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PAPER

Stereoselective vinylogous Mannich reaction of 2-trimethylsilyloxyfuran with *N*-gulosyl nitrones†

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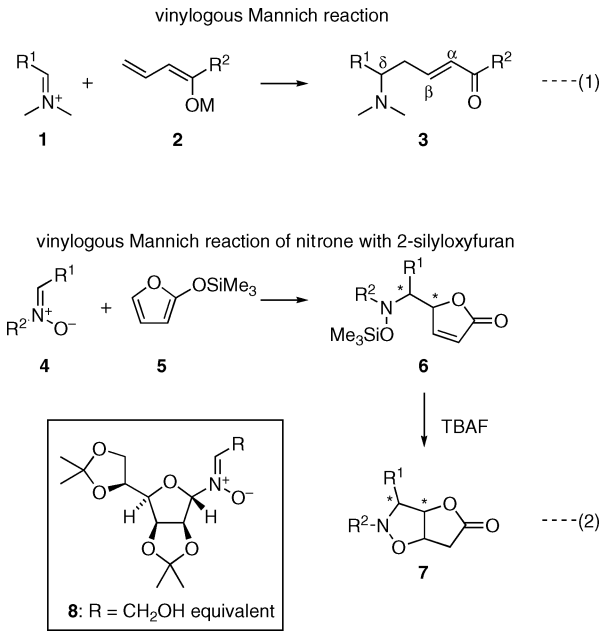
Stereoselective vinylogous Mannich reaction of 2-trimethylsilyloxyfuran with L-gulose-derived chiral nitrones in the presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate was investigated. The selectivity was strongly influenced by the bulkiness of the *C*-substituent of the nitrone: for example, *C*-benzyloxymethyl nitrone afforded four stereoisomers, whereas bulky *C*-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]nitrone gave a single stereoisomer. The latter product was elaborated to afford key synthetic intermediates for polyoxin C and dysiherbaine.

Introduction

Nucleophilic addition reaction of dienolates **2** with imines or iminium ions **1** leading to δ-amino α,β-unsaturated carbonyl compounds **3** is known as the vinylogous Mannich reaction,[1] and is useful in the synthesis of nitrogen-containing natural products and related compounds (Scheme 1, equation 1).[2] In this category, addition reaction of 2-silyloxyfurans to a C–N double bond is very attractive, allowing oxygen functionalities as well as C4-units to be incorporated into nitrogen-containing carbon frameworks.[3,4]

Enantioselective addition reactions of 2-silyloxyfuran and related compounds have been addressed in recent years,[4] and recently diastereoselective addition reactions to C–N double bond compounds bearing chiral auxiliaries have been reported.[3g] Among C–N double bond compounds, nitrones **4** are known to undergo Mannich reaction with 2-silyloxyfuran **5** in the presence of a catalytic amount of TMSOTf to give bicyclic compounds **7** after TBAF treatment of the initial adducts **6** (equation 2).[5,6] Previously, we described diastereoselective addition reaction of 2-trimethylsilyloxyfuran (**5**) to nitrone **8**, which contains a hydroxymethyl group equivalent and an L-gulose-derived chiral auxiliary as an N-substituent; the resulting adduct was elaborated to afford a synthetic intermediate of polyoxin C.[7] Herein, we present a full account of that work, including an additional application of the reaction to synthesis of a key synthetic intermediate of dysiherbaine.



Scheme 1 Vinylogous Mannich reactions.

Results and discussion

1. Stereoselective nucleophilic addition of 2-trimethylsilyloxyfurane 5 to *N*-(2,3:5,6-*O*-isopropylidene-L-gulosyl)nitrones 8

For diastereofacially selective 1,3-dipolar cycloaddition or nucleophilic addition of nitrones, protected glycosyl groups, such as mannosyl[8] and gulosyl groups,[7,9,10] have been used as *N*-chiral auxiliaries. These groups can be removed under mild acidic conditions, whereas removal of benzyl-type auxiliaries, such as the 1-phenylethyl group, generally requires hydrogenolysis (Fig. 1). Although both mannosyl and gulosyl groups often exhibit high stereoselectivity, we have focused on the gulosyl auxiliary because

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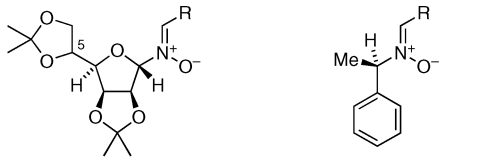
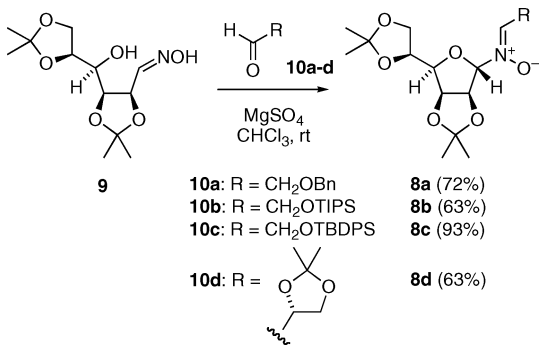


Fig. 1 Nitrones bearing chiral auxiliaries.

(i) both enantiomers are available and (ii) the stereochemistry of the product can be predicted.[7,10]

Our investigation began with preparation of four types of L-gulose-derived nitrone **8**. Treatment of oxime **9**, prepared from 2,3:5,6-*O*-isopropylidene-L-gulonolactone in two steps, with aldehydes **10a–d** in the presence of $MgSO_4$ in $CHCl_3$ at room temperature gave crystalline nitrones **8a–d** (Scheme 2). Since these nitrones were not very stable, they were used immediately for the next step.



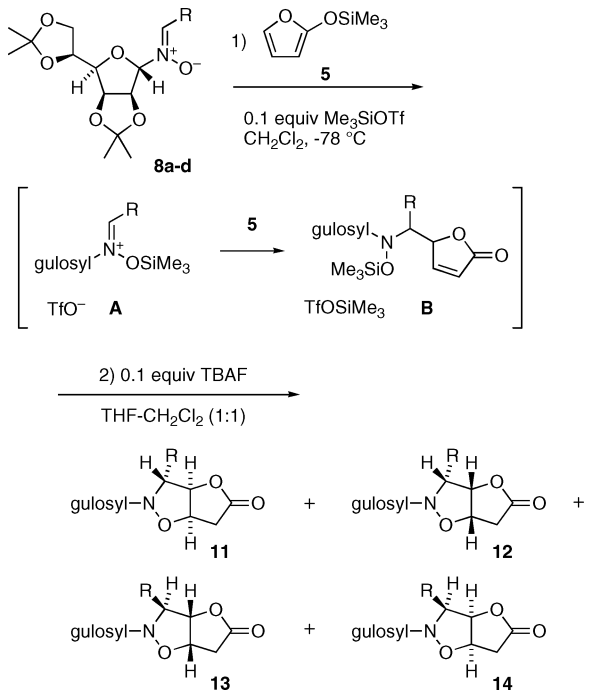
Scheme 2 Synthesis of nitrones **8a–d**.

When nitrones **8a–d** were treated with 2-trimethylsilyloxyfuran (**5**) (1.5 equiv) in the presence of TMSOTf (0.1 equiv) at low temperature, smooth nucleophilic addition to siloxyiminium ion **A** occurred to give butenolides **B** as the initial adducts, and these were further treated with TBAF (0.1 equiv) to afford bicyclic products **11–14** (Scheme 3 and Table 1).

The results, summarized in Table 1, showed that all reactions afforded the adducts **11** as the major products, and nitrones **8** having bulkier substituents exhibited greater stereoselectivity. C-Benzyloxymethyl nitrone **8a** gave a 76 : 13 : 8 : 3 mixture of four isomers **11a–14a** (entry 1). Nitrone **8b**, having a triisopropylsilyloxymethyl group as the substituent R, afforded a 74 : 21 : 5 mixture of three isomers (entry 2). Nitrone **8c** carrying the even bulkier *tert*-butyldiphenylsilyloxymethyl group showed still

Table 1 Addition reaction of nitrones **8a–d** with silyloxyfuran **5**

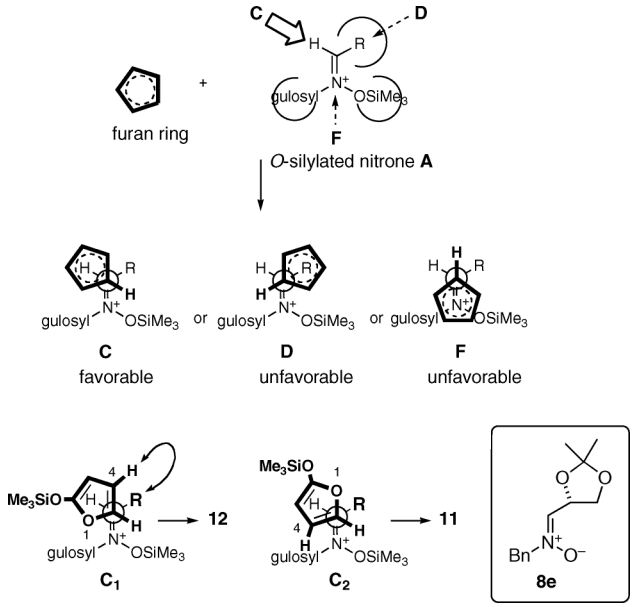
Entry	Nitrone **8** (R)	Yield (%)	Ratio **11** : (**12** + **13** + **14**)
1	**8a** (CH_2OBn)	84	76 : (13 + 8 + 3)
2	**8b** (CH_2OTIPS)	80	74 : (21 + 5)
3	**8c** ($CH_2OTBDPS$)	80	86 : (8 + 6)
4	**8d**	72	>97 : <3



Scheme 3 Addition reaction of nitrones **8a–d** with silyloxyfuran **5**.

greater stereoselectivity (entry 3). Finally, nitrone **8d**, bearing the branched 2,2-dimethyldioxolane ring, exclusively afforded **11d**.

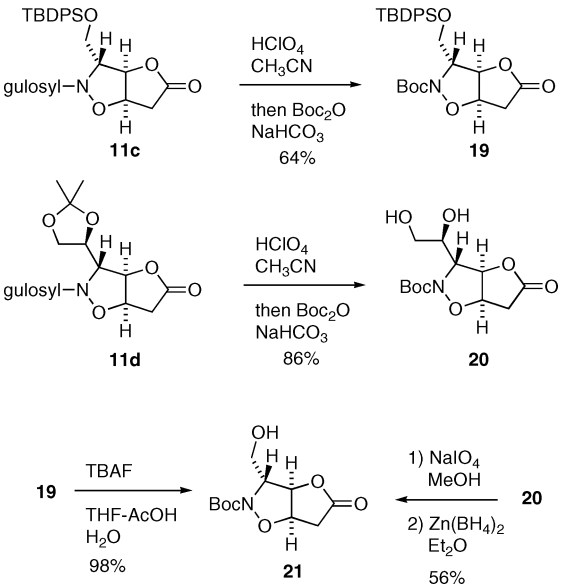
The substituent effect on the stereoselectivity of the present addition reaction of nitrones **8** may be explained in terms of the effect of the bulkiness of the substituent R on the initially generated siloxyiminium ion **A**. The stereochemistry of the products **11–14** of the reaction of nitrone **8** with 2-trimethylsilyloxyfuran **5** should be determined at the step of the addition reaction of furan **5** to siloxyiminium ion **A**, affording the initial adduct **B** (Schemes 3 and 4). Three types of staggered approach of silyloxyfuran **5** to siloxyiminium ion **A** can be considered (see **C**–**F** in Scheme 4; for simplicity, only upper-face approaches of silyloxyfuran to siloxyiminium ion **A** are illustrated). Among the three approach routes **C**–**F**, approach **C** would be more favorable than **D** or **F** because there is less interaction of the furan ring of **5** with substituents of **A**. Approach **C** may be further divided into two transition state models $\mathbf{C_1}$ and $\mathbf{C_2}$, which give opposite relative stereochemistries. Since the 4-position of furan is apparently bulkier than the 1-position is, the use of nitrone having a sterically more demanding *C*-substituent makes model $\mathbf{C_2}$ more favorable than model $\mathbf{C_1}$. Transition state $\mathbf{C_2}$ should exhibit high diastereofacial selectivity because of the closeness between the 4-position and the chiral auxiliary, whereas both antipodal transition states would be possible in the case of $\mathbf{C_1}$. Accordingly, the use of bulky nitrones **8c** and **8d** causes addition reaction of silyloxyfuran **5** to proceed preferentially by way of transition state $\mathbf{C_2}$ to afford **11** with good diastereo- and diastereofacial selectivity. It is known that addition reaction of the *N*-benzyl congener **8e** of **8d** with silyloxyfuran **5** in the presence of TMSOTf gives four stereoisomers of adducts with very low stereoselectivity.[6c] This fact clearly indicates that the stereoselectivity of the present reaction of **8d** arises mainly from the effect of the gulose auxiliary.



Scheme 4 Approach of furan **5** to silylated nitrone.

2. Synthetic studies of polyoxin C from adducts 11c and 11d as intermediates

Thymine and uracil polyoxin Cs (**17a** and **17b**), which are hybrid compounds of nucleosides and α-amino acids, are important as the *C*-terminal amino acid components of polyoxin J (**15**) and nikkomycin Bz (**16**), which exhibit anti-fungal activity (Fig. 2). Therefore, stereoselective syntheses of the unique amino acids **17** have been intensively investigated.[3e,11,12] An efficient method for syntheses of polyoxin Cs would be elaboration of dihydroxy lactone **18**,[12g] and therefore we next examined the synthesis of lactone **18** from adducts **11c** and **11d**, which we obtained stereoselectively as described above. For the synthetic study of polyoxin C, stereochemical correlation of adduct **11c** with **11d** was first conducted (Scheme 5). Hydrolytic removal of the sugar auxiliary of adduct **11c** by acid treatment followed by *N*-protection with a Boc group afforded **19**. Similar treatment of adduct **11d** gave diol **20**. Compound **19** was further treated with TBAF under acidic conditions to provide alcohol **21**, which was also obtained by oxidative cleavage of diol **20**, followed by reduction of the resulting aldehyde with zinc borohydride.



Scheme 5

Compound **21** was next elaborated to dihydroxylactone **18**,[12g] a key synthetic intermediate of polyoxin C (Scheme 6). Reductive cleavage of the *N–O* bond of compound **21** by heating with $Mo(CO)_6$[13] in acetonitrile–water and subsequent treatment with 2,2-dimethoxypropane in the presence of PPTS provided N,O-acetonide **22** in 54% yield. Mesylation of the secondary alcohol of **22** induced β-elimination to yield butenolide **23** in 96% yield. Finally, stereoselective dihydroxylation of butenolide **23** was conducted as described in the literature to afford lactone **18**.

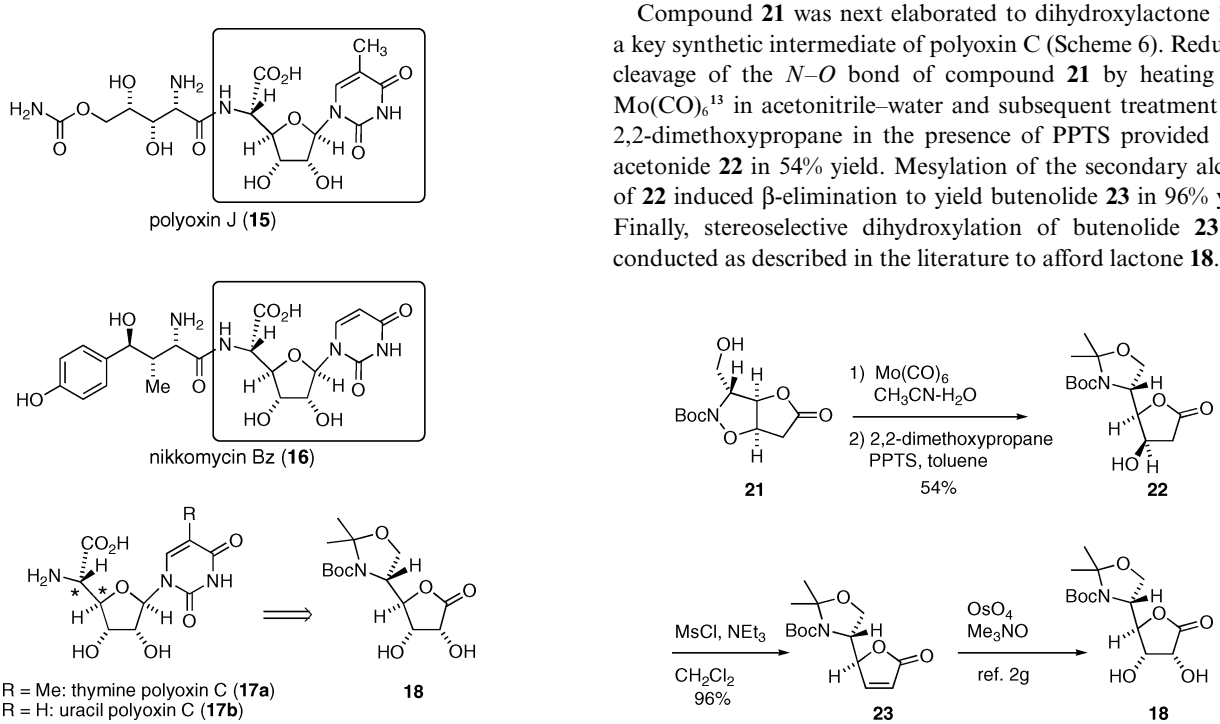


Fig. 2 Structures of polyoxins, nikkomycin Bz, and intermediate **18**.

Scheme 6 Synthesis of lactone **18**.

3. Synthetic studies of dysiherbaine from adduct 11d

Dysiherbaine (**24**), isolated from a Micronesian marine sponge *Dysydea herbacea*, is a strong and selective agonist of non-NMDA type glutamate receptors in the central nervous system (Fig. 3).[14] Owing to this remarkable biological activity, considerable efforts have been made to synthesize the natural product, and several total syntheses of **24** have been reported to date.[15,16] Among them, Hatakeyama's synthesis, in which tricyclic lactone **25** is used as the key synthetic intermediate, seems to be one of the most efficient.[15c,f,16d] Structural consideration of adduct **11d** showed that the stereochemistry of **11d** is in accordance with that of lactone **25** (compare formula **25** with **11d′**). Thus, we next turned our attention to the transformation of adduct **11d** to lactone **25**.

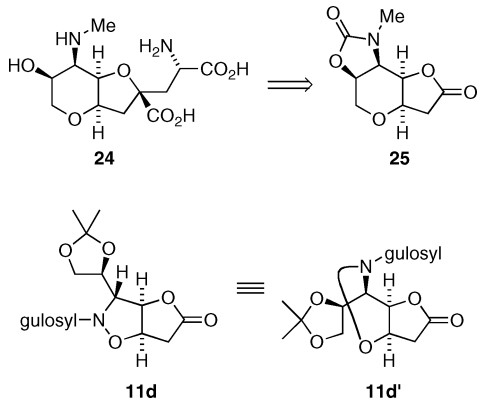
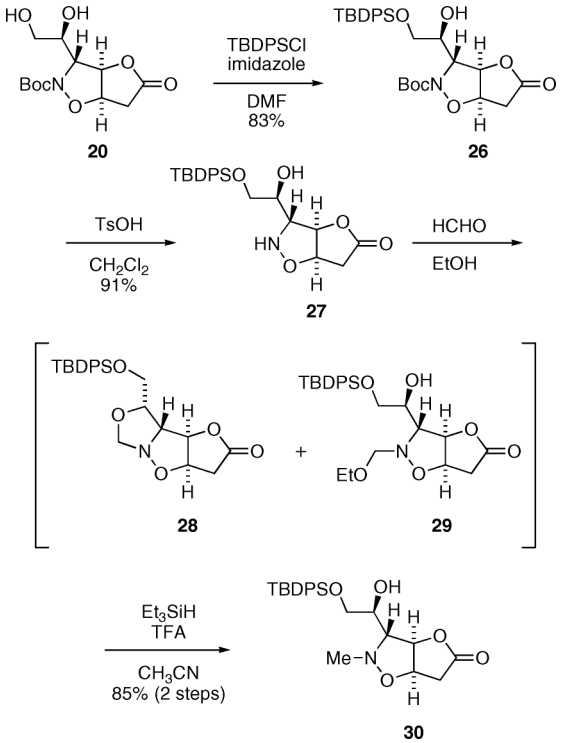


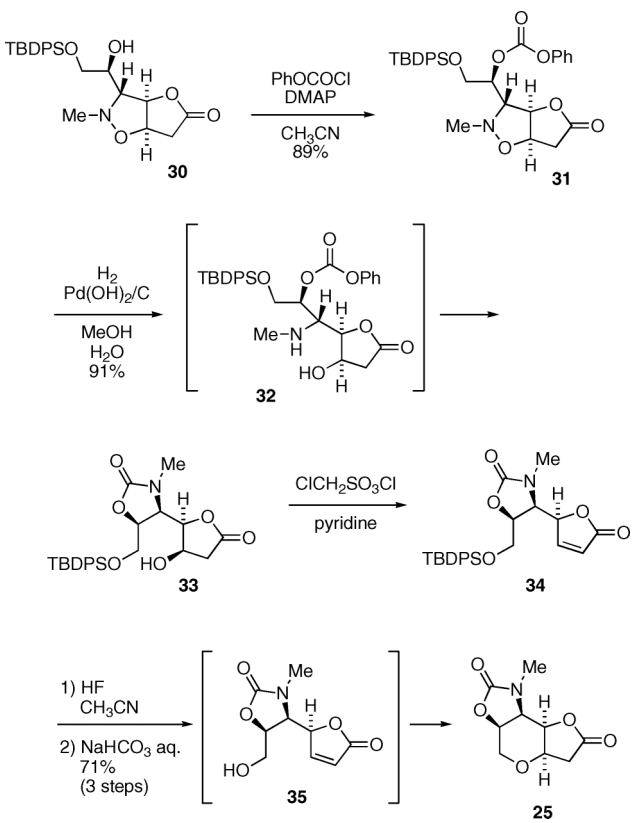
Fig. 3 Stereochemical accordance of adduct **11d** with lactone **25**.

Elaboration to **25** began with monoprotection of diol **20**, prepared in the synthetic study of polyoxin C, with a TBDPS group, affording **26**, from which the Boc group was removed under acidic conditions to give amino alcohol **27**. The key *N*-methylation was conducted by exposure of **27** to formaldehyde in ethanol, followed by treatment of the resulting mixture of **28** and **29** with triethylsilane and trifluoroacetic acid to provide compound **30** (Scheme 7).[17]

The next task was oxazolidinone formation and dihydropyran construction. To this end, phenoxycarbonylation of the secondary hydroxyl group of **30** was first conducted to provide carbonate **31** in 89% yield. When carbonate **31** was exposed to hydrogenolysis conditions, reductive cleavage of the *N*–*O* bond and subsequent ring closure of **32** occurred to give oxazolidinone **33** in 91% yield. Chloromesylation of the secondary hydroxyl group of **33** induced β-elimination to afford butenolide **34**. Finally, dihydropyran formation was accomplished by removal of the silyl protective group of **34** under acidic conditions, followed by intramolecular Michael addition of the primary hydroxyl group of **35** to afford tricyclic lactone **25**, which is a known key intermediate for dysiherbaine (Scheme 8).



Scheme 7 Synthesis of lactone **30** *via* *N*-methylation.



Scheme 8 Synthesis of lactone **25**.

Conclusion

We have explored the stereoselective addition reaction of 2-silyloxyfuran to *N*-gulosylnitrone and have found that the stereoselectivity of the reaction can be controlled by the *N*-chiral auxiliary of the nitrone. It was also found that nitrones with a bulkier *C*-substituent afforded greater stereoselectivity. The products **11c** and **11d** of the present reaction were successfully applied to the synthesis of polyoxin C, and adduct **11d** was transformed to a synthetic intermediate of dysiherbaine.

Experimental

General

Melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-140 or Horiba SEPA-300 digital polarimeter. Infrared spectra (IR) were recorded with a Shimadzu FTIR-8100. ^{1}H NMR spectra were recorded on a JEOL JNM-EX270 (270 MHz), a JEOL JNM-AL300 (300 MHz), a JEOL JNM-GSX400 (400 MHz) or a JEOL JNM-GSX500 (500 MHz) spectrometer. The chemical shifts are expressed in ppm downfield from tetramethylsilane (δ = 0) as an internal standard ($CDCl_3$ solution). ^{13}C NMR spectra were recorded on a JEOL JNM-EX270 (67.5 MHz), a JEOL JNM-AL300 (75 MHz), a JEOL JNM-GSX400 (100 MHz) or a JEOL JNM-GSX500 (125 MHz) spectrometer. The chemical shifts are reported in ppm, relative to the central line of the triplet at 77.0 ppm for $CDCl_3$. Measurements of mass spectra (MS) and high-resolution MS (HRMS) were performed with a JEOL JMS-SX102A or JEOL JMS-DX302 mass spectrometer. Column chromatography was carried out on silica gel (silica gel 40–50 μm neutral, Kanto Chemical Co., Inc.). Merck precoated thin layer chromatography (TLC) plates (silica gel 60 F_{254}, 0.25 mm, Art 5715) were used for the TLC analysis. After extractive workup, organic layers were dried over anhydrous sodium sulfate or anhydrous magnesium sulfate and the solvent was removed by rotary evaporation under reduced pressure.

General procedure for the preparation of adducts 11 from oxime 9 and aldehydes 10

A mixture of oxime **9** (1.0 equiv.), an aldehyde **10** (1.1 equiv.), and $MgSO_4$ in $CHCl_3$ was stirred overnight at room temperature. The mixture was filtered through a pad of Celite®. The filtrate was concentrated *in vacuo*, and the residue was passed through a short column of silica gel to afford nitrone **8** as a colorless solid. Nitrone **8** was used for the next step without further purification. To a stirred solution of nitrone **8** (0.1 mmol) in CH_2Cl_2 (3 mL) was added 2-trimethylsilyloxyfuran (**5**) (0.15 mmol) and TMSOTf (0.01 mmol) at −78 °C. The mixture was stirred at the same temperature for 15 min, then diluted with a saturated solution of $NaHCO_3$, and extracted with CH_2Cl_2. After drying ($MgSO_4$), the organic phase was concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2–THF (1 : 1, 5 mL). TBAF (0.01 mmol) was added at 0 °C, and the mixture was stirred for 10 min. Water (2 mL) was added, and the whole was extracted with CH_2Cl_2. The extract was stirred with $MgSO_4$ and Florisil®. After filtration, the filtrate was concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel to afford adducts **11–14**.

(3*R*,3a*S*,6a*R*)-3-Benzyloxymethyl-*N*-(2′,3′:5′,6′-*O*-diisopropylidene-α-L-gulofuranosyl)tetrahydrofuro[2,3-*d*]isoxazol-5-one (11a)

Following the general procedure, (*Z*)-2-benzyloxy-*N*-(2,3:5,6-*O*-diisopropylidene-α-L-gulofuranosyl)ethylideneamine *N*-oxide (**8a**) (176 mg, 72%) was prepared from oxime **9** (165 mg, 0.60 mmol) and aldehyde **10a** (99.7 mg, 0.66 mmol). It was used for the next step without further purification. **8a**: IR ($CHCl_3$) 3019, 1221, 1213 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23 (3H, s), 1.32 (3H, s), 1.38 (3H, s), 1.40 (3H, s), 3.62 (1H, dd, *J* = 8.4, 7.2 Hz), 4.13 (1H, dd, *J* = 8.4, 6.6 Hz), 4.27 (1H, ddd, *J* = 8.3, 7.2, 6.6 Hz), 4.35 (1H, dd, *J* = 12.9, 4.4 Hz), 4.40 (1H, dd, *J* = 12.9, 4.4 Hz), 4.43 (1H, dd, *J* = 8.3, 4.4 Hz), 4.50 (2H, s), 4.74 (1H, dd, *J* = 6.0, 4.4 Hz), 5.12 (1H, d, *J* = 6.0 Hz), 5.31 (1H, s), 7.08 (1H, t, *J* = 4.4 Hz), 7.21–7.32 (5H, m); MS (EI) *m*/*z*: 408 (M^++1). Following the general procedure, a 76 : 13 : 8 : 3 mixture of bicyclic adducts **11a–14a** (51 mg, 84%) was obtained from nitrone **8a** (50 mg, 0.12 mmol), furan **5** (28 mg, 0.18 mmol), and TMSOTf (2.2 μL, 1.2 μmol). The ratio was estimated by HPLC [JASCO-Fine pack SIL-5, AcOEt–hexane (3 : 2), 1.1 mL min^{-1}, tR: 8.50 (13%), 9.40 (76%), 10.38 (3%), 12.00 (8%)]. The major isomer **11a** was obtained by column chromatography on silica gel with AcOEt–hexane (3 : 2). **11a**: $[\alpha]_D^{17}$ +14.1 (*c* 0.83, $CHCl_3$); IR ($CHCl_3$) 1790 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (3H, s), 1.32 (3H, s), 1.35 (3H, s), 1.43 (3H, s), 2.61 (1H, dd, *J* = 18.7, 1.1 Hz), 2.70 (1H, dd, *J* = 18.7, 5.3 Hz), 3.52–3.58 (2H, m), 3.61 (1H, dd, *J* = 8.4, 7.0 Hz), 3.70 (1H, d, *J* = 10.1 Hz), 3.95 (1H, dd, *J* = 8.3, 3.9 Hz), 4.13 (1H, dd, *J* = 8.4, 7.8 Hz), 4.28 (1H, br ddd, *J* = 8.3, 7.8, 7.0 Hz), 4.45 (1H, d, *J* = 12.1 Hz), 3.53 (1H, d, *J* = 12.1 Hz), 4.59 (1H, dd, *J* = 6.1, 3.9 Hz), 4.64 (1H, br ddd, *J* = 5.4, 4.4, 1.0 Hz), 4.67 (1H, s), 4.85 (1H, d, *J* = 6.1 Hz), 5.10 (1H, br d, *J* = 4.6 Hz), 7.23–7.31 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.9, 25.3, 26.1, 26.8, 34.5, 65.9, 68.6, 68.9, 73.5, 75.6, 77.0, 80.4, 83.7, 84.7, 89.0, 99.6, 109.7, 113.0, 127.7, 127.9, 128.5, 138.0, 174.5; HRMS (EI) *m*/*z* calcd for $C_{25}H_{33}NO_9$ 491.2153, found 491.2148.

(3*R*,3a*S*,6a*R*)-*N*-(2′,3′:5′,6′-*O*-Diisopropylidene-α-L-gulofuranosyl)-3-(triisopropylsilyloxymethyl)tetrahydrofuro[2,3-*d*]isoxazol-5-one (11b)

Following the general procedure, (*Z*)-*N*-(2,3:5,6-*O*-diisopropylidene-α-L-gulofuranosyl)-2-triisopropylsilyloxyethylideneamine *N*-oxide (**8b**) (139 mg, 63%) was prepared from oxime **9** (129 mg, 0.47 mmol) and aldehyde **10b** (110 mg, 0.52 mmol). This material was unstable, and was therefore used for the next step without further purification. Following the general procedure, a 74 : 21 : 5 mixture of bicyclic adducts (70 mg, 80%) was obtained from nitrone **8b** (74 mg, 0.16 mmol), furan **5** (37 mg, 0.24 mmol), and TMSOTf (2.8 μL, 1.6 μmol). The ratio was estimated by ^{1}H NMR (300 MHz). The major isomer **11b** was obtained by column chromatography on silica gel with AcOEt–hexane (1 : 2). **11b**: $[\alpha]_D^{17}$ +3.3 (*c* 0.53, $CHCl_3$); IR ($CHCl_3$) 1786 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (3H, s), 1.07 (18H, s), 1.29 (3H, s), 1.38 (3H, s), 1.41 (3H, s), 1.44 (3H, s), 2.70 (1H, d, *J* = 18.5 Hz), 2.78 (1H, dd, *J* = 18.5, 5.4 Hz), 3.64 (2H, m), 3.66 (1H, dd, *J* = 8.3, 6.4 Hz), 3.99 (1H, dd, *J* = 10.0, 8.3 Hz), 4.00 (1H, dd, *J* = 8.3, 3.9 Hz), 4.19 (1H, dd, *J* = 8.3, 6.6 Hz), 4.33 (1H, br ddd, *J* = 8.3, 6.6, 6.4 Hz), 4.64 (1H, dd, *J* = 6.1, 3.9 Hz), 4.73 (1H, br dd, *J* = 5.4, 4.4 Hz), 4.74 (1H, s), 4.88 (1H, d, *J* = 6.1 Hz), 5.27 (1H, d, *J* = 4.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.0, 18.1, 24.9, 25.5, 26.1, 26.8, 35.3, 62.3, 66.0, 70.1, 75.8, 77.0, 80.5, 83.7, 84.7, 89.1, 99.2, 109.5, 112.8, 173.9; HRMS (EI) *m*/*z* calcd for $C_{27}H_{47}NO_9Si$ 557.3018, found 557.3022.

(3*R*,3a*S*,6a*R*)-3-*tert*-Butyldiphenylsilyloxymethyl-*N*-(2′,3′:5′,6′-*O*-diisopropylidene-α-L-gulofuranosyl)tetrahydrofuro[2,3-*d*]isoxazol-5-one (11c)

Following the general procedure, (*Z*)-2-*tert*-butyldiphenylsilyloxy-*N*-(2,3:5,6-*O*-diisopropylidene-α-L-gulofuranosyl)ethylideneamine

N-oxide (**8c**) (283 mg, 93%) was prepared from oxime **9** (151 mg, 0.55 mmol) and aldehyde **10c** (181 mg, 0.61 mmol). It was used for the next step without further purification. IR ($CHCl_3$) 2994, 1219, 1210 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.04 (9H, s), 1.28 (3H, s), 1.38 (3H, s), 1.43 (3H, s), 1.45 (3H, s), 3.67 (1H, dd, J = 8.3, 6.2 Hz), 4.18 (1H, dd, J = 8.3, 6.2 Hz), 4.32 (1H, br dt, J = 8.8, 6.2 Hz), 4.43 (1H, dd, J = 8.8, 3.9 Hz), 4.61 (2H, br d, J = 3.9 Hz), 4.72 (1H, dd, J = 5.8, 3.9 Hz), 5.10 (1H, d, J = 5.8 Hz), 5.32 (1H, s), 7.14 (1H, t, J = 3.9 Hz), 7.32–7.43 (6H, m), 7.59–7.65 (4H, m); HRMS (EI) m/z calcd for $C_{30}H_{41}NO_7Si$ 555.2650, found 555.2646. Following the general procedure, an 86 : 8 : 6 mixture of bicyclic adducts (91 mg, 80%) was obtained from nitrone **8c** (100 mg, 0.18 mmol), furan **5** (42 mg, 0.27 mmol), and TMSOTf (3.2 µL, 1.8 µmol). The ratio was estimated by HPLC [JASCO-Fine pack SIL-5, AcOEt–hexane (1 : 1), 1.0 mL min^{-1}, tR: 9.04 (86%), 9.40 (76%), 17.08 (6%)]. The major isomer **11c** was obtained by column chromatography on silica gel with AcOEt–hexane (3 : 2). **11c**: mp 166–167 °C (AcOEt–hexane); $[\alpha]_D^{21}$ +10.1 (*c* 0.99, $CHCl_3$); IR ($CHCl_3$) 1790 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.00 (9H, s), 1.10 (3H, s), 1.22 (3H, s), 1.24 (3H, s), 1.36 (3H, s), 2.62 (1H, dd, J = 18.5, 1.5 Hz), 2.70 (1H, dd, J = 18.5, 4.6 Hz), 3.50 (1H, dd, J = 8.3, 7.1 Hz), 3.58 (1H, dd, J = 9.9, 6.4 Hz), 3.63 (1H, ddd, J = 6.4, 3.8, 1.1 Hz), 3.77 (1H, dd, J = 8.2, 4.0 Hz), 3.92 (1H, dd, J = 9.9, 3.8 Hz), 4.08 (1H, dd, J = 8.3, 6.6 Hz), 4.21 (1H, ddd, J = 8.2, 7.1, 6.6 Hz), 4.53 (1H, dd, J = 6.1, 4.0 Hz), 4.65 (1H, td, J = 4.6, 1.5 Hz), 4.67 (1H, s), 4.81 (1H, d, J = 6.1 Hz), 5.16 (1H, dd, J = 4.6, 1.1 Hz), 7.32–7.45 (6H, m), 7.62–7.66 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.4, 25.0, 25.5, 26.2, 26.4, 27.0, 35.0, 62.9, 65.9, 69.5, 75.7, 77.2, 80.5, 83.5, 84.5, 89.0, 99.2, 109.5, 112.9, 127.6, 127.7, 129.7, 129.8, 132.6, 132.9, 135.4, 135.5, 173.9; HRMS (EI) m/z calcd for $C_{34}H_{45}NO_9Si$ 639.2861, found 639.2868. Anal. Calcd for $C_{34}H_{45}NO_9Si$: C, 68.83; H, 7.09; N, 2.19. Found: C, 63.55; H, 7.13; N, 2.16.

[3*R*,3a*S*,6a*R*,(4*S*)]-*N*-(2′,3′:5′,6′-*O*-Diisopropylidene-α-L-gulofuranosyl)-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)tetrahydrofuro-[2,3-*d*]isoxazol-5-one (11d)

(a) Following the general procedure, (4*S*)-(*Z*)-*N*-(2,3:5,6-*O*-diisopropylidene-α-L-gulofuranosyl)(2,2-dimethyl-[1,3]dioxolan-4-yl)methyleneamine *N*-oxide (**8d**) (175 mg, 63%) was prepared from oxime **9** (200 mg, 0.72 mmol) and aldehyde **10d** (103 mg, 0.79 mmol). It was used for the next step without further purification. **8d**: IR ($CHCl_3$) 2992, 1221, 1217 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.29 (3H, s), 1.37 (6H, s), 1.41 (3H, s), 1.43 (3H, s), 1.46 (3H, s), 3.69 (1H, dd, J = 8.4, 7.2 Hz), 3.69 (1H, dd, J = 8.6, 5.7 Hz), 4.18 (1H, dd, J = 8.4, 6.6 Hz), 4.31 (1H, br ddd, J = 8.4, 7.2, 6.6 Hz), 4.33 (1H, t, J = 8.6 Hz), 4.54 (1H, dd, J = 8.4, 4.4 Hz), 4.83 (1H, dd, J = 5.9, 4.4 Hz), 5.09 (1H, br ddd, J = 8.6, 5.7, 5.0 Hz), 5.16 (1H, d, J = 5.9 Hz), 5.31 (1H, s), 7.09 (1H, d, J = 5.0 Hz); HRMS (EI) m/z calcd for $C_{18}H_{29}NO_8$ 387.1891, found 387.1886. Following the general procedure, bicyclic adduct **11d** (55.7 mg, 72%) was obtained as a sole product from nitrone **8d** (60 mg, 0.15 mmol), furan **5** (36 mg, 0.23 mmol), and TMSOTf (2.8 µL, 1.5 µmol). **11d**: mp 172–173 °C (benzene–hexane); $[\alpha]_D^{21}$ +23.7 (*c* 0.90, $CHCl_3$); IR ($CHCl_3$) 1792 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.26 (3H, s), 1.32 (3H, s), 1.36 (3H, s), 1.39 (3H, s), 1.42 (3H, s), 1.44 (3H, s), 2.71 (1H, dd, J = 18.8, 1.0 Hz), 2.79 (1H, dd, J = 18.8, 5.6 Hz), 3.56 (1H, dd, J = 4.6, 1.3 Hz), 3.68 (1H, dd, J = 8.5, 6.7 Hz), 3.79 (1 H, dd, J = 8.8, 5.9 Hz), 4.03 (1 H, dd, J = 8.3, 3.4 Hz), 4.16 (1H, dd, J = 8.8, 5.9 Hz), 4.19 (1 H, dd, J = 8.5, 6.7 Hz), 4.29 (1H, ddd, J = 6.8, 5.9, 4.6 Hz), 4.34 (1H, dt, J = 8.3, 6.7 Hz), 4.65 (1H, s), 4.65 (1H, dd, J = 6.1 3.4 Hz), 4.73 (1H, ddd, J = 5.6, 4.6, 1.0 Hz), 4.90 (1H, d, J = 6.1 Hz), 5.27 (1H, dd, J = 4.6, 1.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7, 25.1, 25.4, 26.2, 26.5, 26.9, 35.1, 66.0, 67.5, 71.9, 73.9, 75.5, 77.5, 80.4, 84.1, 84.7, 87.9, 100.1, 109.7, 109.9, 113.1, 173.6; HRMS (EI) m/z calcd for $C_{22}H_{33}NO_{10}$ 471.2102, found 471.2101. Anal. Calcd for $C_{22}H_{33}NO_{10}$: C, 56.04; H, 7.05; N, 2.97. Found: C, 55.72; H, 6.95, N, 2.93.

(b) Following the general procedure, **11d** (1.19 g, 87%) was obtained as a sole product from nitrone **8d** (1.19 g, 3.06 mmol), furan **5** (717 mg, 4.59 mmol), and TMSOTf (68 mg, 0.306 mmol).

(3*R*,3a*S*,6a*R*)-3-(*tert*-Butyldiphenylsilyloxymethyl)-*N*-(*tert*-butyloxycarbonyl)tetrahydrofuro[2,3-*d*]isoxazol-5-one (19)

To a stirred solution of bicyclic adduct **11c** (500 mg, 0.78 mmol) in CH_3CN (10 mL) was added a 0.96 M solution of $HClO_4$ (1.6 mL, 1.5 mmol). The mixture was stirred at room temperature for 5 h and neutralized with powdered $NaHCO_3$. Then Boc_2O (853 mg, 3.9 mmol) was added, and the mixture was stirred overnight, diluted with water, and extracted with CH_2Cl_2. The organic solution was washed with brine, and dried over $MgSO_4$. After filtration, the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with AcOEt–hexane (1 : 1) to afford **19** (246 mg, 64%) as a colorless oil. $[\alpha]_D^{21}$ −18.8 (*c* 1.32, $CHCl_3$); IR ($CHCl_3$) 1794, 1734, 1429, 1371 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.01 (9H, s), 1.37 (9H, s), 2.68 (1H, dd, J = 19.2, 7.1 Hz), 2.91 (1H, d, J = 19.2 Hz), 3.56 (1H, dd, J = 10.6, 7.7 Hz), 3.82 (1H, dd, J = 10.6, 5.3 Hz), 4.46 (1H, dd, J = 7.7, 5.3 Hz), 4.72 (1H, br dd, J = 7.1, 5.3 Hz), 5.28 (1H, d, J = 5.3 Hz), 7.29–7.41 (6H, m), 7.56–7.60 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.4, 27.1, 28.2, 35.2, 62.1, 67.6, 79.7, 83.9, 86.9, 128.4, 130.5, 130.6, 133.1, 133.2, 136.0, 136.1, 158.0, 173.9; MS (EI) m/z 453 (M+-CO_2), 424, 384, 340, 319. HRMS (EI) m/z calcd for $C_{26}H_{35}NO_4Si$–CO_2 453.2333, found 453.2335.

[3*R*,3a*S*,6a*R*,(2*S*)]-*N*-(*tert*-Butyloxycarbonyl)-3-(1,2-dihydroxyethyl)tetrahydrofuro[2,3-*d*]isoxazol-5-one (20)

To a stirred solution of bicyclic adduct **11d** (258 mg, 0.583 mmol) in CH_3CN (10 mL) was added a 1 M solution of $HClO_4$ (1.17 mL, 1.17 mmol). The mixture was stirred at room temperature for 15 min and neutralized with powdered $NaHCO_3$. Then Boc_2O (636 mg, 2.91 mmol) was added, and the mixture was stirred overnight, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with AcOEt–CH_2Cl_2 (5 : 1) to afford **20** (144 mg, 86%) as a colorless oil. $[\alpha]_D^{21}$ −16.1 (*c* 1.80, $CHCl_3$); IR ($CHCl_3$) 3600, 1794, 1736, 1371 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.49 (9H, s), 2.84 (1H, br s), 2.85 (1H, dd, J = 18.5, 6.9 Hz), 3.00 (1H, d, J = 18.5 Hz), 3.29 (1H, d, J = 7.3 Hz), 3.61 (1H, ddt, J = 9.2, 7.3, 4.0 Hz), 3.77 (1H, dd, J = 15.5, 4.0 Hz), 3.85 (1H, dd, J = 15.5, 4.0 Hz), 4.45 (1H, d, J = 9.2 Hz), 5.03 (1H, br dd, J = 6.9, 5.3 Hz), 5.59 (1H, d, J = 5.3 Hz); ^{13}C NMR (67.8 MHz,

$CDCl_3$) δ 28.0, 35.0, 63.2, 67.5, 69.1, 79.9, 84.3, 86.7, 157.9, 173.9; MS (EI) *m/z* 230 (M^+-*tert*-Bu), 216, 189, 128, 110, 57.

(3*R*,3a*S*,6a*R*)-3-(Hydroxymethyl)-*N*-(*tert*-butyloxycarbonyl)-tetrahydrofuro[2,3-d]isoxazol-5-one (21)

(*a*) Preparation of **21** from **19**. A 1.0 M solution of TBAF (38 µL, 38 µmol) was adjusted to pH 4–5 by adding 80% AcOH. To the mixture was added a solution of **19** (18.7 mg, 37.7 µmol) in THF (2 mL) at 0 °C. The mixture was stirred at room temperature for 3 h, diluted with water, and extracted with AcOEt. The organic phase was dried over $MgSO_4$, and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with AcOEt–hexane (2 : 1) to give **21** (9.6 mg, 98%) as a colorless oil. $[\alpha]_D^{21}$ −23.1 (*c* 0.96, $CHCl_3$); IR ($CHCl_3$) 1794, 1736, 1371 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.49 (9H, s), 2.12 (1H, br s), 2.81 (1H, dd, *J* = 19.2, 7.1 Hz), 3.03 (1H, dd, *J* = 19.2, 0.5 Hz), 3.78 (2H, m), 4.56 (1H, t, *J* = 5.7 Hz), 4.98 (1H, ddd, *J* = 7.1, 5.3, 0.5 Hz), 5.28 (1H, d, *J* = 5.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.1, 34.9, 61.2, 67.9, 79.8, 84.0, 86.6, 157.5, 173.3; HRMS (EI) *m/z* calcd for $C_{11}H_{17}NO_6$ 259.1055, found 259.1064.

(*b*) Preparation of **21** from **20**. A mixture of diol **20** (31.8 mg, 0.11 mmol) and $NaIO_4$ (35.3 mg, 0.16 mmol) in MeOH–H_2O (10 : 1, 2 mL) was stirred at 0 °C for 1 h. After evaporation, the residue was partitioned between water and CH_2Cl_2. The aqueous phase was further extracted with CH_2Cl_2. The combined organic phase was washed with brine, dried over $MgSO_4$, and filtered, and the filtrate was concentrated *in vacuo*. The residue was dissolved in Et_2O (2 mL). To this solution was added a 0.1 M solution of $Zn(BH_4)_2$ in Et_2O (3.3 mL, 0.33 mmol) at 0 °C. After 1 h, 1 N HCl (1 mL) was added, and the mixture was extracted with AcOEt. The AcOEt solution was washed successively with a saturated solution of $NaHCO_3$ and brine, and dried over $MgSO_4$. After filtration, the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with CH_2Cl_2–MeOH (10 : 1) to give **21** (16.0 mg, 56%) as a colorless oil. $[\alpha]_D^{21}$ −22.1 (*c* 0.81, $CHCl_3$). Spectral data of this sample were identical with those obtained in (*a*).

(4*S*)-4-[(2*R*,3*R*)3-Hydroxy-5-oxo-tetrahydro-furan-2-yl]-2,2-dimethyloxazolidine-3-carboxylic acid *tert*-butyl ester (22)

A solution of **21** (142 mg, 0.55 mmol) and $Mo(CO)_6$ (289 mg, 1.1 mmol) in CH_3CN–H_2O (10 : 1, 15 mL) was heated at reflux for 1.5 h. The mixture was filtered through a pad of Celite®, and the filtrate was concentrated *in vacuo*. The residue was passed through a pad of silica gel, and the filtrate was concentrated *in vacuo*. The residue was dissolved in toluene (10 mL) containing 2,2-dimethoxypropane (338 mL, 2.75 mmol) and PPTS (13.8 mg, 55 µmol), and the solution was heated at reflux for 1.5 h. The mixture was concentrated *in vacuo*, and the residue was purified by column chromatography on silica gel with AcOEt–hexane (2 : 3) to give **22** (89.5 mg, 54%). $[\alpha]_D^{21}$ +76.2 (*c* 0.79, $CHCl_3$); IR ($CHCl_3$) 3300, 1800, 1779, 1671, 1402 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.51 (9H, s), 1.54 (3H, s), 1.57 (3H, s), 2.61 (1H, d, *J* = 17.3 Hz), 2.72 (1H, ddd, *J* = 17.3, 4.6, 2.0 Hz), 4.04 (1H, dd, *J* = 9.5, 5.1 Hz), 4.14 (1 H, dd, *J* = 10.2, 2.0 Hz), 4.24 (1H, d, *J* = 9.5 Hz), 4.30 (1H, dd, *J* = 10.2, 5.1 Hz), 4.34 (1H, dt, *J* = 4.6, 2.0 Hz), 5.71 (1H, br t, *J* = 2.0 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 24.2, 27.9, 28.4, 38.8, 54.5, 65.4, 67.3, 82.5, 82.9, 94.4, 154.1, 174.6; HRMS (EI) *m/z* Calcd for $C_{13}H_{20}NO_6$–CH_3 286.1289, found 286.1287.

(4*R*)-4-[(2*S*)-3,4-Dihydro-5-oxo-furan-2-yl]-2,2-dimethyloxazolidine-3-carboxylic acid *tert*-butyl ester (23)

To a stirred solution of **22** (12.9 mg, 42.8 µmol) in CH_2Cl_2 (1 mL) were added MsCl (13 µL, 171 µmol) and Et_3N (47 µL, 342 µmol) at room temperature. The mixture was stirred for 2 h, diluted with water, and extracted with Et_2O. The Et_2O solution was washed with brine, and dried over $MgSO_4$. After filtration, the filtrate was concentrated *in vacuo*. The residue was purified column chromatography on silica gel with AcOEt–hexane (1 : 1) to give **23** (11.6 mg, 96%) as an oil. This compound was used without further purification. IR ($CHCl_3$) 3028, 1794, 1761, 1698, 1686 cm^{-1}; ^{1}H NMR (270 MHz, C_6D_6, 60 °C) δ 1.32 (9H, s), 1.37 (3H, s), 1.53 (3H, s), 3.42 (1H, dd, *J* = 9.2, 5.3 Hz), 3.53 (1H, br s), 3.70 (1H, d, *J* = 9.2 Hz), 4.60 (1H, br s), 5.60 (1H, dd, *J* = 5.7, 2.0 Hz), 6.81 (1H, dd, *J* = 5,7, 1.3 Hz).

(4*R*)-4-[(2*R*,3*R*,4*R*)-3,4-Dihydroxy-5-oxo-tetrahydrofuran-2-yl]-2,2-dimethyloxazolidine-3-carboxylic acid *tert*-butyl ester (18)

Following Garner's procedure, this material was obtained from **23** and Me_3NO, and OsO_4. $[\alpha]_D^{21}$ +31.0 (*c* 0.85, $CHCl_3$), *lit.*[12g] $[\alpha]_D$ +31.8 (*c* 0.87, $CHCl_3$); IR ($CHCl_3$) 2984, 1786, 1695, 1678 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6, 60 °C) δ 1.31 (9H, s), 1.33 (3H, s), 1.48 (3H, s), 2.49 (2H, br s), 3.41 (1H, dd, *J* = 9.4, 5.3 Hz), 3.48 (1H, dd, *J* = 9.4, 5.3 Hz), 3.68 (1H, d, *J* = 9.4 Hz), 4.30 (1H, d, *J* = 9.4 Hz), 4.39 (1 H, br s); ^{13}C NMR (100 MHz, C_6D_6, 60 °C) δ 24.2, 27.9, 28.4, 57.9, 65.6, 69.2, 69.7, 81.1, 84.6, 94.8, 153.2, 174.1; HRMS (EI) *m/z* calcd for $C_{13}H_{20}NO_7$–CH_3 302.1238, found 302.1239.

(3*R*,3a*S*,6a*R*)-3-[(*S*)-(2-*tert*-Butyldiphenylsilyloxy-1-hydroxyethyl)]-2-(*tert*-butyloxycarbonyl)tetrahydrofuro[2,3-*d*]isoxazol-5-one (26)

To a stirred solution of diol **20** (2.23 g, 7.76 mmol) in DMF were added imidazole (1,59 g, 23.3 mmol) and TBDPSCl (2.77 g, 10.1 mmol) at room temperature, and stirring was continued for 30 min. The mixture was partitioned between water and Et_2O, and the organic layer was successively washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane–EtOAc, 2 : 1) to give **26** (3.40 g, 83%) as a colorless oil. $[\alpha]_D^{23}$ −20.6 (*c* 0.30, $CHCl_3$); IR ($CHCl_3$) 1792, 1734 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.09 (9H, s), 1.45 (9H, s), 2.69 (1H, d, *J* = 6.6 Hz), 2.79 (1H, dd, *J* = 19.3, 7.3 Hz), 3.05 (1H, d, *J* = 19.3 Hz), 3.58 (1H, m), 3.78 (1H, dd, *J* = 10.6, 4.3 Hz), 3.86 (1H, dd, *J* = 10.6, 4.6 Hz), 4.58 (1H, d, *J* = 8.5 Hz), 4.97 (1H, dd, *J* = 7.3, 5.2 Hz), 5.57 (1H, d, *J* = 5.2 Hz), 7.35–7.49 (6H, m, Ph), 7.64–7.69 (4H, m, Ph); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 19.2, 26.9, 28.0, 35.0, 63.9, 67.7, 68.9, 79.8, 83.9, 86.5, 127.9, 130.0, 132.5, 135.5, 157.8, 173.9; MS (EI) *m/z* 484 (2.5, -^{t}Bu), 370, 292. *Anal*. Calcd for $C_{28}H_{37}NO_7Si$: C, 63.73; H, 7.07; N, 2.65. Found: C, 63.56; H, 7.21; N, 2.63.

(3*R*,3a*S*,6a*R*)-3-[(*S*)-2-*tert*-Butyldiphenylsilyloxy-1-hydroxyethyl]-tetrahydrofuro[2,3-*d*]isoxazol-5-one (27)

To a stirred solution of **24** (1.45 g, 2.75 mmol) in CH_2Cl_2 (75 ml) was added anhydrous TsOH (1.14 g, 6.60 mmol) at 0 °C, and stirring was continued at room temperature for 7 h. The mixture was poured into a saturated aqueous solution of $NaHCO_3$, and the whole was extracted with $CHCl_3$, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane–EtOAc, 1.7 : 1) to give **25** (1.05 g, 90%) as a colorless oil. $[\alpha]_D^{20}$ +49.4 (*c* 0.22, $CHCl_3$); IR ($CHCl_3$) 1786 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.08 (9H, s, *t*-Bu), 2.64 (1H, d, *J* = 5.3 Hz), 2.68 (1H, dd, *J* = 19.1, 1.3 Hz), 2.84 (1H, dd, *J* = 19.1, 6.7 Hz), 3.53 (1H, m), 3.71 (1H, br), 3.84 (2H, d, *J* = 4.6 Hz), 4.77 (1H, ddd, *J* = 6.7, 6.3, 1.3 Hz), 5.51 (1H, br), 5.83 (1H, dd, *J* = 6.3, 0.9 Hz), 7.37–7.48 (6H, m), 7.63–7.66 (4H, m); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 19.3, 26.9, 34.6, 64.9, 67.9, 68.3, 87.8, 127.9, 130.1, 132.6, 135.5, 173.9. MS (EI) *m*/*z* 370, 293, 292. *Anal*. Calcd for $C_{23}H_{29}NO_5Si$: C, 64.61; H, 6.84; N, 3.28. Found: C, 64.33; H, 7.00; N, 3.30.

(3*R*,3a*S*,6a*R*)-3-[(*S*)-2-*tert*-Butyldiphenylsilyloxy-2-hydroxyethyl]-2-methyl-tetrahydrofuro[2,3-*d*]isoxazole-5-one (30)

To a stirred solution of **27** (1.00 g, 2.35 mmol) in EtOH (5 mL) was added a 35% aqueous solution of HCHO (1.66 mL, 20 mmol) at room temperature, and the mixture was heated at 75 °C for 6 h. After concentration, the residue was dissolved in CH_3CN (50 mL). Trifluoroacetic acid (1.78 mL, 23.5 mmol) and Et_3SiH (2.81 mL, 17.6 mmol) were added at room temperature, and then the mixture was heated at 60 °C for 1.5 h and poured into a saturated aqueous solution of $NaHCO_3$. The whole was extracted with $CHCl_3$. The organic extract was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed on silica gel with (hexane–EtOAc, 1.5 : 1) to give **30** (880 mg, 85%) as colorless oil. $[\alpha]_D^{24}$ –0.3 (*c* 0.48, $CHCl_3$); IR ($CHCl_3$) 1786 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.08 (9H, s), 2.64 (1H, d, *J* = 19.2 Hz), 2.72 (3H, s), 2.73 (1H, dd, *J* = 19.2, 5.5 Hz), 2.95 (1H, dd, *J* = 4.0, 2.4 Hz), 3.78 (1H, m), 3.78 (2H, d, *J* = 4.9 Hz), 4.58 (1H, dd, *J* = 5.5, 4.9 Hz), 5.31 (1H, dd, *J* = 4.9, 2.4 Hz), 7.37–7.48 (6H, m, Ph), 7.63–7.66 (4H, m, Ph); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 19.2, 26.8, 34.2, 44.1, 64.9, 69.0, 75.8, 87.6, 127.9, 130.0, 132.7, 135.5, 174.6. MS (EI) *m*/*z* 441, 384, 307. *Anal*. Calcd for $C_{28}H_{35}NO_7Si$: C, 65.28; H, 7.08; N, 3.17. Found: C, 65.02; H, 7.47; N, 3.09.

(3*R*,3a*S*,6a*R*)-3-[(*S*)-2-*tert*-Butyldiphenylsilyloxyethyl-1-phenyl-carbonyloxy]-2-methyl-tetrahydrofuro[2,3-*d*]isoxazole-5-one (31)

To a stirred solution of **30** (632 mg, 1.43 mmol) and DMAP (350 mg, 2.86 mmol) in CH_3CN (120 mL) was added phenyl chloroformate (336 mg, 2.15 mmol) at 60 °C. After 2 h, further phenyl chloroformate (224 mg, 1.43 mmol) and DMAP (175 mg, 1.43 mmol) were added, and stirring was continued for 2 h at 60 °C. The mixture was poured into a saturated aqueous solution of $NaHCO_3$, and the whole was extracted with AcOEt. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed on silica gel with (hexane–AcOEt, 3 : 1) to give **31** (698 mg, 89%) as a colorless oil and starting **30** (44.8 mg, 7%). **31**: $[\alpha]_D^{24}$ +4.7 (*c* 0.38, $CHCl_3$); IR ($CHCl_3$) 1786, 1767 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.08 (9H, s), 2.65 (1H, dd, *J* = 18.8, 1.3 Hz), 2.72 (3H, s), 2.75 (1H, dd, *J* = 18.8, 5.3 Hz), 3.02 (1H, dd, *J* = 3.0, 2.6 Hz), 3.93 (1H, dd, *J* = 11.5, 5.5 Hz), 3.94 (1H, dd, *J* = 11.5, 6.2 Hz), 4.62 (1H, ddd, *J* = 5.3, 4.6, 1.3 Hz), 5.00 (1H, ddd, *J* = 6.2, 5.5, 2.6 Hz), 5.29 (1H, dd, *J* = 4.6, 3.0 Hz), 7.12–7.48 (11H, Ph), 7.68–7.73 (4H, Ph); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 19.2, 26.7, 33.8, 43.7, 63.1, 74.7, 76.2, 87.4, 126.2, 127.9, 129.5, 129.7, 130.0, 132.5, 135.6, 151.0, 153.0, 174.4. *Anal*. Calcd for $C_{28}H_{35}NO_7Si$: C, 66.29; H, 6.28; N, 2.49. Found: C, 66.18; H, 6.49; N, 2.42.

(4*R*,5*S*)-5-(*tert*-Butyldiphenylsilyloxymethyl)-3-methyl-4-[(2*R*,3*R*)-tetrahydro-3-hydroxy-5-oxofuran-2-yl]oxazolidine-2-one (33)

A mixture of **31** (38.6 mg, 0.071 mmol) and 20% $Pd(OH)_2/C$ (38.6 mg) in MeOH–H_2O (20 : 1, 1 mL) was stirred for 10 h under an atmosphere of hydrogen. The catalyst was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was chromatographed on silica gel with (hexane–EtOAc, 1 : 1.5) to give **33** (30.1 mg, 91%) as a colorless oil. $[\alpha]_D^{18}$ +51.0 (*c* 0.48, $CHCl_3$); IR ($CHCl_3$) 1790, 1747 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.04 (9H, s), 2.53 (1H, d, *J* = 17.4 Hz), 2.60 (1H, dd, *J* = 17.4, 4.6 Hz), 2.99 (3H, s), 3.45 (1H, br), 4.05 (1H, dd, *J* = 11.9, 2.7 Hz), 4.08 (1H, dd, *J* = 11.9, 2.7 Hz), 4.33 (1H, dt, *J* = 8.2, 2.7 Hz), 4.57 (1H, dd, *J* = 8.2, 3.6 Hz), 4.58 (1H, dt, *J* = 9.1, 4.6 Hz), 4.71 (1H, dd, *J* = 9.1, 3.6 Hz), 7.36–7.44 (6H, m), 7.63–7.65 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.1, 22.6, 26.7, 31.2, 31.6, 39.5, 56.4, 62.4, 68.3, 75.9, 80.8, 127.9, 130.1, 132.2, 132.8, 135.4, 135.6, 135.8, 159.1, 173.8. *Anal*. Calcd for $C_{25}H_{31}NO_6Si$: C, 63.94; H, 6.65; N, 2.98. Found: C, 64.01; H, 6.98; N, 2.97.

Hatakeyama's lactone 25

Pyridine (30.8 μL, 0.383 mmol) and chloromethanesulfonyl chloride (17.1 μL, 0.192 mmol) were added to a stirred solution of **33** (30.0 mg, 0.064 mmol) in CH_2Cl_2 (0.4 mL) at 0 °C, and stirring was continued at room temperature for 5 h. The reaction was quenched by adding water, and the whole was extracted with $CHCl_3$. The organic layer was successively washed with 1 N HCl and a saturated aqueous solution of $NaHCO_3$, then dried ($MgSO_4$), and concentrated under reduced pressure to give crude **34**. The crude **34** was dissolved in CH_3CN. A 47% aqueous solution of HF (0.5 mL) was added, and the mixture was heated at 60 °C for 30 h, adjusted to pH 8 by adding $NaHCO_3$, further stirred at room temperature for 3 h, and then partitioned between water and $CHCl_3$. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed on silica gel with (EtOAc–MeOH, 20 : 1) to give **25** (9.6 mg, 71%) as colorless crystals. mp 191–192 °C (EtOAc); *lit*[15c] 199–201 °C (EtOAc); *lit*[16d] 192–193 °C (EtOAc); $[\alpha]_D^{24}$ +128.2 (*c* 0.200, CH_3OH); *lit*[16d] +131.8 (*c* 0.35, CH_3OH); ^1H NMR (270 MHz, CD_3OD) δ 2.53 (1H, d, *J* = 17.2 Hz), 2.89 (1H, dd, *J* = 17.2, 4.3 Hz), 2.90 (3H, s) 3.76 (1H, dd, *J* = 14.2, 2.0 Hz), 4.16 (1H, dd, *J* = 14.2, 1.3 Hz), 4.16 (1H, dd, *J* = 6.9, 5.9 Hz), 4.30 (1H, dd, *J* = 4.3, 2.3 Hz), 4.44 (1H, ddd, *J* = 6.9, 2.0, 1.3 Hz), 4.72 (1H, dd, *J* = 5.9, 2.3 Hz). These physical data are identical with the reported values.[15c,16d]

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