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# 4,5-Unsubstituted 2,3-dihydroisoxazoles in the synthesis of racemic 4-substituted isoxazolidine-5-carbonitriles

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ABSTRACT

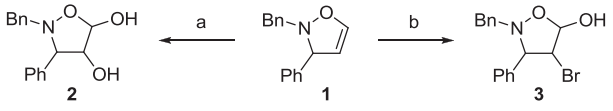
The synthesis of novel types of the 4-hydroxy- and 4-bromosubstituted isoxazolidines is described. Dihydroxylation reactions of 4,5-unsubstituted 2,3-dihydroisoxazoles proceed from the less hindered side and provide the major 3,4-*trans*-isoxazolidine-4,5-diols in good yields. On the other hand, the hydroxybromination reaction of the model 3-phenyl-2,3-dihydroisoxazole predominantly proceeds with 3,4-*cis* selectivity. Isoxazolidine-5-carbonitriles have been prepared from isoxazolidines possessing a good leaving group at C5 by treatment with TMSCN in the presence of TMSOTf.



## 1. Introduction

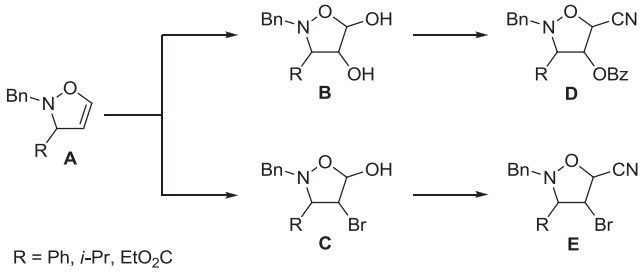
It is well known that small five membered heterocyclic compounds, such as isoxazolidines, pyrrolidines and pyrrazolidines bearing hydroxyl groups are valuable building blocks in medicinal chemistry.[1] Therefore, our general effort has recently focused on the preparation of 4-hydroxysubstituted isoxazolidine-5-carbonitriles and their derivatives as a class of compounds bearing a cyano group, so far not described in the literature, that is, interesting for a versatile potential transformations.

As a part of our continuous research in the field of isoxazolidinyl nucleosides[2] we observed that 4,5-unsubstituted 2,3-dihydroisoxazoles are sometimes formed as byproducts in a process of Vorbrüggen nucleosidation.[3] Based on this observation we have recently developed a novel method for their preparation directly from 5-acetoxyisoxazolidines, which are readily available via 1,3-dipolar cycloaddition of nitrones with vinyl acetate.[4] Recently, we also reported optimal reaction conditions for the preparation of isoxazolidine-4,5-diols **2** and 4-bromoisoxazolidin-5-ols **3** (Scheme 1).[5]




**Scheme 1.** Reagents and conditions: (a) $K_2OsO_4 \cdot 2H_2O$, NMO, water/acetone, 10 °C; (b) NBS, water, THF, 0 °C.

In this paper, we describe an extension of our studies on dihydroxylations and hydroxybrominations of 4,5-unsubstituted 2,3-dihydroisoxazoles (**A**) as well as utilization of resulting isoxazolidine-4,5-diols (**B**) and 4-bromoisoxazolidin-5-ols (**C**) in the synthesis of isoxazolidine-5-carbonitriles (**D**, **E**) (Scheme 2).




**Scheme 2.** General synthetic route to isoxazolidine-5-carbonitriles **D** and **E** from 4,5-unsubstituted 2,3-dihydroisoxazoles **A**.

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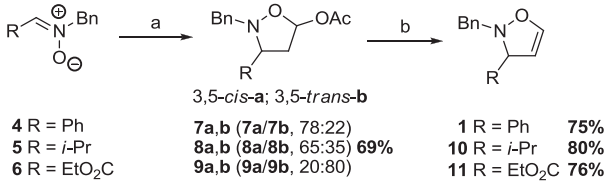
## 2. Results and discussion

### 2.1. Synthesis of 2,3-dihydroisoxazoles

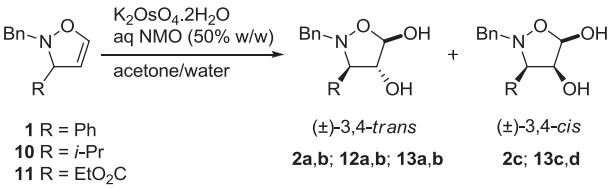
At the beginning, we started with the preparation of initial 5-acetoxyisoxazolidines. 1,3-Dipolar cycloaddition of nitrone **5** with vinyl acetate provided non-separable mixture of 3,5-*cis*- and 3,5-*trans*-5-acetoxyisoxazolidines **8a**, **b** (**8a**/**8b** ratio 65:35) in total yield of 69% (Scheme 3). Analogously to already reported 1,3-dipolar cycloadditions of nitrones **4** and **6** with vinyl acetate,[6,7] the reaction of **5** proceeded preferably through *exo*-TS providing predominantly 3,5-*cis*-isomer **8a**. Subsequently, 2,3-dihydroisoxazole **10** was obtained by reaction of **8a**, **b** with BSTFA [*N*,*O*-bis(trimethylsilyl)trifluoroacetamide] and TMSOTf in anhydrous NMP in very good yield of 80% (Scheme 3). The isoxazoles **1** and **11** were prepared analogously from respective mixtures of 3,5-*cis*- and 3,5-*trans*-isomers of 5-acetoxyisoxazolidines **7a**, **b**[6b] and **9a**, **b**[7] according to procedure we published earlier (Scheme 3).[4] Compared to our results, 2,3-dihydroisoxazole **10** has already been obtained using different method from the corresponding 5-hydroxyisoxazolidine, however in lower yield of 48%.[8]




**Scheme 3.** Reagents and conditions: (a) vinyl acetate, sealed tube, 75 °C; (b) BSTFA, TMSOTf, NMP, 0 °C–rt.

### 2.2. Dihydroxylation reactions

In order to demonstrate utility of 4-unsubstituted 2,3-dihydroisoxazoles in the synthesis of isoxazolidines, we focused our interest on the dihydroxylation of their C4/C5 double bond (Scheme 4).[5] The reaction of **1** with $K_2OsO_4{\cdot}2H_2O$ (0.01 equiv), NMO (2 equiv, 50% w/w in water) in acetone/water (3:1, 0.2 M) provided isoxazolidine-4,5-diol **2** in total yield of 84%. Dihydroxylation afforded two major 3,4-*trans*-isoxazolidines **2a**, **b** along with traces of the minor 3,4-*cis*-4,5-*trans*-isomer **2c** (Scheme 4, Table 1). In the process of searching for the best reaction conditions we found that the amount of $K_2OsO_4{\cdot}2H_2O$, the quantity of water in the reaction mixture and the nature of the NMO removing agent are crucial for successful dihydroxylation. Using more than 0.01 equiv $K_2OsO_4{\cdot}2H_2O$ decreased the yield. A large excess of water accelerated the reaction at lower temperature (10 °C) and avoiding the use of sulfite in the work up improved the total yields. Dihydroxylation reactions of **10** and **11** were carried out in the similar manner as described for **1**.




**Scheme 4.** Dihydroxylations of 2,3-dihydroisoxazoles **1**, **10** and **11**.

We observed that the reactions of **10** and **11** proceeded more slowly and therefore required higher temperature. A mixture of four isomers **13a**–**d** has been formed in the case of the EWG-bearing dihydroisoxazole **11** in total yield of 81% (Table 1, Entry 3). The ratio between **13a**, **b** and **13c**, **d** was established after their conversion into the corresponding acetates.[5] Surprisingly, the dihydroxylation of **10** turned to be more difficult. The presence of water strongly inhibited the reaction and the reaction rate was slightly improved when a higher amount of $K_2OsO_4{\cdot}2H_2O$ and NMO were used (Table 1, Entry 2). Despite the fact that the reaction proceeded with incomplete conversion of **10** and with a disappointingly low yield of isoxazolidine-4,5-diol **12**, only the 3,4-*trans*-isomers **12a**, **b** were formed. The 4,5-*cis*/4,5-*trans* relative configuration of each diastereomer of isoxazolidine-4,5-diols **2**, **12** and **13** was particularly assigned based on the coupling constant and the multiplicity of the proton H-5 as follows. Either none or a small H-4/H-5 coupling constant ($J_{4,5}$–1.8 Hz) indicated 4,5-*trans* configuration with a dihedral angle between H-4 and H-5 protons close to ~90°. A larger H-4/H-5 coupling constant (doublet or multiplet, $J_{4,5}$–4.5 Hz) occurred in 4,5-*cis*-isomers. The stereochemistry of isoxazolidine-4,5-diols **12a**, **b** as well as isoxazolidines **2a**, **b** and **13a**, **b** was later confirmed upon analysis of the NOESY 1D experiments of the corresponding dibenzoates **14a**, **b**–**16a**, **b**, successfully separated by preparative TLC.

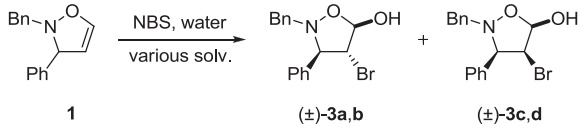
**Table 1**
Dihydroxylation reactions of 2,3-dihydroisoxazoles **1**, **10** and **11**

| Entry | Isoxazoles | Conditions | Isoxazolidines | **a**:**b**:**c**:**d**[b] | Yield (%)[d] |
|---|---|---|---|---|---|
| 1 | **1** | 10 °C, 1.5 h | **2** | 47:47:6:— | 84[e] |
| 2 | **10** | rt, overnight[a] | **12** | 75:25:—:— | 29[d] |
| 3 | **11** | 2 °C–rt, 6 h | **13** | (84):(16)[c] | 81[f] |

[a] The reaction was carried out with 0.03 equiv of $K_2OsO_4{\cdot}2H_2O$ and 2.5 equiv of NMO in neat acetone, the conversion of the initial 2,3-dihydroisoxazole **10** was 75%.
[b] 3,4-*trans*, 4,5-*cis* **a**; 3,4-*trans*, 4,5-*trans* **b**; 3,4-*cis*, 4,5-*trans* **c**; 3,4-*cis*, 4,5-*cis* **d**.
[c] Ratio (**a**+**b**):(**c**+**d**) was determined from the mixture of 4,5-bis(acetoxy) isoxazolidines.
[d] Isolated yield.
[e] The mixture of **2a**, **b**.
[f] The mixture of **13a**–**d**.

### 2.3. Hydroxybromination reactions

Earlier we have demonstrated, hydroxybromination of the 2,3-dihydroisoxazole **1** with NBS (1 equiv) in THF in the presence of water (2 equiv) at 0 °C proceeds unselectively, providing mixture of four diisomeric 4-bromoisoxazolidin-5-ols **3a**–**d** (**3a**/**3b**/**3c**/**3d** ratio 7:43:7:43) in total yield of 68% (Scheme 5, Table 2, Entry 1).[5] Epimeric couples of **3a**, **b** and **3c**, **d** were separated by column chromatography on silica gel and their relative configuration was confirmed based on NOE experiments. Now we explored various reaction parameters and we showed that the amount of water, the reaction temperature and the solvent have a significant effect on the stereochemical outcome (Table 2). Interestingly, all reactions performed at lower temperatures proceeded with 3,4-*cis* selectivity (Table 2, Entries 2, 8–16) giving isoxazolidines **3c**, **d** as major isomers. Higher ratio of water in the mixture and substitution of THF with more polar DMSO at −20 °C significantly improved abundance of **3c**, **d** in the crude reaction mixture (Table 2, Entries 13, 15). It is to be noted that the reaction in DMSO/water at −70 °C did not further improve the 3,4-*cis*/3,4-*trans* ratio, however other unidentified byproducts were present in the crude mixture. We accordingly performed hydroxybrominations of **1** at higher temperatures. Although, the inversion of relative configuration could be expected to favour formation of the 3,4-*trans*-isomers **3a**, **b**, we achieved only




**Scheme 5.** Hydroxybromination reactions of 2,3-dihydroisoxazole **1**.

**Table 2**
Hydroxybromination reactions of 2,3-dihydroisoxazole **1**

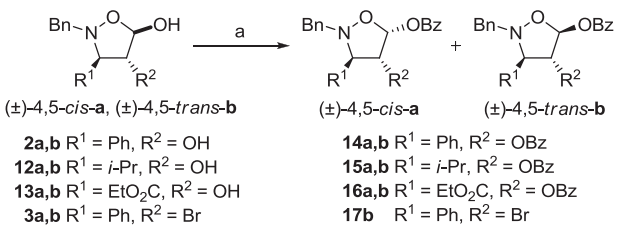
| Entry | Solvent | $T$ (°C) | **3a**, **b**:**3c**, **d**[b] | Entry | Solvent | $T$ (°C) | **3a**, **b**:**3c**, **d**[b] |
|---|---|---|---|---|---|---|---|
| 1 | THF/$H_2O$ (2 equiv)[a] | 0 | 50:50 | 9 | NMP/$H_2O$ (9:1) | −20 | 25:75 |
| 2 | THF/$H_2O$ (9:1) | 0 | 30:70 | 10 | DMF/$H_2O$ (9:1) | −20 | 20:80 |
| 3 | THF/$H_2O$ (9:1) | 20 | 35:65 | 11 | DMA/$H_2O$ (9:1) | −20 | 20:80 |
| 4 | THF/$H_2O$ (9:1) | 40 | 35:65 | 12 | $CH_3CN$/$H_2O$ (9:1) | −20 | 15:85 |
| 5 | THF/$H_2O$ (9:1) | 80 | 40:60 | 13 | DMSO/$H_2O$ (9:1) | −20 | 15:85 |
| 6 | THF/$H_2O$ (2 equiv)[a] | 80 | 50:50 | 14 | $CH_3CN$/$H_2O$ (4:1) | −20 | 15:85 |
| 7 | DMSO/$H_2O$ (9:1) | 80 | 50:50 | 15 | DMSO/$H_2O$ (4:1) | −20 | 10:90 |
| 8 | THF/$H_2O$ (9:1) | −20 | 35:65 | 16 | DMSO/$H_2O$ (7:3) | −70 | 10:90 |

[a] The reaction was carried out in THF using 2 equiv of water.
[b] 4,5-*cis* **a**, **c**; 4,5-*trans* **b**, **d**.

equal ratios of **3a**, **b** and **3c**, **d** (Table 2, Entry 5–7). Reaction of **1** was further optimized giving the best results in DMSO/water (4:1) at −20 °C. Finally, using these conditions, the mixture of isoxazolidines **3a**–**d** was obtained (**3a**, **b**/**3c**, **d** ratio 10:90) in total yield of 82%.

## 2.4. Preparation of 5-benzoyloxyisoxazolidines

With the aim to convert the 4-hydroxy- and 4-bromosubstituted isoxazolidines in their corresponding isoxazolidine-5-carbonitriles, isoxazolidine-4,5-diols **2a**, **b**, **12a**, **b**, **13a**, **b** and 4-bromoisoxazolidin-5-ols **3a**, **b** and **3c**, **d** were benzoylated using standard conditions (Schemes 6 and 8). In all cases both the 4,5-*cis*-**14a**–**16a**, **18a** and 4,5-*trans*-isomers **14b**–**16b**, **18b** were formed with the exception of the reaction of **3a**, **b** that afforded exclusively a single 4,5-*trans*-isomer **17b**. All isoxazolidines **14**–**18** were isolated by flash column chromatography on silica gel. The total yields and the ratios of 4,5-*cis*-**a** and 4,5-*trans*-**b** isomers are summarized in Table 3. Their structure and relative stereochemistry were assigned by NMR studies including NOESY 1D experiments. In accordance with a work concerning determination of configuration and conformation of C5 *O*-ethyl and *O*-acetyl substituted isoxazolidines reported by DeShong et al.,[6a] diastereomers **15a** and **15b** are most stable in conformation where *O*-benzoyl group occupies pseudoaxial position on the five membered ring due to the stabilization of an anomeric effect between a lone pair on the ring oxygen and the pseudoaxial *O*-benzoyl substituent at C5 (Fig. 1). Analysis of the NOESY 1D experiments of each diastereomers **15a** and **15b** unambiguously determined their relative configuration (Fig. 1). Irradiation of proton H-4 of **15a** resulted in enhancement of the signals corresponding to H-5, and the protons of the methyl group of the isopropyl substituent at C3. When H-3 was irradiated, a smaller NOE was obtained for H-4, however a peak enhancement was observed for the methylene protons of the benzyl group at N2.




**Scheme 6.** Reagents and conditions: (a) BzCl, pyridine, DMAP, $CH_2Cl_2$, rt.

**Table 3**
Preparation of 5-benzoyloxyisoxazolidines **14**–**18**

| Entry | Substrates | **a**:**b**[a] | Products | Yield (%)[b] | **a**:**b**[c] |
|---|---|---|---|---|---|
| 1 | **2a**, **b** | 60:40 | **14a**, **b** | 85 | 40:60 |
| 2 | **12a**, **b** | 75:25 | **15a**, **b** | 81 | 40:60 |
| 3 | **13a**, **b** | 60:40 | **16a**, **b** | 85 | 35:65 |
| 4 | **3a**, **b** | 17:83 | **17b** | 70 | <5:>95 |
| 5 | **3c**, **d** | 17:83 | **18a**, **b** | 90 | 40:60 |

[a] Ratio of **a**:**b** used in the reaction.
[b] Isolated total yield.
[c] Ratio of **a**:**b** determined from the crude reaction mixture by $^1$H NMR.

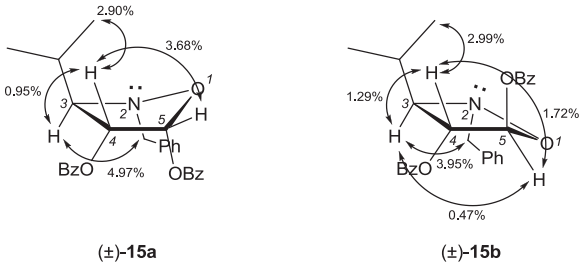



**Fig. 1.** NOE enhancements observed in isoxazolidines **15a** and **15b**. Arrows show the NOESY correlations.

These results strongly suggest the 3,4-*trans*, 4,5-*cis*-isomer. Irradiation of proton H-4 of **15b** resulted in similar enhancement for the signals corresponding to H-3, and the protons of the methyl group of the isopropyl substituent as described above, however enhancement for the signal of H-5 was smaller in comparison with **15a**. Moreover, the signal for H-5 was affected by irradiation of H-3. These results confirmed 3,4-*trans* relative configuration in **15b** and showed that the protons H-4 and H-5 are in the *trans* relationship. As in the above case concerning **15a**, irradiation of H-3 of **15b** led to an increase in the signal for the methylene protons of the benzyl group at N2. Along with the observed NOE enhancements, 4,5-*cis*/4,5-*trans* relative configuration of **15a** and **15b** was assigned based on analysis of the proton coupling constants between H-4 and H-5 nuclei. The minor 4,5-*cis*-isoxazolidine **15a** showed a moderate value of coupling constant between H-4 and H-5 ($J_{4,5}$=4.8 Hz), whereas none H-4/H-5 coupling constant was observed in the major isomer **15b**, indicating its 4,5-*trans* configuration with a dihedral angle between H-4 and H-5 protons of ~90°. The relative configuration of each diastereomer of dibenzoates **14a**, **b** and **16a**, **b** was assigned analogous with above mentioned results obtained for isoxazolidines **15a** and **15b**. The stereochemistry of the isoxazolidines **17b** and **18a** was confirmed by X-ray crystallographic analysis (Fig. 2).[9]

## 2.5. $S_N$-Reactions using TMSCN

Isoxazolidines **14**–**18** bearing benzoyloxy group at C5 are suitable precursors for the synthesis of 5-cyanoisoxazolidines using TMSCN in the presence of TMSOTf (Schemes 7 and 8). Up to now, only one example of preparation of 4-unsubstituted 5-cyanoisoxazolidines is reported in the literature using this method.[10] To the best of our knowledge, we are the first to report the cyanations of 4-hydroxy- and 4-bromosubstituted isoxazolidines. Hence, we focused our attention on the searching for the suitable reaction conditions with regard to the yields and the stereochemistry. We have found that the reaction of isoxazolidines **14a**, **b** with 1.2 equiv of TMSCN in the presence of TMSOTf (1 equiv) at 0 °C in anhydrous $CH_2Cl_2$ (0.5 M) provides the mixture of two isomers 4,5-*cis*-**19a** and 4,5-*trans*-**19b** (**19a**/**19b** ratio 20:80) in 74% yield (Table 4, Entry 1). The cyanations of **15a**, **b** and **16a**, **b** proceeded with even higher diastereoselectivity in favour of 4,5-*trans*-isomers **20b** and **21b** (Table 4, Entries 2, 3). The neighbouring effect

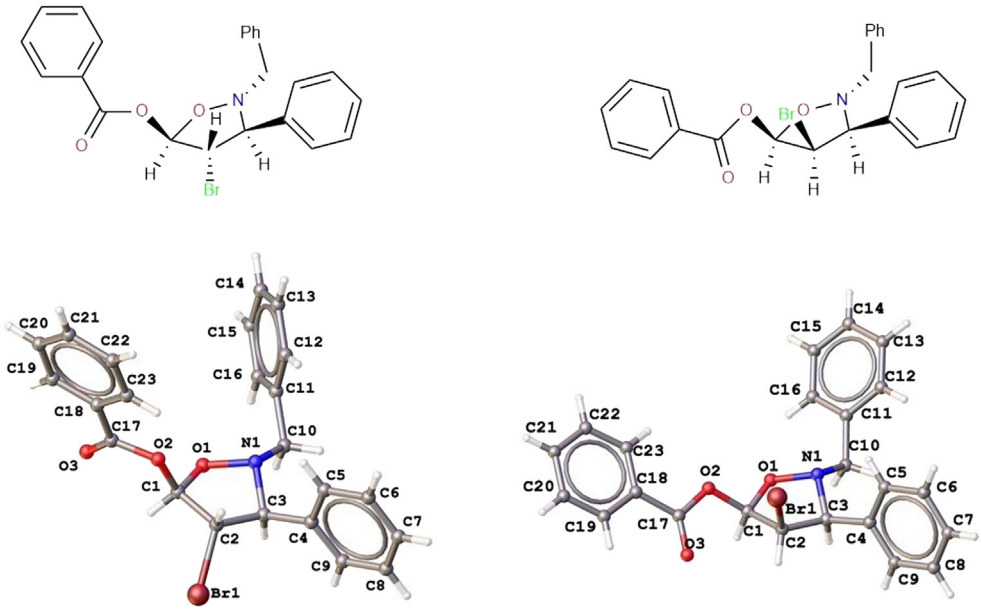
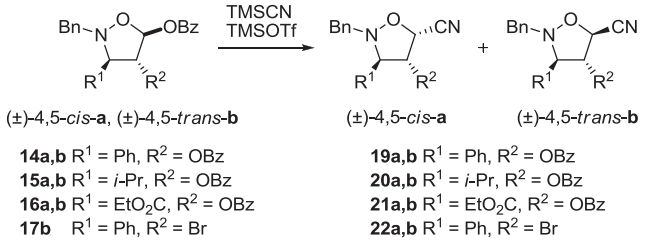
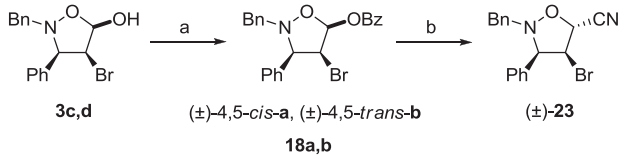



**Fig. 2.** Structures of **17b** (left) and **18a** (right).




**Scheme 7.** Lewis acid-induced cyanations of 5-benzoyloxyisoxazolidines **14**–**17** using TMSCN.




**Scheme 8.** Reagents and conditions: (a) BzCl, pyridine, DMAP, $CH_2Cl_2$, rt; (b) TMSCN, TMSOTf, $CH_3CN$, −20 °C.

of the benzoyl group probably determines the 4,5-*trans* stereoselectivity. The type of solvent, temperature and the substrate concentration are crucial for the successful progress of the reaction. Whereas no cyanations of the isoxazolidines **14a**, **b** and **15a**, **b** occurred in acetonitrile, the use of $CH_2Cl_2$ increased reactivity. All reactions carried out in 0.1 M concentration were less clean then those performed at higher concentrations. We have observed a significant effect of the ester group at C3 in the case of isoxazolidines **16a**, **b**. Herein, the reaction needed to be performed at room temperature with 3 equiv of TMSCN to come to completion. Contrary to original conditions for isoxazolidines **14a**, **b** and **15a**, **b**, the reactivity of **16a**, **b** was improved when acetonitrile and lower concentration were used (Table 4, Entry 3). All reaction conditions and obtained results are summarized in Table 4. The substitution of the C5 benzoyloxy group with cyano group was confirmed by $^1$H and $^{13}$C NMR experiments as follows.

Signals of the H-5 protons for both isomers **19a** and **19b** are shifted to low field compared to H-5 protons of starting isoxazolidines **14a**, **b** [**14a**: $\delta$=6.88 ppm (d); **14b**: $\delta$=6.63 ppm (s); **19a**: $\delta$=4.80 ppm (d); **19b**: $\delta$=5.16 ppm (d)]. Moreover, the signal at 116.6 ppm in the $^{13}$C NMR (**19b**) is typical for the carbon atom of a cyano group. Because, we were not able to separate each diastereomer of isoxazolidines **19a**, **b**, the stereochemistry was assigned from analysis of the NOESY 1D experiments obtained from the corresponding mixture. The results showed that the major isoxazolidine **19b** has a 3,4-*trans*, 4,5-*trans* relative configuration and the minor isoxazolidine **19a** was assigned as 3,4-*trans*, 4,5-*cis*-isomer. Irradiation of proton H-4 of **19a** resulted in signal enhancement of two signals corresponding to H-5 (2.61%), and the ortho protons of the phenyl ring (1.54%) while a smaller peak enhancement was observed for H-3 (0.55%). The signal for H-5 was unaffected by irradiation of H-3. This can occur when phenyl substituent at C3 and the protons H-4 and H-5 are in the *cis* relationship. Likewise as for **19a**, irradiation of proton H-4 of the major **19b** resulted in similar enhancement of the signals corresponding to H-3 (0.59%), and the ortho protons of the phenyl ring at C3 (1.59%), however a smaller NOE was obtained for H-5 (0.98%) in comparison with **19a**. Additionally, irradiation of H-3 led to an increase in the H-5 signal (0.28%). Thus, 3,4-*trans* relative configuration is consistent with that for **19a**, however benzoyloxy group and cyano group are

**Table 4**
Lewis acid-induced cyanations of 5-benzoyloxyisoxazolidines **14**–**18**

| Entry | Substrates | **a**:**b**[a] | Reaction conditions | Products | **a**:**b**[b] | Total yield (%)[c] |
|---|---|---|---|---|---|---|
| 1 | **14a**, **b** | 40:60 | TMSCN (1.2 equiv), TMSOTf (1 equiv), 0 °C, 3 h, $CH_2Cl_2$ (0.5 M) | **19a**, **b** | 20:80 | 74% |
| 2 | **15a**, **b** | 40:60 | TMSCN (1.2 equiv), TMSOTf (1 equiv), 0 °C, 3 h, $CH_2Cl_2$ (0.5 M) | **20a**, **b** | 10:90 | 78% |
| 3 | **16a**, **b** | 35:65 | TMSCN (3 equiv), TMSOTf (1 equiv), rt, 24 h, $CH_3CN$ (0.1 M) | **21a**, **b** | 10:90 | 83% |
| 4 | **17b** | — | TMSCN (1.2 equiv), TMSOTf (1 equiv), 0 °C, 1 h, $CH_2Cl_2$ (0.5 M) | **22a**, **b** | 70:30 | 82% |
| 5 | **18a**, **b** | 40:60 | TMSCN (1.2 equiv), TMSOTf (1 equiv), −20 °C, 1 h, $CH_3CN$ (0.5 M) | **23** | <5:>95 | 82% |

[a] Ratio of **a**:**b** used in the reaction.
[b] Ratio of **a**:**b** determined from the crude reaction mixture by $^1$H NMR.
[c] Isolated yield.

*trans* in the major isomer **19b**. The 4,5-*cis*/4,5-*trans* relative configuration of **19a** and **19b** could be assigned from analysis of H-5 proton coupling constant. The major 4,5-*trans*-isoxazolidine **19b** showed a small coupling constant between H-4 and H-5 ($J_{4,5}$=1.8 Hz), indicating that a dihedral angle between those two protons is close to ~90°, whereas a large H-4/H-5 coupling constant was observed in the minor 4,5-*cis*-isomer **19a** ($J_{4,5}$=6.6 Hz). Similar results were obtained for cyanoisoxazolidines **20a**, **b** and **21a**, **b**. Subsequently, we have carried out cyanations of 4-bromoisoxazolidines **17b** and **18a**, **b** (Table 4, Entries 4, 5). The reaction of **17b** proceeded with poor diastereoselectivity, even afforded more 4,5-*cis*-isomer **22a** (**22a**/**22b** ratio 70:30) to our surprise. Dichloromethane was again a superior solvent to acetonitrile.

On the other hand, the cyanation of the mixture **18a**, **b** in acetonitrile exclusively provided a single 3,4-*cis*, 4,5-*trans*-5-cyanoisoxazolidine **23** in very good yield (82%) (Scheme 8). In analogy with the isoxazolidine-5-carbonitriles **19a**, **b**, 4,5-*cis*/4,5-*trans* relative configuration of each diastereomer of 4-bromoisoxazolidines **22a** and **22b** was unambiguously assigned from analysis of the NOESY 1D experiments for the protons H-3, H-4 and H-5, respectively. In particular, irradiation of H-4 of the major isomer **22a** resulted in enhancement of the signal for H-5 (2.03%). Likewise, when H-5 was irradiated, the signal corresponding to H-4 (2.23%) was enhanced, but no effect upon the intensity of H-3 was observed. On the other hand, irradiation of H-4 of the minor isomer **22b** produced much smaller enhancement of H-5 (0.58%). Similarly, irradiation of H-5 led only to a small increase in H-4 (0.73%). Moreover a peak enhancement was observed for H-3 (0.30%). Above mentioned results clearly showed that the substituents at C4 and C5 of **22a** occupied 4,5-*cis* relative configuration while in **22b** were in the *trans* relationship. These conclusions could be confirmed by analysis of the H-4/H-5 coupling constants. The major 4,5-*cis*-isoxazolidine **22a** showed a large coupling constant between H-4 and H-5 ($J_{4,5}$=7.1 Hz), whereas a small H-4/H-5 coupling constant was observed in the minor isomer **22b** ($J_{4,5}$=2.8 Hz), indicating its 4,5-*trans* configuration. The configuration of 5-cyanoisoxazolidine **23** was also assigned from analysis of the NOESY 1D experiments. The results were similar to those obtained for **22b** and confirmed the 3,4-*cis*, 4,5-*trans* configuration. Irradiation of H-4 had a small effect upon the intensity of H-5 (0.35%), however a large NOE was obtained for H-3 (2.43%). Irradiation of H-3 resulted in a large enhancement of the signal for H-4 (2.50%).

## 3. Conclusion

In conclusion, novel types of the 4-hydroxy- and 4-bromosubstituted isoxazolidines were synthesized from 4,5-unsubstituted 2,3-dihydroisoxazoles using dihydroxylation and hydrobromination reactions. Dihydroxylation reactions with $K_2OsO_4 \cdot 2H_2O$ in the presence of NMO in acetone/water proceeded from the less hindered side and provided the major 3,4-*trans*-isoxazolidine-4,5-diols in good yields with exception of 3-isopropyl-2,3-dihydroisoxazole. On the other hand, the hydrobromination reaction of the model 3-phenyl-2,3-dihydroisoxazole predominantly proceeded with 3,4-*cis* selectivity. In this case, the amount of water, temperature and the type of solvent had a significant effect on the stereochemical outcome of the reaction. In order to prepare isoxazolidine-5-carbonitriles, 4-hydroxy- and 4-bromosubstituted isoxazolidines were transformed into isoxazolidines possessing a good leaving group at C5. Substitution reactions were carried out with TMSCN in the presence of TMSOTf and proceeded with high 4,5-*trans* selectivity. Moreover, reaction of 3,4-*cis*-4-bromoisoxazolidines exclusively afforded single 3,4-*cis*, 4,5-*trans*-isoxazolidine-5-carbonitrile. In general, we observed a strong solvent effect on the course of cyanations depending on the substrate. The presence of an ester group at C3 decreased the reaction rate of both dihydroxylation reaction and cyanation.

## 4. Experimental section

### 4.1. General

All melting points were measured on a Melting Point B-540 apparatus (Büchi) and are uncorrected. HRMS analyses were performed on Orbittrap Velos Pro spectrometer (Thermo Fisher Scientific). Infrared (IR) spectra were recorded on a Nicolet 5700 FT-IR spectrometer with ATR Smart Orbit Diamond adapter (Thermo Electron Corporation) and are reported as wavenumber ($cm^{-1}$). NMR spectra were recorded on a Varian VRX-300 spectrometer ($^1H$, 300 MHz and $^{13}C$, 75.4 MHz) and Varian INOVA-600 spectrometer ($^1H$, 600 MHz and $^{13}C$, 150.8 MHz) in $CDCl_3$ using TMS as the internal standard. All MS analyses were performed on Agilent 1260B LCMS system with multimode ion source (ESI+APCI) in positive mode, 50% scan and 50% SIM. TLC analysis was carried out using TLC Silica gel 60 $F_{254}$ (aluminium sheets, Merck) and visualized by UV light or with permanganate solution followed by heating. Flash column chromatography was performed on Büchi system (Pump Manager C-615 and Fraction Collector C-660) using Normasil 60 silica gel (0.040–0.063 mm) (VWR). All solvents were dried and distilled according to conventional methods. NMP, DCM and acetonitrile were stored over molecular sieves and handled under inert atmosphere. All reagents were purchased from Aldrich, Acros Organics, Alfa-Aesar, Merck and Mikrochem Trade and were used without further purification.

### 4.2. 1,3-Dipolar cycloaddition of nitrone 5 with vinyl acetate

*4.2.1. (±)-2-Benzyl-3-isopropylisoxazolidin-5-yl acetate (**8a**, **b**).* A solution of nitrone **5**[11] (2.9 g, 16.36 mmol) in vinyl acetate (30 mL) was stirred in sealed tube at 75 °C for 24 h. When starting nitrone had been consumed (TLC, ethyl acetate), vinyl acetate was evaporated in vacuo and the products were isolated by flash column chromatography (hexanes/ethyl acetate 80:20) to give the mixture of two diastereoisomers 3,5-*cis*-**8a** and 3,5-*trans*-**8b** (2.98 g, 11.32 mmol, 69%, **8a**/**8b** ratio 65:35) as a colourless oil. $^1H$ NMR data of each diastereomer were extracted from the corresponding mixture. **8a**: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=0.91 (d, 3H, $J$=7.0 Hz), 0.93 (d, 3H, $J$=7.0 Hz), 1.79–1.95 (m, 1H), 2.04 (s, 3H), 2.18 (ddd, 1H, $J$=13.6, 7.0, 1.8 Hz), 2.52 (ddd, 1H, $J$=13.6, 8.4, 6.2 Hz), 2.71–2.78 (m, 1H), 3.92 (d, 1H, $J$=13.9 Hz), 4.07 (d, 1H, $J$=13.9 Hz), 6.30 (dd, 1H, $J$=6.2, 1.8 Hz), 7.22–7.39 (m, 5H); **8b**: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=0.89 (d, 3H, $J$=7.0 Hz), 0.94 (d, 3H, $J$=7.0 Hz), 1.62–1.76 (m, 1H), 2.08 (s, 3H), 2.34 (ddd, 1H, $J$=13.6, 8.4, 5.1 Hz), 2.44 (ddd, 1H, $J$=13.6, 7.0, 1.1 Hz), 2.99–3.07 (m, 1H), 4.02 (d, 1H, $J$=13.6 Hz), 4.19 (d, 1H, $J$=13.6 Hz), 6.33 (d, 1H, $J$=5.1 Hz), 7.22–7.39 (m, 5H); $^{13}C$ NMR data are given for the mixture **8a**, **b**. $^{13}C$ NMR (75.4 MHz, $CDCl_3$): $\delta$=17.0, 18.4, 20.2, 20.7, 21.4, 21.5, 28.9, 31.6, 37.3, 39.1, 61.4, 65.1, 69.0, 69.4, 95.8, 98.2, 127.3 (×2), 128.2, 128.3, 129.1 (×2), 136.9, 137.6, 170.0, 170.6; MS (ESI+APCI): $m/z$ for $C_{15}H_{21}NO_3$ $(M+H)^+$: 264.2.

### 4.3. Elimination reaction in the presence of TMSOTf

*4.3.1. (±)-2-Benzyl-3-isopropyl-2,3-dihydroisoxazole (**10**).* The reaction flask was charged with 5-acetoxyisoxazolidines **8a**, **b** (2.8 g, 10.63 mmol), sealed with a rubber septum and filled with argon. Anhydrous NMP (53 mL) was added followed by BSTFA (3.4 mL, 12.76 mmol). The stirred solution was cooled in an ice/water-bath (2–5 °C) and TMSOTf (0.2 mL, 1.1 mmol) was added. Stirring was continued at room temperature for 1.5 h with exclusion of the moisture. When the initial 5-acetoxyisoxazolidines had been consumed (TLC, hexanes/ethyl acetate 80:20), the reaction mixture

was cooled in an ice/water-bath, satd aqueous $NaHCO_3$ (25 mL) and $Et_2O$ (25 mL) were added and the mixture was vigorously stirred for 5 min. The precipitated solid was dissolved by addition of water (25 mL). Water layer was removed and the organic layer was washed three times with water (20 mL), dried with $Na_2SO_4$ and the solvent was evaporated in vacuo (bath temperature bellow 35 °C). The product was isolated by flash column chromatography (hexanes/ethyl acetate 95:5) to give 2,3-dihydroisoxazole **10** (1.73 g, 8.51 mmol, 80%) as a colourless oil that becomes darker over time. IR (thin film): 2956, 2870, 1622, 1454, 1123, 1049, 1029, 999, 729, 697 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=0.82 (d, 3H, $J$=7.0 Hz), 0.83 (d, 3H, $J$=7.0 Hz), 1.48–1.64 (m, 1H), 3.53–3.56 (m, 1H), 3.77 (d, 1H, $J$=12.9 Hz), 4.13 (d, 1H, $J$=12.9 Hz), 4.86 (t, 1H, $J$=2.9 Hz), 6.42–6.45 (m, 1H), 7.24–7.42 (m, 5H); $^{13}C$ NMR (75.4 MHz, $CDCl_3$): $\delta$=18.1, 18.5, 33.6, 63.9, 75.0, 97.6, 127.4, 128.3, 129.4, 136.9, 141.6; HRMS (ESI): calcd for $C_{13}H_{17}NO$ $(M+H)^+$: 204.1388, found: 204.1379.

### 4.4. Dihydroxylation reactions

*4.4.1. (±)-2-Benzyl-3-isopropylisoxazolidine-4,5-diol (**12a**, **b**).* 2,3-Dihydroisoxazole **10** (400 mg, 1.97 mmol) was dissolved in acetone (10 mL), the solution was cooled to 2 °C (ice/water bath) and aqueous NMO (1.01 mL, 4.93 mmol, 50%, w/w) was added followed by $K_2OsO_4 \cdot 2H_2O$ (22.0 mg, 0.06 mmol). Afterwards, the mixture was vigorously stirred at room temperature over night. Despite of incomplete conversion of the starting 2,3-dihydroisoxazole (TLC, hexanes/ethyl acetate 60:40), the reaction was quenched by dilution with water and repeatedly extracted with $CH_2Cl_2$. The combined organic layers were dried with $Na_2SO_4$, filtered and the solvent was evaporated in vacuo (bath temperature bellow 35 °C). The isoxazolidine-4,5-diols **12a**, **b** were isolated by flash column chromatography (hexanes/ethyl acetate 60:40) as a mixture of two non-separable epimers 3,4-*trans*-4,5-*cis*-**12a** and 3,4-*trans*-4,5-*trans*-**12b** (135 mg, 0.57 mmol, 29%, **12a**/**12b** ratio 75:25) as a colourless oil. NMR data of each diastereomer were extracted from the corresponding mixture. **12a**: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=0.97–1.00 (m, 6H), 1.72–1.86 (m, 1H), 2.75 (dd, 1H, $J$=6.5, 6.1 Hz), 4.06 (d, 1H, $J$=13.4 Hz), 4.16–4.22 (m, 1H), 4.26 (d, 1H, $J$=13.4 Hz), 5.16–5.21 (m, 1H), 7.25–7.39 (m, 5H); $^{13}C$ NMR (75.4 MHz $CDCl_3$): $\delta$=18.6, 19.6, 30.4, 65.9, 75.0, 77.5, 95.6, 127.3, 128.3, 129.0, 137.8; **12b**: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=0.97–1.00 (m, 6H), 1.87–1.99 (m, 1H), 2.55 (dd, 1H, $J$=6.5, 3.8 Hz), 3.93 (d, 1H, $J$=14.2 Hz), 4.25–4.28 (m, 1H), 4.26 (d, 1H, $J$=14.2 Hz), 5.11 (s, 1H), 7.25–7.39 (m, 5H); $^{13}C$ NMR (75.4 MHz, $CDCl_3$): $\delta$=18.1, 20.4, 28.3, 62.1, 78.8, 82.4, 101.6, 127.5, 128.3, 129.2, 137.0; MS (ESI+APCI): $m/z$ for $C_{13}H_{19}NO_3$ $(M+H)^+$: 238.2.

*4.4.2. (±)-Ethyl 2-benzyl-4,5-dihydroxyisoxazolidine-3-carboxylate (**13a**–**d**).* 2,3-Dihydroisoxazole **11**[4] (730 mg, 3.13 mmol) was dissolved in acetone/water (16 mL, 3/1, v/v), the solution was cooled to 2 °C (ice/water bath) and aqueous NMO (1.3 mL, 6.26 mmol, 50%, w/w) was added followed by $K_2OsO_4 \cdot 2H_2O$ (11.5 mg, 0.03 mmol). The mixture was vigorously stirred and the temperature was allowed to rise to room temperature. When starting 2,3-dihydroisoxazole had disappeared after 6 h (TLC, hexanes/ethyl acetate 67:33), the mixture was diluted with water and repeatedly extracted with $CH_2Cl_2$. The combined organic layers were dried with $Na_2SO_4$, filtered and the solvent was evaporated in vacuo (bath temperature bellow 35 °C). The isoxazolidine-4,5-diols **13a**–**d** were isolated by flash column chromatography (hexanes/ethyl acetate 50:50) to give epimeric couple 3,4-*trans*-**13a**, **b** (410 mg, 1.54 mmol, 49%) and epimeric couple 3,4-*cis*-**13c**, **d** (270 mg, 1.01 mmol, 32%) as the colourless oils. NMR data are given for the corresponding epimeric couples. **13a**, **b**: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=1.12–1.24 (m, 6H), 3.53 (d, 1H, $J$=2.9 Hz), 3.64 (d, 1H, $J$=7.0 Hz), 4.03–4.16 (m, 6H), 4.27 (d, 1H, $J$=12.9 Hz), 4.38 (d, 1H, $J$=12.3 Hz), 4.64 (dd, 1H, $J$=7.0, 4.1 Hz), 4.67 (d, 1H, $J$=3.5 Hz), 5.30 (s, 1H), 5.36 (d, 1H, $J$=4.1 Hz), 7.23–7.37 (m, 10H); $^{13}C$ NMR (75.4 MHz, $CDCl_3$): $\delta$=13.9, 14.0, 61.7, 62.0, 62.8, 65.3, 71.4, 73.2, 78.1, 83.8, 95.0, 101.5, 127.8, 127.9, 128.3, 128.4, 129.6, 129.8, 135.3, 135.8, 170.3, 170.6; MS (ESI+APCI): $m/z$ for $C_{13}H_{17}NO_5$ $(M+H)^+$: 268.2; **13c**, **d**: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=1.17–1.25 (m, 6H), 3.59 (d, 1H, $J$=7.6 Hz), 3.98 (d, 1H, $J$=4.1 Hz), 4.08–4.21 (m, 7H), 4.34 (d, 1H, $J$=12.9 Hz), 4.60–4.68 (m, 2H), 5.31–5.38 (m, 2H), 7.28–7.39 (m, 10H); $^{13}C$ NMR (75.4 MHz, $CDCl_3$): $\delta$=14.1 (×2), 61.6, 61.7, 61.8, 65.8, 69.4, 70.0, 75.8, 81.2, 94.4, 101.0, 127.9 (×2), 128.4 (×2), 129.6 (×2), 135.0, 135.7, 168.2, 168.8; MS (ESI+APCI): $m/z$ for $C_{13}H_{17}NO_5$ $(M+H)^+$: 268.2.

### 4.5. Hydroxybromination reactions

*4.5.1. (±)-Benzyl-4-bromo-3-phenylisoxazolidin-5-ol (**3a**–**d**).* A stirred solution of 2,3-dihydroisoxazole **1**[4] (630 mg, 2.65 mmol) in THF/water (53 mL, 9:1, v/v) or in DMSO/water (53 mL, 4:1, v/v) was cooled to −20 °C and solid NBS (460 mg, 2.60 mmol) was added by portions over a period of 30 min. The stirring was continued at this temperature until the initial 2,3-dihydroisoxazole disappeared (30 min, TLC, hexanes/AcOEt 80:20). Thereafter, the mixture was diluted with water (50 mL) and extracted with ether (50 mL). The organic layer was washed with water (2×50 mL), dried with $Na_2SO_4$ and the solvent was evaporated in vacuo. Products were isolated by flash column chromatography (hexanes/AcOEt 90:10) to provide two couples of diastereoisomers 3,4-*trans*-**3a**, **b** and 3,4-*cis*-**3c**, **d** in ratio and with the yield depending on the applied solvent: The reaction carried out in THF/water (9:1, v/v) gave **3a**, **b** (250 mg, 0.75 mmol, 28%) and **3c**, **d** (470 mg, 1.41 mmol, 53%). The reaction performed in DMSO/water (4:1, v/v) afforded **3a**, **b** (70 mg, 0.21 mmol, 8%) and **3c**, **d** (655 mg, 1.96 mmol, 74%). **3a**, **b**, colourless solid, mp 88–89 °C (recrystallized from hexanes, **3a**/**3b** ratio 17:83); IR (thin film): 3460, 3032, 1454, 1070, 1025, 951, 760, 753, 699, 532 $cm^{-1}$; (4,5-*trans*)-**3b**: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=3.46 (br s, 1H), 3.76 (d, 1H, $J$=14.8 Hz), 3.96 (d, 1H, $J$=8.0 Hz), 4.03 (d, 1H, $J$=14.8 Hz), 4.20 (dd, 1H, $J$=8.0, 1.8 Hz), 5.50 (d, 1H, $J$=1.8 Hz), 7.28–7.51 (m, 10H); $^{13}C$ NMR (75.4 Hz, $CDCl_3$): $\delta$=59.5, 59.9, 80.1, 102.1, 127.5, 128.0, 128.3, 128.8, 128.9, 129.1, 134.5, 136.4. Partial $^1H$ NMR data extracted from the mixture of **3a**, **b** for the minor (4,5-*cis*)-**3a**: $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$=4.05 (d, 1H, $J$=13.5 Hz), 4.10 (d, 1H, $J$=13.5 Hz), 4.24 (d, 1H, $J$=10.6 Hz), 4.28 (dd, 1H, $J$=10.0, 4.1 Hz), 5.41 (d, 1H, $J$=4.1 Hz); MS (ESI+APCI): $m/z$ for $C_{16}H_{16}BrNO_2$ $(M+H)^+$: 334.0/336.0; **3c**, **d**, yellowish foam (**3c**/**3d** ratio 17:83); IR (thin film): 3288, 3032, 1454, 1228, 1049, 1015, 751, 717, 693, 517 $cm^{-1}$; (4,5-*trans*)-**3d**: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=3.54 (br s, 1H), 4.02 (d, 1H, $J$=14.2 Hz), 4.23 (d, 1H, $J$=14.2 Hz), 4.49 (d, 1H, $J$=4.3 Hz), 4.57 (d, 1H, $J$=4.3 Hz), 5.60 (s, 1H), 7.28–7.49 (m, 10H); $^{13}C$ NMR (75.4 Hz, $CDCl_3$): $\delta$=59.4, 62.6, 69.7, 102.1, 127.5, 128.3 (×2), 128.4, 128.5, 129.1, 134.8, 136.6. Partial $^1H$ NMR data extracted from the mixture of **3c**, **d** for the minor (4,5-*cis*)-**3c**: $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$=3.79 (d, 1H, $J$=14.7 Hz), 4.18 (d, 1H, $J$=14.7 Hz), 4.19 (d, 1H, $J$=6.5 Hz), 4.83 (dd, 1H, $J$=6.5, 4.7 Hz), 5.46 (d, 1H, $J$=4.7 Hz); MS (ESI+APCI): $m/z$ for $C_{16}H_{16}BrNO_2$ $(M+H)^+$: 334.0/336.0.

### 4.6. Typical experimental procedure for the benzoylation of isoxazolidine-4,5-diols

*4.6.1. (±)-2-Benzyl-3-phenylisoxazolidine-4,5-diyl dibenzoate (**14a**, **b**).* The isoxazolidine-4,5-diols **2a**, **b**[5] (340 mg, 1.25 mmol) were dissolved in anhydrous $CH_2Cl_2$ (13 mL), pyridine (0.42 mL, 5.20 mmol) and DMAP (30 mg, 0.26 mmol) were added followed by benzoyl chloride (0.45 mL, 3.90 mmol). The reaction mixture was stirred at room temperature for 24 h. When no starting isoxazolidine-4,5-diols had been detected by TLC (hexanes/ethyl acetate=60/40), the mixture was diluted with water and extracted with $CH_2Cl_2$ (10 mL) two times. Combined organic layers were

dried over $Na_2SO_4$ and the solvent was evaporated in vacuo. Products were isolated by flash column chromatography (hexanes/diethyl ether 85:15) to provide isoxazolidines **14a**, **b** as a mixture of two epimers 3,4-*trans*, 4,5-*cis*-**14a** and 3,4-*trans*, 4,5-*trans*-**14b** (510 mg, 1.06 mmol, 85%, **14a**/**14b** ratio 40:60) as a colourless oil. With the aim of complete characterization of new compounds, the analytical sample was used in preparative TLC (hexanes/$CH_2Cl_2$ 33:67) to give pure isomers **14a** and **14b**. **14a**, colourless solid, mp 111–113 °C; IR (thin film): 2979, 1716, 1452, 1276, 1250, 1234, 1130, 1097, 1019, 695 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=4.19 (d, 1H, $J$=14.1 Hz, $NCH_2Ph$), 4.31 (d, 1H, $J$=14.1 Hz, $NCH_2Ph$), 4.51 (d, 1H, $J$=8.8 Hz, H-3), 5.70 (dd, 1H, $J$=8.8, 4.1 Hz, H-4), 6.88 (d, 1H, $J$=4.1 Hz, H-5), 7.18–7.61 (m, 12H), 7.90–7.98 (m, 8H); $^{13}C$ NMR (75.4 Hz, $CDCl_3$): $\delta$=62.7, 69.1, 80.3, 93.6, 127.5, 127.8, 128.3, 128.4 (×2), 128.6, 128.8, 128.9 (×2), 129.5, 129.7, 129.8, 133.4, 133.5 135.7, 135.9, 164.8, 165.0; HRMS (ESI): calcd for $C_{30}H_{25}NO_5$ $(M+H)^+$: 480.1811, found: 480.1796; **14b**, colourless oil; IR (thin film): 3032, 1721, 1451, 1248, 1105, 1095, 1059, 1023, 952, 695 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=4.08 (d, 1H, $J$=14.7 Hz, $NCH_2Ph$), 4.17 (d, 1H, $J$=5.3 Hz, H-3), 4.21 (d, 1H, $J$=14.7 Hz, $NCH_2Ph$), 5.84 (d, 1H, $J$=5.3 Hz, H-4), 6.63 (s, 1H, H-5), 7.20–7.63 (m, 12H), 8.03–8.08 (m, 8H); $^{13}C$ NMR (75.4 Hz, $CDCl_3$): $\delta$=60.0, 74.7, 88.4, 98.2, 127.3, 128.0, 128.2, 128.4, 128.5 (×2), 128.8, 128.9 (×2), 129.6, 129.8, 130.0, 133.4, 133.6, 136.0, 136.1, 165.2, 165.3; HRMS (ESI): calcd for $C_{30}H_{25}NO_5$ $(M+H)^+$: 480.1811, found: 480.1798.

*4.6.2. (±)-2-Benzyl-3-isopropylisoxazolidine-4,5-diyl dibenzoate (**15a**, **b**).* The mixture of two epimers 3,4-*trans*, 4,5-*cis*-**15a** and 3,4-*trans*, 4,5-*trans*-**15b** (**15a**/**15b** ratio 40:60); yield 81% (790 mg, 1.8 mmol) after flash column chromatography (hexanes/diethyl ether 90:10), colourless oil. With the aim of complete characterization of new compounds, the analytical sample was used in preparative TLC (hexanes/$CH_2Cl_2$ 33:67) to give pure isomers **15a** and **15b**. **15a**, colourless solid, mp 91–92 °C; IR (thin film): 2970, 1721, 1452, 1279, 1255, 1241, 1126, 1042, 1012, 713 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=0.99–1.04 (m, 6H), 1.89–2.00 (m, 1H), 3.34 (t, 1H, $J$=6.1 Hz), 4.25 (d, 1H, $J$=14.4 Hz), 4.48 (d, 1H, $J$=14.4 Hz), 5.73 (dd, 1H, $J$=6.1, 4.8 Hz), 6.84 (d, 1H, $J$=4.8 Hz), 7.26–8.17 (m, 15H); $^{13}C$ NMR (75.4 MHz, $CDCl_3$): $\delta$=18.6, 19.3, 28.5, 65.6, 71.90, 82.8, 98.4, 127.6, 128.4 (×2), 128.5, 129.0, 129.3, 129.5, 129.7, 129.68, 129.8, 133.4, 133.6, 136.8, 164.7, 165.2; HRMS (ESI): calcd for $C_{27}H_{27}NO_5$ $(M+H)^+$: 446.1967, found: 446.1957; calcd for $C_{27}H_{27}NO_5$ $(M+Na)^+$: 468.1787, found: 468.1775; **15b**, colourless oil; IR (thin film): 2960, 1720, 1451, 1257, 1106, 1079, 1062, 1024, 936, 706 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=0.99–1.04 (m, 3H), 1.18 (d, 3H, $J$=6.5 Hz), 2.00–2.12 (m, 1H), 3.08 (dd, 1H, $J$=6.5, 3.5 Hz), 4.23 (d, 1H, $J$=14.4 Hz), 4.28 (d, 1H, $J$=14.4 Hz), 5.84 (d, 1H, $J$=3.5 Hz), 6.60 (s, 1H), 7.25–8.09 (m, 15H); $^{13}C$ NMR (75.4 MHz, $CDCl_3$): $\delta$=18.0, 20.2, 30.5, 62.3, 75.2, 78.00, 95.6, 127.4, 128.3, 128.4, 128.5, 129.0, 129.7, 129.9, 133.3, 133.5, 129.1, 129.6, 136.5, 165.1, 165.3; HRMS (ESI): calcd for $C_{27}H_{27}NO_5$ $(M+H)^+$: 446.1967, found: 446.1951; calcd for $C_{27}H_{27}NO_5$ $(M+Na)^+$: 468.1787, found: 468.1768.

*4.6.3. (±)-2-Benzyl-3-(ethoxycarbonyl)isoxazolidine-4,5-diyl diben zoate (**16a**, **b**).* The mixture of two epimers 3,4-*trans*, 4,5-*cis*-**16a** and 3,4-*trans*, 4,5-*trans*-**16b** (**16a**/**16b** ratio 35:65); yield 85% (540 mg, 1.14 mmol) after flash column chromatography (hexanes/diethyl ether 90:10), colourless oil. With the aim of complete characterization of new compounds, the analytical sample was used in preparative TLC ($CH_2Cl_2$) to give pure isomers **16a** and **16b**. **16a**, colourless solid, mp 98–100 °C; IR (thin film): 3032, 1740, 1724, 1450, 1244, 1200, 1112, 1065, 1019, 696 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=1.21 (t, 3H, $J$=7.0 Hz), 4.12 (d, 1H, $J$=7.3 Hz), 4.17 (q, 2H, $J$=7.0 Hz), 4.33 (d, 1H, $J$=12.9 Hz), 4.52 (d, 1H, $J$=12.9 Hz), 6.08 (dd, 1H, $J$=7.3, 4.5 Hz), 6.90 (d, 1H, $J$=4.5 Hz), 7.25–7.62 (m, 11H), 7.94–8.01 (m, 4H); $^{13}C$ NMR (75.4 MHz, $CDCl_3$): $\delta$=14.0, 62.1, 65.1, 68.1, 77.5, 94.3, 128.0, 128.5 (x 3), 128.6, 129.2, 129.7, 129.8 (×2), 133.6, 133.7, 135.0, 164.6, 164.9, 168.3; HRMS (ESI): calcd for $C_{27}H_{25}NO_7$ $(M+H)^+$: 476.1709, found: 476.1692; calcd for $C_{27}H_{25}NO_7$ $(M+Na)^+$: 498.1529, found: 498.1509; **16b**, colourless oil; IR (thin film): 2979, 1722, 1451, 1247, 1177, 1095, 1067, 1024, 945, 708 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=1.26 (t, 3H, $J$=7.0 Hz), 3.83 (d, 1H, $J$=3.8 Hz), 4.12–4.30 (m, 2H), 4.37 (s, 2H), 6.13 (d, 1H, $J$=3.8 Hz), 6.66 (s, 1H), 7.29–7.64 (m, 11H), 8.00 (d, 2H, $J$=7.7 Hz), 8.10 (d, 2H, $J$=7.7 Hz); $^{13}C$ NMR (75.4 MHz, $CDCl_3$): $\delta$=14.0, 62.0, 62.1, 71.1, 84.3, 97.7, 127.8, 128.4 (×2), 128.6 (×2), 129.3, 129.7, 129.9, 130.1, 133.5, 133.8, 134.8, 165.2 (×2), 167.6; HRMS (ESI): calcd for $C_{27}H_{25}NO_7$ $(M+H)^+$: 476.1709, found: 476.1690; calcd for $C_{27}H_{25}NO_7$ $(M+Na)^+$: 498.1529, found: 498.1507.

### 4.7. Typical experimental procedure for the benzoylation of 4-bromoisoxazolidin-5-ols

*4.7.1. (±)-2-Benzyl-4-bromo-3-phenylisoxazolidin-5-yl benzoate (**18a**, **b**).* 4-Bromoisoxazolidin-5-ols **3c**, **d** (440 mg, 1.32 mmol) were dissolved in anhydrous $CH_2Cl_2$ (5 mL), pyridine (0.21 mL, 2.60 mmol) and DMAP (30 mg, 0.25 mmol) were added followed by benzoyl chloride (0.23 mL, 1.98 mmol). The reaction mixture was stirred at room temperature 24 h. When no starting isoxazolidin-5-ols had been detected by TLC (hexanes/ethyl acetate 80:20), the mixture was diluted with water (10 mL) and extracted with $CH_2Cl_2$ (10 mL) two times. Combined organic layers were dried over $Na_2SO_4$ and the solvent was evaporated in vacuo. Products were isolated by flash column chromatography (hexanes/ethyl acetate 95:5) to provide two single isoxazolidines 4,5-*cis*-**18a** (220 mg, 0.50 mmol, 39%) and 4,5-*trans*-**18b** (300 mg, 0.68 mmol, 51%) as colourless solids. **18a**, mp 117–118 °C; IR (thin film): 3032, 1712, 1452, 1261, 1064, 1039, 1014, 754, 713, 697 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=3.96 (d, 1H, $J$=14.8 Hz), 4.25 (d, 1H, $J$=8.3 Hz), 4.27 (d, 1H, $J$=14.9 Hz), 4.98 (dd, 1H, $J$=8.3, 5.4 Hz), 6.75 (d, 1H, $J$=5.4 Hz), 7.18–7.64 (m, 13H), 8.10–8.17 (m, 2H); $^{13}C$ NMR (75.4 MHz, $CDCl_3$): $\delta$=55.0, 60.0, 71.3, 93.7, 127.6, 128.3, 128.4, 128.6, 128.7, 129.1, 129.5, 129.7, 130.3, 133.6, 135.9, 136.2, 165.4; HRMS (ESI): calcd for $C_{23}H_{20}Br^{79}NO_3$ $(M+H)^+$: 438.0705, found: 438.0693; calcd for $C_{23}H_{20}Br^{79}NO_3$ $(M+Na)^+$: 460.0524, found: 460.0513; **18b**, mp 129–131 °C; IR (thin film): 3008, 1719, 1450, 1237, 1058, 917, 742, 708, 694, 671 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=4.06 (d, 1H, $J$=14.3 Hz), 4.36 (d, 1H, $J$=14.3 Hz), 4.58 (d, 1H, $J$=4.2 Hz), 4.68 (d, 1H, $J$=4.3 Hz), 6.71 (s, 1H), 7.13–7.72 (m, 12H), 7.90–7.97 (m, 2H), 8.12–8.20 (m, 1H); $^{13}C$ NMR (75.4 MHz, $CDCl_3$): $\delta$=57.8, 61.4, 68.6, 101.1, 127.5, 128.2, 128.4, 128.5 (×2), 128.7, 128.8, 129.1, 129.7, 129.8, 130.5, 133.6, 133.8, 134.5, 135.4, 164.5; HRMS (ESI): calcd for $C_{23}H_{20}Br^{79}NO_3$ $(M+H)^+$: 438.0705, found: 438.0693.

*4.7.2. (±)-2-Benzyl-4-bromo-3-phenylisoxazolidin-5-yl benzoate (**17b**).* Yield 70% (405 mg, 0.92 mmol) after flash column chromatography (hexanes/ethyl acetate 90:10), colourless solid, mp 117–119 °C; IR (thin film): 3032, 1735, 1452, 1246, 1239, 1047, 1021, 954, 754, 696 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=3.92 (d, 1H, $J$=15.0 Hz), 4.12 (s, 1H), 4.12 (d, 1H, $J$=16.0 Hz), 4.51 (dd, 1H, $J$=7.9, 2.1 Hz), 6.64 (d, 1H, $J$=2.0 Hz), 7.15–7.63 (m, 13H), 8.05–8.12 (m, 2H); $^{13}C$ NMR (75.4 MHz, $CDCl_3$): $\delta$=58.4, 59.6, 79.5, 101.4, 127.7, 128.3, 128.5, 128.8, 129.0, 129.4, 129.7, 130.3, 133.8, 134.8, 136.3, 165.7; HRMS (ESI): calcd for $C_{23}H_{20}Br^{79}NO_3$ $(M+H)^+$: 438.0705, found: 438.0692; calcd for $C_{23}H_{20}Br^{79}NO_3$ $(M+Na)^+$: 460.0524, found: 460.0511.

### 4.8. Typical experimental procedure for $S_N$-reaction of isoxazolidinyl-4,5-dibenzoates with TMSCN

*4.8.1. (±)-2-Benzyl-5-cyano-3-phenylisoxazolidin-4-yl benzoate (**19a**, **b**).* The reaction flask was charged with isoxazolidinyl-4,5-dibenzoates **14a**, **b** (340 mg, 0.71 mmol), sealed with a rubber

septum and filled with argon. Anhydrous $CH_2Cl_2$ was added (1.4 mL) followed by TMSCN (115 μL, 0.85 mmol). The solution was cooled to 0 °C with ice-bath, TMSOTf (130 μL, 0.71 mmol) was added and the stirring was continued at this temperature until no starting material was detected (3 h, TLC, hexanes/$CH_2Cl_2$ 33:67). Afterwards, the reaction was quenched with satd aqueous $NaHCO_3$ (5 mL). Subsequently, the mixture was diluted with water (5 mL) and repeatedly extracted with $CH_2Cl_2$ (2×5 mL). Combined organic layers were washed with water (10 mL), dried with $Na_2SO_4$ and the solvent was evaporated in vacuo. Products were isolated by flash column chromatography (hexanes/diethyl ether 85:15) to give the isoxazolidines **19a**, **b** as a mixture of two non-separable isomers 3,4-*trans*-4,5-*cis*-**19a** and 3,4-*trans*-4,5-*trans*-**19b** (205 mg, 0.53 mmol, 74%, **19a**/**19b** ratio 20:80) as a colourless solid. $^1$H NMR data of the major diastereomer **19b** were extracted from the corresponding mixture. **19b**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=3.90 (d, 1H, $J$=15.2 Hz), 4.02 (d, 1H, $J$=5.3 Hz), 4.18 (d, 1H, $J$=15.2 Hz), 4.80 (d, 1H, $J$=1.8 Hz), 5.65 (dd, 1H, $J$=5.3, 1.8 Hz), 7.27–7.65 (m, 13H, Ph), 8.01–8.05 (m, 2H, Ph); $^{13}$C NMR (75.4 Hz, $CDCl_3$): $\delta$=58.7, 70.7, 75.3, 88.1, 116.6, 127.5, 128.2 (×2), 128.3, 128.4, 128.6, 129.2, 129.3, 129.9, 134.0, 134.6, 135.8, 165.7; Partial $^1$H NMR data extracted from the mixture of **19a**, **b** for the minor **19a**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=4.31 (d, 1H, $J$=5.1 Hz, H-3); 5.16 (d, 1H, $J$=6.6 Hz, H-5); 5.75 (dd, 1H, $J$=6.1, 5.1 Hz, H-4); $^{13}$C NMR data are not presented because **19a** was minor and $^{13}$C peaks were ambiguous; MS (ESI+APCI): $m/z$ for $C_{24}H_{20}N_2O_3$ $(M+H)^+$: 385.0.

*4.8.2. (±)-2-Benzyl-5-cyano-3-isopropylisoxazolidin-4-yl benzoate (**20a**, **b**).* The mixture of two non-separable isomers 3,4-*trans*,4,5-*cis*-**20a** and 3,4-*trans*, 4,5-*trans*-**20b** (**20a**/**20b** ratio 10:90), yield 78% (220 mg, 0.63 mmol) after flash column chromatography (hexanes/diethyl ether 90:10), colourless solid. $^1$H NMR data of the major diastereomer **20b** were extracted from the corresponding mixture. **20b**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=1.04 (d, 3H, $J$=7.0 Hz), 1.13 (d, 3H, $J$=7.0 Hz), 1.99–2.09 (m, 1H), 3.06 (t, 1H, $J$=4.8 Hz), 4.00 (d, 1H, $J$=14.7 Hz), 4.27 (d, 1H, $J$=14.7 Hz), 4.70 (d, 1H, $J$=1.5 Hz), 5.64 (dd, 1H, $J$=4.8, 1.5 Hz), 7.28–8.05 (m, 10H); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$=17.1, 19.9, 27.5, 60.0, 70.6, 75.3, 81.9, 116.2, 127.5, 128.2, 128.4, 128.5, 128.7, 129.8, 134.0, 136.2, 165.7; Partial $^1$H NMR data extracted from the mixture of **20a**, **b** for the minor **20a**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=3.22 (dd, 1H, $J$=6.6, 2.9 Hz, H-3), 5.02 (d, 1H, $J$=7.0 Hz, H-5), 5.79 (dd, 1H, $J$=7.0, 2.9 Hz, H-4); $^{13}$C NMR data are not presented because **20a** was very minor; MS (ESI+APCI): $m/z$ for $C_{21}H_{22}N_2O_3$ $(M+H)^+$: 351.2.

*4.8.3. (±)-Ethyl 4-(benzoyloxy)-2-benzyl-5-cyanoisoxazolidine-3-carboxylate (**21a**, **b**).* Reaction flask was charged with isoxazolidinyl-4,5-dibenzoates **16a**, **b** (200 mg, 0.44 mmol), sealed with a rubber septum and filled with argon. Anhydrous acetonitrile was added (4.5 mL) followed by TMSCN (180 μL, 1.32 mmol). The solution was cooled to 0 °C with ice-bath, TMSOTf (80 μL, 0.44 mmol) was added, the mixture was allowed to warm to room temperature and the stirring was continued at this temperature 24 h. Progress of the reaction was monitored by TLC ($CH_2Cl_2$). Afterwards, the mixture was cooled to 0 °C with ice-bath and the reaction was quenched with satd aqueous $NaHCO_3$ (5 mL). Subsequently, the mixture was diluted with water (5 mL) and the solvent was partially evaporated under reduced pressure. The residue was repeatedly extracted with $CH_2Cl_2$ (2×5 mL). Combined organic layers were washed with water (10 mL), dried with $Na_2SO_4$ and the solvent was evaporated in vacuo. Products were isolated by flash column chromatography (hexanes/ethyl acetate 80:20) to give the isoxazolidines **21a**, **b** as a mixture of two non-separable isomers 3,4-*trans*, 4,5-*cis*-**21a** and 3,4-*trans*, 4,5-*trans*-**21b** (135 mg, 0.36 mmol, 83%, **21a**/**21b** ratio 10:90) as a pale yellow sticky oil. $^1$H NMR data of the major diastereomer **21b** were extracted from the corresponding mixture. **21b**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=1.31 (t, 3H, $J$=7.0 Hz), 3.73 (d, 1H, $J$=4.2 Hz), 4.18 (d, 1H, $J$=14.6 Hz), 4.22–4.30 (m, 2H), 4.47 (d, 1H, $J$=14.6 Hz), 4.84 (d, 1H, $J$=1.4 Hz), 6.06 (dd, 1H, $J$=4.2, 1.4 Hz), 7.30–7.65 (m, 8H), 7.98–8.01 (m, 2H); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$=14.0, 60.7, 62.5, 70.3, 72.1, 83.6, 115.4, 127.9, 128.0, 128.4, 128.7, 128.9, 129.9, 134.1, 134.8, 165.5, 166.5; Partial $^1$H NMR data extracted from the mixture of **21a**, **b** for the minor **21a**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=4.02 (d, 1H, $J$=2.8 Hz, H-3), 5.18 (d, 1H, $J$=6.4 Hz, H-5), 6.10 (dd, 1H, $J$=6.4, 2.8 Hz, H-4); $^{13}$C NMR data are not presented because **20a** was very minor; MS (ESI+APCI): $m/z$ for $C_{21}H_{20}N_2O_5$ $(M+H)^+$: 381.0.

### 4.9. Typical experimental procedure for $S_N$-reaction of 4-bromoisoxazolidin-5-ols with TMSCN

*4.9.1. (±)-2-Benzyl-4-bromo-3-phenylisoxazolidine-5-carbonitrile (**23**).* Reaction flask was charged with 4-bromoisoxazolidinyl-5-benzoates **18a**, **b** (200 mg, 0.46 mmol), sealed with a rubber septum and filled with argon. Anhydrous acetonitrile was added (0.90 mL) followed by TMSCN (75 μL, 0.55 mmol). The solution was cooled to −20 °C. TMSOTf (85 μL, 0.46 mmol) was added and the mixture was stirred at this temperature for 1 h until no starting material was detected (TLC, hexanes/$CH_2Cl_2$ 50:50). Afterwards, the reaction was quenched with satd aqueous $NaHCO_3$ (5 mL). Subsequently, the mixture was diluted with water (5 mL) and repeatedly extracted with $CH_2Cl_2$ (2×5 mL). Combined organic layers were washed with water (10 mL), dried with $Na_2SO_4$ and the solvent was evaporated in vacuo. Product was isolated by flash column chromatography (hexanes/$CH_2Cl_2$ 50:50) to give exclusively single 3,4-*cis*, 4,5-*trans*-isoxazolidine **23** (130 mg, 0.38 mmol, 82%) as a colourless sticky oil. IR (thin film): 3030, 1495, 1454, 1293, 1070, 1028, 996, 754, 697, 518 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=3.91 (d, 1H, $J$=14.5 Hz), 4.16 (d, 1H, $J$=14.5 Hz), 4.30 (d, 1H, $J$=6.5 Hz), 4.87 (dd, 1H, $J$=6.5, 4.7 Hz), 4.94 (d, 1H, $J$=4.7 Hz), 7.29–7.46 (m, 10H); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$=55.2, 60.4, 72.7, 72.9, 115.7, 128.0, 128.6, 128.7, 129.1, 129.2, 129.3, 134.1, 135.7; HRMS (ESI): calcd for $C_{17}H_{15}Br^{79}N_2O$ $(M+H)^+$: 343.0446, found: 343.0431; calcd for $C_{17}H_{15}Br^{79}N_2O$ $(M+Na)^+$: 365.0265, found: 365.0250.

*4.9.2. (±)-2-Benzyl-4-bromo-3-phenylisoxazolidine-5-carbonitrile (**22a**, **b**).* Reaction was performed in anhydrous $CH_2Cl_2$ at 0 °C for 1 h according to the procedure described above. The products were isolated by flash column chromatography (hexanes/$CH_2Cl_2$ 50:50) to give pure isomers 4,5-*cis*-**22a** (90 mg, 0.26 mmol, 56%) and 4,5-*trans*-**22b** (40 mg, 0.12 mmol, 26%). **22a**, colourless solid, mp 108–109 °C; IR (thin film): 2985, 1493, 1451, 1190, 1003, 975, 763, 746, 725, 694 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=4.00 (d, 1H, $J$=14.2 Hz), 4.07 (d, 1H, $J$=14.2 Hz), 4.19 (d, 1H, $J$=8.7 Hz), 4.43 (dd, 1H, $J$=8.7, 7.1 Hz), 5.10 (d, 1H, $J$=7.1 Hz), 7.26–7.49 (m, 10H); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$=51.6, 61.0, 70.4, 77.8, 115.2, 128.0 (×2), 128.5, 129.1, 129.3, 129.6, 133.8, 135.9; HRMS (ESI): calcd for $C_{17}H_{15}Br^{79}N_2O$ $(M+H)^+$: 343.0446, found: 343.0434; calcd for $C_{17}H_{15}Br^{79}N_2O$ $(M+Na)^+$: 365.0265, found: 365.0255; **22b**, colourless solid; mp 72–75 °C; IR (thin film): 3035, 1495, 1455, 1188, 1051, 971, 758, 746, 696, 527 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=3.84 (d, 1H, $J$=15.0 Hz), 4.01 (d, 1H, $J$=7.0 Hz), 4.10 (d, 1H, $J$=15.0 Hz), 4.56 (dd, 1H, $J$=7.0, 2.8 Hz), 4.90 (d, 1H, $J$=2.8 Hz), 7.24–7.55 (m, 10H); $^{13}$C NMR (75.4 MHz, $CDCl_3$): $\delta$=56.3, 58.8, 72.8, 79.9, 117.0, 127.8, 128.1, 128.4, 128.5, 129.5, 129.6, 133.8, 135.7; HRMS (ESI): calcd for $C_{17}H_{15}Br^{79}N_2O$ $(M+H)^+$: 343.0446, found: 343.0437.

### 4.10. Crystallography

Data collection and cell refinement were carried out using a κ-axis diffractometer Kuma KM4 CCD at 293 K with graphite monochromated Mo Kα radiation for both compounds. The diffraction intensities were corrected for Lorentz and polarization factors. The

structures were solved by direct methods using SIR-2011[12] (**17b**) or charge flipping method using SUPERFLIP[13] (**18a**) and refined by the full-matrix least-squares procedure with SHELXL-2014.[14] Geometrical analyses were performed with SHELXL-2014. Absolute configuration of **18a** has been confirmed using Flack[15] ($x$=−0.013(6)) and Hooft[16] ($y$=−0.006(2)) parameters, and the chirality of carbon atoms has been confirmed using PLATON program[17] for C1(S), C2(R) and C3(S). The structures were drawn with OLEX2 package.[18] Crystal data and conditions of data collection and refinement are reported in Table 5.

**Table 5**
Crystallographic data for compounds **17b** and **18a**

| | **17b** | **18a** |
|---|---|---|
| Chemical formula | $C_{23}H_{20}BrNO_3$ | $C_{23}H_{20}BrNO_3$ |
| $M_r$ | 438.31 | 438.31 |
| Cell setting, space group | Triclinic, *P*-1 | Orthorhombic, $Pna2_1$ |
| $T$ (K) | 293 | 293 |
| $A$ (Å) | 9.2238(4) | 11.6470(3) |
| $B$ (Å) | 10.4662(4) | 22.3036(5) |
| $C$ (Å) | 11.4729(5) | 7.3826(1) |
| $\alpha$ (°) | 76.889(3) | 90 |
| $\beta$ (°) | 86.778(3) | 90 |
| $\gamma$ (°) | 70.195(4) | 90 |
| $V$ (Å$^3$) | 1014.64(8) | 1917.78(7) |
| $Z$ | 2 | 4 |
| Radiation type | Mo Kα | Mo Kα |
| $\mu$ (mm$^{-1}$) | 2.049 | 2.168 |
| Crystal size (mm) | 0.59×0.37×0.26 | 0.37×0.34×0.23 |
| Diffractometer | Kuma KM4 CCD | Kuma KM4 CCD |
| Abs correction | CrysAlisPro | CrysAlisPro |
| $T_{min}$, $T_{max}$ | 0.512, 0.728 | 0.495, 0.761 |
| $S$ | 1.036 | 1.058 |
| $R_1$ [$F^2>2\sigma(F^2)$], $wR_2(F^2)$ | 0.0399, 0.1142 | 0.0247, 0.0630 |
| Data/restrains/parameters | 4132/0/253 | 3922/1/253 |

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