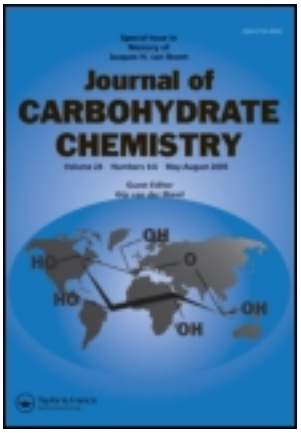

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Ram Chandra Mishra [a], Neetu Tewari [a], Shyam Sunder Verma [a], Rama Pati Tripathi [a], Manish Kumar [b] & Praveen Kumar Shukla [b]

[a] Division of Medicinal Chemistry, Central Drug Research Institute, Lucknow, 226001, India

[b] Medical Mycology, Central Drug Research Institute, Lucknow, India

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Diastereoselective Synthesis and Antifungal Activity of Glycosyl Isoxazolines[#]

Ram Chandra Mishra,[1] Neetu Tewari,[1] Shyam Sunder Verma,[1] Rama Pati Tripathi,[1,*] Manish Kumar,[2] and Praveen Kumar Shukla[2]

[1]Divisions of Medicinal Chemistry and [2]Medical Mycology, Central Drug Research Institute, Lucknow, India

CONTENTS

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[*]Correspondence: Rama Pati Tripathi, Division of Medicinal Chemistry, Central Drug Research Institute, Lucknow 226001, India; Fax: +91-522-2223938, 2223405; E-mail: rpt_56@yahoo.com.

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ABSTRACT

Glycosyl nitrile oxides, generated *in situ* by reaction of glycosyl oximes (**3a**, **3b**, **4**) with *N*-chlorosuccinimide and DBU, on 1,3-dipolar cycloaddition with substituted alkenes resulted in glycosyl isoxazolines (**5**, **7**–**28**) in diastereoselective manner. The extent of diastereoselection varies with the nature of substituents both in sugar and alkenes. The compounds synthesized were screened *in vitro* against many fungi wherein two of the compounds (**12**, **23**) showed significant inhibition against *Sporothrix schenckii*, *Trychophyton mentagrophytes*, and *Cryptococcus neoformans* with MIC of 12.5 and 6.25 μg/mL, respectively.

Key Words: Cycloaddition; Isoxazoline; DBU; Antifungal activity.

INTRODUCTION

1,3-Dipolar cycloaddition reactions of nitrones and nitrile oxides with alkenes for the synthesis of five membered heterocycles of synthetic and biological importance is known for quite some time.[1–3] Isoxazolines, isosters of oxazolidinones, which are well-known antibacterial agents, have recently been reported to be of great significance as antibacterial and antifungal agents.[4,5]

The stereochemistry in 1,3-dipolar cycloadditions is controlled either by choosing an appropriate substrate or controlling the geometry of the transition state during progress of the reaction by agents acting as catalyst or co-catalyst. If the alkene, or the 1,3-dipole, contains a chiral center(s), the approach towards one of the faces of the alkene or 1,3-dipole can be discriminated (diastereofacial selectivity) leading to a diastereoselectivity. The exo/endo selectivity is also diastereoselectivity, but for clarity endo/exo or cis-trans selectivity terms are preferred.

Existing reports for 1,3-dipolar additions using optically active nitrile oxides are scanty but of great synthetic value.[6–8] Application of chiral nitrile oxides generated *in situ* by reaction of oximes with *N*-bromosuccinimide in the presence of bases such as pyridine or triethylamine to get isoxazolines diastereoselectively have recently been reported[9] to prepare biologically active compounds. Synthetic application of carbohydrate-derived chiral building blocks as precursors for the synthesis of nitrogenated compounds such as amino sugars, alkaloids, and amino acids has been reported since long ago.[10,11] Asymmetric 1,3-dipolar cycloaddition utilizing either chiral nitrile oxide or chiral dipolarophile because of its versatility in the construction of diastereomerically pure compounds like amino alcohol, β-hydroxy ketones, amino acids, and many antibiotics are of much importance.[12] Carbohydrate-derived chiral nitrones have been used in asymmetric synthesis of fused or bridged isoxazoline, oxepans, and pyrans.[10] Keeping the aforementioned facts in mind and in the continuation of our work on the development of sugar derivatives as chemotherapeutic agents,[13] we were prompted to synthesize glycosylated isoxazolines, which may serve as intermediates for the synthesis of a variety of compounds. The compounds synthesized were screened against *Candida albicans*, *Candida parapsilosis* (ATCC 22019), *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Sporothrix schenckii*, and *Trychophyton mentagrophytes*.

RESULTS AND DISCUSSION

The glycosyl oximes[14] (**3a**, **3b**, **4**) were prepared from the respective uloses (**1a**, **1b**, **2**) by reaction with hydroxylamine hydrochloride separately in good yields. Glycosyl oximes on reaction with *N*-cholorosuccinimide led to the formation of intermediate glycosyl hydroxamoyl chlorides, which on treatment with diazabicyclo undecene (DBU) separately *in situ* resulted in glycosyl nitrile oxides. The intermediate nitrile oxides, so generated, on reaction with different dipolarophiles (alkenes) gave 3- glycosyl-2-isoxazolines in good yields with varying diastereoselection.

Thus reaction of glycosyl ulose **1a** with hydroxylamine hydrochloride resulted in a 1 : 1 mixture of syn/anti oxime **3a**, which on treatment with *N*-chlorosuccinimide gave the intermediate glycosyl hydroxamoyl chloride. *In situ* reaction of the intermediate hydroxamoyl chloride with DBU resulted in the formation of glycosyl nitrile oxide (unisolated), which on treatment with ethyl acrylate at 0°C gave a mixture of products from which only two products could be isolated by column chromatography. The faster-moving compound was found to be a diastereomeric mixture of 5-carbethoxy-3-(3′-*O*-methyl-1′, 2′-*O*-isopropylidene-tetrahydro-1′, 4′-furanos-4′-yl)-isoxazole (**5**). The two diastereomers formed were separated by repetitive column chromatography and characterized individually. The structure of compound **5** was established on the basis of spectral data and analysis. Compound **5** (major diastereoisomer) in IR spectrum exhibited absorption band at 1744 and 1625 cm^{-1}, indicating the presence of COOEt and C═N moieties, respectively. In the ^1H NMR spectrum a *dd* signal for two protons at δ 3.4 while a one-proton *m* at δ 4.99 accounted for the H-4 and H-5 of the isoxazoline ring, respectively. In ^{13}C NMR spectrum a signal corresponding to C═N appeared at δ 157 and signals corresponding to C-4 and C-5 of the isoxazoline ring appeared at δ 40.0 and 87.0, respectively, besides other usual signals. The minor diastereoisomer showed a *dd* for H-5 at δ 5.00 with $J = 9.6$ and 8.4 Hz, and an *m* at δ 3.40–3.34 accounted for methylene protons at C-4. In ^{13}C NMR there were slight differecnces in δ values of all the carbons. The second product, isolated from column, was found to be a furoxan derivative (**6**, 20%) formed by dimerization of the nitrile oxide. Its structure was also established on the basis of spectroscopic data and analysis. MS (FAB) of compound **6** showed a peak at 431 corresponding to $(M + H)^+$, while in the ^1H NMR spectrum all the proton signals in sugar moiety were duplicated and no proton signal corresponding to isoxazoline ring was observed. It is appropriate to mention here that when triethyl amine was used as a base instead of DBU in the aforementioned reaction, the yield of the isoxazoline is low and furoxan is the major product. Further, formation of hydroxamoyl chloride in the presence of triethyl amine is slow and always accompanied with a darkening of the reaction mixture while with DBU, hydroxamoyl formation followed by the addition of alkene is completed within 2–4 h and reaction mixture is comparatively clean.

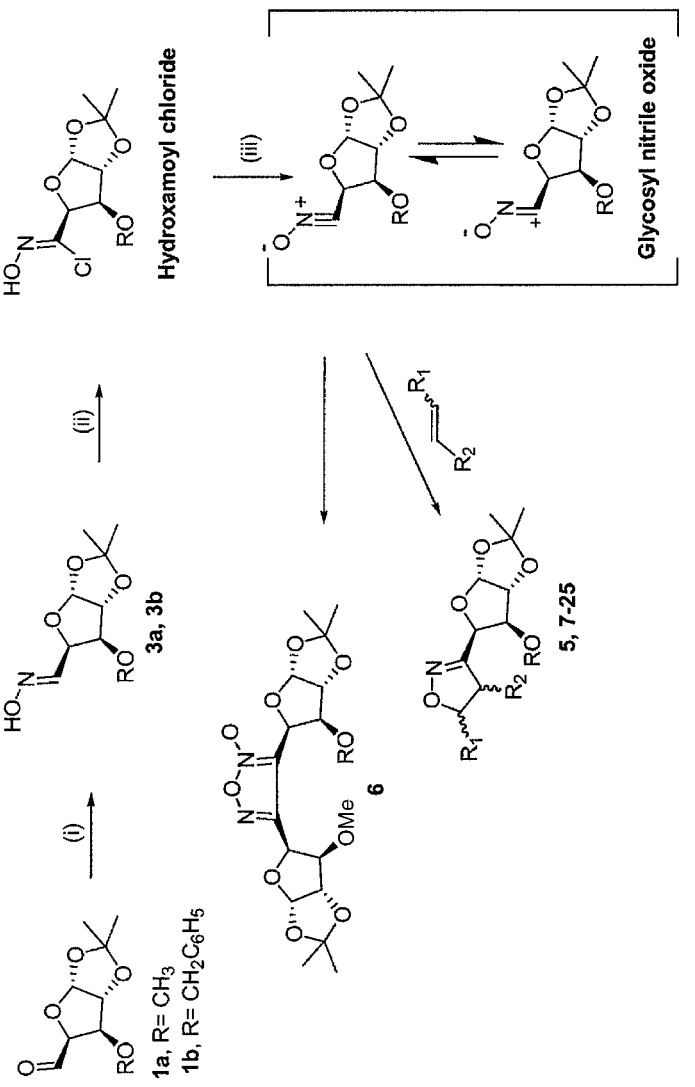
Similarly, reaction of **3a** with dipolarophiles including ethyl vinyl ether, vinyl acetate, methyl vinyl ketone, acrylo nitrile, allyl bromide, 2-allyl phenol, 4-allyl anisole, allyl alcohol, and crotonic acid separately resulted in the formation of respective glycosyl isoxazolines (**7**–**14**) as diastereomeric mixture in fair to good yields. Diastereomers could be separated in the reaction of ethyl vinyl ether and acrylonitrile with **3a** and characterized individually as major (**7**, **10**) and minor isomers. Minor isomer of **7** in ^1H NMR shows a *d* signal for H-5, while in major isomer it appeared as *dd*. Similarly for compound **10**, H-5 appeared as a *t* in the minor isomer while in major isomer as *m* at δ 5.21.

It is interesting to note that the reaction of crotonic acid with **3a** gave regioisomeric glycosyl isoxazoline (**15**) with 4-carboxy and 5-methyl substituents as distereoisomeric mixture. It is speculated that due to the electron-withdrawing effect of COOH, the polarization is in such a manner that electron density is more at β carbon to carboxyl group, which results in compound **15**. However, the formation of other regioisomer in minor amounts cannot be ruled out, because many unisolable products were observed on tlc plates. The structure of the compound **15** was elucidated on the basis of IR, MS (FAB), NMR spectral data and analysis. Compound **15** in the IR spectrum exhibited absorption band at 3352, 1769, and 1658 cm^{-1} indicating the presence of COOH and C═N moieties, respectively. MS (FAB) showed peak at m/z 302 corresponding to $(M + H)^+$. In ^1H NMR spectrum an *m* for one proton at δ 7.22 accounted for the H-4 and another *m* at δ 1.81 for H-5 of the isoxazoline ring. The ^{13}C NMR spectrum showed signals corresponding to COOH and C═N at δ 164.4 and δ 163.8, respectively, while signals at δ 149.5 & 118.5 accounted for C-4 and C-5 of the isoxazoline ring, respectively, besides other usual signals for sugar moiety.

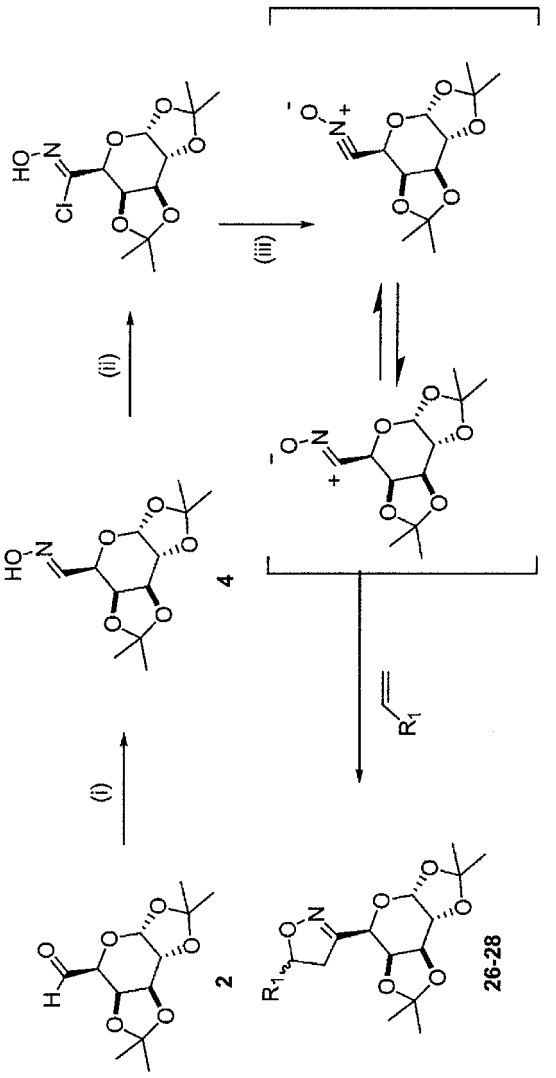
In the next attempt a glycosyl oxime with bulky 3-*O*-benzyl substituent was chosen as starting material to see whether there is any improvement on diastereoselection due to steric effect. Thus the reaction of oxime **3b** with *N*-chlorosuccinimide leads to the formation of intermediate hydroxamoyl chloride, which on treatment with DBU results in the respective nitrile oxide and the latter, on *in situ* reaction with ethyl acrylate, gave compound **16** in 75% yield as diastereomeric mixture. Some minor products, observed on thin layer chromatography plates formed in the reaction, could not be isolated. The structure of the compound **16** was elucidated on the basis of IR, FABMS, NMR spectral data, and analysis. Compound **16** in the IR spectrum exhibited absorption band at 1744 and 1625 cm^{-1}, indicating the presence of COOEt and C═N moieties, respectively. The MS (FAB) showed peak at m/z 392 corresponding to $(M + H)^+$, and in the ^1H NMR spectrum an *m* for two protons at δ 3.40 while a one-proton *m* at δ 4.93 accounted the H-4 and H-5 of the isoxazoline ring, respectively (Sch. 1). The ^{13}C NMR showed two signals corresponding to C═N at δ 157.3 and 156.7 for each diastereomer, while signals at δ 40.5 and δ 40.5 accounted for C-4 of the two diastereomers and another signal at δ 85.3 corresponded to C-5 of the isoxazoline ring, respectively, besides other usual signals (Sch. 2).

Similar reaction of **3b** with *N*-chlorosuccinimide followed by treatment with DBU and subsequent cycloaddition of ethyl vinyl ether, vinyl acetate, methyl vinyl ketone, acrylonitrile, allyl bromide, 2-allyl phenol, 4-allyl anisole, and allyl alcohol separately resulted in the formation of respective glycosyl isoxazolines (**17**–**24**) in good yield with marginal diastereoselection (Tab. 1). The structures of all the products were determined on the basis of spectroscopic data and analysis. However, reaction of **3b** with crotonic acid here too resulted in regioisomeric glycosyl isoxazoline (**25**) with 4-carboxyl and 5-methyl substituents.

The ^1H NMR spectrum of all the glycosyl isoxazolines, except compound **25**, showed characteristic signals for H-4 and H-5 of isoxazoline ring as *d*, *dd*, or *m* at around δ 3.5 and as *t*, *dd*, or *m* at around δ 5.0, respectively, while H-4′ (sugar ring) in all the compounds appeared downfield at around δ 5.1–5.2. In ^{13}C NMR C-5 in all the compounds was observed around δ 65.0–87.0 (δ 102.6 in compound **7**) depending upon the nature of substituents, while C-4 in these compounds appeared between δ 37.0–41.0. All the compounds showed $(M + H)^+$ peaks in their FAB MS. Only a marginal diastereoselection was noticed in most of the cases. It is appropriate to mention here that all the spots observed on



Scheme 1.



Scheme 2. Reagents & condition: (i) NH_2OH, DMAP, Alcohol, Pyridine, rt (ii) NCS, CH_3CN, rt (iii) DBU, 0° to rt.

Table 1. Glycosyl isoxazolines synthesized.

Entry	Compound no.	R	R_1	R_2	% Yield	Ratio of isomers[#]
1	**5**	CH_3	$COOC_2H_5$	H	70	75 : 25
2	**7**	CH_3	OC_2H_5	H	60	60 : 40
3	**8**	CH_3	$OCOCH_3$	H	60	62 : 38
4	**9**	CH_3	$COCH_3$	H	54	55 : 45
5	**10**	CH_3	CN	H	55	55 : 45
6	**11**	CH_3	CH_2Br	H	58	60 : 40
7	**12**	CH_3	CH_2PhOH	H	75	75 : 25
8	**13**	CH_3	CH_2PhOCH_3	H	79	65 : 35
9	**14**	CH_3	CH_2OH	H	60	55 : 45
10	**15**	CH_3	CH_3	COOH	58	60 : 40
11	**16**	CH_2Ph	$COOC_2H_5$	H	75	80 : 20
12	**17**	CH_2Ph	OC_2H_5	H	65	65 : 35
13	**18**	CH_2Ph	$OCOCH_3$	H	75	65 : 35
14	**19**	CH_2Ph	$COCH_3$	H	59	60 : 40
15	**20**	CH_2Ph	CN	H	50	62 : 38
16	**21**	CH_2Ph	CH_2Br	H	80	70 : 30
17	**22**	CH_2Ph	CH_2PhOH	H	75	90 : 10
18	**23**	CH_2Ph	CH_2PhOCH_3	H	80	75 : 25
19	**24**	CH_2Ph	CH_2OH	H	65	65 : 35
20	**25**	CH_2Ph	CH_3	COOH	55	65 : 35
21	**26**	—	$COOC_2H_5$	H	65	60 : 40
22	**27**	—	CH_2PhOH	H	55	70 : 30
23	**28**	—	CH_2OH	H	75	60 : 40

[#]Determined on the basis of integration of ^{1}H NMR signal.

tlc plates in the reactions could not be isolated, thus the possibility of regioisomeric isoxazolines cannot be ruled out in few cases.

Compound **25** in its IR spectrum exhibited absorption bands at 3280, 1770, 1658, and 1587 cm^{-1} corresponding to carboxylic acid and C═N moieties; MS (FAB) showed peak corresponding to $(M + H)^+$ at m/z 378. In ^{1}H NMR a broad singlet at δ 9.64 exchangeable with D_2O corresponds to carboxyl proton, while H-4 and H-5 of the isoxazoline ring appeared as *m* at δ 7.13 and δ 1.94 a *m*, respectively, beside other usual signals. In ^{13}C NMR spectrum of compound **25** signals corresponding to COOH and C═N of the isoxazoline ring appeared at δ 173.0 and 164.3, beside other usual signals.

Among all the compounds (**5**, **7**–**25**) the maximum diastereoselection (9 : 1) was noticed in reaction of **3b** with 2-allyl phenol for compound **22**. As changing the substituent in the sugar ring did not improve the diastereoselection, we were curious to compare the diastereoselectivity of furanose and pyranose skeletons at least with three alkenes, ethyl acrylate, allyl alcohol, and 2-allyl phenol. Thus, galactopyranosyl oxime (**4**), obtained from the galactopyranosyl ulose (**2**)[15] and hydroxylamine hydrochloride, on treatment with *N*-chlorosuccinimide resulted in the unisolated galactopyranosyl hydroxamoyl chloride, which on addition of DBU gave glycosyl nitrile oxide and the latter on *in situ* reaction with ethyl acrylate gave a diastereoisomeric mixture of galactopyranosyl isoxazolines (**26**) in 65% yield. The structure of **26** was elucidated on the basis of IR, NMR, and MS spectral data. The

MS showed the peak at m/z 372 corresponding to $(M+H)^+$, while the IR spectrum exhibited an absorption band at 1745 cm^{-1} and 1631 cm^{-1} corresponding to COOEt and C═N of the isoxazoline ring, respectively. In the ^1H NMR spectrum two *m* were observed at δ 4.82 and δ 3.45, each accounting for diastereomeric H-5 and H-4, respectively, in the isoxazoline ring, besides other usual signals.

Similar sequence of reactions of galactopyranosyl oxime with *N*-chlorosuccinimide treatment with DBU followed by cycloaddition of 2-allyl phenol resulted in compound **27** as diastereomeric mixture (7 : 3). The structural elucidation was carried out using IR, FABMS, and NMR spectroscopy. The IR spectrum exhibited absorption bands at 3467, 2985, and 1597 cm^{-1} corresponding to –OH, ArCH, and C═N of the isoxazoline moiety, while FAB MS showed $(M+H)^+$ at m/z 406. In the ^1H NMR spectrum a broad singlet at δ 6.70 accounted for aromatic –OH, and two *m* at δ 5.65 and 3.09 accounted for the H-5 and H-4 of the isoxazoline ring. ^{13}C NMR showed characteristic signals at δ 158.2, 65.5, 65.8, and 37.2 for C═N, C-5 (diastereomeric), and C-4. Similar cycloadditon of allyl alcohol with the nitrile oxide, generated from galactopyranosyl oxime, gave a diastereomeric mixture of isoxazoline **28** in 75% yield. Compound **28** in IR exhibited absorption bands at 3469 cm^{-1} and 1599 cm^{-1}, while FAB MS showed base peak at 330 $(M+H)^+$. In ^1H NMR an *m* at δ 4.67 for three protons accounted H-5 of the isoxazoline ring and H-3′ & H-5′ of the sugar ring, while two *dd* at δ 3.23 and 2.94 corresponded to H-4 of the isoxazoline ring. In ^{13}C NMR signals at δ 65.47 and 65.35 were accounted for diastereomeric C-5 and a signal at δ 37.03 was assigned for C-4 of the isoxazoline ring beside other usual signals.

Formation of two diastereoisomers, endo/exo or syn/anti, in different ratios could be rationalized considering the Houk and Felkin Anh models of the transition states formed during the reaction. The major products in allyl derivatives arise from a transition state **I** in which the largest group occupies the anti position, the medium group the inside position, and the smallest group the outside position,[2,16] the medium and smallest group being the same proton in all the cases. The minor products may arise from the transition state **II**, in which the location of the largest group is outside or inside. The outside position is more sterically demanding than the inside due to the angle of approach of the nitrile oxide oxygen.

Similarly for vinyl derivatives major products may be formed from the transition state **III** and the minor products from a transition state **IV** if we consider the Houck model[2] or Felkin model. However, if hyperconjugative effect is taken into consideration, the transition state **V** gives the major isomer because the electron-withdrawing substituents are known to occupy the inside or outside positions in order to exert minimal electron withdrawal from the alkene, as this addition is presumed to be mildly electrophilic in nature. Because outside position is more sterically demanding[16] the major product arises from **V** while the minor one from **VI** (Fig. 1). As evident from the results and transition states proposed, the diastereoselectivity is mainly dependent on the size and nature of substituent in alkene and almost independent of sugar substituents (Fig. 2).

Antifungal Evaluation of the Compounds

The minimum inhibitory concentration (MIC) for each compound against the test fungi was determined using a broth micro-dilution technique as per guidelines

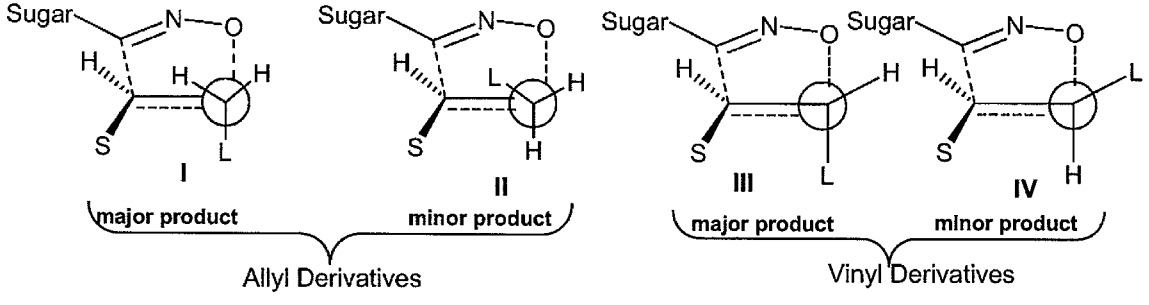


Figure 1. Transition state models for isoxazoline formation.

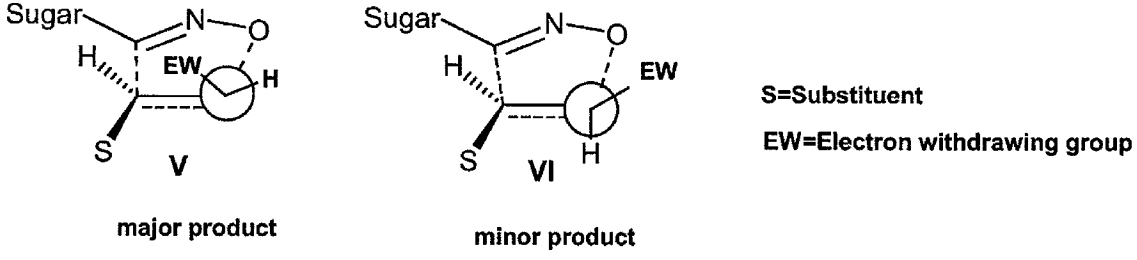


Figure 2. Hyperconjugative effect transition state models for isoxazoline formation.

of NCCLS M-27A[17]. The MIC of standard antifungals and synthetic compounds were measured in 96 well tissue culture plates (Cellstar Greiner Bio One, Germany) using RPMI 1640 media buffered with MOPS (3-[*N*-Morpholino] propanesulfonic acid) (Sigma Chemical Co.). Starting inocula of test cultures were maintained at $1.0-5.0 \times 10^3$ cfu/mL. All the compounds were tested between the range of 50–0.78 μg/mL. Microtiter plates were incubated at 35°C in a moist, dark chamber, and MICs were recorded spectrophotometrically (Softmax pro® 4.3, Versamax microplate reader, Molecular Devices) after 48 h for *Candida* spp. and 72 h for *Cryptococcus* spp. and mycelial fungi, while for *T. mentegrophytes* it was documented after 96 h.

Antifungal Activity

It is evident from the antifungal activity data (Tab. 2) that except compound **14** all the compounds belonging to glycosyl isoxazolines exhibited inhibition of fungal growth at a concentration ranging from 50 μg/mL to 6.25 μg/mL. A glycosyl isoxazoline (**23**) with a hydrophobic 3′-*O*-benzyl substituent in the sugar ring was found to be the most active against the dermatophyte *T. mentagrophytes* (MIC 6.25 μg/mL). Compound **12** with 3′-*O*-methyl substituent and compound **22** with a hydroxy substituent at C-5 of isoxazoline moiety were less potent with an MIC value of 12.5 μg/mL, indicating the importance of hydrophobicity in fungal growth inhibition. Because compound **23** is a diastereoisomeric mixture and it was the most active compound in the series, we were interested to see the activity of individual diastereoisomers. Repetitive column chromatography led to separation of only the major isomer in pure form, and the minor isomer was always contaminated with the major isomer. The pure major diastereoisomer and mixture of minor and major isomers were screened separately. It was found that the major has an

Table 2. Antifungal activity of glycosylisoxazolines showing MIC against different fungal strains.

Compd. no.	Cn	Ss	Tm	Compd. no.	Cn	Ss	Tm
5	25 (50)	25 (25)	25 (25)	**17**	25	50	50
7	25 (25)	12.5 (25)	25 (6.25)	**18**	50	50	50
8	25	50	25	**19**	12.5	50	25
9	25	25	50	**20**	25	50	50
10	50 (25)	50 (25)	50 (6.25)	**21**	25	25	25
11	25	12.5	50	**22**	12.5	50	12.5
12	12.5	50	12.5	**23**	25 (25)	>50	6.25 (>12.5)
13	25	50	12.5	**24**	25	25	12.5
14	>50	>50	>50	**25**	nd	nd	nd
15	12.5	50	50	**26**	12.5	50	50
16	12.5	50	25	**27**	25	50	50
Ketoconazole	0.12	0.50	0.25	**28**	12.5	50	50

Figures in ( ) indicate MIC for minor isomers in given cases.
Cn = *Cryptococcus neoformans*; Tm = *Trychophyton mentagrophytes*; Ss = *Sporothrix schenckii*. The compounds did not show any activity against *Candidia albicans*, *Candida parapsilosis* (ATCC 22019), and *Aspergillus fumigatus* at the concentrations tested.

MIC of 6.25 μg/mL while the minor isomer (contaminated with the major isomer) has an MIC of >12.5 μg/mL. The dermatophytes including *T. mentagrophytes* in patients with advanced HIV infection can extend to large area of the body,[18] hence this series of compounds offers a lead to further optimization in order to get better and safer antidermatophytic agents.

EXPERIMENTAL

General methods. Thin-layer chromatography was carried out on silica gel (Kiesel 60-F254, Merck) and spots were developed in iodine vapors and also by spraying with 5% sulfuric acid in alcohol followed by heating at 100°C. Column chromatography was carried out on flash silica gel (230–400 mesh, Merck) using the indicated eluent. IR spectra were recorded as thin films on KBr plates with a Perkin Elmer 881 spectrophotometer. NMR spectra were recorded on Bruker spectrometers, 200 and 300 MHz, and reference used was $CDCl_3$. Chemical shifts were given as δ ppm values and J values were given in Hertz (Hz). Elemental analyses were performed on a Perkin-Elmer 2400 II elemental analyzer. The optical rotations were measured in a 1.0 dm tube with Jasco dip-140 polarimeter in chloroform. The excess of the reagents or solvents were evaporated under reduced pressure at a bath temperature between the ranges 55°C and 60°C.

General Procedure for the preparation of compounds 3a, 3b & 4: 5-Deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-oximinyl-α-D-xylofuranose (3a). A mixture of 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranos-5-ulose (**1**, 10.0 g, 49.5 mmol), hydroxylamine hydrochloride (3.48 g, 50.0 mmol), and dimethyl aminopyridine (6.1 g, 50.0 mmol) in ethanol and pyridine (25 mL each) was magnetically stirred at room temperature for 2 h. The solvent was evaporated under reduced pressure and the crude mass, thus obtained, was dissolved in ethylacetate (2 × 100 mL), washed with water (2 × 20 mL), and dried (Na_2SO_4). Solvents evaporated under reduced pressure to get syrup which on column chromatography (SiO_2) using hexane:ethyl acetate (17 : 3) as eluant afforded the required compound **3a** as colorless viscous oil, Rf 0.55 (hexane:ethyl acetate, 7 : 3); $[\alpha]_D^{20}$ −32.6° (*c* 0.175, $CHCl_3$), MS (FAB) = m/z 218 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 3396, 2989, 2836, 2143, 1710, 1630, 1457, 1379; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.47 (d, J = 7.3 Hz, 1H, CH═N, anti isomer), 6.90 (d, J = 3.4 Hz, 1H, CH═N, syn isomer), 5.96 (d, J = 2.5 Hz, 2H, diastereomeric H-1'), 5.20 (dd, J = 3.4 and 3.3 Hz, 1H, H-4, syn isomer), 4.73 (dd, J = 7.3 and 3.3 Hz, 1H, H-4, anti isomer), 4.61 (d, J = 2.5 Hz, 2H, H-2 of each isomer), 4.15 and 3.81 (d, J = 3.3 Hz, 1H, H-3 of each isomer), 3.40 and 3.39 (s, 3H, OCH_3 of each isomer), 2.10 (s, exchangable with D_2O, 1H, N-OH), 1.51 and 1.33 [each s, 12H, $C(CH_3)_2$ of each isomer].

Anal. Calcd for $C_9H_{15}NO_5$: C, 49.76; H, 6.96; N, 6.45. Found: C, 49.93; H, 7.11; N, 6.32.

3-*O*-Benzyl-5-deoxy-1,2-O-isopropylidene-5-oximinyl-α-D-xylofuranose (3b). Colorless Solid, Mp 159°C, Rf 0.65 (hexane:ethyl acetate, 7:3); $[\alpha]_D^{20}$ −42.7° (*c* 0.275, $CHCl_3$), MS (FAB) = m/z 294 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 3412, 3251, 2995, 2371, 2162, 1628, 1450, 1384; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.67 (s, 1H, CH═N),

7.30 (m, 5H, ArH), 6.98 (d, $J = 3.9$ Hz, 1H, CH═N), 5.99 (d, $J = 3.7$ Hz, 1H, H-1), 5.23 (m, 1H, H-4), 4.61 (m, 3H, H-2 and $-OCH_2Ph$), 4.37 (d, $J = 3.2$ Hz, 1H, H-3), 1.50 and 1.32 [s, 6H, $C(CH_3)_2$].

Anal. Calcd for $C_{15}H_{19}NO_5$: C, 61.42; H, 6.53; N, 4.78. Found C, 61.65; H, 6.73; N, 4.55.

6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-oximinyl-α-D-galactopyranose (4). Colorless Solid, Mp 82°C, Rf 0.60 (hexane:ethyl acetate, 7:3); $[\alpha]_D^{25}$ −53.4° (*c* 0.28, $CHCl_3$); MS (FAB) = m/z 274 $(M + H)^+$; IR (Neat): ν_{max} cm^{-1} 3396, 2989, 2836, 2143, 1710, 1630, 1457, 1379; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.48 (d, $J = 7.3$ Hz, 1H, CH═N, anti isomer), 6.80 (d, $J = 3.4$ Hz, 1H, CH═N, syn isomer) 5.57 (d, $J = 4.9$ Hz, 2H, diastereomeric H-1'), 4.66 (m, 2H, H-3, and H-2), 4.33 (m, 2H, H-4, and H-5) 1.55, 1.51 and 1.33 [s, 12H, $C(CH_3)_2$ of each isomer].

Anal. Calcd for $C_{12}H_{19}NO_6$: C, 52.74; H, 7.01; N, 5.13. Found: C, 52.74; H, 7.01; N, 5.13.

General Procedure for the preparation of compounds 5, 7–28: 5(*R*,*S*)-Carbethoxy-3-[(*1'R*, *2'R*, *3'S*, *4'R*)-1',2'-*O*-isopropylidene-3'-*O*-methyl-tetrahydrofuranos-4'-yl]-2-isoxazoline (5). To a stirring solution of compound **3a** (0.6 g, 2.76 mmol) in acetonitrile (7.0 mL) at 0°C *N*-chlorosuccinimide (0.37 g, 2.80 mmol) was added and stirring continued for 1.5 h. Conversion of the oxime to chloroxime was monitored by thin layer chromatography. DBU (0.42 g, 2.76 mmol) was slowly added to the reaction mixture followed by addition of ethyl acrylate (1.4 g, 14.0 mmol) and the reaction continued for 4 h. Solvent was evaporated and the residue obtained was dissolved in ethyl acetate (50 mL), washed with water (2 × 25 mL), and saturated solution of NaCl (2 × 25 mL), and dried (Na_2SO_4). The solvent evaporated under reduced pressure to get a crude product, which was chromatographed over SiO_2 using hexane:ethyl acetate (17 : 3) as eluent to give compound **5** major isomer as colorless oil, Rf 0.70 (hexane:ethyl acetate, 7:3); $[\alpha]_D^{25}$ +49.1° (*c* 0.175, $CHCl_3$), MS (FAB) = m/z 316 $(M + H)^+$; IR (Neat): ν_{max} cm^{-1} 2985, 2362, 1744, 1625, 1540, 1377; ^1H NMR ($CDCl_3$, 200 MHz): δ 5.96 (d, $J = 3.6$ Hz, 1H, H-1'), 5.13 (d, $J = 3.6$ Hz, 1H, H-4') 4.99 (t, $J = 9.6$ Hz, 1 H, H-5), 4.60 (d, $J = 3.6$ Hz, 1H, H-2'), 4.24 (q, $J = 7.2$ Hz, OCH_2), 3.89 (d, $J = 3.6$ Hz, 1H, H-3'), 3.40–3.36 (m, 2H, H-4 isoxazoline ring), 3.38 (s, 3H, OCH_3), 1.50 and 1.33 [s, 3H, $C(CH_3)_2$], 1.28 (t, $J = 7.2$ Hz, $-OCH_2CH_3$).^{13}C NMR ($CDCl_3$): δ 170.6 (C = O), 157.1 (C = N); 112.7 [$C(CH_3)_2$]; 105.0 (C-1'); 87.3 (C-5), 81.8 (C-2'); 77.7 (C-4'); 76.2 (C-3); 62.2 (OCH_2); 58.4 (OCH_3), 40.5 (C-4); 27.2, 26.7 [$>C(CH_3)_2$] and 14.5 (CH_2CH_3).

Compound **5** minor isomer: MS (FAB) = m/z 316 $(M + H)^+$; ^1H NMR ($CDCl_3$, 200 MHz): δ 5.97 (d, $J = 3.6$ Hz, 1H, H-1'), 5.14 (d, $J = 3.3$ Hz, 1H, H-4') 5.00 (dd, $J = 9.6$ and 8.4 Hz, 1 H, H-5), 4.61 (d, $J = 3.6$ Hz, 1H, H-2'), 4.25 (q, $J = 7.2$ Hz, OCH_2), 3.91 (d, $J = 3.3$ Hz, 1H, H-3'), 3.40–3.34 (m, 2H, H-4 isoxazoline ring), 3.38 (s, 3H, OCH_3), 1.50 and 1.33 [s, 3H, $C(CH_3)_2$], 1.28 (t, $J = 7.2$ Hz, $-OCH_2CH_3$).

Anal. Calcd for $C_{14}H_{21}NO_7$: C, 53.33; H, 6.71; N, 4.44. Found: C, 53.46; H, 6.92; N, 4.31.

3,4-*Bis*-[(*1'R,2'R,3'S,4'R*)-1',2'-*O*-isopropylidene-3'-*O*-methyl-tetrahydrofuranos-4'-yl]-1,2,5-oxadizole-2-oxide (6). Colorless oil, Rf 0.40 (hexane:ethyl acetate, 7:3); MS (FAB) = m/z 431 $(M + H)^+$; IR (Neat): ν_{max} cm^{-1} 2988, 2839, 1609, 1475, 1379; ^1H NMR ($CDCl_3$, 200 MHz): δ 6.07 and 6.01 (each d, $J = 3.6$ Hz, each 1H, H-1'), 5.55

and 5.28 (each d, $J = 3.0$ and 3.3 Hz, each 1H, H-4′), 4.67 (d, $J = 3.6$ Hz, 2H, H-2′), 4.17 and 3.89 (each d, $J = 3.0$ and 3.3 Hz, each 1H, H-3′), 3.33 and 3.29 (each s, each 3H, OCH_3), 1.53 and 1.36 [each s, each 6H, C (CH_3)$_2$].

Anal. Calcd for $C_{18}H_{26}N_2O_{10}$: C, 50.23; H, 6.09; N, 6.51; O, 37.17 Found: C, 50.43; H, 6.37; N, 6.32.

5(*R*,*S*)-Ethoxy-3-[(*1′R,2′R,3′S,4′R*)-1′,2′-*O*-isopropylidene-3′-*O*-methyltetrahydrofuranos-4′-yl]-2-isoxazoline (7). Major isomer: white solid m.p. 84°C, Rf 0.65 (hexane:ethyl acetate, 3 : 1); $[\alpha]_D^{25}$ −86.5° (*c* 0.275, $CHCl_3$), MS (FAB) = m/z 288 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 2983, 2362, 1616, 1453, 1378, 1300 ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.96 (d, $J = 3.6$ Hz, 1H, H-1), 5.55 (dd, $J = 6.5$ and 2.3 Hz, 1H, H-5), 5.11 (d, $J = 3.2$ Hz, 1H, H-4′), 4.59 (d, $J = 3.6$ Hz, 1H, H-2′), 3.90 (d, $J = 3.2$ Hz, 1H, H-3′), 3.84 and 3.55 (each m, 2H, $-OCH_2CH_3$), 3.36 (s, 3H, OCH_3), 3.06 (dd, $J = 12.5$ and 6.5 Hz, 1H, H- 4_A), 2.98 (dd, $J = 12.5$ and 2.3 Hz, 1H, H-4_B),1.50 and 1.33 [s, 6H, C (CH_3)$_2$], 1.28 (t, $J = 7.0$ Hz, -CH_2CH_3).

Minor isomer: Colorless oil, Rf 0.67 (hexane:ethyl acetate, 3 : 1); $[\alpha]_D^{25}$ +23.5° (*c* 0.275, $CHCl_3$), MS (FAB) = m/z 288 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 2983, 2362, 1616, 1453, 1378, 1300 ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.96 (d, $J = 3.3$ Hz, 1H, H-1), 5.56 (d, $J = 6.0$ Hz, 1H, H-5), 5.13 (d, $J = 2.7$ Hz, 1H, H-4′), 4.61 (d, $J = 3.3$ Hz, 1H, H-2′), 3.90 (d, $J = 2.7$ Hz, 1H, H-3′), 3.83 and 3.56 (each m, 2H, $-OCH_A$ & $-OCH_B$), 3.38 (s, 3H, $-OCH_3$), 3.14 (dd, $J = 18.0$ and 6.0 Hz, 1H, H-4_A), 3.02 (d, $J = 18.0$ Hz, 1H, H-4_B), 1.52 and 1.35 [s, 6H, C (CH_3)$_2$], 1.20 (t, $J = 7.0$ Hz, $-CH_2CH_3$). ^{13}C NMR ($CDCl_3$): δ 157.7 (C═N); 112.1 [$C(CH_3)_2$]; 105.1 (C-1′); 102.6 (C-5), 86.7 (C-2′); 81.4 (C-4′); 76.0 (C-3); 63.3 (OCH_2); 57.9 (OCH_3), 42.3 (C-4); 26.8, 26.2 [>$C(CH_3)_2$] and 14.9 (CH_2CH_3).

Anal. Calcd for $C_{13}H_{21}NO_6$: C, 54.35; H, 7.37; N, 4.88. Found: C, 54.71; H, 7.41; N, 4.67.

5(*R*,*S*)-Acetoxy-3-[(1′*R,2′R,3′S,4′R*)-1′,2′-*O*-isopropylidene-3′-*O*-methyltetrahydrofuranos-4′-yl]-2-isoxazoline (8). Colorless oil, Rf 0.60 (hexane:ethyl acetate, 4 : 1); $[\alpha]_D^{25}$ − 38.6° (*c* 0.21, $CHCl_3$), MS (FAB) = m/z 302 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 2992, 2258, 1775, 1635, 1564, 1458, 1379; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.68 (dd, $J = 6.4$ and 1.4 Hz, 1H, H-5), 5.98 (d, $J = 3.6$ Hz, 1H, H-1′), 5.16 (d, $J = 3.3$ Hz, 1H, H-4′),4.63 (d, $J = 3.6$ Hz, 1H, diastereomeric H-2′), 3.93 (d, $J = 3.3$ Hz, 1H, diastereomeric H-3′), 3.41 and 3.35 (s, 3H, diastereomeric $-OCH_3$), 3.26 (dd, $J = 6.4$ and 1.4 Hz, 1H, H-4_A) 3.16 (dd, $J = 16.6$ Hz, 1H, H-4_B) 2.05 (s, 3H, $-COCH_3$), 1.51 and 1.34 [s, 6H, C (CH_3)$_2$].

Anal. Calcd for $C_{13}H_{19}NO_7$: C, 51.82; H, 6.36; N, 4.65. Found: C, 52.12; H, 6.47; N, 4.44.

5(*R*,*S*)-Acetyl-3-[(*1′R,2′R,3′S,4′R*)-1′,2′-*O*-isopropylidene-3′-*O*-methyltetrahydrofuranos-4′-yl]-2-isoxazoline (9). Colorless oil, Rf 0.70 (hexane:ethyl acetate, 7:3); $[\alpha]_D^{25}$−34.7° (*c* 0.375, $CHCl_3$), MS (FAB) = m/z 286 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 2988, 2362, 1722, 1627, 1438, 1376; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.96 (d, $J = 3.7$ Hz, 1H, H-1′), 5.10 (d, $J = 3.5$Hz, 1H, diastereomeric H-4′), 4.85 (m, 1H, H-5), 4.61 (d, $J = 3.7$ Hz, 1H, diastereomeric H-2′), 3.89 (d, $J = 3.5$ Hz, 1H, diastereomeric H-3′), 3.41 (s, 3H, OCH_3), 3.34 (m, 2H, H-4), 2.26 (s, 3H, $COCH_3$), 1.50 and 1.34 [s, 6H, C(CH_3)$_2$].

Anal. Calcd for $C_{13}H_{19}NO_6$: C, 54.73; H, 6.71; N, 4.91. Found: C, 54.97; H, 6.91; N, 4.83.

5(R,S)-Cyano-3-[(*1′R,2′R,3′S,4′R*)-1′,2′-*O*-isopropylidene-3′-*O*-methyltetrahydrofuranos-4′-yl]-2-isoxazoline (10). Major isomer: White solid, Mp 78°C, Rf 0.55 (hexane : ethyl acetate, 7 : 3); $[\alpha]_D^{25}$ −21.0° (*c* 0.25, $CHCl_3$), MS (FAB) = *m*/*z* 269 $(M + H)^+$; IR (Neat): ν_{max} cm^{-1} 2933, 2950, 2845, 2362, 1638, 1453, 1383; ^1H NMR ($CDCl_3$, 200 MHz): δ 5.97 (d, $J = 3.6$ Hz, 1H, H-1′), 5.21 (m, 1H, H-5), 5.17 (d, $J = 3.6$ Hz, 1H, H-4′), 4.64 (d, $J = 3.6$ Hz, 1H, H-2′), 3.95 (d, $J = 3.6$ Hz, 1H, H-3′), 3.49 (m, 2H, H-4), 3.45 (s, 3H, OCH_3), 1.51 and 1.35 [s, 6H, C $(CH_3)_2$]. ^{13}C NMR ($CDCl_3$): δ 158.0 (C═N); 117.5 (C≡N); 112.9 [$C(CH_3)_2$]; 105.9 (C-1′); 87.5 (C-2′); 81.9 (C-4′); 75.6 (C-3); 66.3 (C-5); 58.8 (OCH_3), 42.4 (C-4); 27.3, 26.6 [>C(*C*$H_3)_2$].

Anal. Calcd for $C_{13}H_{18}N_2O_5$: C, 55.31; H, 6.43; N, 9.92. Found: C, 55.58; H, 6.70; N, 9.78.

Minor isomer: colorless oil, Rf 0.57, (hexane:ethyl acetate, 7:3); $[\alpha]_D^{25}$ −42.5° (*c* 0.30, $CHCl_3$), MS (FAB) = *m*/*z* 269 $(M + H)^+$; IR (Neat): ν_{max} cm^{-1} 2933, 2950, 2845, 2362, 1638, 1453, 1383; ^1H NMR ($CDCl_3$, 200 MHz): δ 5.97 (d, $J = 3.6$ Hz, 1H, H-1′), 5.21 (t, $J = 6.2$ Hz, 1H, H-5), 5.17 (d, $J = 3.6$ Hz, 1H, H-4′), 4.64 (d, $J = 3.6$ Hz, 1H, H-2′), 3.95 (d, $J = 3.6$ Hz, 1H, H-3′), 3.49 (d, $J = 6.2$ Hz, 2H, H-4), 3.45 (s, 3H, OCH_3), 1.51 and 1.35 [s, 6H, C $(CH_3)_2$]. ^{13}C NMR ($CDCl_3$): δ 157.8 (C═N); 117.4 (C≡N); 112.9 [$C(CH_3)_2$]; 105.9 (C-1′); 87.3 (C-2′); 81.7 (C-4′); 75.4 (C-3); 66.7 (C-5), 58.4 (OCH_3), 42.2 (C-4); 27.3, 26.6 [>C(*C*$H_3)_2$].

5(*R*,*S*)-Bromomethyl-3-[(*1′R,2′R,3′S,4′R*)-1′,2′-*O*-isopropylidene-3′-*O*-methyl-tetrahydrofuranos-4′-yl]-2-isoxazoline (11). Colorless oil, Rf 0.60 (hexane:ethyl acetate, 7:3); $[\alpha]_D^{25}$ +3.4° (*c* 0.4125, $CHCl_3$), MS (FAB) = *m*/*z* 336 $(M + H)^+$; IR (Neat): ν_{max} cm^{-1} 2984, 2937, 2367, 1623, 1442, 1378; ^1H NMR ($CDCl_3$, 200 MHz): δ 5.98 (d, $J = 3.7$ Hz, 1H, diastereomeric H-1′), 5.09 (d, $J = 3.6$ Hz, 1H, H-4′), 4.82 (m, 1H, H-5), 4.62 (d, $J = 3.7$ Hz, 1H, diastereomeric H-2′), 3.90 and 3.95 (d, $J = 3.6$ Hz, 1H, diastereomeric H-3′), 3.56, 3.40 (s, 3H, diastereomeric $-OCH_3$), 3.30 (m, 2H, H-4), 1.50, 1.48, 1.34, and 1.32 [s, 6H, C $(CH_3)_2$]; ^{13}C NMR ($CDCl_3$): δ 157.4 (C═N); 112.2 [$C(CH_3)_2$]; 105.9, 105.7 (C-1′); 87.5 (C-5), 84.8 (C-2′); 81.9, 81.8 (C-4′); 79.5, 76.3 (C- 3′); 59.2 and 58.3 ($-OCH_3$), 40.7 (C-4); 33.2 (CH_2Br), 27.3, 27.2 and 26.5 [>C(*C*$H_3)_2$].

Anal. Calcd for $C_{12}H_{18}BrNO_5$: C, 42.87; H, 5.40; N, 4.17. Found: C, 43.12; H, 5.71; N, 4.02.

5(*R*,*S*)-(2-Hydroxy phenylmethyl)-3-[(*1′R,2′R,3′S,4′R*)-1′,2′-*O*-isopropylidene-3′-*O*-methyl-tetrahydrofuranos-4′-yl]-2-isoxazoline (12). Colorless oil, Rf 0.65 (hexane : ethyl acetate, 7:3); $[\alpha]_D^{25}$ −34.2° (*c* 0.275, $CHCl_3$); MS (FAB) = *m*/*z* 350 $(M + H)^+$; IR (Neat): ν_{max} cm^{-1} 3404, 2936, 2364, 1599, 1454, 1376, 1220; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.12 (m, 4H, ArH), 5.97 (d, $J = 3.8$ Hz, 1H, H-1′), 5.08 (m, 1H, H-5), 4.84 (d, $J = 3.6$ Hz, 1H, H-4′), 4.60 (d, $J = 3.8$ Hz, 1H, H-2′), 3.87 (d, $J = 3.6$ Hz, 1H, H-3′), 3.46 (dd, $J = 5.1$ and 1.4 Hz, 2H, CH_2Ar), 3.40 (s, 3H, OCH_3), 3.33 (m, 2H, H-4), 1.49, 1.45, 1.35, and 1.30 [s, 6H, diastereomeric $C(CH_3)_2$]. ^{13}C NMR ($CDCl_3$): δ 159.4, 158.9 (C═N); 155.6, 127.5 (ArC), 132.3, 132.0, 121.0, 120.9, 117.4, 117.3(ArCH), 112.7 [$C(CH_3)_2$]; 105.6, 105.7 (C-1′); 87.4, 87.1 (C-5), 82.0 (C-2′), 81.8

(C-4′), 76.3 (C-3′), 58.4 ($-OCH_3$), 40.6, 40.2 ($ArCH_2$), 36.5, 36.2 (C-4), 27.3, 27.2 and 26.7 [$C(CH_3)_2$].

Anal. Calcd for $C_{18}H_{23}NO_6$: C, 61.88; H, 6.64; N, 4.01. Found: C, 62.09; H, 6.92; N, 3.97.

5(*R,S*)-(4-Methoxy phenylmethyl)-3-[(*1′R,2′R,3′S,4′R*)-1′,2′-*O*-isopropylidene-3′-*O*-methyl-tetrahydrofuranos-4′-yl]-2-isoxazoline (13). Colorless oil, Rf 0.65 (hexane:ethyl acetate, 3 : 1); $[\alpha]_D^{25}$ −17.6° (*c* 0.375, $CHCl_3$), MS (FAB) = *m/z* 364 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 2987, 2936, 1612, 1514, 1458, 1377; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.14 and 6.84 (d, *J* = 6.6 Hz, 2H, ArH), 5.94 (d, *J* = 3.7 Hz, 1H, H-1′), 5.07 (d, *J* = 3.4 Hz, 1H, H-4′), 4.70 (m, 1H, H-5), 4.59 (d, *J* = 3.7 Hz, 1H, H-2′), 3.87 (d, *J* = 3.4 Hz, 1H, H-3′), 3.78 (s, 3H, $-ArOCH_3$), 3.35 (s, 3H, $-OCH_3$), 2.98 (m, 2H, $ArCH_2$), 2.84 (m, 2H, H-4), 1.50 and 1.33 [s, 6H, C $(CH_3)_2$].

Anal. Calcd for $C_{19}H_{25}NO_6$: C, 62.80; H, 6.93; N, 3.85. Found: C, 62.98; H, 7.19; N, 3.61.

5(*R,S*)-Hydroxymethyl-3-[(*1′R,2′R,3′S,4′R*)-1′,2′-*O*-isopropylidene-3-*O*-methyltetrahydrofuranos-4′-yl]-2-isoxazoline (14). Colorless oil, Rf 0.35 (hexane:ethyl acetate, 3 : 2); $[\alpha]_D^{25}$ −76.1° (c 0.3625, $CHCl_3$), MS (FAB) = *m/z* 274 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} ^1H NMR ($CDCl_3$, 200 MHz): δ 5.98 (d, *J* = 3.7 Hz, 1H, H-1′), 5.09 (d, *J* = 3.3 Hz, 1H, diastereomeric H-4′), 4.80 (m. 1H, H-5), 4.62 (d, *J* = 3.7 Hz, 1H, H-2′), 3.90 (d, *J* = 3.5 Hz, 1H, H-3′), 3.72 (dd, *J* = 13.6 and 2.9 Hz, -CH_AOH), 3.58 (dd, *J* = 13.6 and 5.4 Hz, $-CH_BOH$), 3.39 (s, 3 H, $-OCH_3$), 3.18 (dd, *J* = 18.0 and 10.8 Hz, $-H\text{-}4_A$), 2.95 (dd, *J* = 18.0 and 8.0 Hz, $H\text{-}4_B$), 1.51 and 1.34 [s, 6H, $C(CH_3)_2$]. ^{13}C NMR ($CDCl_3$): δ 157.9 (C═N); 112.6 [$C(CH_3)_2$]; 105.6 (C-1′); 87.19, 87.04 (C-5), 81.9 (C-2′); 81.2 (C-4′); 76.5, 76.4 (C-3); 64.0, 63.9 (CH_2OH), 58.4 (OCH_3), 37.7, 37.6 (C-4); 27.2, 26.6 [$>C(CH_3)_2$].

Anal. Calcd for $C_{12}H_{19}NO_6$: C, 52.74; H, 7.01; N, 5.13. Found: C, 52.96; H, 7.32; N, 5.01.

5(*R,S*)-Carboxy-3-[(*1′R,2′R,3′S,4′R*)-1′,2′-*O*-isopropylidene-3′-*O*-methyltetrahydrofuranos-4′-yl]-2-isoxazoline (15). Colorless oil, Rf 0.40 (hexane:ethyl acetate, 1:1); $[\alpha]_D^{25}$ −41° (*c* 0.4, $CHCl_3$), MS (FAB) = *m/z* 302 $(M+H)^+$; IR (Neat): $\nu_{max}cm^{-1}$ 3352, 2937, 2362, 1769, 1709, 1658, 1622, 1447, 1378; ^1H NMR ($CDCl_3$, 200 MHz): δ 9.76 (bs, exchangeable with D_2O, 1H, −COOH), 7.22 (m, 1H, H-4), 5.99, 5.91 (d, *J* = 3.6 Hz, 1H, diastereomeric H-1′), 4.84 (d, *J* = 3.3 Hz, 1H, H-4′), 4.59 (d, *J* = 3.6 Hz, 1H, H-2′), 4.13 (d, *J* = 3.3 Hz, 1H, H-3′), 3.43 (s, 3H, -OCH_3), 1.95 (d, *J* = 6.9 Hz, 3H, CH_3), 1.81 (m, 1H, H-5) 1.49 and 1.33 [s, H, $C(CH_3)_2$]. ^{13}C NMR ($CDCl_3$): δ 164.4 (C = O), 163.8 (C═N); 149.5 (C-4), 118.6 (C-5), 113.3 [$C(CH_3)_2$]; 106.09 (C-1′); 84.8 (C-2′); 81.9 (C-4′); 81.3 (C-3); 59.4 and 58.6 (OCH_3), 27.3, 26.7 [$>C(CH_3)_2$], 18.8 (CH_3).

Anal. Calcd for $C_{13}H_{19}NO_7$: C, 51.82; H, 6.36; N, 4.65. Found: C, 52.07; H, 6.54; N, 4.48.

5(*R,S*)-Carbethoxy-3-[(*1′R,2′R,3′S,4′R*)-3′-*O*-benzyl-1′,2′-*O*-isopropylidenetetrahydrofuranos-4′-yl]-2-isoxazoline (16). Colorless oil, Rf 0.70 (hexane:ethyl acetate, 7:3); $[\alpha]_D^{25}$ +30.5° (*c* 0.4, $CHCl_3$), MS (FAB) = *m/z* 392 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 2986, 2361, 1745, 1620, 1448, 1377, 1215. ^1H NMR ($CDCl_3$, 200 MHz): δ 7.32 (m, 5H, ArH)

5.99 (d, $J = 3.7$ Hz, 1H, H-1′), 5.15 (d, $J = 3.2$ Hz, 1H, H-4′); 4.93 (t, $J = 9.3$ Hz, 1H, H-5) 4.57 (m, 2H, OCH_APh and H-2′), 4.17 (m, 4H, $-OCH_2$, OCH_BPh and H-3′); 3.40 (m, 2H, H-4); 1.49 and 1.32 [each s, each 3H, C $(CH_3)_2$], 1.25 (t, $J = 7.1$ Hz, $-OCH_2CH_3$).^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.6 (C—O), 157.3 and 156.7 (C═N); 137.3, (ArC), 129.0, 128.9, 128.5, 128.4, 128.0 (ArCH), 112.7 [$C(CH_3)_2$]; 105.7 (C-1′); 85.3 (C-2′); 84.8 (C-4′); 82.6, 82.57 (C-3); 72.8 ($-OCH_2Ph$), 62.2, 62.0 ($-OCH_2$), 40.6, 40.5 (C-4); 27.2, 26.7 [$>C(CH_3)_2$], 14.5 (CH_3).

Anal. Calcd for $C_{20}H_{25}NO_7$: C, 61.37; H, 6.44; N, 3.58. Found: C, 61.64; H, 6.57; N, 3.32.

5(*R,S*)-Ethoxy-3-[(*1′R,2′R,3′S,4′R*)-3′-*O*-benzyl-1′,2′-*O*-isopropylidene-tetrahydrofuranos-4′-yl]2-isoxazoline (17). Colorless oil, Rf 0.65 (hexane:ethyl acetate, 3:1); $[\alpha]_D^{20}$ -23.8° (*c* 0.275, $CHCl_3$), MS (FAB) = m/z 364 $(M + H)^+$; IR (Neat): ν_{max} cm^{-1} 2981, 2362, 1626, 1456, 1377; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.35 (m, 5H, ArH), 6.00 (d, $J = 3.1$ Hz, 1H, diastereomeric H-1′), 5.54 (m, 1H, diastereomeric H-5), 5.15 (d, $J = 3.3$ Hz, 1H, H-4′), 4.64 (m, 3H, H-2′ and $-OCH_2Ph$), 4.13 (d, $J = 3.3$ Hz, 1H, H-3′), 3.86 and 3.53 (each m, 2H, $-OCH_2CH_3$), 1.49 and 1.33 [s, 6H, C $(CH_3)_2$].

Anal. Calcd for $C_{19}H_{25}NO_6$: C, 62.80; H, 6.93; N, 3.85. Found: C, 62.96; H, 7.11; N, 3.68.

5(*R,S*)-Acetoxy-3-[(*1′R,2′R,3′S,4′R*)-3′-*O*-benzyl-1′,2′-*O*-isopropylidene-tetrahydrofuranos-4′-yl]-2-isoxazoline (18). Colorless oil, Rf 0.65 (hexane:ethyl acetate, 3:1); $[\alpha]_D^{25}$ – 38.2° (*c* 0.738, $CHCl_3$), MS (FAB) = m/z 318 $(M\text{-}OCOCH_3)^+$; IR (Neat): ν_{max} cm^{-1} 3022, 2937, 1751, 1610, 1456, 1377; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.34 and 7.21 (m, 5H, ArH), 6.66 (m, 1H, H-5), 6.00 (d, $J = 3.5$ Hz, 1H, H-1′), 5.20 (d, $J = 3.4$ Hz,1H, H-4′), 4.64 (m, 2H, $-OCH_APh$ and H-2′), 4.47 (d, $J = 11.6$ Hz, 1H, $-OCH_BPh$), 4.17 (d, $J = 3.4$ Hz, 1H, H-3′), 3.23 (m, 2H, H-4), 2.03 and 1.90 (s, 3H, diastereomeric $COCH_3$), 1.50 and 1.33 [s, 6H, C $(CH_3)_2$]; ^{13}C NMR ($CDCl_3$): δ 170.4, 169.9 (C—O), 158.0 (C═N); 137.4, 137.1 (ArC), 129.1, 128.9, 128.6, 128.4, 128.2, 128.0, 127.8 (ArCH), 112.8 ad 109.9 [$C(CH_3)_2$]; 105.8, 105.7 (C-1′); 95.8, 95.7 (C-5); 85.2, 84.9 (C-2′); 82.8, 82.6 (C-4′); 76.3, 76.1 (C-3′); 72.9, 72.7 ($-OCH_2Ph$); 42.8, 42.6 (C-4); 27.3, 26.7 [$>C(CH_3)_2$], 21.4, 21.2 ($COCH_3$).

Anal. Calcd for $C_{19}H_{23}NO_7$: C, 60.47; H, 6.14; N, 3.71. Found: C, 60.68; H, 6.32; N, 3.58.

5(*R,S*)-Acetyl-3′-*O*-benzyl-3-[(*1′R,2′R,3′S,4′R*)-1′,2′-*O*-isopropylidene-tetrahydrofuranos-4′-yl]-2-isoxazoline (19). Colorless oil, Rf 0.65 (hexane:ethyl acetate, 3:1); $[\alpha]_D^{25}$ -24.5° (*c* 0.2, $CHCl_3$), MS (FAB) = m/z 362 $(M + H)^+$; IR (Neat): ν_{max} cm^{-1} 2987, 2935, 2363, 1722, 1624, 1496, 1449, 1377; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.33 and 7.23 (m, 5H, ArH), 6.00 (d, $J = 3.7$ Hz, 1H, H-1′), 5.12 (m, 1H, diastereomeric H-4′), 4.81 (m, 1H, diastereomeric H-5), 4.61 (m, 3H, $-OCH_2Ph$ and H-2′), 4.15, 4.13 (d, $J = 3.6$ Hz, 1H, diastereomeric H-3′), 3.29 (m, 2H, H-4), 2.25, 2.13 (s, 3H, diastereomeric $COCH_3$), 1.50 and 1.33 [s, 6H, $C(CH_3)_2$].

Anal. Calcd for $C_{19}H_{23}NO_6$: C, 63.15; H, 6.41; N, 3.88. Found: C, 63.44; H, 6.71; N, 3.64.

5(*R*,*S*)-Cyano-3-[(*1′R,2′R,3′S,4′R*)-3′-*O*-benzyl-1′,2′-*O*-isopropylidene-tetrahydrofuranos-4′-yl]-2-isoxazoline (20). Colorless oil, Rf 0.60 (hexane:ethyl acetate, 7:3); $[\alpha]_D^{25}$ -21.9° (*c* 0.4875, $CHCl_3$), MS (FAB) = m/z 345 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 2988, 2936, 2364, 1620, 1453, 1379, 1314, 1218; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.35 and 7.22 (m, 5H, ArH), 6.00 (d, $J = 3.7$ Hz, 1H, H-1′), 5.18 (d, $J = 3.5$ Hz, 1H, diastereomeric H-4′), 5.08 (t, $J = 8.5$ Hz, 1H, H-5), 4.65 (m, 2H, H-2 and $-OCH_BPh$), 4.46 (d, $J = 11.6$ Hz, 1H, $-OCH_APh$), 4.17 (d, $J = 3.5$ Hz, 1H, H-3′), 3.51 and 3.44 (d, 2H, H-4), 1.51 and 1.34 [each s, each 3H, $C(CH_3)_2$]; ^{13}C NMR ($CDCl_3$): δ, 157.9 (C═N); 136.7 (Ar-C), 129.2, 128.8, 128.6, 128.0 (Ar-CH), 117.0 (C═N), 112.9 [$C(CH_3)_2$]; 105.9 (C-1′); 85.4, 84.8 (C-4′); 83.4 (C-2′); 76.1, 75.7 (C-3′); 73.1, 72.9 ($-OCH_2Ph$), 66.3, 66.2 (C-5), 42.3 (C-4); 27.3, and 26.7 [$>C(CH_3)_2$].

Anal. Calcd for $C_{19}H_{22}N_2O_5$: C, 63.67; H, 6.19; N, 7.82. Found: C, 63.89; H, 6.34; N, 7.66.

5(*R*,*S*)-Bromomethyl-3-[(*1′R,2′R,3′S,4′R*)-3′-*O*-benzyl-1′,2′-*O*-isopropylidene-tetrahydrofuranos-4′-yl]-2-isoxazoline (21). Colorless oil. Rf 0.65 (hexane:ethyl acetate, 7:3); $[\alpha]_D^{25}$ +3.2 (*c* 0.98, $CHCl_3$); MS (FAB) = m/z 412 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 2985, 2365, 2144, 1631, 1452, 1377, 1312; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.33 (m, 5H, ArH), 6.01 (d, $J = 3.6$ Hz, 1H, H-1′), 5.13 (d, $J = 3.5$ Hz, 1H, H-4′), 4.80 (m, 1H, H-5), 4.66 (m, 2H, H-2′ and $-OCH_APh$), 4.50 (d, $J = 11.6$ Hz, 1H, $-OCH_BPh$), 4.16 (d, $J = 3.5$ Hz, 1H, diastereomeric H-3′), 3.46 (dd, $J = 10.3$ and 4.6 Hz, 1H, $H\text{-}4_A$), 3.23 (m, 3H, $H\text{-}4_A$ and CH_2Br), 1.55, 1.50, and 1.30 [s, 6H, $C(CH_3)_2$].

Anal. Calcd for $C_{18}H_{22}BrNO_5$: C, 52.44; H, 5.38; N, 3.40. Found: C, 52.70; H, 5.57; N, 3.32.

5(*R*,*S*)-(2-Hydroxy phenylmethyl)-3-[(*1′R,2′R,3′S,4′R*)-3′-*O*-benzyl-1′,2′-*O* isopropylidene-tetrahydrofuranos-4′-yl]-2-isoxazoline (22). Colorless oil, Rf 0.70 (hexane:ethyl acetate, 7:3); $[\alpha]_D^{25}$ -42.5° (*c* 0.15, $CHCl_3$), MS (FAB) = m/z 426 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 3395, 2985, 2366, 1592, 1493, 1456, 1377; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.32 (m, 9H, ArH), 6.60 (s, exchangeable with D_2O, 1H, ArOH), 6.01, 5.97 (d, $J = 3.8$ Hz, 1H, diastereomeric H-1′), 5.07 (d, $J = 3.5$ Hz, 1H, H-4′), 4.87 (m, 1H, H-5), 4.61 (m, 3H, $-OCH_2Ph$ and diastereomeric H-2′), 4.13, 4.08 (d, $J = 3.5$ Hz, 1H, distereomeric H-3), 3.40 (d, $J = 6.4$ Hz, 1H, $-CH_APhOH$), 3.16 (dd, $J = 18.8$ and 10.2 Hz, 1H, $H\text{-}4_A$) 2.95 (m, 2H, CH_BPhOH and H-4B), 1.48, 1.47, 1.31 [s, 6H, diastereomeric $C(CH_3)_2$], ^{13}C NMR ($CDCl_3$): δ 159.3 (C═N); 155.4, 149.5, 137.4 (ArC), 132.1, 130.7, 128.5, 128.3, 127.6, 121.0, and 117.4 (ArCH), 112.7 [$C(CH_3)_2$], 105.7, 105.6 (C-1′), 85.2 (C-2′), 83.0 (C-4′), 81.9 (C-3′), 78.4, 76.6 (C-5), 73.8 (OCH_2Ph), 40.75 (CH_2-Ar), 36.6, 36.4 (C-4), 27.38, 27.3, 26.8, and 26.73 [$C(CH_3)_2$].

Anal. Calcd for $C_{24}H_{27}NO_6$: C, 67.75; H, 6.40; N, 3.29. Found: C, 67.96; H, 6.69; N, 3.12.

5-(4-Methoxyphenylmethyl)-3-[(*1′R,2′R,3′S,4′R*)-3′-*O*-benzyl-1′,2′-*O*-isopropylidene-tetrahydrofuranos-4′-yl]-2-isoxazoline (23). *Major isomer*: Colorless oil, Rf 0.70 (hexane:ethyl acetate, 3 : 1); $[\alpha]_D^{25}$ $+8.64^\circ$ (*c* 0.3125, $CHCl_3$), MS (FAB) = m/z 440 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 2994, 2936, 2365, 1612, 1513, 1457, 1378; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.30 (m, 6H, ArH), 6. 85 (m, 3H, ArH), 5.98 (d, $J = 3.4$ Hz, 1H, H-1′), 5.12 (d, $J = 3.6$ Hz, 1H, H-4′), 4.65 (m, 3H, H-5, H-2′ and $-OCH_APh$), 4.48

(d, $J = 11.7$ Hz, 1H, $-OCH_BPh$), 4.16 (d, $J = 3.6$ Hz, 1H, H-3), 3.78 (s, 3H, Ar-OCH_3), 3.10–2.62 (m, 4H, CH_2Ar and H-4), 1.42 and 1.26 [s, 6H, $C(CH_3)_2$]; ^{13}C NMR ($CDCl_3$): δ 158.8 (C═N); 137.4 (ArC), 130.69, 129.40, 128.6, 128.2, 127.9, and 114.4 (ArCH), 112.6 [$C(CH_3)_2$], 105.6 (C-1′), 85.4 (C-2′), 82.7 (C-4′), 82.0 (C-3′), 76.8 (C-5), 72.8 (OCH_2Ph), 55.6 (Ar-OCH_3), 40.70 (CH_2-Ar), 40.3 (C-4), 27.28, and 26.73 [$C(CH_3)_2$].

Anal. Calcd for $C_{25}H_{29}NO_6$: C, 68.32; H, 6.65; N, 3.19. Found: C, 68.54; H, 6.81; N, 3.07.

5(*R*,*S*)-Hydroxymethyl-3-[(*1′R,2′R,3′S,4′R*)-3′-*O*-benzyl-1′,2′-*O*-isopropylidenetetrahydrofuranos-4′-yl]-2-isoxazoline (24). Colorless oil, Rf 0.40 (hexane:ethyl acetate, 3:2); $[\alpha]_D^{25} -11^\circ$ (*c* 0.28, $CHCl_3$), MS (FAB) = m/z 350 $(M + H)^+$; IR (Neat): $\nu_{max}cm^{-1}$ 3426, 2934, 2365, 1628, 1454, 1379; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.33, (m, 5H, ArH), 6.01 (d, $J = 3.3$ Hz, 1H, H-1′), 5.10 (d, $J = 3.3$ Hz, 1H, H-4′), 4.67 (m. 3H, H-5,$-OCH_APh$ and H-2′), 4.51 (d, $J = 11.4$ Hz, 1H,$-OCH_BPh$), 4.15 (d, $J = 3.3$ Hz, 1H, H-3′), 3.58 (dd, $J = 12.0$ and 3.0 Hz, $-CH_AOH$), 3.46 (dd, $J = 12.0$ and 5.7 Hz, $-CH_BOH$), 3.09 (dd, $J = 17.4$ and 10.8 Hz, $-H\text{-}4_A$), 2.95 (dd, $J = 17.4$ and 7.8 Hz, $H\text{-}4_B$), 1.50 and 1.34 [s, 6H, $C(CH_3)_2$]. ^{13}C NMR ($CDCl_3$): δ 158.1, 157.9 (C═N); 137.3 (ArC), 129.0, 128.6, 128.3, 128.0 (ArCH), 112.7 [$C(CH_3)_2$], 105.7 (C-1′), 85.2 (C-2′), 82.6, 82.5 (C-4′), 81.1 (C-3′), 76.6 (C-5), 73.4 (OCH_2Ph), 64.1, 63.9 (CH_2OH), 37.7 (C-4), 27.25 and 26.70 [$C(CH_3)_2$].

Anal. Calcd for $C_{18}H_{23}NO_6$: C, 61.88; H, 6.64; N, 4.01. Found: C, 62.06; H, 6.82; N, 3.91.

5(*R*,*S*)-Carboxy-3-[(*1′R,2′R,3′S,4′R*)-3′-*O*-benzyl-1′,2′-*O*-isopropylidenetetrahydrofuranos-4′-yl]-2-isoxazoline (25). Colorless oil, Rf 0.45 (hexane:ethyl acetate, 1 : 1); $[\alpha]_D^{25} -27.6^\circ$ (*c* 0.1375, $CHCl_3$), MS (FAB) = m/z 378 $(M + H)^+$; IR (Neat): ν_{max} cm^{-1} 3280, 2984, 2933, 2362, 1770, 1708, 1658, 1587, 1481, 1379; ^1H NMR ($CDCl_3$, 200 MHz): δ 9.65 (bs, 1H, exchangeable with D_2O, COOH), 7.23 (m, 5H, ArH), 7.13 (m, 1H, H-4), 6.00 (m, 1H, diastereomeric H-1′), 4.88 (d, $J = 3.2$ Hz, 1H, H-4′), 4.60 (m, 3H, $-OCH_2$ and H-2′), 4.37, 4.10 (d, $J = 3.2$ Hz, 1H, diastereomeric H-3′), 1.94 (m, 1H, H-5), 1.47, 1.30 (s, 3H, $C(CH_3)_2$], 1.27 (d, $J = 6.9$ Hz, 3H, CH_3).

Anal. Calcd for $C_{19}H_{23}NO_7$: C, 60.47; H, 6.14; N, 3.71. Found: C, 60.47; H, 6.14; N, 3.71.

5(*R*,*S*)-Ethoxy-3-[(*1′R,2′R,3′S,4′R*)-1′,2′:3′,4′-di-*O*-isopropylidenetetrahydropyranos-5′-yl]-2-isoxazoline (26). Colorless oil, Rf 0.65 (hexane:ethyl acetate, 4:1); $[\alpha]_D^{20} -60.4^\circ$ (*c* 0.275, $CHCl_3$); MS (FAB) = m/z 372 $(M + H)^+$; IR (Neat): ν_{max} cm^{-1} 2980, 2939, 2365, 1745, 1631, 1445, 1377, 1223; ^1H NMR ($CDCl_3$, 200 MHz): δ 5.54 (d, $J = 4.9$ Hz, 1H, H-1′), 5.10 (m, 1H, H-5′), 4.82 (m, 1H, H-5), 4.34 (dd, $J = 7.7$ and 2.3 Hz, 1H, H-3′), 4.33 (m, 4H, $-OCH_2$, H-2′ and H-4′), 3.45 (m, 2H, H-4), 1.55, 1.46, 1.34, and 1.33 [s, 12H, $C(CH_3)_2$], 1.30 (t, $J = 7.1$ Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.8, 170.4 (C═O), 157.9 (C═N); 110.02, 109.48 [$C(CH_3)_2$]; 96.6 (C-1′); 78.1 (C-2′); 77.5, 76.8 (C-4′); 70.6 (C-3′); 71.0 (C-5); 69.4 (C-5′); 62.15 (OCH_2); 40.38, 40.18 (C-4); 26.4, 26.3, 25.2, and 24.6 [$C(CH_3)_2$].

Anal. Calcd for $C_{17}H_{25}NO_8$: C, 54.98; H, 6.79; N, 3.77. Found: C, 55.22; H, 6.95; N, 3.58.

5(*R*,*S*)-(2-Hydroxy phenylmethyl)-3-[(*1′R, 2′R, 3′R, 4′S*) 1′,2′:3′,4′-di-*O*-isopropylidene-tetrahydropyranos-5′-yl]-2-isoxazoline (27). Colorless oil; Rf 0.65 (hexane:ethyl acetate, 7:3); $[\alpha]_D^{20}$ −23.6° (*c* 0.2875, $CHCl_3$); MS (FAB) = *m*/*z* 405 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 3467, 2985, 2362, 1747, 1597, 1455, 1374; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.03 (m, 2H, ArH), 6.86 (m, 2H, ArH), 6.70 (bs, 1H, ArOH), 5.65 (m, 1H, H-5), 5.55 (d, *J* = 4.7 Hz, 1H, diastereomeric H-1′), 4.62 (m, 2H, H-5′ and H-3′), 4.31 (m, 4H, H-2′, H-4′ and CH_2Ar)), 3.09 (m, 2H, H-4), 1.51, 1.43, and 1.31 [s, 12H, $C(CH_3)_2$]. ^{13}C NMR ($CDCl_3$, 50 MHz): δ 158.2 (C═N); 145.6, 137.2 (ArC), 128.9, 128.4, 128.3 (ArCH) 109.6, 108.9 [$C(CH_3)_2$]; 96.1 (C-1′); 80.2 (C-2′); 73.5, 73.4 (C-4′); 70.3 (C-3′); 72.8 (C-5′), 65.8, 65.5 (diastereomeric C-5), 40.4 (CH_2Ar), 37.2 (C-4); 25.6, 25.3, 24.5, and 24.2 [>$C(CH_3)_2$].

Anal. Calcd for $C_{21}H_{27}NO_7$: C, 62.21; H, 6.71; N, 3.45. Found: C, 62.31; H, 6.88; N, 3.39.

5(*R*,*S*)-(Hydroxymethyl)-3-[(*1′R,2′R,3′R,4′S*)-1′,2′:3′,4′-tetrahydropyranos-5′-yl]-2-isoxazoline (28). Colorless solid Mp 124°C; Rf 0.35 (hexane:ethyl acetate, 7:3); $[\alpha]_D^{25}$ −76.1° (*c* 0.3625, $CHCl_3$); MS (FAB) = *m*/*z* 330 $(M+H)^+$; IR (Neat): ν_{max} cm^{-1} 3469, 2985, 2929, 2362, 1744 1599, 1446, 1379; ^1H NMR ($CDCl_3$, 200 MHz): δ 5.55 (d, *J* = 4.9 Hz, 1H, H-1′), 4.67 (m, 3H, H-5, H-5′, and H-3′), 4.34 (m, 2H, H-2′, and H-4′), 3.66 (m, 2H, diastereomeric CH_2OH), 3.23 (dd, *J* = 17.5 and 10.4 Hz, 1H, H-4_A), 2.94 (dd, *J* = 17.5 and 7.4 Hz, 1H, H-4_B), 1.55, 1.46, and 1.34 [s, 12H, $C(CH_3)_2$]. ^{13}C NMR ($CDCl_3$, 50 MHz): δ 158.3 (C═N); 109.6, 108.9 [$C(CH_3)_2$]; 96.1 (C-1′); 80.4 (C-2′); 73.6, 73.5 (C- 4′); 70.6 (C-3′); 72.8 (C-5′), 65.47 and 65.35 (diastereomeric C-5), 63.7 (CH_2OH), 37.03 (C-4); 25.9, 25.8, 24.7, and 24.2 [>$C(CH_3)_2$].

Anal. Calcd for $C_{15}H_{23}NO_7$: C, 54.70; H, 7.04; N, 4.25. Found: C, 54.99; H, 7.23; N, 4.17.

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