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Reactivity difference between diphosgene and phosgene in reaction with (2,3-*anti*)-3-amino-1,2-diols

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Abstract—In reactions of (2,3-*anti*)-3-amino-1,2-diols with diphosgene and phosgene and their conversion into 1,3-oxazolidin-2-ones, some differences in the stereochemistry of the reactions have been found with these two reagents. The reactions with phosgene afforded the expected *cis*-oxazolidinones, and in the reaction with diphosgene under the same reaction conditions, the *trans*-oxazolidinones were also obtained.

1. Introduction

The synthesis of chiral 4,5-disubstituted 1,3-oxazolidin-2-ones has received special attention, because these structural units are present in molecules with pharmaceutical interest such as cytoxazone[1] and they are also useful chiral auxiliaries for asymmetric synthesis.[2]

Different methods described in the literature for the preparation of 1,3-oxazolidin-2-ones use *N*-Boc derivatives of 1,2-amino alcohols as starting materials. The reaction with sodium hydride,[3] for example, affords oxazolidin-2-ones without changes in the configuration of the carbon supporting the hydroxyl group. By contrast, the conversion of the alcohol function into a good leaving group, reaction with methanesulfonyl chloride[4] or reaction with triphenylphosphine-DEAD,[5] affords the cyclisation products with inverted configuration.

There are recent reports in the literature related with synthesis of 1,3-oxazolidin-2-ones from *N*-acylamino alcohols with unexpected stereochemical results. One example is the reaction of *N*-Boc amino alcohols with mesyl chloride, which not only gave oxazolidinones with inversion of the configuration as expected, but also gave some oxazolidinones with retention of configuration due to competition between S_N1 and S_N2 mechanisms.[6] Other exception with unexpected stereochemical results is the carboxylation of 1,2-amino alcohols followed by Mitsunobo reaction. The reaction is reported[7] to be substituent dependent affording oxazolidinones with retention, when the N atom is substituted with hydrogen, or inversion when it is substituted with carbon. Other examples of retention of configuration in intramolecular versions of Mitsunobo reaction are attributed to steric congestion at the hydroxyl reaction centre.[8]

1,3-Oxazolidin-2-ones can also be prepared from 1,2-amino alcohols as starting materials using reagents such as phosgene,[9] diphosgene (trichloromethyl chloroformate),[10] carbonyl diimidazol,[11] etc. In all these reactions, the configuration of the stereocentres of the starting amino alcohols is retained in the oxazolidinone. The formation of these cyclic carbamates is a procedure used to establish the configuration of the stereocentres of 1,2-amino alcohols,[12] because the stereochemical assignment is easier in the cyclic derivatives.

As a part of our current interest in the reactivity of amino alcohols,[13–17] we have studied in this work the reaction of different compounds containing the 1,2-amino alcohol unit with diphosgene and phosgene and we have found some exceptions to the general rule that establish that the reaction of 1,2-amino alcohols with both reagents affords the same stereochemical results and proceeds with retention of configuration. These exceptions have been found working with some compounds containing the (2,3-*anti*)-3-amino-1,2-diol moiety.

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2. Results and discussion

In the course of a work on reactivity of polyfunctionalized molecules, we studied the reaction of 3-amino-1,2-diol **1a**[18] with diphosgene and triethylamine. The result was similar to the same reaction reported in the literature[19] for other aminodiols and *cis*-oxazolidinone **2a** (70%) was obtained. The reaction of **1a** with phosgene afforded a similar result with the formation of **2a** (75%) (Scheme 1) (Table 1, entry 1).

When similar reactions were attempted with 3-amino-1,2-diol **1b**,[13] different stereochemical results were observed with these two reagents. In the reaction of aminodiol **1b** with diphosgene, the *trans*-oxazolidinone **3b**[17] (45%) was obtained, along with the cis isomer **2b** (16%) and a small amount of the six-membered oxazinone **4b**[17] (8%). However, when aminodiol (**1b**) reacted with phosgene, instead of diphosgene, *cis*-oxazolidinone **2b** (70%) was obtained, with no traces of the *trans*-oxazolidinone (Table 1, entry 2).

Other examples of inversion on the oxygen-bearing centre were observed in the reactions of the *N*-carbon substituted 3-amino-1,2-diols **1c**[13] and **1d**.[21] In the reaction of aminodiol (**1c**) with diphosgene in triethylamine, *trans*-oxazolidinone (**3c**) was obtained as major product (30%), along with *cis*-oxazolidinone **2c** (16%) and a small amount of oxazinone **4c** (12%) (Table 1, entry 3). In the reaction aminodiol (**1d**) with diphosgene in triethylamine, *trans*-oxazolidinone **3d** (18%) was obtained along with oxazinone **4d** (11%) and carbonate **5d** (40%) (Table 1, entry 4).

In contrast with the reaction of aminodiols **1c** and **1d** with diphosgene, in the reaction with phosgene, the exceptional inversion was not observed. The reaction of **1c** with phosgene afforded cis isomer **2c** (20%) and carbonate **6c** (46%) as a major product (Table 1, entry 3) and in the reaction of **1d** with phosgene only carbonate **5d** (70%) was obtained (Table 1, entry 4). The isolation of carbonate **6c** as a carbamoyl chloride derivative was probably due to the presence of an excess of phosgene in these experiments.[20]

This trend in the formation of the carbonate with increasing steric hindrance on the *N*-substituent was observed for aminodiol **1e**.[21] In this case with both reagents, diphosgene and phosgene, carbonate **5e** was the only isolated product from the reactions (Table 1, entry 5).

The reactions of the 1,2-amino alcohols, (1*R*,2*S*)-(−)-norephedrine and (1*R*,2*S*)-(−)-ephedrine, molecules without the primary hydroxyl group of our previous examples were also studied. The reaction with diphosgene in triethylamine afforded, in both cases, the corresponding *cis*-oxazolidinones reported in the literature,[22] without stereochemical inversion in the oxygen-bearing centres. This result induced us to think that the presence of a vicinal primary hydroxyl group was necessary for the unexpected stereochemical inversions observed in the cases of **1b–d**. The hypothesis of the necessary presence of the vicinal primary hydroxyl group was confirmed when we studied the reaction of the partially protected aminodiols **1f**, **1g**[23] and **1h** with diphosgene in triethylamine. Here again there was not observed any inversion on the oxygen-bearing centre and *cis*-oxazolidinones **2f** (80%), **2g** (73%) and **2h** (71%) were obtained, respectively.

Table 1. Reaction of aminodiols **1a–e** with diphosgene and phosgene

Entry	Starting material	Diphosgene/Et_3N	Phosgene/Et_3N
1	**1a**	**2a** (70%)	**2a** (75%)
2	**1b**	**2b** (16%)+**3b** (45%)+**4b** (8%)	**2b** (70%)
3	**1c**	**2c** (16%)+**3c** (30%)+**4c** (12%)	**2c** (20%)+**6c** (46%)
4	**1d**	**3d** (18%)+**4d** (11%)+**5d** (40%)	**5d** (70%)
5	**1e**	**5e** (96%)	**5e** (97%)

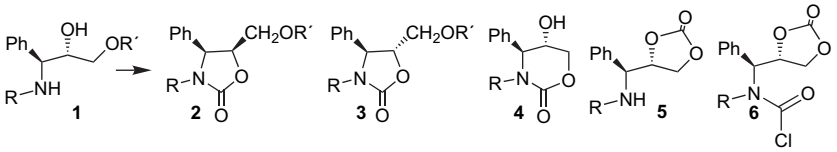
The proposed mechanism (Scheme 2) accounts for the stereochemical differences in the reaction of (2,3-*anti*)-3-amino-1,2-diols (**1b–d**) with diphosgene and the formation of *trans*-oxazolidinones (**3**) and *cis*-oxazolidinones **2**, through the intermediates (**7–11**).

After the initial attack of the amino group of 3-amino-1,2-diol (**1**) to diphosgene and formation of carbamate (**7**), an intramolecular attack of the secondary hydroxyl group (path 1) to the carbamate with the elimination of phosgene would explain the formation of *cis*-oxazolidinones (**2**).

For the formation of *trans*-oxazolidinones (**3**), we suggest an initial acid–base equilibrium (path 2) between **7** and **8** in the presence of Et_3N. The transfer of the trichloromethyl group from the carbamate to the primary alcoxide function would afford intermediate (**9**), which could be converted into epoxide (**10**) by attack of the secondary hydroxyl group and extrusion of phosgene. The intramolecular attack of the carbamate to the epoxide at C2 would afford the corresponding alcoxide (**11**) with inverted configuration at C2, whose protonated species are *trans*-oxazolidinones (**3**).

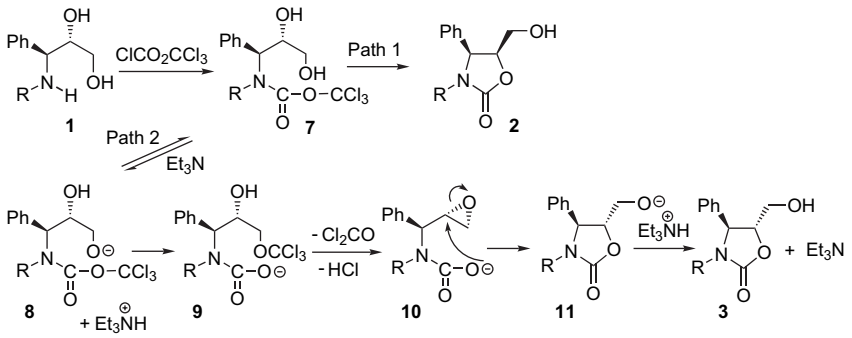
The formation of oxazinones (**4**), in experiments where *trans*-oxazolidinones (**3**) were isolated, could be explained through intermediate (**10**), by an intramolecular attack of the carbamate to the epoxide at C1. This fact would be an additional support to the proposed mechanism for the reaction of 3-amino-1,2-diols with diphosgene.

The use of diphosgene and the presence of a primary hydroxy group are essential conditions for the observed



a R=H, R´=H; **b** R=CH_3, R´=H; **c** R=Et, R´=H; **d** R=CH_2Ph, R´=H; **e** R=Ph_2CH, R´=H; **f** R=H, R´=TBDMS; **g** R=CH_3, R´=TBDMS; **h** R=Ph_2CH, R´=TBDMS

Scheme 1.



Scheme 2.

inversion to take place, according to the mechanism. The amino substitution looks not necessary. The fact that the presence of oxazolidinone **3a** (path 2) could not be detected in the reaction of **1a** (R=H) with diphosgene, can be due to the low concentration of this product as a result of a more favourable process through path 1 in relation with path 2, or the existence of a competitive mechanism through an isocyanate.[7]

3. Conclusion

In conclusion, we have presented for the first time examples with different stereochemical behaviour in reactions between diphosgene and phosgene with (2,3-*anti*)-3-amino-1,2-diols affording 1,3-oxazolidin-2-ones. These results must be considered when the configuration of stereocentres in oxazolidinones had to be established in relation with the stereochemistry of the starting amino alcohols.

4. Experimental

4.1. General

Unless otherwise specified, materials were purchased from commercial suppliers and used without further purification. Solvents were distilled prior to use. Thin-layer chromatography was performed on Merck 60F254 sheets. Preparative column chromatography was performed on Merck Kieselgel 60 (230–240 mesh) silica gel. IR spectra were recorded on a FTIR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with an Avance DPX Bruker 500 MHz or an Avance 400 MHz Bruker or an Avance DRX Bruker 300 MHz spectrometers, in $CDCl_3$ solutions. Chemical shifts were recorded in parts per million (ppm), downfield from internal Me_4Si. The carbon multiplicity was determined by edited HSQC and DEPT experiments. High-resolution mass spectral data were obtained on a VG Autospec, TRIO 1000 (Fisons) instrument. FAB or EI at 70 eV was used as ionisation mode in mass spectra.

The structure of all the compounds and their stereochemistry was determined spectroscopically and by comparison with the data of compounds of similar structure reported in the literature. Every ^{1}H and ^{13}C NMR signals have been assigned by single and multiple bond ^{1}H–^{13}C and ^{1}H–^{1}H NMR correlations. When required, 1D and 2D NOESY experiments were performed in order to determine relative configurations.

4.2. Preparation of the starting materials 1f, 1g and 1h

A solution of the corresponding aminodiol **1a**,[18] **1b**[13] or **1e**[21] (6.0 mmol), *tert*-butyldimethylsilyl chloride (0.9 g, 6.5 mmol), imidazole (1.0 g, 14.9 mmol) in dichloromethane (12 mL) was stirred at room temperature for 24 h. The reaction mixture was washed with water, dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography on silica gel eluting with hexane/ethyl acetate (1:1) to afford compounds **1f**, **1g**[23] and **1h**, respectively. In the reaction with aminodiol (**1a**) in the addition of compound **1f**, the disilylated product was also obtained.

4.2.1. 3-(*tert*-Butyldimethylsilyloxy)-1-amino-1-phenylpropan-2-ol (1f). Yield 30% (28% of the disilyl derivative was also isolated from the reaction mixture). Colourless oil. IR (KBr): ν_{max} 3370, 2928, 2857, 1254, 1114 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 6H), 0.91 (s, 9H), 3.70 (m, 2H), 3.96 (m, 1H), 4.28 (d, 1H, J=5.5 Hz), 7.25 (m, 5H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −4.7 (q), −4.2 (q), 18.2 (s), 25.9 (q), 58.1 (d), 64.3 (t), 75.0 (d), 127.2 (d), 127.6 (d), 128.6 (d), 142.7 (s). HRMS (MH^+) 282.1907. Calculated for $C_{15}H_{28}NO_2Si$ 282.1889.

4.2.2. 3-(*tert*-Butyldimethylsilyloxy)-1-benzhydrylamino-1-phenylpropan-2-ol (1h). Yield 90%. White solid. Mp 80–81 °C. IR (KBr): ν_{max} 3478, 2928, 2857, 1255, 1100 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.31 (br s, 1H), 3.47 (dd, 1H, J=10.5, 5.0 Hz); 3.61 (dd, 1H, J=10.5, 3.5 Hz); 3.77 (br s, 1H), 3.83 (d, 1H, J=6.0 Hz), 7.33 (m, 15H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −5.4 (q), −5.3 (q), 18.3 (s), 26.0 (q), 62.8 (d), 63.7 (d), 64.9 (t), 73.9 (d), 127.3 (d), 127.4 (d), 127.5 (d), 127.6 (d), 128.0 (d), 128.1 (d), 128.4 (d), 128.6 (d), 128.7 (d), 140.2 (s), 143.9 (s), 144.2 (s); HRFAB *m/z* calcd for $[M+1]^+$ $C_{28}H_{38}NO_2Si$ 448.2671, found: 448.2680.

4.3. General procedure for the reactions of amino alcohols (1) with diphosgene or phosgene[19]

Trichloromethyl chloroformate (0.17 mL, 1.4 mmol) in CH_2Cl_2 (0.15 mL) or a solution of phosgene in toluene (0.87 mL, 8.28 mmol) was slowly added to the corresponding aminodiol **1a–h** (2.76 mmol) in CH_2Cl_2/Et_3N (1:1) mixture (35 mL) at −20 °C. After stirring for 3 h, the reaction mixture was quenched by the addition of H_2O (15 mL). After decantation and CH_2Cl_2 extraction (3×25 mL), the combined organic layers were washed with brine, dried

(Na_2SO_4) and concentrated to dryness. The complex mixtures were purified by silica gel column chromatography using hexane/EtOAc mixtures as eluent.

4.3.1. From 3-amino-3-phenyl-1,2-propanediol[18] (1a). The reaction with diphosgene afforded 1,3-oxazolidin-2-one (**2a**) (70%); the reaction with phosgene 1,3-oxazolidin-2-one (**2a**) (75%).

4.3.1.1. *cis*-5-Hydroxymethyl-4-phenyl-1,3-oxazolidin-2-one (2a). Colourless oil. IR (KBr): ν_{max} 3336, 1745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.17 (dd, 1H, J=12.5, 4.0 Hz, CH_2–O), 3.31 (dd, 1H, J=12.5, 4.0 Hz, CH_2–O), 4.87 (td, 1H, J=8.5, 4.0 Hz, *H*-5), 5.03 (d, 1H, J=8.5 Hz, *H*-4), 6.31(br s, N*H*), 7.26 (m, 2H), 7.36 (m, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 57.8 (d), 62.0 (t), 80.8 (d), 127.4 (d), 128.9 (d), 129.0 (d), 135.9 (s), 159.9 (s); HREI-MS *m/z* calcd for $[M]^+$ $C_{10}H_{11}NO_3$ 193.0738, found: 193.0719.

4.3.2. From 3-methylamino-3-phenyl-1,2-propanediol[13] (1b). The reaction with diphosgene afforded a mixture of *cis*-1,3-oxazolidin-2-one (**2b**) (16%), *trans*-1,3-oxazolidin-2-one[17] (**3b**) (45%) and tetrahydro-1,3-oxazin-2-one[17] (**4b**) (8%); the reaction with phosgene afforded *cis*-oxazolidinone (**2b**) (70%).

4.3.2.1. *cis*-5-Hydroxymethyl-3-methyl-4-phenyl-1,3-oxazolidin-2-one (2b). White solid. Mp 69–70 °C. IR: ν_{max} 3502, 1744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.77 (s, 3H), 3.18 (dd, 1H, J=12.0, 3.0 Hz, CH_2–O), 3.32 (m, 1H, CH_2–O), 4.82 (m, 2H, *H*-4+*H*-5), 7.17 (m, 2H), 7.39 (m, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 29.6 (q), 62.1 (t), 63.4 (d), 77.8 (d), 127.6 (d), 129.1 (d), 129.4 (d), 133.6 (s), 158.6 (s); HREI-MS *m/z* calcd for $[M]^+$ $C_{11}H_{13}NO_3$ 207.0853, found: 207.0895.

4.3.3. From 3-ethylamino-3-phenyl-1,2-propanediol[13] (1c). The reaction with diphosgene afforded a mixture of *cis*-1,3-oxazolidin-2-one (**2c**) (16%), *trans*-1,3-oxazolidin-2-one (**3c**) (30%) and tetrahydro-1,3-oxazin-2-one (**4c**) (12%); the reaction with phosgene afforded 1,3-oxazolidin-2-one (**2c**) (20%) and carbamoyl chloride **6c** (46%).

4.3.3.1. *cis*-5-Hydroxymethyl-3-ethyl-4-phenyl-1,3-oxazolidin-2-one (2c). Colourless oil. IR (KBr): ν_{max} 3430, 1742 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.19 (t, 3H, J=7.0 Hz), 2.75 (dq, 1H, J=14.0, 7.0 Hz, CH_2–N), 3.10 (dd, 1H, J=12.5, 4.5 Hz, CH_2–O), 3.10 (dd, 1H, J=12.5, 8.0 Hz, CH_2–O), 3.53 (dq, 1H, J=14.0, 7.0 Hz, CH_2–N), 4.76 (m, 1H, *H*-5), 4.84 (d, 1H, J=8.5, *H*-4), 7.05 (m, 2H), 7.40 (m, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 12.7 (q), 37.3 (t), 60.8 (d), 62.5 (t), 78.1 (d), 127.8 (d), 129.3 (d), 129.5 (d), 133.9 (s), 158.1 (s); HREI-MS *m/z* calcd for $[M]^+$ $C_{12}H_{15}NO_3$ 221.1051, found: 221.1040.

4.3.3.2. *trans*-5-Hydroxymethyl-3-ethyl-4-phenyl-1,3-oxazolidin-2-one (3c). Colourless oil. IR (KBr): ν_{max} 3419, 1740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.09 (t, 3H, J=7.0 Hz), 2.61 (br s, 1H, O*H*), 2.89 (dq, 1H, J=14.0, 7.0 Hz, CH_2–N), 3.52 (dq, 1H, J=14.0, 7.0 Hz, CH_2–N), 3.70 (dd, 1H, J=13.0 and 3.5 Hz, CH_2–O), 3.97 (dd, 1H, J=13.0, 3.0 Hz, CH_2–O), 4.34 (ddd, 1H, J=7.0, 3.5, 3.0 Hz, *H*-5), 4.76 (d, 1H, J=7.0 Hz, *H*-4), 7.34 (m, 2H), 7.42 (m, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 12.4 (q), 37.4 (t), 60.7 (d), 61.9 (t), 82.3 (d), 127.3 (d), 129.3 (d), 129.6 (d), 138.0 (s), 157.9 (s). HREI-MS *m/z* calcd for $[M]^+$ $C_{12}H_{15}NO_3$ 221.1051, found: 221.1033.

4.3.3.3. 5-Hydroxy-3-ethyl-4-phenyltetrahydro-1,3-oxazin-2-one (4c). White solid. Mp 132–133 °C. IR (KBr): ν_{max} 3380, 3272, 1672 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.17 (t, 3H, J=7.0 Hz), 2.87 (dq, 1H, J=14.0, 7.0 Hz, CH_2–N), 3.77 (dq, 1H, J=14.0, 7.0 Hz, CH_2–N), 4.02 (d, 1H, J=2.0 Hz, *H*-5), 4.15 (dt, 1H, J=12.0, 2.0 Hz, *H*-6eq), 4.21 (dd, 1H, J=11.8, 1.3 Hz, *H*-6ax), 4.62 (br s, 1H, *H*-4), 7.28 (m, 2H), 7.37 (m, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 12.2 (q), 43.6 (t), 65.3 (d), 66.8 (t), 67.2 (d), 126.5 (d), 128.4 (d), 129.1 (d), 138.5 (s), 153.7 (s); HRFAB-MS *m/z* calcd for $[M+1]^+$ $C_{12}H_{16}NO_3$ 222.1130, found: 222.1120.

4.3.3.4. Ethyl-[(2-oxo-1,3-dioxolan-4-yl)(phenyl)methyl]-carbamoyl chloride (6c). White solid. Mp 85–86 °C (hexane/chloroform). IR (KBr): ν_{max} 1814, 1728 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, 3H, J=7.0 Hz, CH_2–CH_3), 3.30 (dq, 1H, J=21.0, 7.0 Hz, CH_2–CH_3), 3.61 (dq, 1H, J=21.0, 7.0 Hz, CH_2–CH_3), 4.33 (dd, 1H, J=8.5, 7.0 Hz, *H*-5), 4.66 (t, 1H, J=8.5 Hz, *H*-5), 4.87 (d, J=8.5 Hz, 1H, Ph-C*H*-N), 5.52 (m, 1H, *H*-4), 7.42 (s, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (q), 45.9 (t), 65.4 (d), 67.3 (t), 76.7 (d), 126.5 (d), 128.4 (d), 129.4 (d), 134.8 (s), 150.9 (s), 154.1 (s); HREI-MS *m/z* calcd for $[M]^+$ $C_{13}H_{14}NO_4Cl$ 283.0611, found: 283.0590.

4.3.4. From 3-benzylamino-3-phenyl-1,2-propanediol[21] (1d). The reaction with diphosgene afforded a mixture of *trans*-1,3-oxazolidin-2-one (**3d**) (18%), tetrahydro-1,3-oxazin-2-one (**4d**) (11%) and 1,3-dioxolan-2-one (**5d**) (40%); the reaction with phosgene afforded 1,3-dioxolan-2-one (**5d**) (70%).

4.3.4.1. *trans*-5-Hydroxymethyl-3-benzyl-4-phenyl-1,3-oxazolidin-2-one (3d). Yield 18%. Oil. IR (KBr): ν_{max} 3422, 1744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.50 (dd, 1H, J=12.7, 3.7 Hz, CH_2–O), 3.55 (d, 1H, J=15.0 Hz, CH_2–N), 3.75 (dd, 1H, J=12.5, 3.0 Hz, CH_2–O), 4.26 (m, 1H, *H*-5), 4.39 (d, 1H, J=7.0 Hz, *H*-4), 4.74 (d, 1H, J=15.0 Hz, CH_2–N), 7.04 (m, 2H), 7.15 (m, 6H), 7.30 (m, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 46.1 (t), 60.3 (d), 61.8 (t), 82.5 (d), 127.4 (d), 127.8 (d), 128.1 (d), 128.5 (d), 128.9 (d), 129.5 (d), 135.3 (s), 137.5 (s), 158.2 (s); HREI-MS *m/z* calcd for $[M]^+$ $C_{17}H_{17}NO_3$ 283.1208, found: 283.1211.

4.3.4.2. 3-Benzyl-5-hydroxy-4-phenyl-1,3-oxazinan-2-one (4d). White solid. Mp 200–201 °C. IR (KBr): ν_{max} 3442, 1704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.65 (d, 1H, J=15.5 Hz, CH_2N), 4.16 (dt, 1H, J=13.0, 2.0 Hz, *H*-6eq), 4.34 (dd, 1H, J=13.0, 1.6 Hz, *H*-6ax), 4.59 (br s, 1H, *H*-4), 4.68 (m, 1H, *H*-5), 5.47 (d, 1H, J=15.5 Hz, CH_2–N), 7.30 (m, 5H, *Ph*–CH_2N), 7.46 (m, 5H, *Ph*-C4); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 50.7 (t), 60.8 (d), 64.1 (t), 73.1 (d), 126.7, 128.1 (d), 128.3 (d), 129.1 (d), 129.3 (d), 129.9 (d), 136.1 (s), 136.3 (s), 152.8 (s); HREI-MS *m/z* calcd for $[M]^+$ $C_{17}H_{17}NO_3$ 283.1208, found: 283.1114.

4.3.4.3. 4-[(Benzylamino)(phenyl)methyl]-1,3-dioxolan-2-one (5d). White solid. Mp 90–91 °C. IR (KBr): ν_{max} 3324, 1775, 1177 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.58 (d, 1H, J=13.0 Hz, CH_2–Ph), 3.80 (d, 1H, J=13.0 Hz, CH_2–Ph), 3.96 (d, 1H, J=6.0 Hz, Ph–CH-NH), 4.34 (t, 1H, J=8.5 Hz, H-5), 4.50 (t, 1H, J=8.5 Hz, H-5), 4.83 (ddd, 1H, J=13.0, 8.5, 6.0 Hz, H-4), 7.29 (m, 3H), 7.35 (m, 4H), 7.44 (m, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 51.1 (t), 62.6 (d), 66.7 (t), 79.2 (d), 127.5 (d), 127.8 (d), 127.9 (d), 128.5 (d), 128.8 (d), 129.4 (d), 136.9 (s), 139.6 (s), 155.0 (s); HRFAB-MS m/z calcd for $[M+H]^+$ $C_{17}H_{18}NO_3$ 284.1286, found: 284.1288.

4.3.5. From 3-benzhydrylamino-3-phenyl-1,2-propanediol[21] (1e). The reaction with diphosgene afforded 1,3-dioxolan-2-one (**5e**) (96%); the reaction with phosgene afforded 1,3-dioxolan-2-one (**5e**) (97%).

4.3.5.1. 4-[(Benzhydrylamino)(phenyl)methyl-1,3-dioxolan-2-one (5e). White solid. Mp 69–70 °C (hexane/chloroform). IR (KBr): ν_{max} 1753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.76 (d, 1H, J=6.0 Hz, Ph–CH–NH), 4.39 (t, 1H, J=8.0 Hz, H-5), 4.46 (t, 1H, J=8.0 Hz, H-5), 4.68 (s, 1H, CH–Ph_2), 4.91 (dd, 1H, J=8.0, 6.0 Hz, H-4), 7.25 (m, 4H), 7.32 (m, 8H), 7.42 (m, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 61.7 (d), 63.6 (d), 67.2 (t), 79.1 (d), 127.2 (d), 127.4 (d), 127.5 (d), 127.6 (d), 127.9 (d), 128.0 (d), 128.1 (d), 128.3 (d), 128.6 (d), 128.7 (d), 128.9 (d), 129.0 (d), 129.3 (d), 136.7 (s), 142.2 (s), 143.7 (s), 155.1 (s); HREI-MS m/z calcd for $[M]^+$ $C_{23}H_{21}NO_3$ 359.1521, found: 359.1531.

4.3.6. From 3-(*tert*-butyldimethylsilyloxy)-1-amino-1-phenylpropan-2-ol (1f). The reaction with diphosgene afforded 1,3-oxazolidin-2-one (**2f**) (80%).

4.3.6.1. *cis*-5-(*tert*-Butyldimethylsilyloxymethyl)-4-phenyl-1,3-oxazolidin-2-one (2f). White solid. Mp 103–104 °C. IR: ν_{max} 3226, 1737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ −0.14 (s, 3H), −0.09 (s, 3H), 0.82 (s, 9H), 3.28 (dd, 1H, J=11.0, 6 Hz, CH_2–O), 3.46 (dd, 1H, J=11.0, 6.0 Hz, CH_2–O), 4.84 (m, 1H, H-5), 4.98 (d, 1H, J=8.5 Hz, H-4), 6.3 (br s, 1H, NH), 7.28 (m, H), 7.36 (m, H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −5.5 (q), −5.1 (q), 18.4 (s), 25.9 (q), 58.7 (d), 61.8 (t), 80.5 (d), 127.5 (d), 128.9 (d), 129.0 (d), 136.4 (s), 159.7 (s); HRFAB-MS m/z calcd for $[M+H]^+$ $C_{16}H_{26}NO_3Si$ 308.1681, found: 308.1686.

4.3.7. From 3 (*tert*-butyldimethylsilyloxy)1-methylamino-1-phenyl-propan-2-ol[23] (1g). The reaction with diphosgene afforded *cis*-1,3-oxazolidin-2-one (**2g**) (73%).

4.3.7.1. *cis*-5-(*tert*-Butyldimethylsilyloxymethyl)-3-methyl-4-phenyl-1,3-oxazolidin-2-one (2g). White solid. Mp 117–118 °C. IR: ν_{max} 3417, 1753, 1445 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ −0.17 (s, 3H), −0.10 (s, 3H), 0.79 (s, 9H), 2.75 (s, 3H), 3.23 (dd, 1H, J=11.0, 6.0 Hz, CH_2–O), 3.48 (dd, 1H, J=11.0, 5.0 Hz, CH_2–O), 4.75 (m, 2H, H-4+H-5), 7.16 (m, 2H), 7.35 (m, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −4.9 (q), −4.8 (c), 18.3 (s), 25.9 (q), 29.7 (q), 61.6 (t), 64.2 (d), 77.4 (d), 127.9 (d), 128.9 (d), 129.2 (d), 133.9 (s), 158.5 (s); HREI-MS m/z calcd for $[M]^+$ $C_{17}H_{27}NO_3Si$ 321.1760, found: 321.1783.

4.3.8. From 3-(*tert*-butyldimethylsilyloxy)-1-benzhydrylamino-1-phenylpropan-2-ol (1h). The reaction with diphosgene afforded *cis*-1,3-oxazolidin-2-one (**2h**) (71%).

4.3.8.1. *cis*-3-Benzhydrylamino-5-(*tert*-butyldimethylsilyloxy)-4-phenyl-1,3-oxazolidin-2-one (2h). Colourless oil. IR (KBr): ν_{max} 3484, 1756, 1105, 837 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ −0.17 (s, 3H); −0.11 (s, 3H); 3.22 (dd, 1H, J=11.0, 7.0 Hz, CH_2–O), 3.51 (dd, 1H, J=11.0, 6.0 Hz, CH_2–O), 4.79 (d, 1H, J=8.0 Hz, H-4), 4.89 (m, 1H, H-5); 7.01 (m, 10H), 7.27 (m, 3H), 7.34 (m, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −5.8 (q), −5.7 (q), 18.1 (s), 25.9 (q), 45.9 (d), 61.3 (t), 62.3 (d), 78.3 (d), 126.3 (d), 126.8 (d), 127.1 (d), 127.2 (d), 127.3 (d), 127.7 (d), 128.0 (d), 128.1 (d), 128.3 (d), 128.4 (d), 128.7 (d), 128.8 (d), 128.9 (d), 129.0 (d), 129.7 (d), 135.1 (s), 137.7 (s), 139.5 (s), 157.7 (s); HRFAB m/z calcd for $[M+H]^+$ $C_{29}H_{36}NO_3Si$ 474.2464, found: 474.2486.

4.4. General procedure for the deprotection of the silyl ethers with KF

A mixture of 5-(*tert*-butyldimethylsilyloxymethyl)-1,3-oxazolidin-2-one **2f**, **2g** or **2h** (4.7 mmol), potassium fluoride (800 mg, 14.0 mmol) and methanol (10 mL) was heated to reflux for 3 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel, eluting with hexane/ethyl acetate mixture to afford the corresponding 1,3-oxazolidin-2-one (**2a**) (90%), (**2b**) (94%) or **2e** (96%).

4.4.1. *cis*-3-Benzhydrylamino-5-hydroxymethyl-4-phenyl-1,3-oxazolidin-2-one (2e). From the deprotection of **2h**. Colourless oil. IR (KBr): ν_{max} 3430, 1744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.18 (dd, 1H, J=12.0, 7.5 Hz, CH_2–O), 3.23 (br s, 1H, OH), 3.35 (dd, 1H, J=12.0, 7.5 Hz, 1H, CH_2–O), 4.84 (d, 1H, J=8.0 Hz, H-4), 4.94 (m, 1H, H-5), 5.93 (s, 1H), 7.07 (m, 4H), 7.23 (m, 4H), 7.30 (m, 7H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 52.4 (d), 61.7 (t), 61.9 (d), 62.3 (d), 78.7 (d), 127.3 (d), 127.4 (d), 127.9 (d), 128.1 (d), 128.2 (d), 128.3 (d), 128.7 (d), 129.7 (d), 134.9 (s), 137.7 (s), 139.3 (s), 157.8 (s); HREI-MS m/z calcd for $[M]^+$ $C_{23}H_{21}NO_3$ 359.1521, found: 359.1481.

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