting compounds **12d**,**e**. In particular, C2−C3 fragmentation products were never observed.

Then, (*E*,2*S*,3*S*,4*S*)-3,4-bis(benzyloxy)-6-methoxyhex-5-en-2-ol **14**, available from the *O*-benzyl derivative of L-rhamnal, was converted into the ketoxime **16** as an *E*/*Z* stereoisomeric mixture (Scheme 5). Subsequent treatment with mesyl chloride, as described previously, led almost quantitatively to the formation of the corresponding mesyl derivative as the only reaction product (*E*/*Z* mixture); that is, no by-products of either the Beckmann fragmentation or the Beckmann rearrangement reactions were detected. Note also that C2−C3 heterolytic cleavage products were never detected.



Scheme 5. Reagents and conditions: a) PDC, CH_3CN, 4-Å molecular sieves, room temp. (95%); b) $NH_2OH{\cdot}HCl$, NEt_3, EtOH/THF 1:1, 40 °C (80%); c) CH_3SO_2Cl, NEt_3, CH_2Cl_2, room temp. (90%)

All the above results indicate that the benzyloxy group at the C3-position did not assist the heterolytic cleavage de-



a: R^1 = Bn; R^2 = 2',3',4',6'-tetra-*O*-benzyl-β-D-glucopyranosyl
b: R^1 = Bn; R^2 = 2',3',4',6'-tetra-*O*-benzyl-α-D-glucopyranosyl
c: R^1 = Bn; R^2 = 2',3',4',6'-tetra-*O*-benzyl-β-D-galactopyranosyl
d: R^1 = 2',3',4',6'-tetra-*O*-benzyl-α-D-galactopyranosyl; R^2 = Bn
e: R^1 = 2',3',4',6'-tetra-*O*-benzyl-β-D-glucopyranosyl; R^2 = Bn

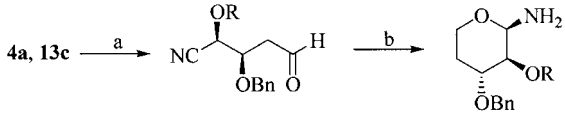
Scheme 4. Reagents and conditions: a) PDC, CH_3CN, 4-Å molecular sieves, room temp. (90−95%); b) $NH_2OH{\cdot}HCl$, NEt_3, EtOH/THF 1:1, 40 °C (75−80%); c) CH_3SO_2Cl, NEt_3, CH_2Cl_2, room temp. (30−70%)

spite being adjacent to the reaction center possibly due to some steric interaction involved in the formation of the transition state and the necessary stereochemistry of the reaction pathway (Scheme 3). As has been described in the literature, effective assistance requires a transition state in which both of the carbon atoms involved in the fragmentation, the leaving group on the nitrogen and the "assisting atom" lie in or near a common plane, as shown in Scheme 3.[2−4,12,13] To the best of our knowledge, there is no evidence in the literature of such highly regio- and stereocontrolled assistance in the Beckmann fragmentation reaction.

Synthetic Application

The compounds obtained from the Beckmann fragmentation are precursors of δ-hydroxynitriles and they can be utilized in strategies leading to the synthesis of protected pyranosylamines by reductive cyclization.[18] The reductive cyclization of hydroxynitriles to provide glycosylamines is a known reaction.[28,29] However, owing to the biological activity of this class of cyclic *N*,*O*-acetals, glycosylamines are a central motif in *N*-linked glycopeptides and glycoproteins,[30−32] the development of new synthetic strategies remains an important goal.[33]

Some pyranosylamines, such as **19a**,**b** (Scheme 6), were synthesized starting with the preparation of (2*R*,3*R*)-2,3-di-*O*-substituted-5-oxopentanenitriles **18a**,**b**, which were easily and almost quantitatively obtained from **4a** and **13a**, respectively, by treatment with acid as catalyst in THF. Upon exposure to sodium borohydride in ethanol, **18a**,**b** were first converted into the corresponding δ-hydroxynitriles and subsequent reductive cyclization afforded the new pyranosylamines **19a**,**b** in acceptable yields (55%) as the only reaction products. In both cases, reductive cyclization resulted in the preferential formation of the β anomer, as previously reported for these reactions.[18] However, it is worth noting that in the case of compounds **19**, the β configuration means an axial orientation, as shown by the ^{13}C NMR analysis of the C1 atom shielded at around 77 ppm.[18] This sequence thus allows a simple approach to a library of stereodefined pyranosylamines.



18a,b **19a,b**

a: R = Bn
b: R = 2',3',4',6'-tetra-*O*-benzyl-β-D-galactopyranosyl

Scheme 6. Reagents and conditions: a) THF/4 N HCl (5:1), room temp.; b) $NaBH_4$, THF/EtOH (1:1), reflux

Conclusions

In conclusion, we have found that acyclic, differentially and densely functionalised ketoximes successfully undergo the Beckmann fragmentation reaction to give enantiopure (*E*)-2,3-*O*-disubstituted-5-methoxypent-4-enenitriles, precursors of biologically active compounds. Then the regio- and stereocontrolled participation of an adjacent coplanar *trans*/*anti* ether oxygen, which generates a carbonium-oxonium ion as the active electrofugal group, was unambiguously demonstrated. The results give a new insight into both the mechanism and the stereochemical requirements of the neighboring groups in the electronically assisted carbon-cleavage reaction and provides scope to broaden the synthetic utility of this reaction.

Experimental Section

General: ^1H (200 MHz) and ^{13}C NMR (50.3 MHz) spectra were recorded with a Varian Gemini 200 spectrometer with $CDCl_3$ as the solvent and internal standard. IR spectra were recorded with an IR Equinox 55 Bruker spectrometer. HRMS spectra were recorded with a Micromass Q-TOF *micro* Mass Spectrometer (Waters). Optical rotations were measured by using the sodium D line of a DIP 370 Jasco digital polarimeter. Yields are given for isolated products after column chromatography showed a single spot on TLC and when no impurities were detected in the ^1H NMR spectra. All reactions were performed under N_2 in flame-dried glassware. All solvents and commercially available reagents were used without further purification unless otherwise noted. All reactions were monitored by thin-layer chromatography (TLC) carried out on Merck F-254 silica glass plates visualized with UV/light and heat-gun treatment with 2 N H_2SO_4 solution. Column chromatography was performed using Merck silica gel 60 (230−400 mesh).

Starting Materials: All the starting materials were prepared from their corresponding glycals or glycosyl glycals.[15,16,24] Since compounds **5a**,**b** and **10b**,**e** have not been described before, we report the analytical data in the Expt. Sect..

Linear Methoxy Alcohol 5a: Compound **5a** was prepared from perbenzylated D-xilal (200 mg, 0.67 mmol) by following our previously described method,[15,16] and was obtained as a viscous oil (122 mg, 55%). $[\alpha]_D = +48.7$ ($c = 1.1$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu} = 3300, 3150, 3090, 1690, 1650, 1625, 1520, 1430, 1380, 1230, 1120, 1090\ cm^{-1}$. ^1H NMR: $\delta = 7.52-7.30$ (m, 10 H, Ph), 6.55 (d, $J = 12.5$ Hz, 1 H, 1-H), 4.90−4.52 (m, 6 H, 2-H, 4-H, 2 CH_2Ph), 3.80 (dd, $J = 5.0, 7.0$ Hz, 1 H, 3-H), 3.80 (m, 2 H, 5-H_A, 5-H_B), 3.58 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 152.7 (C-1), 138.2, 137.5 (C_{quat}, Ph), 128.2, 127.9, 127.5, 127.4 (Ph), 98.7 (C-2), 79.5, 78.1 (C-3, C-4), 72.5, 70.4 (CH_2Ph), 63.8 (C-5), 55.5 (OCH_3) ppm. HRMS: calcd. for $C_{20}H_{24}O_4$: 346.2018 $[M + NH_4]^+$; found: 346.2015.

Linear Methoxy Alcohol 5b: Compound **5b** was prepared from perbenzylated D-arabinal (200 mg, 0.67 mmol) by following our previously described method,[15,16] and was obtained as a viscous oil (122 mg, 55%). $[\alpha]_D = +58.7$ ($c = 1.3$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu} = 3300, 3150, 3090, 1690, 1650, 1625, 1520, 1430, 1380, 1230, 1120, 1090\ cm^{-1}$. ^1H NMR: $\delta = 7.52-7.30$ (m, 10 H, Ph), 6.58 (d, $J = 12.3$ Hz, 1 H, 1-H), 4.90−4.60 (m, 5 H, CH_2Ph, H_A of CH_2Ph, 2-H, 4-H), 4.42 (d, $J = 12.0$ Hz, 1 H, H_B of CH_2Ph), 3.92 (dd, $J = 8.0, 6.0$ Hz, 1 H, 3-H), 3.80 (m, 2 H, 5-H_A, 5-H_B), 3.65 (s, 3 H, OCH_3) ppm. ^{13}C NMR: $\delta = 151.7$ (C-1), 138.2 (C_{quat}, Ph), 128.2, 127.8, 127.6, 127.4 (Ph), 99.7 (C-2), 81.5, 78.1 (C-3, C-4), 72.7, 69.3 (CH_2Ph), 62.2 (C-5), 55.9 (OCH_3) ppm. HRMS: calcd. for $C_{20}H_{24}O_4$: 346.2018 $[M + NH_4]^+$; found: 346.2013.

Linear Methoxy Alcohol 10b: Compound **10b** was prepared from perbenzylated maltal (200 mg, 0.23 mmol) by following our previously described method,[15,16] and was obtained as a viscous oil (124 mg, 60%). $[\alpha]_D = +72.3$ ($c = 1.3$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3300, 3140, 3050, 1690, 1655, 1630, 1530, 1430, 1380, 1230, 1120, 1090 cm^{-1}. ^1H NMR: $\delta = 7.42-7.20$ (m, 30 H, Ph), 6.20 (d, J = 12.7 Hz, 1 H, 1-H), 5.21−4.40 (m, 17 H, 6 CH_2Ph, 1′-H, 2′-H, 3′-H, 4′-H, 2-H), 4.35−4.10 (m, 2 H, 3-H, 4-H), 4.02−3.60 (m, 6 H, 5′-H, 6′-H_A, 6′-H_B, 5-H, 6-H_A, 6-H_B), 3.47 (s, 3 H, OCH_3), 2.78 (br. s, OH) ppm. ^{13}C NMR: $\delta = 152.8$ (C-1), 138.3, 137.8, 137.6, 137.4, 137.0 (C_{quat}, Ph), 128.0, 127.8, 127.7, 127.6, 127.5, 126.4 (Ph), 99.3 (C-1′), 97.2 (C-2), 81.5, 79.8, 79.4, 77.2, 76.7, 75.9 (C-2′, C-3′, C-4′, C-5′, C-3, C-4), 75.1, 74.6, 74.4, 73.2, 72.9 (CH_2Ph), 70.0 (C-5), 69.4, 68.0 (C-6′, C-6) ppm. HRMS: calcd. for $C_{55}H_{60}O_{10}$: 898.4530 $[M + NH_4]^+$; found: 898.4538.

Linear Methoxy Alcohol 10e: Compound **10e** was prepared from perbenzylated gentiobial[24] (200 mg, 0.23 mmol) by following our previously described method,[15,16] and was obtained as a viscous oil (124 mg, 60%). $[\alpha]_D = +5.6$ ($c = 1.3$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3300, 3140, 3050, 1690, 1655, 1630, 1530, 1430, 1380, 1230, 1120, 1090 cm^{-1}. ^1H NMR: $\delta = 7.45-7.25$ (m, 30 H, Ph), 6.60 (d, J = 12.5 Hz, 1 H, 1-H), 5.21−4.40 (m, 17 H, 6 CH_2Ph, 1′-H, 2′-H, 3′-H, 4′-H, 2-H), 4.35−4.0 (m, 2 H, 3-H, 4-H), 4.0−3.62 (m, 6 H, 5′-H, 6′-H_A, 6′-H_B, 5-H, 6-H_A, 6-H_B), 3.62 (s, 3 H, OCH_3), 2.78 (br. s, OH) ppm. ^{13}C NMR: $\delta = 150.7$ (C-1), 138.1, 138.0, 137.9, 137.6, 137.5 (C_{quat}, Ph), 127.9, 127.8, 127.7, 127.6, 127.4, 127.3, 127.1, 127.0 (Ph), 103.9 (C-1′), 99.1 (C-2), 84.2, 81.9, 81.5, 77.3, 76.8, 74.3 (C-2′, C-3′, C-4′, C-5′, C-3, C-4), 75.2, 74.3, 73.9, 73.1, 72.1 (CH_2Ph), 69.8 (C-5), 69.1, 68.4 (C-6′, C-6) ppm. HRMS: calcd. for $C_{55}H_{60}O_{10}$: 898.4530 $[M + NH_4]^+$; found: 898.4528.

Synthesis of Ketones 2a,b, 11a−e and 15 and Aldehydes 6a,b. General Procedure: The appropriate alcohol (0.23 mmol) was dissolved in dry CH_3CN (7 mL) in the presence of powdered molecular sieves (4 Å, 2 g·mmol^{-1}) and the mixture was treated with PDC (0.17 g, 0.46 mmol). The reaction mixture was stirred at room temperature overnight and then was filtered through Celite, washing with CH_3CN. After evaporation of the solvent under reduced pressure the crude product was purified by column chromatography.

Ketone 2a: This compound was prepared by the general procedure from **1a** (200 mg, 0.44 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 8:2) to give **2a** as a viscous oil (189 mg, 95%). $[\alpha]_D = -57.0$ ($c = 1.3$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3150, 3090, 1730, 1695, 1625, 1520, 1500, 1230, 1190, 1120, 1090 cm^{-1}. ^1H NMR: $\delta = 7.38-7.17$ (m, 15 H, Ph), 6.44 (d, J = 12.8 Hz, 1 H, 6-H), 4.79 (dd, J = 12.8, 9.4 Hz, 1 H, 5-H), 4.67−4.18 (m, 8 H, 3 CH_2Ph, 1-H_A, 1-H_B), 4.16 (dd, J = 9.4, 3.8 Hz, 1 H, 4-H), 3.94 (d, J = 3.8 Hz, 1 H, 3-H), 3.48 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 207.3 (CO), 151.6 (C-6), 137.6, 137.2, 136.8 (C_{quat}, Ph), 128.2, 128.0, 127.9, 127.7, 127.3 (Ph), 97.8 (C-5), 86.6 (C-3), 77.6 (C-4), 74.2, 74.0, 72.9 (CH_2Ph), 69.3 (C-1), 55.7 (OCH_3) ppm. HRMS: calcd. for $C_{28}H_{30}O_5$: 464.2437 $[M + NH_4]^+$; found: 464.2433.

Ketone 2b: This compound was prepared by the general procedure from **1b** (200 mg, 0.44 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 8:2) to give **2b** as a viscous oil (183 mg, 92%). $[\alpha]_D = -21.0$ ($c = 1.2$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3145, 3090, 1720, 1695, 1625, 1525, 1510, 1500, 1230, 1190, 1130, 1080 cm^{-1}. ^1H NMR: $\delta = 7.40-7.20$, (m, 15 H, Ph), 6.55 (d, J = 12.7 Hz, 1 H, 6-H), 4.72 (dd, J = 2.7, 9.8 Hz, 1 H, 5-H), 4.62−4.32 (m, 8 H, 3 CH_2Ph, 1-H_A, 1-H_B), 4.10−3.94 (m, 2 H, 3-H, 4-H), 3.52 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 207.0 (CO), 152.1 (C-6), 138.0, 137.3 (C_{quat}, Ph), 128.3, 128.0, 127.8, 127.5, 127.4 (Ph), 98.1 (C-5), 85.4 (C-3), 78.4 (C-4), 74.0, 73.2, 73.0 (CH_2Ph), 69.3 (C-1), 56.0 (OCH_3) ppm. HRMS: calcd. for $C_{28}H_{30}O_5$: 464.2437 $[M + NH_4]^+$; found: 464.2439.

Aldehyde 6a: This compound was prepared by the general procedure from **5a** (122 mg, 0.37 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 8:2) to give **6a** as a viscous oil (97 mg, 80%). $[\alpha]_D = +11.3$ ($c = 1.5$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3150, 3090, 2700, 1730, 1680, 1670, 1600, 1530, 1420, 1230, 1100, 1090 cm^{-1}. ^1H NMR: δ = 9.91 (d, J = 1.8 Hz, 1 H, H−CO), 7.52−7.25 (m, 10 H, Ph), 6.56 (d, J = 12.8 Hz, 1 H, 5-H), 4.80 (dd, J = 12.8, 9.2 Hz, 1 H, 4-H), 4.82 (d, J = 9.0 Hz, 1 H, H_A of CH_2Ph), 4.60 (s, 2 H, CH_2Ph), 4.39 (d, J = 9.0 Hz, 1 H, H_B of CH_2Ph), 4.09 (dd, J = 9.2, 4.8 Hz, 1 H, 3-H), 3.94 (dd, J = 4.8, 1.8 Hz, 1 H, 2-H), 3.60 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 201.8 (CO), 152.0 (C-5), 137.9, 137.3 (C_{quat}, Ph), 128.3, 127.9, 127.4 (Ph), 98.1 (C-4), 77.3, 76.1 (C-3, C-2), 72.8, 70.3 (CH_2Ph), 54.7 (OCH_3) ppm. HRMS: calcd. for $C_{20}H_{22}O_4$: 344.1862 $[M + NH_4]^+$; found: 344.1865.

Aldehyde 6b: This compound was prepared by the general procedure from **5b** (122 mg, 0.37 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 8:2) to give **6b** as a viscous oil (97 mg, 80%). $[\alpha]_D = +32.7$ ($c = 1.5$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3150, 3090, 2700, 1730, 1680, 1670, 1600, 1530, 1420, 1230, 1100, 1090 cm^{-1}. ^1H NMR: δ = 9.91 (d, J = 1.8 Hz 1 H, H−CO), 7.52−7.25 (m, 10 H, Ph), 6.56 (d, J = 12.8 Hz, 1 H, 5-H), 4.80 (dd, J = 12.8, 9.2 Hz, 1 H, 4-H), 4.82−4.60 (m, 3 H, CH_2Ph, H_A of CH_2Ph), 4.39 (d, J = 2.0 Hz, 1 H, H_B of CH_2Ph), 4.09 (dd, J = 9.2, 4.8 Hz, 1 H, 3-H) 3.94 (dd, J = 4.8, 1.8 Hz, 1 H, 2-H), 3.60 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 201.8 (CO), 152.0 (C-5), 137.9, 137.3 (C_{quat}, Ph), 128.3, 128.0, 127.4 (Ph), 98.1 (C-4), 85.3, 77.3 (C-3, C-2), 72.8, 69.1 (CH_2Ph), 55.8 (OCH_3) ppm. HRMS: calcd. for $C_{20}H_{22}O_4$: 344.1862 $[M + NH_4]^+$; found: 344.1859.

Ketone 11a: This compound was prepared by the general procedure from **10a** (200 mg, 0.23 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 8:2) to give **11a** as an amorphous powder (184 mg, 92%). $[\alpha]_D = -14.0$ ($c = 1.3$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3060, 3020, 3010, 1730, 1690, 1550, 1510, 1420, 1290, 1180, 1100, 1090 cm^{-1}. ^1H NMR: $\delta = 7.40-7.25$ (m, 30 H, Ph), 6.56 (d, J = 12.0 Hz, 1 H, 6-H), 5.10−4.80 (m, 6 H, 2 CH_2Ph, 3-H, 5-H), 4.71−4.42 (m, 12 H, 4 CH_2Ph, 1′-H, 2′-H, 4′-H, 4-H), 4.40−4.23 (m, 4 H, 3′-H, 5′-H, 6′-H_A, 6′-H_B), 3.82 (m, 2 H, 1-H_A, 1-H_B), 3.50 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 206.6 (CO), 151.3 (C-6), 138.1, 137.9, 137.7, 137.1 (C_{quat}, Ph), 127.9, 127.8, 127.7, 127.6, 127.4, 127.3, 127.1, 127.0 (Ph), 101.6 (C-1′), 97.9 (C-5), 84.2, 83.6, 81.4, 77.6, 77.3, 74.7 (C-2′, C-3′, C-4′, C-5′, C-3, C-4), 74.5, 74.3, 73.0, 72.4 (CH_2Ph), 69.0, 68.2 (C-6′, C-1), 55.4 (OCH_3) ppm. HRMS: calcd. for $C_{55}H_{58}O_{10}$: 896.4374 $[M + NH_4]^+$; found: 896.4377.

Ketone 11b: This compound was prepared by the general procedure from **10b** (200 mg, 0.23 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 8:2) to give **11b** as a viscous oil (184 mg, 92%). $[\alpha]_D = +68.9$ ($c = 1.1$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3050, 3025, 3010, 1728, 1690, 1555, 1515, 1420, 1280, 1160, 1100, 1090 cm^{-1}. ^1H NMR: $\delta = 7.50-7.30$ (m, 30 H, Ph), 6.52 (d, J = 13 Hz, 1 H, 6-H), 5.10 (d, J = 3.2 Hz, 1 H, 1′-H), 5.02−4.60 (m, 5 H, 2 CH_2Ph, H-5), 4.58−4.42 (m, 12 H, 4 CH_2Ph, 2′-H, 4′-H, 3-H, 4-H), 4.30−3.52 (m, 6 H, 3′-H, 5′-H, 6′-H_A, 6′-H_B, 1-H_A, 1-H_B), 3.48 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 205.3 (CO), 152.1 (C-6), 138.7, 138.3, 138.1, 137.8, 137.3 (C_{quat}, Ph), 128.3, 128.2, 128.1, 128.0, 127.8, 127.6, 127.5, 127.4 (Ph), 99.2 (C-1′), 97.7 (C-5), 84.5, 81.5, 79.6, 77.8, 77.4 (C-2′, C-3′, C-4′, C-5′, C-4), 75.4, 74.8, 74.3, 73.3,

73.1, 72.6 (CH_2Ph), 71.1 (C-3), 69.3, 68.2 (C-6′, C-1), 55.8 (OCH_3) ppm. HRMS: calcd. for $C_{55}H_{58}O_{10}$: 896.4374 $[M + NH_4]^+$; found: 896.4380.

Ketone 11c: This compound was prepared by the general procedure from **10c** (200 mg, 0.23 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 8:2) to give **11c** as an amorphous powder (187 mg, 94%). $[\alpha]_D = -5.1$ ($c = 1.1$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3060, 3020, 3010, 1730, 1696, 1545, 1510, 1416, 1290, 1180, 1100, 1048 cm^{-1}. ^1H NMR: $\delta = 7.41-7.26$ (m, 30 H, Ph), 6.52 (d, J = 12.9 Hz, 1 H, 6-H), 5.00 (d, J = 12.9 Hz, 1 H, H_A of CH_2Ph), 4.89 (dd, J = 12.9, 3.0 Hz, 1 H, 5-H), 4.71−4.22 (m, 16 H, H_B of CH_2Ph, 5 CH_2Ph, 1′-H, 2′-H, 3′-H, 4′-H, 4-H), 4.13 (dd, J = 9.2, 3.3 Hz, 1 H, 3-H), 3.92 (d, J = 7.5 Hz, 1 H, 1-H_A), 3.88 (d, J = 7.5 Hz, 1 H, 1-H_B), 3.60−3.48 (m, 3 H, 5′-H, 6′-H_A, 6′-H_B), 3.47 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 207.1 (CO), 151.3 (C-6), 138.6, 138.5, 138.1, 137.9, 137.6, 137.5 (C_{quat}, Ph), 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 127.5, 127.3 (Ph), 102.3 (C-1′), 98.4 (C-5), 84.1, 82.2, 79.0, 78.0, 75.0, 72.8 (C-2′, C-3′, C-4′, C-5′, C-3, C-4), 69.3, 68.5 (C-6′, C-1), 55.7 (OCH_3) ppm. HRMS: calcd. for $C_{55}H_{58}O_{10}$: 896.4374 $[M + NH_4]^+$; found: 896.4376.

Ketone 11d: This compound was prepared by the general procedure from **10d** (200 mg, 0.23 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 8:2) to give **11d** as a viscous oil (179 mg, 90%). $[\alpha]_D = +19.5$ ($c = 1.1$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3050, 3015, 3010, 1730, 1690, 1555, 1520, 1430, 1280, 1160, 1110, 1090 cm^{-1}. ^1H NMR: $\delta = 7.45-7.30$ (m, 30 H, Ph), 6.32 (d, J = 13.1 Hz, 1 H, 6-H), 5.05 (d, J = 4.2 Hz, 1 H, 1′-H), 5.03−4.65 (m, 5 H, 2 CH_2Ph, 5-H), 4.58−4.42 (m, 12 H, 4 CH_2Ph, 2′-H, 4′-H, 3-H, 4-H), 4.35−3.52 (m, 6 H, 3′-H, 5′-H, 6′-H_A, 6′-H_B, 1-H_A, 1-H_B), 3.42 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 206.7 (CO), 151.4 (C-6), 138.5, 138.3, 138.0, 137.5, 136.5 (C_{quat}, Ph), 128.0, 127.9, 127.8, 127.7, 127.6, 127.4, 127.3, 127.1, 126.9 (Ph), 97.6 (C-1′), 96.7 (C-5), 86.5, 78.2, 77.8, 77.4 (C-2′, C-3′, C-4′, C-5′, C-4), 75.4, 74.8, 74.3, 73.3, 73.1, 72.6 (CH_2Ph), 70.1 (C-3), 69.2, 67.9 (C-6′, C-1), 55.5 (OCH_3) ppm. HRMS: calcd. for $C_{55}H_{58}O_{10}$: 896.4374 $[M + NH_4]^+$; found: 896.4370.

Ketone 11e: This compound was prepared by the general procedure from **10e** (200 mg, 0.23 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 8:2) to give **11e** as an amorphous powder (179 mg, 90%). $[\alpha]_D = +2.6$ ($c = 1.2$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3060, 3020, 3010, 1730, 1696, 1545, 1510, 1416, 1290, 1180, 1100, 1048 cm^{-1}. ^1H NMR: $\delta = 7.41-7.26$ (m, 30 H, Ph), 6.58 (d, J = 12.5 Hz, 1 H, 6-H), 5.00−4.22 (m, 17 H, 6 CH_2Ph, 1′-H, 2′-H, 3′-H, 4′-H, 5-H), 4.13−3.88 (m, 1 H, 3-H), 3.92 (d, J = 7.5 Hz, 1 H, 1-H_A), 3.88 (d, J = 7.5 Hz, 1 H, 1-H_B), 3.60−3.48 (m, 4 H, 5′-H, 6′-H_A, 6′-H_B, 4-H), 3.51 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 205.4 (CO), 151.4 (C-6), 138.1, 137.9, 137.6, 137.5 (C_{quat}, Ph), 127.8, 127.7, 127.6, 127.5, 127.3, 127.2, 127.0 (Ph), 102.9 (C-1′), 97.6 (C-5), 86.1, 83.9, 81.5, 76.7, 75.1, 74.4 (C-2′, C-3′, C-4′, C-5′, C-3, C-4), 74.5, 74.1, 73.7, 73.1, 72.9 (CH_2Ph), 70.2, 68.9 (C-6′, C-1), 55.4 (OCH_3) ppm. HRMS: calcd. for $C_{55}H_{58}O_{10}$: 896.4374 $[M + NH_4]^+$; found: 896.4376.

Ketone 15: This compound was prepared by the general procedure from **14** (200 mg, 0.58 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 8:2) to give **15** as a viscous oil (189 mg, 95%). $[\alpha]_D = +95.2$ ($c = 1.1$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3100, 3050, 1730, 1695, 1625, 1525, 1510, 1500, 1380, 1230, 1190, 1130 cm^{-1}. ^1H NMR: $\delta = 7.35-7.15$ (m, 10 H, Ph), 6.44 (d, J = 12.5 Hz, 1 H, 6-H), 4.80 (dd, J = 12.5, 9.1 Hz, 1 H, 5-H), 4.72 (d, J = 13.7 Hz, 1 H, H_A of CH_2Ph), 4.57 (d, J = 12.5 Hz, 1 H, H_A of CH_2Ph), 4.45 (d, J = 12.5 Hz, 1 H, H_B of CH_2Ph), 4.24 (d, J = 13.7 Hz, 1 H, H_B of CH_2Ph), 3.98 (dd, J = 9.1, 4.1 Hz, 1 H, 4-H), 3.74 (d, J = 4.1 Hz, 1 H, 3-H), 3.48 (s, 3 H, OCH_3), 2.24 (s, 3 H, CH_3) ppm. ^{13}C NMR: δ = 209.8 (CO), 151.5 (C-6), 137.8, 137.1 (C_{quat}, Ph), 128.2, 128.0, 127.7, 127.5, 127.3 (Ph), 98.2 (C-5), 88.1, 77.8 (C-4, C-3), 76.3, 69.3 (CH_2Ph), 55.7 (OCH_3), 27.4 (C-1) ppm. HRMS: calcd. for $C_{21}H_{24}O_4$: 358.2018 $[M + NH_4]^+$; found: 358.2015.

Synthesis of Ketoximes 3a,b, 12a−e and 16 and Aldoximes 7a,b. General Procedure: NEt_3 (0.19 g, 1.86 mmol) and $NH_2OH{\cdot}HCl$ (44·mg, 0.62 mmol) were added to a solution of the appropriate carbonilic compound (0.21 mmol) in freshly distilled THF (3 mL) and abs. EtOH (3 mL). The solution was stirred at 40 °C overnight. After evaporation of the solvent under reduced pressure the crude product was taken up with Et_2O and washed in a separating funnel with H_2O (till neutral), brine, dried with anhydrous Na_2SO_4 and the solvent removed. The residue was then purified by column chromatography.

Ketoxime 3a (*E*/*Z*): This compound was prepared by the general procedure from **2a** (189 mg, 0.42 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 75:25) to give **3a** as a viscous oil (156 mg, 80%). IR ($CHCl_3$): $\tilde{\nu}$ = 3577, 3355, 3090, 3080, 1610, 1460, 1095, 1075, 1040 cm^{-1}. ^1H NMR: $\delta = 7.45-7.22$ (m, 15 H, Ph), 6.65 (d, J = 14 Hz, 1 H, 6-H), 5.22−5.02 (m, 1 H, 5-H), 5.00−4.60 (m, 8 H, 3 CH_2Ph, 1-H_A, 1-H_B), 4.58−4.43 (m, 1 H, 3-H), 4.40−4.30 (m, 1 H, 4-H), 3.70 (s, 3 H, OCH_3), 3.30 (br. s, OH) ppm. ^{13}C NMR: δ = 156.8, 156.6 (C-2), 151.6, 151.5 (C-6), 138.6, 138.3, 138.0, 137.5, 137.6 (C_{quat}, Ph), 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3 (Ph), 99.1, 98.6 (C-5), 81.9, 78.8, 78.0, 77.1 (C-3, C-4), 73.5, 73.2, 72.9, 72.1 (CH_2Ph), 69.7, 67.9 (C-1), 55.8 (OCH_3) ppm. HRMS: calcd. for $C_{28}H_{31}NO_5$: 479.2546 $[M + NH_4]^+$; found: 479.2543.

Ketoxime 3b (*E*/*Z*): This compound was prepared by the general procedure from **2b** (183 mg, 0.41 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 75:25) to give **3b** as a viscous oil (151 mg, 80%). IR ($CHCl_3$): $\tilde{\nu}$ = 3578, 3350, 3090, 3080, 1615, 1520, 1510, 1500, 1460, 1100, 1075, 1040 cm^{-1}. ^1H NMR: δ ($CDCl_3$): 7.45−7.12 (m, 15 H, Ph), 6.48 (d, J = 13.3 Hz, 1 H, 6-H), 5.01−4.62 (m, 10 H, 3 CH_2Ph, 1-H_A, 1-H_B, 3-H, 5-H), 4.18 (dd, J = 9.3, 7.0 Hz, 1 H, 4-H), 3.53 (s, 3 H, OCH_3), 3.30 (br. s, OH) ppm. ^{13}C NMR: δ = 155.8 (C-2), 151.3 (C-6), 138.1, 138.0, 137.9, 137.8, 137.4 (C_{quat}, Ph), 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.2, 127.0, 126.8 (Ph), 99.4, 98.9 (C-5), 80.0, 77.8, 77.1, 76.8 (C-3, C-4), 75.9, 75.2, 72.9, 72.3, 72.2, 71.1 (CH_2Ph), 68.8, 67.0 (C-1), 55.3 (OCH_3) ppm. HRMS: calcd. for $C_{28}H_{31}NO_5$: 479.2546 $[M + NH_4]^+$; found: 479.2541.

Aldoxime 7a (*E*/*Z*): This compound was prepared by the general procedure from **6a** (97 mg, 0.30 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 75:25) to give **7a** as a viscous oil (91 mg, 90%). IR ($CHCl_3$): $\tilde{\nu}$ = 3568, 3340, 3078, 3070, 1625, 1560, 1520, 1510, 1470, 1100, 1085, 1030 cm^{-1}. ^1H NMR: δ = 8.68 (br. s, OH), 7.38 (d, J = 7.9 Hz, 1 H, 1-H), 7.40−7.20 (m, 10 H, Ph), 6.40 (d, J = 12.3 Hz, 1 H, 5-H), 4.72−4.62 (m, 3 H, CH_2Ph, H-4), 4.42 (t, J = 12.3 Hz, 2 H, CH_2Ph), 3.98 (dd, J = 7.9, 5.7 Hz, 1 H, 2-H), 3.85 (dd, J = 5.7, 3.3 Hz, 1 H, 3-H), 3.53 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 152.3 (C-1), 149.6 (C-5), 138.2, 137.7 (C_{quat}, Ph), 128.2, 128.1, 128.0, 127.9, 127.6, 127.4, 127.3 (Ph), 98.8 (C-4), 77.7, 76.8 (C-2, C-3), 71.0, 69.2 (CH_2Ph), 55.9 (OCH_3) ppm. HRMS: calcd. for $C_{20}H_{23}NO_4$: 359.1971 $[M + NH_4]^+$; found: 359.1975.

Aldoxime 7b (*E*/*Z*): This compound was prepared by the general procedure from **6b** (97 mg, 0.30 mmol) followed by column chro-

matography (SiO_2; *n*-hexane/EtOAc, 75:25) to give **7b** as a viscous oil (91 mg, 90%). IR ($CHCl_3$): $\tilde{\nu}$ = 3578, 3350, 3090, 3070, 1620, 1530, 1510, 1500, 1470, 1100, 1085, 1030 cm^{-1}. ^1H NMR: δ = 8.68 (br. s, OH), 7.38 (d, J = 7.9 Hz, 1 H, 1-H), 7.40−7.20 (m, 10 H, Ph), 6.48 (d, J = 12.9 Hz, 1 H, 5-H), 4.72−4.62 (m, 3 H, CH_2Ph, H-4), 4.42 (t, J = 12.3 Hz, 2 H, CH_2Ph), 3.98 (dd, J = 7.9, 6.1 Hz, 1 H, 2-H), 3.85 (dd, J = 6.1, 3.7 Hz, 1 H, 3-H), 3.53 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 151.9 (C-1), 149.6 (C-5), 138.2, 137.7 (C_{quat}, Ph), 128.2, 128.0, 127.9, 127.8, 127.6, 127.5, 127.3 (Ph), 98.8 (C-4), 78.7, 77.9 (C-2, C-3), 71.0, 69.2 (CH_2Ph), 55.9 (OCH_3) ppm. HRMS: calcd. for $C_{20}H_{23}NO_4$: 359.1971 $[M + NH_4]^+$; found: 359.1969.

Ketoxime 12a (*E*/*Z*): This compound was prepared by the general procedure from **11a** (184 mg, 0.21 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 75:25) to give **12a** as a viscous oil (150 mg, 80%). IR ($CHCl_3$): $\tilde{\nu}$ = 3570, 3358, 3078, 3080, 1620, 1457, 1120, 1100, 1090, 1065, 1040, 1028 cm^{-1}. ^1H NMR: δ = 7.48−7.15 (m, 30 H, Ph), 6.45 (m, 1 H, 6-H), 5.05−4.38 (m, 14 H, 6 CH_2Ph, 1′-H, 5-H), 4.36−4.20 (m, 7 H, 2′-H, 3′-H, 4′-H, 6′-H_A, 6′-H_B, 3-H, 4-H), 3.72−3.45 (m, 3 H, 5′-H, 1-H_A, 1-H_B), 3.45 (s, 1.7 of 3 H, OCH_3), 3.43 (s, 1.3 of 3 H, OCH_3) ppm. ^{13}C NMR: δ = 155.5, 155.0 (C-2), 151.3, 151.1 (C-6), 138.4, 138.2, 138.1, 138.0, 137.8, 137.6, 137.5, 137.3 (C_{quat}, Ph), 127.9, 127.8, 127.7, 127.6, 127.5, 127.3, 127.2, 126.9, 126.7 (Ph), 100.6, 100.2 (C-1′), 98.6 (C-5), 84.3, 81.7, 81.5, 78.6, 77.4, 76.8, 75.9, 75.2, 74.8, 74.1, 73.9, 73.0 (C-2′, C-3′, C-4′, C-5′, C-3, C-4), 75.4, 75.1, 74.9, 73.8, 73.5, 73.2, 73.1, 72.7, 70.0, 69.9, 69.0, 68.2, 67.6 (CH_2Ph, C-6′, C-1), 55.3 (OCH_3) ppm. HRMS: calcd. for $C_{55}H_{59}NO_{10}$: 911.4483 $[M + NH_4]^+$; found: 911.4489.

Ketoxime 12b (*E*/*Z*): This compound was prepared by the general procedure from **11b** (184 mg, 0.21 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 75:25) to give **12b** as a viscous oil (146 mg, 78%). IR ($CHCl_3$): $\tilde{\nu}$ = 3570, 3358, 3078, 3080, 1620, 1457, 1120, 1100, 1090, 1065, 1040, 1028 cm^{-1}. ^1H NMR: δ = 7.40−7.15 (m, 30 H, Ph), 6.50 (m, 1 H, 6-H), 5.15−4.38 (m, 14 H, 6 CH_2Ph, 1′-H, 5-H), 4.36−4.20 (m, 7 H, 2′-H, 3′-H, 4′-H, 6′-H_A, 6′-H_B, 3-H, 4-H), 3.72−3.45 (m, 3 H, 5′-H, 1-H_A, 1-H_B), 3.45 (s, 1.7 of 3 H, OCH_3), 3.43 (s, 1.3 of 3 H, OCH_3) ppm. ^{13}C NMR: δ = 155.1, 149.1 (C-2), 152.3, 151.1 (C-6), 138.4, 138.3, 138.1, 137.9, 137.7, 137.6, 137.4, 137.3 (C_{quat}, Ph), 127.9, 127.8, 127.7, 127.6, 127.3, 127.2, 126.9, 126.7, 126.6 (Ph), 99.0, 98.6, 97.6 (C-1′, C-5), 84.3, 81.7, 81.5, 79.6, 77.4, 76.7, 75.8, 75.2, 74.7, 74.0, 71.9, 71.2 (C-2′, C-3′, C-4′, C-5′, C-3, C-4), 75.4, 75.1, 74.9, 73.8, 73.5, 73.2, 73.1, 72.7, 70.0, 69.9, 69.0, 68.2, 67.6 (CH_2Ph, C-6′, C-1), 55.3 (OCH_3) ppm. HRMS: calcd. for $C_{55}H_{59}NO_{10}$: 911.4483 $[M + NH_4]^+$; found: 911.4480.

Ketoxime 12c (*E*/*Z*): This compound was prepared by the general procedure from **11c** (187 mg, 0.21 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 75:25) to give **12c** as a viscous oil (150 mg, 80%). IR ($CHCl_3$): $\tilde{\nu}$ = 3570, 3357, 3088, 3080, 1618, 1457, 1110, 1065, 1040 cm^{-1}. ^1H NMR: δ = 7.48−7.15 (m, 30 H, Ph), 6.48 (m, 1 H, 6-H), 5.05−4.38 (m, 14 H, 6 CH_2Ph, 1′-H, 5-H), 4.35−4.15 (m, 7 H, 2′-H, 3′-H, 4′-H, 6′-H_A, 6′-H_B, 3-H, 4-H), 3.92 (m, 1 H, 5′-H), 3.72−3.45 (m, 2 H, 1-H_A, 1-H_B), 3.45 (s, 1.7 of 3 H, OCH_3), 3.43 (s, 1.3 of 3 H, OCH_3) ppm. ^{13}C NMR: δ = 156.3, 155.7 (C-2), 151.7, 151.5 (C-6), 139.2, 139.1, 139.0, 138.8, 138.6, 138.5, 138.2, 138.0 (C_{quat}, Ph), 128.6, 128.4, 128.3, 128.1, 127.9, 127.8, 127.6, 127.5, 127.4 (Ph), 101.8, 101.2 (C-1′), 99.4 (C-5), 82.7, 82.5, 79.6, 79.5, 79.4, 78.6, 77.8, 74.8, 74.1, 73.7 (C-2′, C-3′, C-4′, C-5′, C-3, C-4), 75.4, 75.1, 74.9, 73.8, 73.5, 73.2, 73.1, 72.7, 70.0, 69.9, 68.8, 68.7, 68.3 (CH_2Ph, C-6′, C-1), 56.2, 56.0 (OCH_3) ppm. HRMS: calcd. for $C_{55}H_{59}NO_{10}$: 911.4483 $[M + NH_4]^+$; found: 911.4485.

Ketoxime 12d (*E*/*Z*): This compound was prepared by the general procedure from **11d** (179 mg, 0.20 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 75:25) to give **12d** as a viscous oil (137 mg, 75%). IR ($CHCl_3$): $\tilde{\nu}$ = 3570, 3358, 3078, 3080, 1620, 1457, 1120, 1100, 1090, 1065, 1040, 1028 cm^{-1}. ^1H NMR: δ = 7.40−7.15 (m, 30 H, Ph), 6.50 (m, 1 H, 6-H), 5.15−4.38 (m, 14 H, 6 CH_2Ph, 1′-H, 5-H), 4.36−4.20 (m, 7 H, 2′-H, 3′-H, 4′-H, 6′-H_A, 6′-H_B, 3-H, 4-H), 3.72−3.45 (m, 3 H, 5′-H, 1-H_A, 1-H_B), 3.45 (s, 1.7 of 3 H, OCH_3), 3.43 (s, 1.3 of 3 H, OCH_3) ppm. ^{13}C NMR: δ = 156.1, 155.4 (C-2), 152.3, 151.4 (C-6), 138.5, 138.4, 138.3, 138.1, 138.0, 137.8, 137.7, 137.6 (C_{quat}, Ph), 127.9, 127.8, 127.6, 127.5, 127.4, 127.1, 127.0, 126.9, 126.8, 126.7 (Ph), 98.1, 97.9, 97.6 (C-1′, C-5), 82.9, 82.1, 79.9, 79.6, 77.4, 76.7, 75.8, 75.2, 74.7, 74.0, 71.9, 71.2 (C-2′, C-3′, C-4′, C-5′, C-3, C-4), 75.4, 75.1, 74.9, 73.8, 73.5, 73.2, 73.1, 72.7, 70.0, 69.9, 69.0, 68.2, 67.6 (CH_2Ph, C-6′, C-1), 55.3 (OCH_3) ppm. HRMS: calcd. for $C_{55}H_{59}NO_{10}$: 911.4483 $[M + NH_4]^+$; found: 911.4488.

Ketoxime 12e (*E*/*Z*): This compound was prepared by the general procedure from **11e** (179 mg, 0.20 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 75:25) to give **12e** as a viscous oil (140 mg, 77%). IR ($CHCl_3$): $\tilde{\nu}$ = 3570, 3357, 3088, 3080, 1618, 1457, 1110, 1065, 1040 cm^{-1}. ^1H NMR: δ = 7.48−7.15 (m, 30 H, Ph), 6.46 (m, 1 H, 6-H), 5.03−4.38 (m, 14 H, 6 CH_2Ph, 1′-H, 5-H), 4.30−4.15 (m, 7 H, 2′-H, 3′-H, 4′-H, 6′-H_A, 6′-H_B, 3-H, 4-H), 3.92 (m, 1 H, 5′-H), 3.70−3.43 (m, 2 H, 1-H_A, 1-H_B), 3.45 (s, 1.5 of 3 H, OCH_3), 3.41 (s, 1.5 of 3 H, OCH_3) ppm. ^{13}C NMR: δ = 155.3, 154.7 (C-2), 151.4, 151.0 (C-6), 139.2, 139.0, 138.9, 138.7, 138.6, 138.3, 137.9, 137.0 (C_{quat}, Ph), 128.8, 128.6, 128.4, 128.3, 128.2, 128.1, 127.9, 127.6 127.4, 127.2, 127.0 (Ph), 102.8, 102.4 (C-1′), 97.4 (C-5), 85.7, 83.9, 81.5, 79.5, 79.2, 78.6, 77.8, 74.8, 74.1, 73.7 (C-2′, C-3′, C-4′, C-5′, C-3, C-4), 75.4, 75.1, 74.9, 73.8, 73.5, 73.2, 73.1, 72.7, 70.0, 69.9, 68.8, 68.7, 68.3 (CH_2Ph, C-6′, C-1), 55.2, 55.0 (OCH_3) ppm. HRMS: calcd. for $C_{55}H_{59}NO_{10}$: 911.4483 $[M + NH_4]^+$; found: 911.4487.

Ketoxime 16 (*E*/*Z*): This compound was prepared by the general procedure from **15** (189 mg, 0.55 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 75:25) to give **16** as a viscous oil (158 mg, 80%). IR ($CHCl_3$): $\tilde{\nu}$ = 3578, 3350, 3090, 3080, 1615, 1520, 1510, 1500, 1460, 1100, 1075, 1040 cm^{-1}. ^1H NMR: δ = 7.60−7.25 (m, 10 H, Ph), 6.40 (d, 0.6 of J = 6.3 Hz, 1 H, 6-H), 6.36 (d, 0.4 of J = 6.3 Hz, 1 H, 6-H), 5.05−4.42 (m, 5 H, 2 CH_2Ph, 5-H), 4.15−3.97 (m, 2 H, 3-H, 4-H), 3.56 (s, 3 H, OCH_3), 2.05 (s, 1.2 of 3 H, CH_3), 1.98 (s, 1.8 of 3 H, CH_3) ppm. ^{13}C NMR: δ = 157.9, 156.7 (C-2), 150.8 (C-6), 138.1, 137.5, 137.3 (C_{quat}, Ph), 127.7, 127.5, 127.3, 127.1, 127.0, 126.8 (Ph), 98.5, 98.3 (C-5), 83.5, 78.4, 77.4, 76.4 (C-3, C-4), 72.3, 71.0, 69.3, 69.1 (CH_2Ph), 55.4 (OCH_3), 15.9, 9.8 (C-1) ppm. HRMS: calcd. for $C_{21}H_{25}NO_4$: 373.2127 $[M + NH_4]^+$; found: 373.2130.

Synthesis of Nitriles 4a,b, 8b, 13a−c and 17. General Procedure: CH_3SO_2Cl (55 mg, 0.48 mmol) was added to a stirred solution of the appropriate oxime (0.16 mmol) in dry CH_2Cl_2 (4 mL) and NEt_3 (140 mg, 1.44 mmol). After stirring for 30 min at room temperature, the solvent was evaporated at reduced pressure and the residue was taken up with Et_2O, washed in a separating funnel with H_2O (till neutral), brine, dried with anhydrous Na_2SO_4 and the solvent removed. The crude product was then purified by column chromatography.

Nitrile 4a: This compound was prepared by the general procedure from **3a** (156 mg, 0.34 mmol) followed by column chromatography

(SiO_2; *n*-hexane/EtOAc, 85:15) to give **4a** as a viscous oil (66 mg, 60%). $[\alpha]_D = -45.2$ ($c = 1.4$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu} = 3100, 2900, 1600, 1480, 1360, 1190, 1110, 1040, 1018$ cm^{-1}. ^1H NMR: $\delta = 7.50-7.20$ (m, 10 H, Ph), 6.59 (d, $J = 12.9$ Hz, 1 H, 5-H), 4.88 (d, $J = 11.7$ Hz, 1 H, H_A of CH_2Ph), 4.79 (dd, $J = 12.9, 8.7$ Hz, 1 H, 4-H), 4.67 (s, 2 H, CH_2Ph), 4.58 (d, $J = 11.7$ Hz, 1 H, H_B of CH_2Ph), 4.28 (d, $J = 5.4$ Hz, 1 H, 2-H), 3.95 (dd, $J = 8.7, 5.4$ Hz, 1 H, 3-H), 3.62 (s, 3 H, OCH_3) ppm. ^{13}C NMR: $\delta = 153.3$ (C-5), 137.6, 135.8 (C_{quat}, Ph), 128.7, 128.5, 128.3, 127.7 (Ph), 116.6 (CN), 97.0 (C-4), 76.6 (C-3), 72.5 (CH_2Ph), 71.6 (C-2), 69.8 (CH_2Ph), 56.1 (OCH_3) ppm. HRMS: calcd. for $C_{20}H_{21}NO_3$: 341.1865 $[M + NH_4]^+$; found: 341.1870.

Nitrile 4a: This compound was prepared by the general procedure from **7a** (91 mg, 0.27 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 85:15) to give **4a** (77 mg, 90%).

Nitrile 4a: This compound was prepared by the general procedure from **12d** (137 mg, 0.15 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 85:15) to give **4a** (15 mg, 30%).

Nitrile 4a: This compound was prepared by the general procedure from **12e** (140 mg, 0.16 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 85:15) to give **4a** (20 mg, 40%).

Nitrile 4b: This compound was prepared by the general procedure from **3b** (151 mg, 0.33 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 85:15) to give **4b** as a viscous oil (64 mg, 60%). $[\alpha]_D = +18.0$ ($c = 1.4$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu} = 3100, 3090, 3070, 1680, 1618, 1587, 1540, 1500, 1420, 1400, 1390, 1020$ cm^{-1}. ^1H NMR: $\delta = 7.50-7.20$ (m, 10 H, Ph), 6.62 (d, $J = 13.3$ Hz, 1 H, 5-H), 4.98 (d, $J = 11.6$ Hz, 1 H, H_A of CH_2Ph), 4.75−4.60 (m, 3 H, CH_2Ph, 4-H), 4.58 (d, $J = 11.6$ Hz, 1 H, H_B of CH_2Ph), 4.20 (d, $J = 6.0$ Hz, 1 H, 2-H), 4.05 (dd, $J = 6.6, 6.0$ Hz, 1 H, 3-H), 3.55 (s, 3 H, OCH_3) ppm. ^{13}C NMR: $\delta = 152.9$ (C-5), 137.4, 135.7 (C_{quat}, Ph), 128.7, 128.5, 128.4, 128.3, 127.5 (Ph), 116.8 (CN), 97.4 (C-4), 76.6 (C-3), 72.3 (CH_2Ph), 71.3 (C-2), 69.7 (CH_2Ph), 56.0 (OCH_3) ppm. HRMS: calcd. for $C_{20}H_{21}NO_3$: 341.1865 $[M + NH_4]^+$; found: 341.1862.

Nitrile 8b: This compound was prepared by the general procedure from **7b** (91 mg, 0.27 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 85:15) to give **8b** (the enantiomer of **4b**) as a viscous oil (77 mg, 90%). $[\alpha]_D = -18.2$ ($c = 1.3$, $CHCl_3$).

Nitrile 13a: This compound was prepared by the general procedure from **12a** (150 mg, 0.17 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 85:15) to give **13a** as a viscous oil (76 mg, 60%). $[\alpha]_D = -25.6$ ($c = 1.4$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu} = 3048, 3046, 3022, 3018, 1696, 1540, 1500, 1415, 1220, 1182, 1098, 1022$ cm^{-1}. ^1H NMR: $\delta = 7.40-7.26$ (m, 25 H, Ph), 6.60 (d, $J = 13.2$ Hz, 1 H, 5-H), 4.90−4.40 (m, 16 H, 5 CH_2Ph, 1′-H, 2′-H, 3′-H, 4′-H, 2-H, 4-H), 4.05 (dd, $J = 9.8, 5.0$ Hz, 1 H, 3-H), 3.65−3.45 (m, 3 H, 5′-H, 6′-H_A, 6′-H_B), 3.40 (s, 3 H, OCH_3) ppm. ^{13}C NMR: $\delta = 153.0$ (C-5), 138.0, 137.6, 137.4, 137.1 (C_{quat}, Ph), 127.9, 127.8, 127.6, 127.3, 127.1 (Ph), 115.6 (CN), 100.6 (C-1′), 96.4 (C-4), 83.7, 80.9, 76.7, 75.6, 74.5, (C-2′, C-3′, C-4′, C-5′, C-3), 75.1, 74.4, 74.1, 72.9, 69.1 (CH_2Ph), 68.6 (C-2), 67.9 (C-6′), 55.5 (OCH_3) ppm. HRMS: calcd. for $C_{48}H_{51}NO_8$: 787.3802 $[M + NH_4]^+$; found: 787.3805.

Nitrile 13b: This compound was prepared by the general procedure from **12b** (146 mg, 0.16 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 85:15) to give **13b** as a viscous oil (68 mg, 55%). $[\alpha]_D = +44.0$ ($c = 1.1$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu} = 3033, 3030, 3020, 3010, 1696, 1540, 1510, 1410, 1222, 1182, 1098, 1020$ cm^{-1}. ^1H NMR: $\delta = 7.40-7.10$ (m, 25 H, Ph), 6.78 (d, $J = 12.6$ Hz, 1 H, 5-H), 5.00 (d, $J = 6.3$ Hz, 1 H, 1′-H), 4.96 (d, $J = 13.5$ Hz, 1 H, H_A of CH_2Ph), 4.84 (dd, $J = 12.6, 7.5$ Hz, 1 H, 4-H), 4.81 (d, $J = 13.5$ Hz, 1 H, H_B of CH_2Ph), 4.74−4.38 (m, 11 H, 4 CH_2Ph, 2′-H, 3′-H, 4′-H), 4.32 (d, $J = 6.9$ Hz, 1 H, 2-H), 4.02 (dd, $J = 7.5, 6.9$ Hz, 1 H, 3-H), 3.80−3.50 (m, 3 H, 5′-H, 6′-H_A, 6′-H_B), 3.56 (s, 3 H, OCH_3) ppm. ^{13}C NMR: $\delta = 153.5$ (C-5), 138.5, 138.0, 137.8, 137.6 (C_{quat}, Ph), 128.2, 127.9, 127.5 (Ph), 116.6 (CN), 99.6 (C-1′), 96.5 (C-4), 81.5, 79.3, 77.2, 71.5 (C-2′, C-3′, C-4′, C-5′, C-3), 70.9 (C-2), 75.6, 75.0, 73.5, 72.8, 69.7, 67.6 (CH_2Ph, C-6′), 56.2 (OCH_3) ppm. HRMS: calcd. for $C_{48}H_{51}NO_8$: 787.3802 $[M + NH_4]^+$; found: 787.3807.

Nitrile 13c: This compound was prepared by the general procedure from **12c** (150 mg, 0.17 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 85:15) to give **13c** as a viscous oil (76 mg, 60%). $[\alpha]_D = -37.0$ ($c = 1.4$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu} = 3058, 3022, 3018, 1760, 1698, 1540, 1500, 1418, 1300, 1180, 1100, 1048$ cm^{-1}. ^1H NMR: $\delta = 7.40-7.26$ (m, 25 H, Ph), 6.58 (d, $J = 12.6$ Hz, 1 H, 5-H), 4.95−4.59 (m, 10 H, 4 CH_2Ph, H_A of CH_2Ph, 4-H), 4.43 (m, 4 H, H_B of CH_2Ph, 1′-H, 2′-H, 2-H), 4.05 (dd, $J = 9.3, 9.3$ Hz, 1 H, 3-H), 3.91 (d, $J = 2.7$ Hz, 1 H, 4′-H), 3.81 (dd, $J = 9.9, 9.0$ Hz, 1 H, 5′-H), 3.62−3.51 (m, 3 H, 3′-H, 6′-H_A, 6′-H_B), 3.47 (s, 3 H, OCH_3) ppm. ^{13}C NMR: $\delta = 153.3$ (C-5), 138.2, 138.0, 137.9, 137.7, 137.4 (C_{quat}, Ph), 128.3, 128.0, 127.8, 127.7, 127.4 (Ph), 116.1 (CN), 101.2 (C-1′), 96.9 (C-4), 81.6, 78.6, 75.8, 73.7, 73.4 (C-2′, C-3′, C-4′, C-5′, C-3), 74.9, 74.6, 73.5, 73.3, 69.49 (CH_2Ph), 68.7 (C-2), 68.3 (C-6′), 55.9 (OCH_3) ppm. HRMS: calcd. for $C_{48}H_{51}NO_8$: 787.3802 $[M + NH_4]^+$; found: 787.3803.

Mesylate 17 (*E*/*Z*): This compound was prepared by the general procedure from **16** (158 mg, 0.44 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 85:15) to give **17** as a viscous oil (172 mg, 90%). IR ($CHCl_3$): $\tilde{\nu} = 3578, 3350, 3090, 3071, 1630, 1520, 1510, 1480, 1460, 1100, 1075, 1040$ cm^{-1}. ^1H NMR: $\delta = 7.40-7.20$ (m, 10 H, Ph), 6.58 (d, 0.1 of $J = 13.3$ Hz, 1 H, 6-H), 6.47 (d, 0.9 of $J = 13.3$ Hz, 1 H, 6-H), 4.80−4.32 (m, 6 H, 2 CH_2Ph, 3-H, 5-H), 3.84 (dd, $J = 9.9, 4.7$ Hz, 1 H, 4-H), 3.53 (s, 0.1 of 3 H, OCH_3), 3.48 (s, 0.9 of 3 H, OCH_3), 2.94 (s, 3 H, CH_3SO_2), 2.04 (s, 3 H, CH_3) ppm. ^{13}C NMR: $\delta = 168.5$ (C-2), 153.6, 152.0 (C-6), 137.9, 136.8 (C_{quat}, Ph), 128.4, 128.1, 127.8, 127.6, 127.5 126.8 (Ph), 97.7, 95.3 (C-5), 81.7, 77.9, 77.6 (C-3, C-4), 73.2, 70.1, 69.4 (CH_2Ph), 56.1, 55.9 (OCH_3), 36.2 (CH_3SO_2), 16.6 (C-1) ppm. HRMS: calcd. for $C_{22}H_{27}NO_6S$: 451.1903 $[M + NH_4]^+$; found: 451.1907.

Preparation of Aldehydes 18a,b. General Procedure: 4 M HCl (1 mL) was added to a solution of the appropriate enol ether (0.60 mmol) in THF (5 mL) and then stirred at room temperature for 4 h. The reaction mixture was diluted with Et_2O and washed in a separating funnel with $NaHCO_3$, H_2O, brine and dried with anhydrous Na_2SO_4. After evaporation of the solvent under reduced pressure the crude product was purified by column chromatography.

Aldehyde 18a: This compound was prepared by the general procedure from **4a** (150 mg, 0.46 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 7:3) to give **18a** as a viscous oil (122 mg, 85%). $[\alpha]_D = -22.5$ ($c = 1.4$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu} = 3100, 2900, 2700, 1700, 1500, 1480, 1360, 1190, 1110, 1040, 1018$ cm^{-1}. ^1H NMR: $\delta = 9.72$ (t, $J = 1.5$ Hz, 1 H, H−CO), 7.45−7.27, (m, 10 H, Ph), 4.82 (d, $J = 12.0$ Hz, 1 H, H_A of CH_2Ph), 4.64 (s, 2 H, CH_2Ph), 4.49 (d, $J = 12.0$ Hz, 1 H, H_B of CH_2Ph), 4.22 (m, 2 H, 2-H, 3-H), 2.88 (dd, $J = 5.7, 1.5$ Hz, 2 H, 4-H) ppm. ^{13}C NMR: $\delta = 198.0$ (CO), 136.8, 135.0 (C_{quat}, Ph), 128.6, 128.4, 128.0, 127.9 (Ph), 116.1 (CN), 73.5, 72.74 (CH_2Ph), 73.0, 69.1 (C-2, C-3),

45.0 (C-4) ppm. HRMS: calcd. for $C_{19}H_{19}NO_3$: 327.1709 [M + NH_4]$^+$; found: 327.1703.

Aldehyde 18b: This compound was prepared by the general procedure from **13c** (152 mg, 0.20 mmol) followed by column chromatography (SiO_2; *n*-hexane/EtOAc, 7:3) to give **18b** as a viscous oil (117 mg, 80%). $[\alpha]_D = -42.5$ ($c = 1.6$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3090, 3050, 2910, 2700, 1705, 1510, 1480, 1360, 1188, 1110, 1050, 1018 cm^{-1}. ^{1}H NMR: $\delta = 9.72$ (t, $J = 1.6$ Hz, 1 H, H-CO), 7.45−7.27 (m, 25 H, Ph), 4.92−4.58 (m, 11 H, 5 CH_2Ph, 1′-H), 4.42−4.30 (m, 2 H, 2′-H, 3-H), 4.05 (d, $J = 2.7$ Hz, 1 H, 4′-H), 3.81 (dd, $J = 9.3$, 9.3 Hz, 1 H, 5′-H), 3.62−3.51 (m, 4 H, 3′-H, 6′-H_A, 6′-H_B, 2-H), 2.90−2.82 (m, 2 H, 4-H_A, 4-H_B) ppm. ^{13}C NMR: δ = 197.8 (CO), 138.4, 138.2, 138.1, 137.9, 137.5 (C_{quat}, Ph), 128.6, 128.5, 128.3, 128.1, 127.4 (Ph), 116.1 (CN), 101.6 (C-1′), 81.6, 78.6, 75.8, 73.7, 73.4 (C-2′, C-3′, C-4′, C-5′, C-3), 74.9, 74.6, 73.5, 73.3, 69.49 (CH_2Ph), 68.7 (C-2), 68.3 (C-6′), 41.8 (C-4) ppm. HRMS: calcd. for $C_{46}H_{47}NO_8$: 759.3645 [M + NH_4]$^+$; found: 759.3648.

Synthesis of Pyranosylamine 19a: $NaBH_4$ (59 mg, 1.5 mmol) was added to a solution of **18a** (120 mg, 0.39 mmol) in dry THF (2 mL) and abs. EtOH (2 mL). The mixture was refluxed for 1.5 h and the solvent was removed under reduced pressure. The residue was taken up with Et_2O/EtOAc, 1:1, washed in a separating funnel with H_2O (till neutral), brine, dried with anhydrous Na_2SO_4 and the solvent removed. The crude product was then purified by column chromatography (SiO_2; *n*-hexane/EtOAc, 6:4) to give **19a** as a viscous oil (67 mg, 55% yield). $[\alpha]_D = +12.8$ ($c = 1.1$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3390, 3350, 3010, 2990, 1690, 1510, 1480, 1360, 1188, 1110, 1050, 1018 cm^{-1}. ^{1}H NMR: δ = 7.36−7.20 (m, 10 H, Ph), 4.72−4.43 (m, 5 H, 2 CH_2Ph, 1-H), 3.82−3.62 (m, 4 H, 2-H, 3-H, 5-H_A, 5-H_B), 2.63 (br. s, 2 H, NH_2), 1.98−1.80 (m, 2 H, 4-H_A, 4-H_B) ppm. ^{13}C NMR: δ = 137.9, 137.7 (C_{quat}, Ph), 128.3, 127.5, 127.2, 127.0 (Ph), 77.7, 77.1, 63.9 (C-1, C-2, C-3), 71.6 (CH_2Ph), 59.6 (C-5), 33.9 (C-4) ppm. HRMS: calcd. for $C_{19}H_{23}NO_3$: 331.2022 [M + NH_4]$^+$; found: 331.2028.

Synthesis of Pyranosylamine 19b: This compound was prepared from **18b** (117 mg, 0.16 mmol) in accord with the procedure described for **19a**, refluxing the reaction mixture for 4 h. The crude product was purified by column chromatography (SiO_2; *n*-hexane/EtOAc, 7:3) to give **19b** as a viscous oil (65 mg, 55% yield). $[\alpha]_D = -17.5$ ($c = 1.2$, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3389, 3350, 3012, 2990, 1692, 1516, 1478, 1360, 1188, 1110, 1048, 1013 cm^{-1}. ^{1}H NMR: δ = 7.42−7.20 (m, 25 H, Ph), 5.12−4.52 (m, 12 H, 4 CH_2Ph, 1′-H, 2′-H, 3′-H, 1-H), 4.43 (s, 2 H, CH_2Ph), 3.95−3.83 (m, 3 H, 4′-H, 2-H, 3-H), 3.80−3.68 (m, 3 H, 5′-H, 6′-H_A, 6′-H_B), 3.62−3.52 (m, 2 H, 5-H_A, 5-H_B), 2.05−1.85 (m, 2 H, 4-H_A, 4-H_B), 1.72 (br. s, 2 H, NH_2) ppm. ^{13}C NMR: δ = 137.9, 137.7, 137.2, 137.0 (C_{quat}, Ph), 128.0, 127.8, 127.6, 127.3, 127.0 (Ph), 101.3 (C-1′), 81.4, 78.3, 76.6, 75.4, 74.7, 73.3, 67.9, (C-2′, C-3′, C-4′, C-5′, C-1, C-2, C-3), 74.5, 74.4, 73.5, 73.0 (CH_2Ph), 67.6 (C-6′), 58.7 (C-5), 32.7 (C-4) ppm. HRMS: calcd. for $C_{46}H_{51}NO_8$: 763.3958 [M + NH_4]$^+$; found: 763.3960.

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