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Kinetic and thermodynamic aspects in the 1,3-dipolar cycloaddition of five-membered cyclic nitrones to α,β-unsaturated γ- and δ-lactones

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Abstract—The 1,3-dipolar cycloaddition of five-membered ring nitrones to the α,β-unsaturated δ-lactones is kinetically controlled, whereas the same reactions involving γ-lactones, upon heating and prolonged reaction times, display visible reversibility of the reaction and as the consequence, the formation of the more stable, thermodynamic products can be observed. Owing to this and to the high stereoselectivity of the cycloaddition, δ-lactones can be used for kinetic resolution of racemic nitrones whereas γ-ones cannot. In addition the reversibility of the cycloaddition, as well as racemization of 5-substituted 2-(5*H*)-furanones (γ-lactones), complicates the composition of the post-reaction mixtures and may lead to the formation of partially racemic adducts. The possible asymmetric transformation of cycloaddition involving γ-lactones, which eventually provide the most stable thermodynamic products in high yield, cannot be performed due to the low stability of cyclic nitrones which undergo decomposition.

1. Introduction

Recently we have reported that the 1,3-dipolar cycloaddition of nitrones **1**–**4** to α,β-unsaturated γ-**5**, **6** and δ-lactones **7**–**10** constitutes an interesting example of a double asymmetric induction, where the chirality elements of each reactant may influence stereoselectivity either in concert or in opposite manner.[1–5] Although, in general, 1,3-dipolar cycloaddition involving nitrones is thermally reversible,[6] the results of our investigations have been interpreted on the assumption that the cycloaddition is kinetically controlled. In the case of δ-lactones, such an assumption appeared reasonable since we have never observed any reversibility of these reactions. In the case of γ-lactones, however, upon heating and prolongation of the reaction time, the reversibility of the cycloaddition has been observed, and the presence of more stable thermodynamic products has been detected. Moreover, in the case of γ-lactone **6**, a partial racemization can occur and consequently adducts derived from **6** and *ent*-**6** are formed.

Contrary to the corresponding additions involving δ-lactones, where only the *exo* approach of reactants was observed, with the exception of the formation of a small amount of the *endo* adduct reported by Font et al.[7] for compound **7**, γ-lactones **5** and **6** can add nitrone in both the *exo* and *endo* mode. Recently Langlois et al.[8] have reported the *endo* approach of oxazoline N-oxide and unsaturated δ-lactone in the mismatched pair and explained that by the interaction between the positively charged imino-ether fragment in the nitrone and the lactone carbonyl group. The *endo* addition of the reactants is energetically more demanding than the *exo* addition and might occur if none of the substituents present in the lactone or nitrone hinders such approach and when there is an additional secondary interaction that favors the *endo* transition state.

The high preference of the *anti* addition to the terminal acetoxymethyl group in the δ-lactones **8**–**10** and to the 3-*tert*-butoxy group of the nitrones **2** and **3** has been observed. The 4-*tert*-butoxy substituent present in **3** played a secondary role. In the case of mismatched pairs, the configuration of the 4-*O*-acetoxy substituent in lactones **9** and **10** becomes the decisive factor controlling the outcome of the addition.[4]

The cycloaddition of 2 mol equiv of racemic δ-lactones **8**/*ent*-**8** and nitrones **2** or **3** showed significant kinetic resolutions.[1,2] In the case of the nitrone **2**, D-glycero lactone **8** was less reactive and could be isolated in 95% yield and

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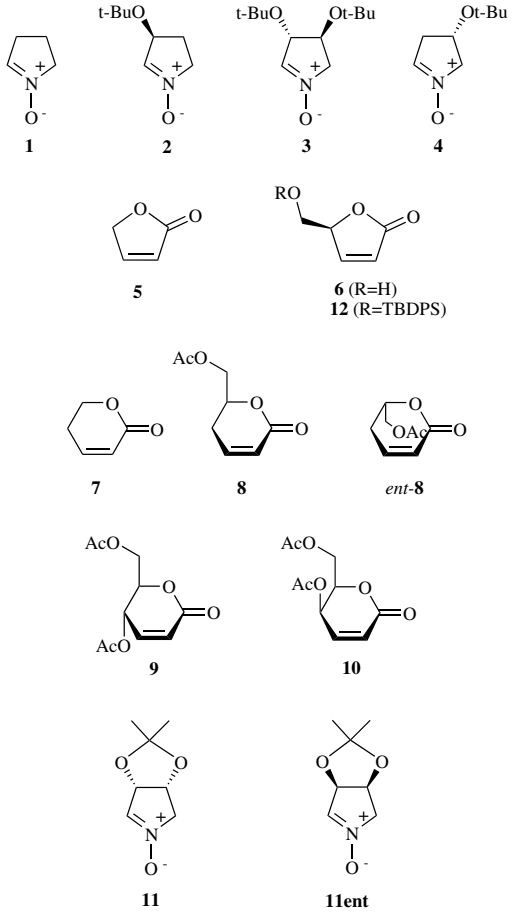
81% ee,[2] whereas in the case of nitrone **3**, L-glycero lactone *ent*-**8** is less reactive and was isolated in 86% yield and 77% ee.[1]



The lack of the *endo* approach of reactants in the case of δ-lactones **8**–**10** suggested the examination of the cycloaddition involving racemic nitrone **11**/*ent*-**11**. One would expect an effective kinetic resolution of **11**/*ent*-**11** using both δ-lactones **9**, **10** and γ-lactone **12**. Moreover, in the case of mismatched pairs at higher temperature, or under high pressure, due to steric reasons, one could expect the *endo* addition even for δ-lactones.

The stereocontrolled formation of the desired configuration of the cycloadduct will allow us to design an efficient target-oriented synthesis. Recently, using nitrones **2** and **3**, and lactones **7** and **10**, we have demonstrated a convenient approach to indolizidine[3,9] and pyrrolizidine[10] alkaloids.

2. Results and discussion

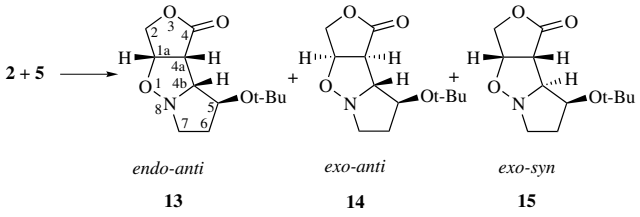
Reaction between lactone **5** and nitrone **2** in toluene solution at room temperature afforded two adducts *endo-anti* **13** and *exo-anti* **14** in a ratio of about 1:3, respectively, and in 75% yield (Table 1).[5] The same reaction in boiling toluene revealed after 48 h the presence of *exo-syn* adduct **15**. Prolongation of the reaction time led to a reduction of the content of the *endo* compound **13**. After 5 days,

Table 1. Cycloaddition of **2** and **5** in toluene solution under reflux

Entry	Time (h)	Yield (%)	Cycloadducts ratio[a] (%)		
			13	**14**	**15**
1	48	73	17	64	19
2	96	67	12	67	29
3	120	65	8	46	46
4	196	56	4	35	58
5	48[b]	75	25	75	—

[a] All data are average of five runs.
[b] Reaction performed at room temperature.[5]

the proportion of **13**:**14**:**15** was found to be 1:6:6 whereas after 7 days it was 1:9:14, respectively (Scheme 1). At the same time the yield of the reaction was decreased to 65% and 56%. Under the same condition the *exo-anti* adduct **14** underwent slow rearrangement to the *exo-syn* **15**; after 7 days of reflux the mixture contained 40% of **14** and 60% of **15** (Table 2). It shows that the adduct *exo-syn* **15**, not observed under kinetic control of the reaction, is thermodynamically the most stable one (Tables 1 and 2). It should be stressed that our results throw a new light on the work of the Brandi et al. published in a review article,[11] which for the cycloaddition of the nitrone **2** and the lactone **5** reported the formation of two *exo* adducts **14** and **15** in a ratio of about 5:1, respectively; the *endo* adduct **13** has not been found. The configuration of adducts **13**–**15** was established by NMR spectra and confirmed by X-ray analysis (Fig. 1).[12]



Scheme 1.

Table 2. Isomerization of **14** (*exo-anti*) in toluene

Entry	Time	Ratio of **14**/**15**[a]
1	24 h	93:7
2	48 h	63:37
3	90 h	48:52
4	7 d	39:61
5	12 d	30:61
6	16 d	40:60

[a] All data are average of three runs.

A similar transformation was observed for the adducts of the mismatched pair, nitrone **2** and lactone **6** (Table 3). The previously reported standard reaction in toluene solution (47 h at room temperature followed by 1 h reflux[†]) provided a mixture of three products **16**–**18** in a ratio of about 21:27:52 (Scheme 2). The prolongation of the reaction time to 96 h under reflux showed 4% of **19**. The *endo*

[†] Examination of 1-h reflux of the reaction mixture did not show any change of the adducts' ratio.

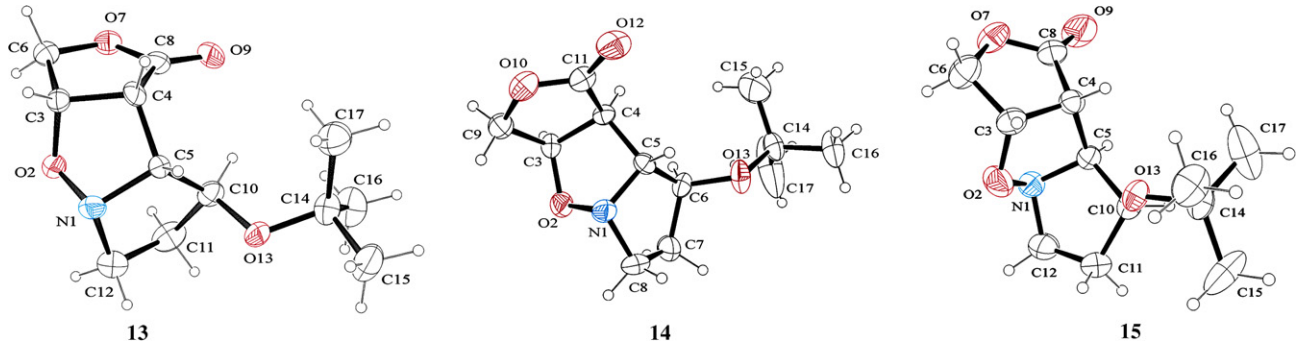


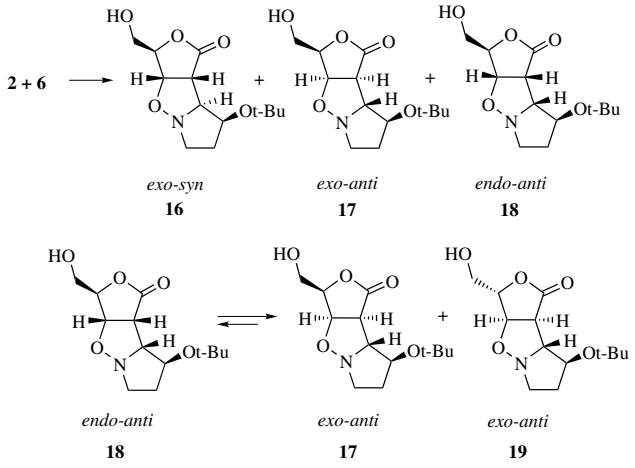
Figure 1. Molecular structures of the compounds **13**–**15** with the crystallographical numbering scheme.[12]

Table 3. Cycloaddition of nitrone **2** to the lactone **6**

Entry	Solvent	Additive	Time	Yield (%)	Cycloadducts ratio[a] (%)			
					16	**17**	**18**	**19**
1	PhMe	—	47 h (rt) 1 h (reflux)	89	21	27	52	—
2	PhMe	—	48 h (reflux)	72	23	23	48	6
3	PhMe	Et_3N (10%)	54 h (rt), 1 h (reflux)	66	18	24	43	15
4	PhMe	Et_3N (10%)	60 h (reflux)	75	11	15	39	35
5	Et_3N	—	9 d (rt)	90	—	11	25	64
6	Et_3N	—	5 d (reflux)	66	8	15	42	35
7	Et_3N	H_2O (5%)	7 d (rt)	41	—	—	20	80

[a] All data are average of five runs.

adduct **18** which was the main product of the cycloaddition, refluxed in toluene solution for 24 h showed the unreacted substrate and two new products: the *exo-anti* adduct **17** and the cycloadduct **19** in a ratio of about 8:1:3, respectively. Observation of the formation of the adduct **19** which should be thermodynamically the most stable (the matched approach of **2** and *ent*-**6**) suggested a possible shift of the reaction towards **19** as the sole product upon prolongation of the reaction time. As a consequence of such an asymmetric transformation, lactone **6** could be used in both enantiomeric forms or as a racemate since the configuration of the final product would be determined by the configuration of nitrone **2**. To accelerate the racemization of lactone **6**,[13] triethylamine was added. The highest content of **19** (**19**:**18** equal 4:1) was found for the use of triethylamine in the presence of a small amount of water as the solvent (Table 3). The overall yield of the transformation, however, was decreased significantly to afford products in 41% only. It was shown that upon prolongation of heating and in the presence of a base, both reactants (the nitrone and the lactone) underwent decomposition.



Scheme 2.

Racemic nitrone **11**/*ent*-**11** was obtained from D-arabinose following known procedure.[14] The reaction sequence proceeds via an intermediate that belongs to C_s symmetry point group. Enantiomerically pure nitrone **11** can be obtained by an alternative way involving intramolecular alkylation of an oxime.[15–17]

In the case of cycloaddition between racemic nitrone **11**/*ent*-**11** and lactones **8** and **10** one could expect that matched pairs, involving **11**, should approach almost exclusively in the *anti-exo* mode to provide adducts **20** and **21**, respectively, whereas mismatched pairs involving *ent*-**11** could react via both *exo* and *endo* mode.

The cycloaddition of lactone **8** to 2 equiv of the racemate **11**/*ent*-**11** at room temperature for 5 days resulted in a visible kinetic resolution and exclusively afforded adduct **20** in 79% yield and unreacted nitrone *ent*-**11** with 64% ee in 60% yield (Table 4). Reaction between **8** and 1 equiv of **11**/*ent*-**11** in boiling toluene for 4 days gave besides **20** (92%) adduct **22** (8%) in low 22% yield. The reaction of enantiomerically pure nitrone *ent*-**11** with **8** under the same conditions showed two products, adducts **22** and **24**, in the ratio of about 4:1, respectively, in 51% yield; product of the *endo* approach **26** was not found.

Similar results were obtained for lactone **10** and the racemate **11**/*ent*-**11**. 1:2 Proportion of reactants, after 6 days, afforded adduct **21** as a sole product in 82% yield and the

Table 4. Kinetic resolution of nitrones **11**/**11*ent*** by lactones **8**, **10** and **12**

Entry	Lactone	Nitrone	Lactone/nitrone ratio	Temperature	Time	Yield (%)	Diastereoisomers' ratio (%)
1	**8**	**11**/**11*ent***	1:2	rt	5 d	79	100(**20**)
2	**8**	**11**/**11*ent***	1:1	rt	6 d	36	100(**20**)
3	**8**	**11**/**11*ent***	1:1	Reflux	4 d	22	92(**20**), 8(**24**)
4	**8**	**11*ent***	1:1	Reflux	5 d	51	80(**22**), 20(**24**)
5	**9**	**11**/**11*ent***	1:2	rt	7 d	79	95(**28**), 5(**29**)
6	**9**	**11**/**11*ent***	1:1	rt	8 d	36	67(**28**), 33(**29**)
7	**9**	**11*ent***	1:1	Reflux	3 d	51	64(**28**), 36(**29**)
8	**10**	**11**/**11*ent***	1:2	rt	6 d	82	100(**21**)
9	**10**	**11**/**11*ent***	1:1	rt	7 d	65	82(**21**), 12(**25**), 6(**23**)
10	**10**	**11**/**11*ent***	1:1	Reflux	5 d	33	67(**25**), 33(**21**)
11	**10**[a]	**11*ent***	1:1	50 °C	24 h	74	67(**25**), 33(**23**)
12	**12**	**11**/**11*ent***	1:1	rt	7 d	68	71(**30**), 23(**32**), 6(**31**)
13	**12**	**11**/**11*ent***	1:1	Reflux	7 d	49	57(**30**), 41(**32**), 2(**31**)
14	**12**	**11**/**11*ent***	1:2	rt	7 d	95	76(**30**), 24(**32**)
15	**12**	**11**/**11*ent***	1:2	Reflux	7 d	72	58(**30**), 28(**32**), 14(**31**)
16	**12**	**11*ent***	1:1	rt	14 d	84	80(**32**), 20(**31**)
17	**12**/**12*ent***[b]	**1**/**11*ent***	1:1	rt	5 d	64	95(*rac*-**30**), 2(*rac*-**32**), 3(*rac*-**31**)

[a] Reaction performed under high pressure (11 kbar).
[b] Obtained via racemization of **12** under basic condition (Et_3N in aq EtOH, 1 h).[13]

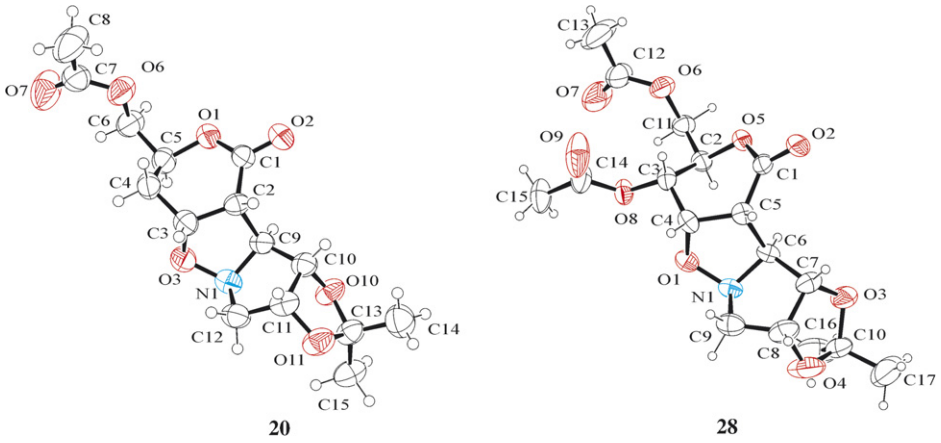
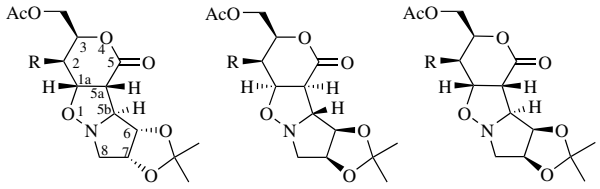
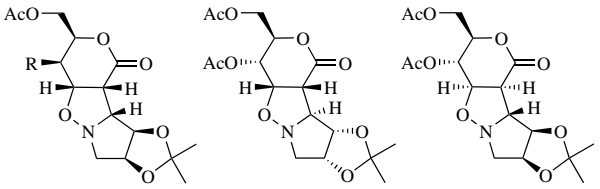


Figure 2. Molecular structure of the compounds **20** and **28** with the crystallographical numbering scheme.[3]

unreacted nitrone *ent*-**11** in 53% yield (Table 4). Optically pure nitrone *ent*-**11** was obtained when the cycloaddition involved 1.6 equiv of the racemate **11**/*ent*-**11**. Under the same conditions, 1:1 proportion of reactants, besides **21**, led to unseparable mixture of two other adducts **23** and **25**, in the ratio of about 82:12:6, respectively, in 65% yield. Reaction of enantiomerically pure nitrone *ent*-**11** with **10** at 50 °C for 24 h showed two products, adduct **23** and **25** in the ratio of about 2:1, respectively, in 74% yield. In the case of both mismatched pairs **8**/*ent*-**11** and **10**/*ent*-**11** cycloaddition proceeded in lower yields than in corresponding matched pairs **8**/**11** and **10**/**11** providing *exo* adducts only (Table 4). The formation of *endo* adducts **26** and **27** was not observed. The configuration of compounds **20**–**25** was proven by ^1H NMR, coupling constants between H-1a, H-2, H-5a, H-5b and H-6 protons and NOEs. Additionally the structure and configuration of **20** was confirmed by X-ray crystal structure determination (Fig. 2).[12]

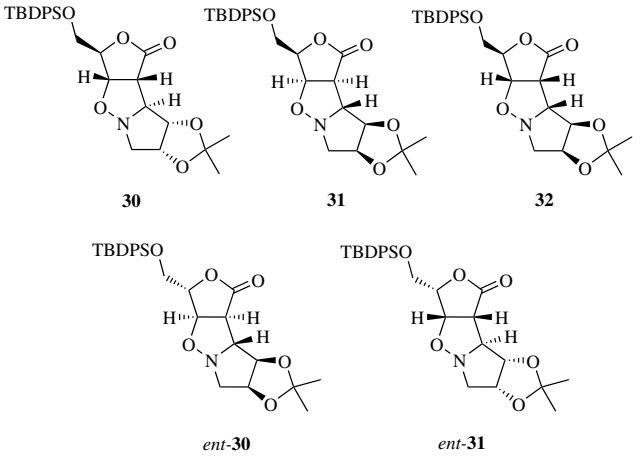
Cycloaddition of D-*erythro* lactone **9** with 2 equiv of racemic nitrone **11**/*ent*-**11** at room temperature for 7 days afforded two adducts **28** and **29** in a ratio of about 95:5, respectively, and 79% yield.





Under the same conditions and a 1:1 ratio of both reactants, adducts **28** and **29** were formed in a ratio of

about 2:1, respectively; the yield of the reaction dropped to 36%. Cycloaddition of **9** with 1 equiv of **11**/*ent*-**11** in boiling toluene for 3 days provided **28** and **29** in a ratio of about 2:1 and in 51% yield. The structure and configuration of **28** was proven by X-ray crystallography (Fig. 2).[12]



In order to increase the stability of dipolarophile, for the investigation of the cycloaddition between racemic nitrone **11**/*ent*-**11** and a chiral γ-lactone, we decided to use *tert*-butyldiphenylsilyl-protected compound **12**. Bearing in mind the results of the cycloaddition of **2** and **6**, presented above, one could expect that the cycloaddition of the γ-lactone **12** with racemic nitrone **11**/*ent*-**11** under kinetic control would lead to an interesting kinetic resolution providing the *exo* adduct **30** with **11** and the *endo* one **32** with *ent*-**11**.

Cycloaddition of lactone **12** to 1 equiv of the racemate **11**/*ent*-**11** at room temperature for 7 days led to the formation of three adducts **30**–**32** in a ratio of about 71:6:23, respectively, in 68% overall yield (Table 4).

Under reflux for 7 days, the content of the *endo* adduct **32** raised significantly and only trace amounts of compound **31** were detected (Table 4). The yield, however, dropped to 49%. Cycloaddition of **12** with 2 equiv of racemic nitrone **11**/*ent*-**11** at room temperature for 7 days afforded two adducts **30** and **32** in a ratio of about 3:1, respectively. Under reflux in toluene solution the content of adducts derived from *ent*-**11** was increased. Reaction of **12** with *ent*-**11** provided adducts **32** and **31** in a ratio of 4:1, respectively. The proportions of stereoisomers **30**–**32** were determined by HPLC. One can expect, however, that reversibility of the cycloaddition and racemization of the lactone **12** can provide enantiomeric forms of adducts: **30*ent*** by epimerization of **31** at C-2 and **31*ent*** by similar epimerization of **30**. Both processes should eventually result in the decrease of enantiomeric excess of **30** and **31**. The process of racemization of **31** cannot be observed due to the low content of this stereoisomer in the reaction mixture and the highest stability of the adduct **30**. The first process, however, the formation of *ent*-**30** from **31** can be easily observed. For example, heating of the mixture of adducts **32** and **31** (in the ratio 4:1) in toluene solution revealed the formation of *ent*-**30** after 3 days to give an *ent*-**30**:**31**:**32** ratio equal to 12:67:21, respectively. The prolongation of the reaction time, however, decreased the content of **31** and **32**, whereas it did not significantly increase the content of *ent*-**30**. This was caused by the decomposition of the nitrone *ent*-**11**, formed via *retro*-cycloaddition, and testified that its decomposition was faster than the cycloaddition to both enantiomeric forms of the lactone **12**/*ent*-**12**. The presence of *ent*-**30** was detected by NMR spectra and by HPLC on the chiral column[‡] and compared with the chromatogram of the racemic adduct **30**/*ent*-**30** obtained by cycloaddition of both racemic nitrone and lactone.

3. Conclusions

The results we have reported herein show that δ-lactones are attractive dipolarophiles which can be used for the kinetic resolution of a racemic nitrone. This resulted from the fact that cycloadditions involving δ-lactones are not reversible and usually form one predominating adduct, or in many cases, produce a single product. The corresponding transformations involving γ-lactones are more complicated. As we showed, cycloadditions to γ-lactones proceeded with lower diastereoselectivity, when compared with the cycloaddition to six-membered ones because of the possible formation of *endo* adducts. Moreover, the reversibility of cycloaddition, as well as racemization of 5-substituted 2-(5*H*)-furanones, additionally complicates the composition of the post-reaction mixtures and may lead to the formation of partially racemic products. The possible asymmetric transformation, which eventually would provide the most stable thermodynamic product, cannot be performed effectively due to the low stability of cyclic nitrones. As a result, γ-lactones are less attractive in target-oriented synthesis.

4. Experimental

4.1. General

Melting points were determined by using Köfler hot-stage apparatus with microscope and are uncorrected. Proton and carbon NMR spectra were recorded on a Bruker DRX 500 Avance Spectrometer at 500 MHz and 125 MHz, respectively, using deuterated solvents and TMS as an internal standard. Chemical shifts are reported as δ values in ppm and coupling constants are in Hertz. Infrared spectra were obtained on an FT IR-1600 Perkin–Elmer spectrophotometer. The optical rotations were measured with a JASCO J-1020 digital polarimeter. High resolution mass spectra were recorded on ESI-TOF Mariner spectrometer (Perspective Biosystem). X-ray analysis was performed on Nonius MACH3 diffractometer. HPLC chromatography was recorded on Merck LaChrom

[‡] HPLC: column Chiralcel® OD-H, hexane:*i*-propanol 90:10, 1 mL/min, retention times: 15.7 min **30**, 27.3 min **30*ent***.

chromatograph equipped with Hitachi Pump L-2130 and Hitachi Diode Array Detector L-2450.

Thin layer chromatography (TLC) was performed on aluminium sheets silica gel 60 F_{254} ($20 \times 20 \times 0.2$) from Merck. Column chromatography (CC) was carried out using Merck silica gel 230–400 mesh. The TLC spots were visualized by treatment with alcoholic solution of ninhydrine (spray) and heating.

All solvents were dried and purified by the standard techniques.

Nitrone **2**,[18] lactones **5**[19] and **6**[20] were obtained following literature procedure. Silylated lactone **12** were prepared according to literature procedure.[21] Racemic nitrone **11**/*ent*-**11** was obtained from D-arabinose following known procedure.[14] Enantiomerically pure nitrones **11** and *ent*-**11** were obtained by intramolecular alkylation of corresponding 2,3-*O*-isopropylidene-D- and L-erythrose oxime.[15–17]

4.2. Cycloaddition of lactones 5 and 6 to nitrone 2

General procedure: A solution of lactone **5** or **6** (0.375 mmol) and nitrone **2** (78.5 mg, 0.500 mmol) in solvent (Table 1; 5 mL) was stirred under nitrogen for periods of time as shown in Table 1. Subsequently, the solvent was evaporated and the product isolated by chromatography using hexane–ethyl acetate 1:2 v/v as an eluent. Two fractions were collected; the first one contained both *exo*-adducts.[§] (TLC, R_f 0.5, ethyl acetate–hexane 2:1) while the second fraction contained *endo*-adduct (TLC, R_f 0.3, ethyl acetate–hexane 2:1).

4.3. Isomerization of 14 (*exo-anti*)

4.3.1. General procedure. Solution of 30 mg of adduct **14** (0.124 mmol) in 5 mL of dry toluene was heated at reflux under nitrogen for appropriate period of time (Table 2). Subsequently, the solvent was evaporated and mixture of **14/15** was isolated by chromatography on silica gel using hexane–ethyl acetate 1:2 v/v as an eluent.

4.3.2. (1a*S*,4a*R*,4b*S*,5*S*)-5-*tert*-Butoxy-hexahydrofuro[3,4-*d*]pyrrolo[1,2-*b*]isoxazol-4(3*H*)-one 15. Mp 102–103 °C (benzene–diethyl ether 1:1); $[\alpha]_D = +1.2$ (*c* 0.4, CH_2Cl_2); IR (film): *v* 1771 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 4.13 (1H, ddd, *J* 7.1, 5.3, 1.7 Hz, H-1a), 4.03 (1H, dd, *J* 10.4, 1.7 Hz, H-2), 3.74 (1H, dd, *J* 7.3, 1.3 Hz, H-4b), 3.59–3.54 (2H, m, H-2′, H-5), 3.35 (1H, dd, *J* 7.1, 1.3 Hz, H-4a), 3.11 (1H, ddd, *J* 13.3, 7.7, 3.6 Hz, H-7), 2.58 (1H, ddd, *J* 13.3, 10.0, 7.0 Hz, H-7′), 1.64 (1H, dddd, *J* 12.8, 10.0, 7.7, 5.9 Hz, H-6), 1.46 (1H, dddd, *J* 12.8, 7.2, 7.0, 3.6 Hz, H-6′), 0.97 (9H, s, *t*-Bu); ^{13}C NMR (125 MHz, C_6D_6) δ: 177.1, 77.6, 73.9, 73.7, 72.5, 71.5, 53.2, 50.1, 34.1, 28.2; HR MS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{12}H_{20}NO_4$ 242.1387. Found 242.1379.

[§] The **14**:**15** ratio was determined by NMR spectra in benzene-d_6.

4.4. Cycloaddition of lactone 8 to nitrone *ent*-11

4.4.1. General procedure. Lactone **8** (34 mg, 0.2 mmol) and nitrone **11***ent* (31 mg, 0.2 mmol) were dissolved in dry toluene (5 mL) and refluxed for 5 days under a nitrogen atmosphere. The reaction progress was monitored by TLC chromatography (hexane–ethyl acetate 1:4). After the solvent was evaporated, the residue was chromatographed (ethyl acetate–hexane 70:30 v/v) to afford **22** (27 mg, 41%, $R_f = 0.28$) and **24** (7 mg, 10%, $R_f = 0.45$).

4.4.2. (1a*R*,3*S*,5a*R*,5b*S*,6*S*,7*R*)-3-Acetoxymethyl-hexahydro-6,7-*O*-isopropylidenedioxy-pyrrolo[1,2-*b*]-pyrano[3,4-*d*]-isoxazol-5(3*H*)-one 20. Mp 100–102 °C; $[\alpha]_D = +37.3$ (*c* 0.9, CH_2Cl_2); IR(film): *v* 1740, 1234 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 4.89 (ddd, 1H, *J* 6.6, 5.2, 1.0 Hz, H-7), 4.86 (d, 1H, *J* 6.6 Hz, H-6), 4.80 (dddd, 1H, *J* 11.3, 5.4, 3.6, 2.0 Hz, H-3), 4.74 (ddd, 1H, *J* 8.8, 3.7, 2.0 Hz, H-1a), 4.26 (dd, 1H, *J* 12.2, 3.6 Hz, CH*H*OAc), 4.20 (dd, 1H, *J* 12.2, 5.4 Hz, CH*H*OAc), 3.86 (d, 1H, *J* 7.9 Hz, H-5b), 3.50 (dd, 1H, *J* 12.3, 1.0 Hz, H-8), 3.23 (dd, 1H, *J* 8.8, 7.9 Hz, H-5a), 2.97 (dd, 1H, *J* 12.3, 5.2 Hz, H-8′), 2.10 (s, 3H, OAc), 2.00 (dt, 1H, *J* 15.1, 2.0 Hz, H-2), 1.91 (ddd, 1H, *J* 11.3, 3.7 Hz, H-2′), 1.50, 1.31 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.4, 168.7, 112.3, 81.4, 78.5, 76.4, 73.0, 72.6, 64.8, 58.3, 49.2, 29.7, 26.2, 24.7, 20.6; MS HR (ESI) *m*/*z* $[M+Na]^+$, Calcd for $C_{15}H_{21}NO_7Na$: 350.1210. Found: 350.1227.

4.4.3. (1a*S*,3*S*,5a*S*,5b*R*,6*R*,7*S*)-3-Acetoxymethyl-hexahydro-6,7-*O*-isopropylidenedioxy-pyrrolo[1,2-*b*]-pyrano[3,4-*d*]-isoxazol-5(3*H*)-one 22. Colourless crystals; mp 158–161 °C; $[\alpha]_D = -3.7$ (*c* 0.4, CH_2Cl_2); IR(film): *v* 1747, 1241 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 4.92 (ddd, 1H, *J* 6.5, 5.5, 2.5 Hz, H-7), 4.86 (dd, 1H, *J* 6.5, 1.9 Hz, H-6), 4.67 (ddd, 1H, *J* 10.3, 9.5, 6.7 Hz, H-1a), 4.40 (dddd, 1H, *J* 11.8, 5.9, 3.6, 1.5 Hz, H-3), 4.26 (dd, 1H, *J* 12.1, 3.6 Hz, C*H*HOAc), 4.22 (dd, 1H, *J* 12.1, 5.9 Hz, CH*H*OAc), 4.07 (dd, 1H, *J* 5.9, 1.9 Hz, H-5b), 3.43 (dd, 1H, *J* 13.1, 2.5 Hz, H-8), 3.28 (dd, 1H, *J* 9.5, 5.9 Hz, H-5a), 3.18 (dd, 1H, *J* 13.1, 5.5 Hz, H-8′), 2.22 (ddd, 1H, *J* 13.7, 6.7, 1.5 Hz, H-2), 2.10 (s, 3H, OAc), 1.77 (ddd, 1H, *J* 13.7, 11.8, 10.3 Hz, H-2′), 1.52, 1.32 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.6, 169.4, 113.1, 83.5, 79.5, 74.7, 73.5, 72.4, 65.0, 59.9, 49.6, 30.3, 26.6, 24.9, 20.7; HR MS (ESI) *m*/*z* $[M+Na]^+$, Calcd for $C_{15}H_{21}NO_7Na$: 350.1210. Found: 350.1231.

4.4.4. (1a*R*,3*S*,5a*R*,5b*S*,6*R*,7*S*)-3-Acetoxymethyl-hexahydro-6,7-*O*-isopropylidenedioxy-pyrrolo[1,2-*b*]-pyrano[3,4-*d*]-isoxazol-5(3*H*)-one 24. Colourless oil; $[\alpha]_D = +20.5$ (*c* 0.1, CH_2Cl_2); IR(film): 1739, 1733, 1229 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 5.08 (dddd, 1H, *J* 11.2, 5.5, 3.4, 2.1 Hz, H-3), 4.86 (ddd, 1H, *J* 6.3, 5.3, 1.0 Hz, H-7), 4.80 (dd, 1H, *J* 6.3, 5.3 Hz, H-6), 4.65 (ddd, 1H, *J* 8.0, 3.4, 3.2 Hz, H-1a), 4.27 (dd, 1H, *J* 12.2, 3.4 Hz, C*H*HOAc), 4.20 (dd, 1H, *J* 12.2, 5.5 Hz, CH*H*OAc), 3.88 (dd, 1H, *J* 8.0, 1.2 Hz, H-5a), 3.77 (dd, 1H, *J* 5.3, 1.2 Hz, H-5b), 3.63 (br d, 1H, *J* 15.5 Hz, H-8), 3.05 (dd, 1H, *J* 15.5, 5.3 Hz, H-8′), 2.10 (s, 3H, OAc), 2.05 (ddd, 1H, *J* 14.5, 3.2, 2.1 Hz, H-2), 1.84 (ddd, 1H, *J* 14.5, 11.2, 3.4 Hz, H-2′), 1.49, 1.33 (2s, 6H, $C(CH_3)_2$); HR MS (ESI) *m*/*z*

$[M+Na]^+$, Calcd for $C_{15}H_{21}NO_7Na$: 350.1210. Found 350.1222.

4.5. Kinetic resolution of 11/*ent*-11

4.5.1. General procedure. Lactone **10** (228 mg, 1.0 mmol) and racemic nitrone **11**/*ent*-**11** (267 mg, 1.6 mmol) were dissolved in dry toluene (40 mL) and the reaction was carried out for 6 days at room temperature (under nitrogen). The reaction was monitored by TLC chromatography (hexane–ethyl acetate 1:1, $R_f = 0.28$). After this, the solvent was evaporated and residue purified by column chromatography—at first cycloadduct **21** was eluted by using a mixture of hexane–ethyl acetate (1:1 v/v) and then residue on column was eluted by a mixture of methylene chloride–methanol (90:10 v/v) affording 110 mg of pure *ent*-**11** (39%) as colourless crystals. The optical purity of (+)-*ent*-**11** was confirmed by chiral HPLC chromatography. Chiral HPLC chromatography: Chiralpak AS®, *i*-propanol (100%), sample concentration 1 mg/mL, flow rate 0.3 mL/min, retention times: 66.0 min (−)-**11** and 72.6 min (+)-***ent*-11**.

4.5.2. (+)-3,4-Isopropylidenodioxypyrroline-1-oxide *ent*-11. Mp 101.5–102.5 °C; $[\alpha]_D^{30} = +26.1$ (*c* 0.56, CH_2Cl_2); Ref. 14b $[\alpha]_D^{20} = +27.7$ (*c* 0.46, CH_2Cl_2); for **11**: Ref. 14b $[\alpha]_D^{20} = -28$ (*c* 0.46, CH_2Cl_2); Ref. 15 $[\alpha]_D^{26} = -26.3$ (*c* 0.50, CH_2Cl_2); Ref. 16 $[\alpha]_D = -26.5$ (*c* 0.83, CH_2Cl_2); IR(film): *v* 1580 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) *δ*: 6.89 (q, 1H, *J* 1.6 Hz, H-2), 5.30 (br d, 1H, *J* 6.4 Hz, H-3), 4.92 (ddd, 1H, *J* 6.5, 5.2, 1.3 Hz, H-4), 4.14 (ddd, 1H, *J* 15.2, 5.4, 1.9 Hz, H-5), 4.06 (dq, 1H, *J* 15.2, 1.3 Hz, H-5′), 1.46, 1.39 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 132.5, 112.2, 79.8, 73.6, 67.9, 27.2, 25.7; HR MS (ESI) *m*/*z* $[M+H]^+$, Calcd for $C_7H_{12}NO_3$: 158.0812. Found: 158.0804; HPLC: retention time 72.6 min.

4.5.3. (1a*S*,2*R*,3*R*,5a*R*,5b*S*,6*S*,7*R*)-2-Acetoxy-3-acetoxymethyl-hexahydro-6,7-*O*-isopropylidenedioxy-pyrrolo[1,2-*b*]-pyrano[3,4-*d*]isoxazol-5(3*H*)-one 21. Colourless crystals; mp 106–108 °C; $[\alpha]_D = +30.7$ (*c* 0.8, CH_2Cl_2); IR(film): *v* 1747, 1223 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) *δ*: 5.08 (dd, 1H, *J* 2.6, 1.1 Hz, H-2), 4.93 (dd, 1H, *J* 6.2, 1.1 Hz, H-3), 4.91 (ddd, 1H, *J* 6.6, 5.5, 2.1 Hz, H-7), 4.80 (dd, 1H, *J* 6.6, 1.8 Hz, H-6), 4.51 (dd, 1H, *J* 8.6, 2.6 Hz, H-1a), 4.23 (m, 2H, C*H*$_2$OAc), 3.85 (dd, 1H, *J* 6.5, 1.8 Hz, H-5b), 3.44 (dd, 1H, *J* 13.0, 2.1 Hz, H-8), 3.38 (dd, 1H, *J* 8.6, 6.5 Hz, H-5a), 3.08 (dd, 1H, *J* 13.0, 5.5 Hz, H-8′), 2.11, 2.09 (2s, 6H, 2 × OAc), 1.50, 1.31 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 170.2, 169.3, 167.4, 113.1, 82.4, 79.1, 76.5, 75.1, 73.7, 65.8, 61.8, 59.3, 48.6, 26.4, 24.7, 20.6, 20.6; HR MS (ESI) *m*/*z* $[M+Na]^+$, Calcd for $C_{17}H_{23}NO_9Na$: 408.1265. Found: 408.1284.

4.5.4. (1a*R*,2*R*,3*R*,5a*S*,5b*R*,6*R*,7*S*)-2-Acetoxy-3-acetoxymethyl-hexahydro-6,7-*O*-isopropylidenedioxy-pyrrolo[1,2-*b*]-pyrano[3,4-*d*]isoxazol-5(3*H*)-one 23. ^1H NMR (500 MHz, C_6D_6) taken for the mixture **23** and **25**, *δ*: 4.84 (dd, 1H, *J* 2.0, 1.1 Hz, H-2), 4.78 (ddd, 1H, *J* 6.9, 5.6, 1.1 Hz, H-3), 4.43 (ddd, 1H, *J* 6.6, 5.8, 3.8 Hz, H-7), 4.28 (d, 1H, *J* 7.9 Hz, H-1a), 4.18 (dd, 1H, *J* 6.6, 2.7 Hz, H-6), 4.09 (dd, 1H, *J* 11.6, 6.9 Hz, C*H*HOAc), 4.05 (dd, 1H, *J* 11.6, 5.6 Hz, CH*H*OAc), 3.46 (dd, 1H, *J* 3.3, 2.7 Hz, H-5b), 3.11 (dd, 1H, *J* 13.8, 3.8 Hz, H-8), 3.00 (dd, 1H, *J* 13.8, 5.8 Hz, H-8′), 2.53 (ddd, 1H, *J* 7.9, 3.3, 2.0 Hz, H-5a), 1.56, 1.53 (2s, 6H, 2 × OAc), 1.46, 1.16 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) taken for the mixture **23** and **25**, *δ*: 170.3, 169.7, 169.5, 114.3, 85.5, 80.7, 75.8, 74.1, 72.8, 67.7, 61.8, 60.4, 51.0, 26.9, 24.8, 20.7, 20.7; HR MS (ESI) *m*/*z* $[M+Na]^+$ taken for the mixture **23** and **25**, Calcd for $C_{17}H_{23}NO_9Na$: 408.1265. Found: 408.1265.

4.5.5. (1a*S*,2*R*,3*R*,5a*R*,5b*S*,6*R*,7*S*)-2-Acetoxy-3-acetoxymethyl-hexahydro-6,7-*O*-isopropylidenedioxy-pyrrolo[1,2-*b*]-pyrano[3,4-*d*]isoxazol-5(3*H*)-one 25. ^1H NMR (500 MHz, C_6D_6) taken for the mixture **23** and **25**, *δ*: 5.30 (ddd, 1H, *J* 6.8, 5.4, 1.4 Hz, H-3), 5.28 (dd, 1H, *J* 3.5, 1.4 Hz, H-2), 4.58 (dd, 1H, *J* 8.2, 3.5 Hz, H-1a), 4.23 (dd, 1H, *J* 11.7, 6.8 Hz, C*H*HOAc), 4.14 (dd, 1H, *J* 11.7, 5.4 Hz, CH*H*OAc), 4.10 (dd, 1H, *J* 6.3, 5.3 Hz, H-7), 4.00 (d, 1H, *J* 8.2 Hz, H-5a), 3.96 (dd, 1H, *J* 6.3, 5.2 Hz, H-6), 3.53 (d, 1H, *J* 15.7 Hz, H-8), 3.24 (d, 1H, *J* 5.2 Hz, H-5b), 2.35 (dd, 1H, *J* 15.7, 5.3 Hz, H-8′), 1.57, 1.44 (2s, 6H, 2 × OAc), 1.37, 1.06 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) taken for the mixture **23** and **25**, *δ*: 170.3, 169.6, 169.4, 113.2, 82.9, 82.0, 75.2, 75.2, 74.3, 66.6, 62.1, 59.8, 47.3, 26.2, 23.9, 20.7, 20.7.

4.5.6. (1a*S*,2*S*,3*R*,5a*R*,5b*S*,6*S*,7*R*)-2-Acetoxy-3-acetoxymethyl-hexahydro-6,7-*O*-isopropylidenedioxy-pyrrolo[1,2-*b*]-pyrano[3,4-*d*]isoxazol-5(3*H*)-one 28. Colourless crystals; mp 63–65 °C; $[\alpha]_D = +95.2$ (*c* 0.8, CH_2Cl_2); IR(film): *v* 1746, 1218 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) *δ*: 5.10 (dd, 1H, *J* 9.4, 3.4 Hz, H-2), 4.99 (ddd, 1H, *J* 9.4, 3.9, 2.6 Hz, H-3), 4.94 (ddd, 1H, *J* 6.6, 5.6, 3.1 Hz, H-7), 4.76 (dd, 1H, *J* 6.6, 2.7 Hz, H-6), 4.74 (dd, 1H, *J* 8.4, 3.4 Hz, H-1a), 4.37 (dd, 1H, *J* 12.6, 3.9 Hz, C*H*HOAc), 4.28 (dd, 1H, *J* 12.6, 2.6 Hz, CH*H*OAc), 3.92 (dd, 1H, *J* 4.9, 2.7 Hz, H-5b), 3.56 (dd, 1H, *J* 8.4, 4.9 Hz, H-5a), 3.38 (dd, 1H, *J* 13.6, 3.1 Hz, H-8), 3.32 (dd, 1H, *J* 13.6, 5.6 Hz, H-8′), 2.12, 2.08 (2s, 6H, 2 × OAc), 1.50, 1.32 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 170.3, 169.6, 167.3, 113.7, 83.3, 79.8, 77.3, 73.4, 72.0, 66.3, 61.4, 60.2, 50.8, 26.6, 24.8, 20.7, 20.6; HR MS (ESI) *m*/*z* $[M+Na]^+$, Calcd for $C_{17}H_{23}NO_9Na$: 408.1265. Found: 408.1272.

4.5.7. (1a*R*,2*S*,3*R*,5a*S*,5b*R*,6*R*,7*S*)-2-Acetoxy-3-acetoxymethyl-hexahydro-6,7-*O*-isopropylidenedioxy-pyrrolo[1,2-*b*]-pyrano[3,4-*d*]isoxazol-5(3*H*)-one 29. Colourless oil; $[\alpha]_D = -2.9$ (*c* 0.2, CH_2Cl_2); IR(film): *v* 1745, 1203 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) *δ*: 5.22 (dd, 1H, *J* 9.1, 7.6 Hz, H-2), 4.96 (ddd, 1H, *J* 6.6, 5.8, 3.8 Hz, H-7), 4.76 (dd, 1H, *J* 6.6, 3.2 Hz, H-6), 4.49 (dd, 1H, *J* 9.6, 7.6 Hz, H-1a), 4.43 (ddd, 1H, *J* 9.1, 5.1, 2.5 Hz, H-3), 4.38 (dd, 1H, *J* 12.4, 5.1 Hz, C*H*HOAc), 4.22 (dd, 1H, *J* 12.4, 2.5 Hz, CH*H*OAc), 4.10 (dd, 1H, *J* 3.8, 3.2 Hz, H-5b), 3.64 (dd, 1H, *J* 9.6, 3.8 Hz, H-5a), 3.42 (dd, 1H, *J* 13.9, 5.8 Hz, H-8), 3.32 (dd, 1H, *J* 13.9, 3.8 Hz, H-8′), 2.11, 2.08 (2s, 6H, 2 × OAc), 1.52, 1.33 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 170.5, 168.9, 167.8, 114.1, 84.7, 80.6, 76.3, 75.5, 74.7, 67.0, 61.2, 60.4, 50.2, 26.9, 24.9,

20.7, 20.6; HR MS (ESI) m/z $[M+Na]^+$, Calcd for $C_{17}H_{23}NO_9Na$: 408.1265. Found: 408.1276.

4.6. Synthesis of lactone 12

4.6.1. (5*S*)-5-(*tert*-Butyldiphenylsiloxymethyl)-2(5*H*)-furanone 12. To a solution of **6** (1.016 g, 8.9 mmol) and imidazole (0.864 g, 12.7 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added *tert*-butyldiphenylsilyl chloride (3.143 g, 2.9 mL, 11.4 mmol). After 45 min, the reaction was quenched by addition of water (20 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3×10 mL). The combined organic extracts were dried over sodium sulfate. Evaporation of the solvent followed by chromatographical purification yielded **12** (2.923 g, 97%) as colourless crystals: mp 79–81 °C (diethyl ether–benzene 1:1), Ref. 22 79–80 °C; $[\alpha]_D^{25} = -80.6$ (c 1.33, CH_2Cl_2), Ref. 22 $[\alpha]_D^{22} = -83.0$ (c 1.6, CH_2Cl_2); IR(film): ν 1755 cm^{-1}; ^1H NMR (500 MHz, C_6D_6 without aromatic protons) δ: 6.40 (dd, 1H, J 5.7, 1.6 Hz, H-3), 5.63 (dd, 1H, J 5.7, 2.0 Hz, H-4), 4.31 (dddd, 1H, J 4.4, 4.3, 2.0, 1.6 Hz, H-5), 3.52 (dd, 1H, J 11.0, 4.3 Hz, C*H*HOSiPh$_2$*t*-Bu), 3.37 (dd, 1H, J 11.0, 4.4 Hz, CH*H*OSiPh$_2$*t*-Bu), 1.07 (s, 9H, *t*-Bu); ^{13}C NMR (125 MHz, C_6D_6) δ: 171.9, 152.7, 122.7, 82.7, 63.5, 26.9, 19.4; HR MS (ESI) m/z $[M+Na]^+$, Calcd for $C_{21}H_{24}O_3NaSi$: 375.13869. Found: 375.13859.

4.7. Cycloaddition of lactone 12 to racemic nitrone 11/*ent*-11

4.7.1. General procedure. Solution of lactone **12** and nitrone **11**/***ent*-11** in dry toluene (10 mL) was stirred at ambient temperature under nitrogen (for reagents' ratio see Table 4). The reaction progress was monitored by HPLC chromatography (LiChrospher Si60®, hexane–isopropanol 97:3 v/v, flow rate 1 mL/min, sample concentration 1 mg/mL, retention times: 9.1 min **30**, 9.5 min **32**, 12.5 min **12** and 28.4 min **31**). After that solvent was evaporated, the adducts were isolated by chromatography on silica gel by using mixture of hexane and ethyl acetate as a eluent (5:1 v/v).

4.7.2. (1a*S*,2*R*,4a*R*,4b*S*,5*S*,6*R*)-2-*tert*-Butyldiphenylsiloxymethyl-hexahydro-5,6-*O*-isopropylidenedioxy-pyrrolo-[1,2-*b*]-furo[3,4-*d*]isoxazol-4(3*H*)-one 30. Colourless oil; $[\alpha]_D = +22.5$ (c 0.4, CH_2Cl_2); IR(film): ν 1776, 1113 cm^{-1}; ^1H NMR (500 MHz, C_6D_6, without aromatic protons) δ: 4.62 (ddd, 1H, J 6.7, 6.0, 4.5 Hz, H-6), 4.49 (dd, 1H, J 7.5, 1.3 Hz, H-1a), 4.30 (ddd, 1H, J 2.9, 2.3, 1.3 Hz, H-2), 4.26 (dd, 1H, J 6.7, 4.1 Hz, H-5), 4.03 (dd, 1H, J 4.1, 1.6 Hz, H-4b), 3.54 (dd, 1H, J 11.4, 2.9 Hz, C*H*HOSiPh$_2$*t*-Bu), 3.43 (dd, 1H, J 7.5, 1.6 Hz, H-4a), 3.34 (dd, 1H, J 14.2, 6.0 Hz, H-7), 3.26 (dd, 1H, J 11.4, 2.3 Hz, CH*H*OSiPh$_2$*t*-Bu), 3.08 (dd, 1H, J 14.2, 4.5 Hz, H-7′), 1.38, 1.16 (2s, 6H, C(CH$_3$)$_2$), 1.06 (s, 9H, *t*-Bu); ^{13}C NMR (125 MHz, C_6D_6) δ: 174.9, 114.5, 85.8, 85.0, 81.8, 78.7, 76.6, 64.3, 60.8, 54.2, 27.2, 26.9, 25.2, 19.3; HR MS (ESI) m/z $[M+H]^+$, Calcd for $C_{28}H_{36}NO_6Si$: 510.23064. Found: 510.2311.

4.7.3. (1a*S*,2*R*,4a*R*,4b*R*,5*R*,6*S*)-2-*tert*-Butyldiphenylsiloxymethyl-hexahydro-5,6-*O*-isopropylidenedioxy-pyrrolo-[1,2-*b*]-furo[3,4-*d*]isoxazol-4(3*H*)-one 32. Colourless oil; $[\alpha]_D = -5.6$ (c 0.2, CH_2Cl_2); IR(film): ν 1775, 1112 cm^{-1}; ^1H NMR (500 MHz, C_6D_6, without aromatic protons) δ: 5.38 (dd, 1H, J 6.5, 1.8 Hz, H-5), 4.71 (ddd, 1H, J 6.5, 5.7, 2.8 Hz, H-6), 4.48 (d, 1H, J 6.8 Hz, H-1a), 4.08 (dd, 1H, J 2.9, 1.9 Hz, H-2), 3.94 (dd, 1H, J 8.8, 1.8 Hz, H-4b), 3.58 (dd, 1H, J 11.5, 2.9 Hz, CH*H*OSiPh$_2$*t*-Bu), 3.46 (dd, 1H, J 8.8, 6.8 Hz, H-4a), 3.41 (dd, 1H, J 13.3, 2.9 Hz, H-7), 3.15 (dd, 1H, J 13.3, 5.7 Hz, H-7′), 3.10 (dd, 1H, J 11.5, 1.9 Hz, C*H*HOSiPh$_2$*t*-Bu), 1.49, 1.14 (2s, 6H, C(CH$_3$)$_2$), 1.02 (s, 9H, *t*-Bu); ^{13}C NMR (125 MHz, C_6D_6) δ: 175.1, 112.6, 83.1, 83.1, 80.3, 79.9, 74.4, 64.2, 61.6, 52.1, 27.0, 26.8, 24.9, 19.2; HR MS (ESI) m/z $[M+Na]^+$, Calcd for $C_{28}H_{35}NO_6NaSi$: 532.21259. Found: 532.2109.

4.7.4. (1a*R*,2*R*,4a*S*,4b*R*,5*R*,6*S*)-2-*tert*-Butyldiphenyl-siloxymethyl-hexahydro-5,6-*O*-isopropylidenedioxy-pyrrolo[1,2-*b*]-furo[3,4-*d*]isoxazol-4(3*H*)-one 31. Colourless oil; $[\alpha]_D = -11.5$ (c 0.25, CH_2Cl_2); IR(film): ν 1775, 1112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, without aromatic protons) δ: 4.97 (ddd, 1H, J 6.5, 6.0, 4.5 Hz, H-6), 4.80 (dd, 1H, J 7.2, 5.2, Hz, H-1a), 4.60 (dd, 1H, J 6.5, 4.9 Hz, H-5), 4.58 (ddd, 1H, J 6.6, 6.0, 5.2 Hz, H-2), 4.03 (dd, 1H, J 10.9, 6.0 Hz, C*H*HOSiPh$_2$*t*-Bu), 3.99 (dd, 1H, J 10.9, 6.6 Hz, CH*H*OSiPh$_2$*t*-Bu), 3.88 (d, 1H, J 4.9 Hz, H-4b), 3.68 (d, 1H, J 7.2 Hz, H-4a), 3.54 (dd, 1H, J 14.6, 6.0 Hz, H-7), 3.14 (dd, 1H, J 14.6, 4.5 Hz, H-7′), 1.52, 1.33 (2s, 6 H, C(CH$_3$)$_2$), 1.06 (s, 9H, *t*-Bu); ^{13}C NMR (125 MHz, C_6D_6) δ: 174.1, 114.7, 85.4, 82.8, 82.0, 76.0, 75.9, 62.0, 61.1, 53.6, 27.2, 27.0, 25.1, 19.5; HR MS (ESI) m/z $[M+Na]^+$, Calcd for $C_{28}H_{35}NO_6NaSi$: 532.21259. Found: 532.2146.

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