Diastereoselective Radical Bromination of 5,6-Dihydro-4*H*-1,2-oxazines and Subsequent Substitution Reactions with Nitrogen Nucleophiles

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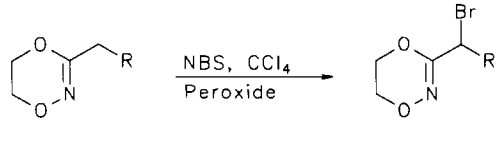
5,6-Dihydro-4*H*-1,2-oxazines **1a–b**, **2**, and **3** are easily brominated at C-4 with *N*-bromosuccinimide/dibenzoyl peroxide in tetrachloromethane. The bromo substituent is incorporated with surprisingly high diastereoselectivity *trans* to the substituent at C-6. 4-Bromo-5,6-dihydro-4*H*-1,2-oxazines are useful reagents for substitution reactions with N-nucleophiles such as primary amines and azide ions. Inversion of configuration at C-4 provides derivatives of 4-amino-1,2-oxazines with uniform relative configuration. As a minor byproduct the dibromo adduct **7** is obtained by bromination of **3**. The dehydrohalogenation of this compound allows the synthesis of the 4-bromo-6*H*-1,2-oxazine **12**. The presented reaction sequence thus constitutes an "umpolung" reaction that allows the introduction of nucleophiles into a position of the oxazine ring that so far was accessible only for electrophiles. The diastereoselectivity of the bromination reaction is discussed.

Shatzmiller and coworkers[1] have shown that lithiated 1,2-oxazines can be brominated at C-4 by bromine. However, their systems did not allow any statement about the stereochemistry of the ionic bromination.

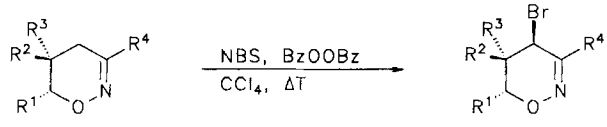
With regard to our previous work on 1,2-oxazines[2–6] and their application as building blocks with latent 1,4-functionality a 4-brominated species seems to be very promising due to the various possibilities of further functionalization. Taking into account that there are severe restrictions concerning the substitution patterns tolerated in deprotonation/electrophilic substitution reactions[5] it was desirable to develop an alternative approach to 4-bromo-1,2-oxazines.

Since linear oxime ethers[7] and cyclic oxime ethers like 5,6-dihydro-1,4,2-dioxazine[8] have been brominated in the presence of *N*-bromosuccinimide (NBS) and dibenzoyl peroxide (BzOOBz) in the α-position in a radical-type substitution reaction[9] we tried to apply this method to 5,6-dihydro-4*H*-1,2-oxazines.



Radical Bromination of 5,6-Dihydro-4*H*-1,2-oxazines

When 1,2-oxazines **1–3** were exposed to similar reaction conditions as mentioned above we obtained the 4-brominated heterocycles **4–6** in good yield. The conversion into the 4-bromo-1,2-oxazines was usually not complete but chromatographic separation of starting material, product and succinimide was possible without any difficulties.



1a	R^1 = $N(SiMe_3)_2$,	R^2 = Me,	R^3 = H,	R^4 = Ph	65%	**4a**
1b	R^1 = $N(SiMe_3)_2$,	R^2 = Me,	R^3 = H,	R^4 = CO_2Et	70%	**4b**
1c	R^1 = $N(SiMe_3)_2$,	R^2 = Me,	R^3 = H,	R^4 = CF_3	0%	**4c**
2	R^1 = CH_2SiMe_3,	R^2 = R^3 = H,	R^4 = Ph		74%[*]	**5**
3	R^1 = OEt,	R^2 = R^3 = H,	R^4 = Ph		69%[*]	*cis-/trans*-**6**

[*] established by ^{1}H-NMR spectra of the crude product

Different substituents are tolerated at C-6 of the 1,2-oxazines, and the reaction occurs readily with 3-phenyl- and 3-ethoxycarbonyl-substituted derivatives. On the other hand we failed to brominate the 3-CF_3-substituted compound **1c** and observed only decomposition.

Commonly, 4-bromo-1,2-oxazines are stable solid products, but compound **5** decomposes readily after exposure to air at room temperature. It was therefore used as a crude product for further reactions. Both possible diastereoisomers of **6** (*trans*:*cis* = 85:15) were formed during the reaction of **3**. This was the only example where the bromination was not highly stereoselective. In addition, the doubly halogenated **7** was isolated as a minor byproduct in 8.5% yield.

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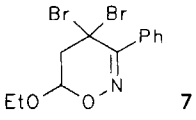


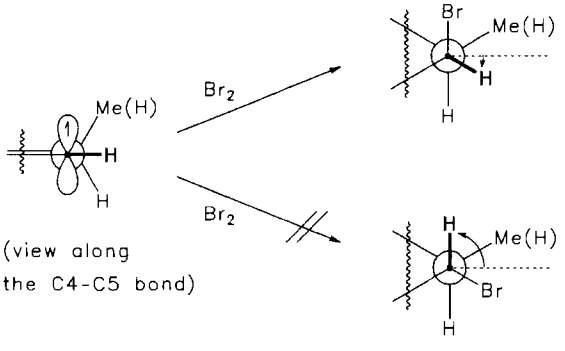
7

The compounds **1a**[10], **1b**[10], **1c**[10] and **2**[3] have a half-chair conformation that is fixed by a large pseudoequatorial substituent at C-6. It can be assumed that this conformation is maintained in a distorted manner even after the halogenation. The stereochemistry of the bromine incorporation can therefore be deduced from the coupling constants of the remaining 4-H signal in the ^{1}H-NMR spectra. The values of 3.4 and 3.5 Hz are typical of the 4-H-equatorial 5-H-axial substitution pattern in **4a** and **4b**. The equatorial-equatorial coupling constant of 1.7 Hz for the 4-H atom in **5** proves the pseudoaxial position of bromine in this case.

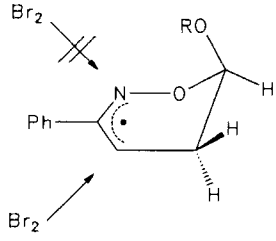
Discussion of the Stereoselective Bromination of 1,2-Oxazines

The bromination of 1,2-oxazines **1**–**3** occurrs with surprisingly high diastereoselectivity. The stereochemistry of the reaction seems to depend mainly on the pseudoequatorial position of the substituent at C-6 and the resulting half-chair conformation[10,11,12] of the rings in **1a**, **1b**, and **2**. The 5-methyl group is apparently of minor importance as proved by the selective formation of *trans*-configurated **5** starting from **2**.

The radical-type bromination of the structurally related 4-*tert*-butylcyclohexene[13] (which has a less effectively fixed half-chair conformation) shows a *trans*:*cis* selectivity of 5:1. Stereoelectronic effects have a crucial influence on the regio- and stereochemistry of radical-type reactions[14]. The first step in the bromination reaction of 1,2-oxazines is the abstraction of the pseudoaxial 4-H atom. The homolytic cleavage of this bond is facilitated by its coplanarity to the adjacent π-system. However, the configuration of **4a**, **4b**, and **5** is determined during the attack of bromine on the planar π-radical in the second reaction step. We suggest that torsional effects[15] play the decisive role in this step. The 4-H atom has to change its position during the conversion of the sp^2-radical to the sp^3-hybridized 4-bromo-1,2-oxazine. In case of a pseudoequatorial attack of bromine the 4-H atom has to pass the adjacent 5-substituent (H or CH_3). This unfavourable interaction is circumvented by pseudoaxial attack of bromine thus leading to products **4a**, **4b**, and **5**.

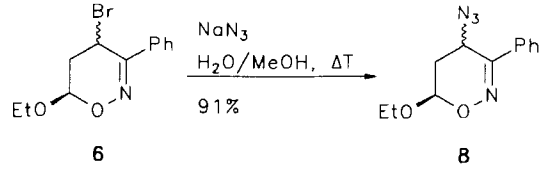


The previously discussed stereoelectronic and torsional effects do not seem to dominate the bromination of **3**. Due to its anomeric effect[3] the 6-ethoxy substituent occupies the pseudoaxial position in the half-chair conformation of **3**. This group thus effectively shields one side of the formed oxazine radical leading to *trans*-**6** as the major product. In addition, the incorporation of bromine into the pseudoaxial 4-position to give *cis*-**6** should cause significant destabilizing 1,3-repulsion. The opposing influence of these steric effects and the torsional effect leads to diminished diastereoselectivity and the formation of a mixture of *cis*-**6** and *trans*-**6**. They may also facilitate the generation of doubly brominated **7**.

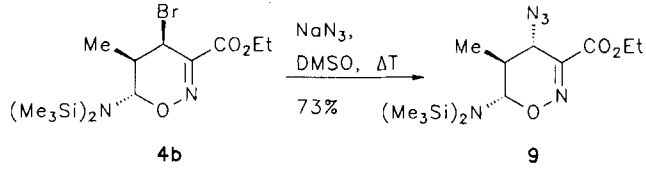


Nucleophilic Substitution Reactions

Presumably due to a severe distortion of the half-chair conformation, the ^{1}H-NMR spectra of *cis*-**6** and *trans*-**6** did not allow an unambiguous establishment of the stereochemistry of these compounds. Reliable assignments were only possible after S_N2 reaction of the *cis*/*trans* mixture with azide ions in refluxing water/methanol. 4-Azido-1,2-oxazine **8** was obtained in very good yield and with unchanged but inverted diastereomeric ratio. Being a smaller substituent, N_3 causes less distortion of the oxazine ring thus making it possible to obtain clearly interpretable spectra.



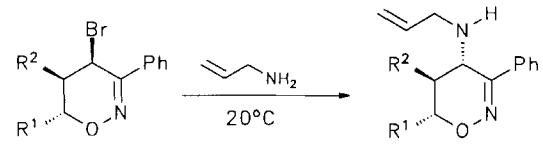
6 **8**



4b **9**

S_N2 reaction of **4b** with NaN_3 provided the 1,2-oxazine **9**. In this case dimethyl sulfoxide (DMSO)[16] was used as a solvent to avoid desilylation by water or methanol[17,18]. Allylamine also allowed clean S_N2 reactions. Using the am-

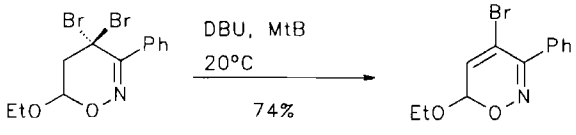
ine as a solvent, we obtained the 1,2-oxazines **10** and **11** even at room temperature in very good yield.



4a R^1 = $N(SiMe_3)_2$, R^2 = Me 81% **10**
5 R^1 = CH_2SiMe_3, R^2 = H 72% **11**

Dehydrohalogenation Reactions

Not unexpectedly, the attempt to dehydrohalogenate 4-bromo-1,2-oxazine **4a** by treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) failed at room temperature. After 18 h, 88% of unchanged starting material was recovered. On the other hand, the dibromo compound **7** could easily be dehydrohalogenated under these conditions. The resulting 4-bromo-6*H*-1,2-oxazine **12** is the first example of an 1,2-oxazine with this substitution pattern, which is very promising for further synthetic transformations.



7 **12**

Conclusion

The sequence of radical-type bromination and nucleophilic substitution makes possible the introduction of nucleophiles into the pseudoequatorial position at C-4 of the heterocycle **2** and of *N*-silylated 1,2-oxazines **1a** and **1b**. This establishes "umpolung" of reactivity since this position was so far only accessible to electrophiles after lithiation at C-4[5,19,20]. The radical bromination of 1,2-oxazines provides a diastereoselective access to highly functionalized N,O-heterocycles, thus enhancing the synthetic potential of these compounds.

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Experimental

^{1}H NMR: Solvent deuteriochloroform, Bruker ARX 300, AC 300 or WM 300 (300 MHz), internal standard tetramethylsilane (δ = 0.00), chloroform (δ = 7.25). – ^{13}C NMR: Solvent deuteriochloroform, Bruker ARX 300, AC 300 or WM 300 (75.5 MHz); internal standard tetramethylsilane (δ = 0.00), deuteriochloroform (δ = 77.0). – IR: Perkin-Elmer IR-197 or IR-325 (KBr pellets or films). – MS: Varian MAT 311A. – Melting points (uncorrected): Büchi SMP 20. – Boiling points: The temperature in the oven of a Büchi GKR 50 bulb-to-bulb distillation apparatus (kugelrohr oven) is given. – Elemental analysis: Perkin-Elmer CHN 240B. – All solvents were dried by standard methods. The experiments were carried out with the exclusion of moisture.

General Procedure for the Preparation of 4-Bromo-5,6-dihydro-4H-1,2-oxazines: The 1,2-oxazine and 1–1.2 equivalents of *N*-bromosuccinimide were dissolved in tetrachloromethane (2–5 ml/1 mmol of 1,2-oxazine). A small amount of dibenzoyl peroxide was added and the mixture was refluxed for the indicated time. The dark solution was allowed to cool to room temperature and was filtered through a sintered glass plug which contained a pad (ca. 5 cm) of Celite. The filtrate was concentrated in vacuo and a ^{1}H-NMR spectrum of the residue was recorded. The crude product (mixture of product, starting material and succinimide) was purified by chromatography over neutral alumina (activity III) with *n*-hexane/ethyl acetate (4:1). Experimental, analytical, and spectroscopic data are compiled in Tables 1, 2, 3, and 4.

Reactions of 4-Bromo-1,2-oxazines with N-Nucleophiles

cis/trans-4-Azido-6-ethoxy-5,6-dihydro-3-phenyl-4H-1,2-oxazine (**8**): 0.769 g (2.71 mmol) of **6** (*trans*:*cis* = 95:5) was mixed with 0.264 g (4.06 mmol) of NaN_3, 15 ml of methanol and 12 ml of water. The refluxing mixture was stirred for 3 h. The reaction mixture was treated with water (15 ml), cooled to room temperature and extracted with dichloromethane (3 × 15 ml). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to afford 0.609 g (91%) of **8** as a viscous, slightly yellow oil that became an almost colourless solid (m.p. 56–57°C) at room temperature. The diastereomeric ratio of the crude product (*trans*:*cis* = 5:95) was established by ^{1}H-NMR spectroscopy. Chromatographic purification (neutral alumina, activity III, *n*-hexane/ethyl acetate, 4:1, yield 76%) did not alter the diastereomeric ratio or the melting point. Analytical data of **8** are compiled in Table 4.

trans-**8**: ^{1}H NMR ($CDCl_3$): δ = 7.65–7.61, 7.46–7.40 (2 m, 5H, Ph), 5.20 (dd, *J* = 4.2, 2.8 Hz, 1H, 6H), 4.61 (dd, *J* = 9.3, 7.2 Hz, 1H, 4-H_{ax}), 3.96–3.84, 3.78–3.58, 1.19 (2 m, t, *J* = 7.0 Hz, 1H, 1H, 3H, OEt), 2.50–2.43, 2.33–2.24 (2 m, 2H, 5-H). – ^{13}C NMR ($CDCl_3$): δ = 154.7 (s, C-3), 133.3, 129.8, 128.4, 126.7 (s, 3 d, Ph), 96.5 (d, C-6), 64.5, 14.8 (t, q, OEt), 48.8 (d, C-4), 29.7 (t, C-5).
cis-**8**: ^{1}H NMR ($CDCl_3$): δ = 7.82–7.76, 7.48–7.40 (2 m, 5H, Ph), 5.30 (dd, *J* = 2.9, 2.1 Hz, 1H, 6H), 4.10 (dd, *J* = 7.0, 0.8 Hz, 1H, 4-H_{eq}), 3.92, 3.65, 1.26 (2 m_c, t, *J* = 7.0 Hz, 1H, 1H, 3H, OEt), 2.53–2.47, 2.35–2.27 (2 m, 2H, 5-H). – ^{13}C NMR ($CDCl_3$): δ = 152.9 (s, C-3), 133.3, 130.3, 128.7, 126.0 (s, 3 d, Ph), 93.0 (C-6), 64.4, 14.7 (t, q, OEt), 44.3 (d, C-4), 30.6 (t, C-5).

Ethyl r-4-Azido-c-6-[bis(trimethylsilyl)amino]-5,6-dihydro-t-5-methyl-4H-1,2-oxazine-3-carboxylate (**9**): A solution of 0.178 g (0.435 mmol) of **4b** and 0.075 g (1.15 mmol) of NaN_3 in 3 ml of DMSO was stirred and heated for 2 h to 60–70°C. After cooling to room temperature and addition of 30 ml of water the solution was extracted with dichloromethane (3 × 10 ml). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to afford 0.128 g (79%) of **9** as a dark yellow, highly viscous oil. The diastereomerically pure (according to ^{1}H-NMR spectra) crude product was purified by adsorptive filtration (1.5 × 15 cm neutral alumina, activity III, *n*-hexane/ethyl acetate, 4:1). Pure **9** (0.118 g, 73%) was obtained as a colourless, highly viscous oil that slowly crystallized (m.p. 78–81°C). Analytical data of **9** are compiled in Table 4. – ^{1}H NMR ($CDCl_3$): δ = 4.58 (d, *J* = 10.7 Hz, 1H, 6H), 4.36, 1.38 (q, t, *J* = 6.8 Hz, 2H, 3H, CO_2Et), 3.97 (d, *J* = 9.9 Hz, 1H, 4-H_{ax}), 2.13 (m_c, 1H, 5-H_{ax}), 1.14 (d, *J* = 6.8 Hz, 3H, Me), 0.19 [s, 18H, $N(SiMe_3)_2$]. – ^{13}C NMR ($CDCl_3$): δ = 162.6, 62.1,

Table 1. Bromination of the 1,2-oxazines **1a–1c**, **2**, and **3** with NBS

1,2-Oxazine	[g (mmol)]	NBS [g (mmol)]	time [h]	Product	*trans:cis*[a]	Yield [g (%)]
1a	0.335 (1.00)	0.172 (0.97)	4	**4a**	>97:3	0.260 (65)
1b	0.663 (2.01)	0.363 (2.04)	3	**4b**	>97:3	0.578 (70)
1c	1.05 (3.22)	0.572 (3.22)	2	start. mat.	-	-
1c	1.03 (3.16)	0.937 (5.26)	4	-[b]	-	-
2	0.478 (1.93)	0.380 (2.13)	2.5	**5**	>97:3	0.562 (74)[c]
3	2.05 (10.0)	1.80 (10.1)	2.5	**6**	85:15	2.57[d]

[a] Based on 6-substituent and bromo substitutent. – [b] Decomposition. – [c] Crude product: **5**:**2** ratio = 78:22 (slightly yellow solid that turned brown within minutes if exposed to air at room temperature). – [d] Crude product contained 75% **6** (*trans:cis* = 85:15), 9% dibromo adduct **7** and 16% of starting material **3**. Recrystallisation of 2.41 g of crude product provided 0.861 g (38%) of *trans*-**6**. Chromatography of the residue (1.55 g) provided 0.291 g (8.5%, m.p. 69–72°C) of **7**, 0.868 g of *trans*-**6**:**3** mixture (63:37) and 1.68 g (6.3%) of *cis*-**6**.

Table 2. ^{1}H-NMR data of the 1,2-oxazines **4a**, **4b**, and **5–7** ($CDCl_3$, 300 MHz, δ values, *J* in Hz)

1,2-Oxazine	6-H (1H)	4-H_{eq} (1H)	5-H (2H)	3-R (5H)	6-R'
4a[a]	5.38 (d, *J*= 10.4)	5.07 (d, *J* = 3.4)	2.35 (dqd, *J* = 10.4, 6.7, 3.4)[b]	7.38-7.40, 7.73-7.77 (2m, Ph)	0.27 [s, 18H, $N(SiMe_3)_2$]
4b[c]	5.29 (d, *J*= 10.5)	5.04 (d, *J* = 3.5)	2.17 (m_c)[b]	4.34, 1.36 (m_c, t, *J* = 7.2, CO_2Et)	0.21 [s, 18H, $N(SiMe_3)_2$]
5	4.50 (m_c)	5.04 (dd, *J* = 4.2, 1.7)	2.51 (dt, *J* = 15.2, 1.7)[d], 2.26 (ddd, *J* = 15.2, 11.5, 4.2)[b]	7.35-7.44, 7.68-7.75 (2m, Ph)	1.00, 1.25 (2dd, *J* = 14.4, 6.1, *J* = 14.4, 8.4, 1H, 1H, CH_2Si), 0.16 (s, 9H, $SiMe_3$)
cis-**6**	5.58 (t, *J*= 2.8)	4.90 (dd, *J* = 6.4, 2.1)	2.60-2.76 (m)	7.25-7.49, 7.66-7.69 (2m, Ph)	3.93, 3.66, 1.25 (2m_c, t, *J* = 7.0, 1H, 1H, 3H, OEt)
trans-**6**	5.37 (dd, *J*= 7.0, 2.7)	-[e]	2.50-2.74 (m)	7.40-7.42, 7.66-7.69 (2m, Ph)	4.05, 3.73, 1.28 (2m_c, t, *J* = 7.1, 1H, 1H, 3H, OEt)
7	5.38 (dd, *J*= 8.1, 2.5)	-	3.22, 3.38 (J_{AB}= 14.8, J_{AX}= 2.5, J_{BX}= 8.1)	7.36-7.66, 7.85-7.92 (2m, Ph)	4.06, 3.74, 1.29 (2m_c, t, *J* = 7.1, 1H, 1H, 3H, OEt)

[a] 5-Me: 1.21 (d, *J* = 6.7, 3H). – [b] 5-H_{ax} (1H). – [c] 5-Me: 1.13 (d, *J* = 6.7, 3H). – [d] 5-H_{eq} (1H). – [e] 4-H_{ax}: 5.10 (t, *J* = 5.4, 1H).

Table 3. ^{13}C-NMR data of the 1,2-oxazines **4a**, **4b**, and **5–7** ($CDCl_3$, 75.5 MHz, δ values, multiplicity)

1,2-Oxazine	C-3	C-6	C-4	C-5	5-CH_3	3-R (s, 3d, Ph)	6-R'
4a	151.9 (s)	90.3 (d)	34.4 (d)	46.7 (d)	15.7 (q)	133.2, 125.7, 128.5, 129.5	2.5, 4.2 [2q, $N(SiMe_3)_2$]
4b	147.5 (s)	92.4 (d)	33.1 (d)	44.2 (d)	15.3[a] (q)	162.0, 62.2, 14.0[a],[b]	2.2, 4.1 [2q, $N(SiMe_3)_2$]
5	152.4 (s)	71.0 (d)	34.9 (d)	36.9 (t)	-	133.6, 125.8, 128.4, 129.4	22.2, -0.7 (t, q, CH_2SiMe_3)
cis-**6**	154.6 (s)	94.0 (d)	27.1 (d)	32.8 (t)	-	133.7, 126.2, 128.3, 129.8	64.1, 14.9 (t, q, OEt)
trans-**6**	154.1 (s)	97.2 (d)	34.0 (d)	34.8 (t)	-	133.2, 126.0, 128.3, 129.7	65.3, 15.0 (t, q, OEt)
7	154.4 (s)	98.4 (d)	46.0 (s)	49.4 (t)	-	133.3, 127.8, 129.1, 129.6	65.9, 15.1 (t, q, OEt)

[a] Exchangeable assignments. – [b] (s, t, q, CO_2Et).

15.5* (s, t, q, CO_2Et), 147.6 (s, C-3), 94.8 (d, C-6), 61.8 (d, C-4), 37.4 (d, C-5), 14.1* (q, Me), 4.1, 2.3 [2 q, $N(SiMe_3)_2$]; assignments marked with an asterisk are exchangeable.

r-4-(Allylamino)-c-6-[bis(trimethylsilyl)amino]-5,6-dihydro-t-5-methyl-3-phenyl-4H-1,2-oxazine (**10**): 0.152 g (0.368 mmol) of **4a** was stirred for 3 d at room temperature in 1.5 ml of allylamine. Addition of water (10 ml), extraction with dichloromethane (3 × 10 ml), drying ($MgSO_4$) of the combined extracts and removal of the solvent in vacuo gave 0.143 g (100%) of crude product in diastereomerically pure form. Further purification by chromatography (1.5 × 15 cm, neutral alumina, activity III, *n*-hexane/ethyl acetate, 4:1) afforded in the first fraction 0.116 (81%) of **10** as a highly viscous oil that slowly crystallized (m.p. 82–83°C) at room temperature. Analytical data of **10** are compiled in Table 4. – ^{1}H NMR ($CDCl_3$): δ = 7.62–7.56, 7.42–7.33 (2 m, 5H, Ph), 5.59 (m_c, 1H, =CH), 4.95–4.88 (m, 2H, $=CH_2$), 4.53 (d, *J* = 10.5 Hz, 6-H), 3.62

(d, J = 9.2 Hz, 4-H_{ax}), 3.01, 2.76 (2 ddt, J = 13.6, 5.6, 1.2 Hz, J = 13.6, 6.1, 1.2 Hz, 2H, CH_2N), 2.37 (m_c, 1H, 5-H_{ax}), 1.39 (br. s, 1H, NH), 1.13 (d, J = 6.7 Hz, 3H, Me), 0.24 [s, 18H, $N(SiMe_3)_2$]. – ^{13}C NMR ($CDCl_3$): δ = 159.0 (s, C-3), 134.8, 129.1, 128.5, 126.6 (s, 3 d, Ph), 136.3 (d, =CH), 115.9 (t, $=CH_2$), 93.7 (d, C-6), 59.2 (d, C-4), 46.2 (t, CH_2N), 35.7 (d, C-5), 16.0 (q, Me), 3.5 [q, $N(SiMe_3)_2$].

Table 4. Analytical data of 1,2-oxazines **4a**, **4b**, and **6**–**12**

1,2-Oxazine	mp [°C]	IR ν [cm^{-1}]	elemental analysis calcd./found C H N
4a[a]	98-100	1585 (C=N), 1245 (Si-C)	$C_{17}H_{29}BrN_2OSi_2$ (413.5) 49.38 7.07 6.77 49.47 7.01 6.69
4b	72-73	1720 (C=O), 1570 (C=N), 1250 (Si-C)	$C_{14}H_{29}BrN_2O_3Si_2$ (409.5) 41.06 7.14 6.84 41.32 7.13 6.86
6[b]	61-65[c]	1575 (C=N)	$C_{12}H_{14}BrNO_2$ (284.2) 50.71 4.97 4.93 50.75 4.94 4.79
7	69-72	1585 (C=N)	$C_{12}H_{13}Br_2NO_2$ (363.1) 39.69 3.61 3.86 40.11 3.57 3.86
8[b]	56-57	2100 (N_3), 1560 (C=N)	$C_{12}H_{14}N_4O_2$ (246.3) 58.52 5.73 22.75 58.39 5.66 22.79
9	78-81	2100 (N_3), 1705 (C=O), 1580 (C=N), 1250 (Si-C)	$C_{14}H_{29}N_5O_3Si_2$ (371.6) 45.25 7.87 18.85 44.86 7.84 18.82
10	82-83	3360 (N-H), 1650 (C=C), 1595 (C=N), 1245 (Si-C)	$C_{20}H_{35}N_3OSi_2$ (389.7) 61.64 9.05 10.78 61.38 9.01 10.65
11	-[d]	3320 (N-H), 1635 (C=C), 1585 (C=N), 1245 (Si-C)	$C_{17}H_{26}N_2OSi$ (302.5) 67.50 8.66 9.26 67.61 8.53 9.18
12	-[d]	1610 (C=C), 1570 (C=N)	$C_{12}H_{12}BrNO_2$ (282.1) 51.09 4.29 4.96 51.26 4.35 4.88

[a] MS (EI, 70 eV): *m/z* (%) = 414, 412 (M^+, 2), 399, 397 (M^+ – CH_3, 10), 333 (M^+ – Br, 6), 234 (26), 144 (35), 73 [$Si(CH_3)_3$, 100], 45 (11). – [b] *cis*/trans mixture. – [c] *trans* Isomers. – [d] Highly viscous oil.

cis-4-(Allylamino)-5,6-dihydro-3-phenyl-6-(trimethylsilyl)methyl-4H-1,2-oxazine (**11**): The crude product from the bromination reaction of 1,2-oxazine **2** (0.457 g, **5**:**2** = 78:22, content of **5**: 1.15 mmol) was stirred for 4 d at room temperature in 5 ml of allylamine. Usual workup afforded 0.445 g of dark brown, viscous crude product. Purification by chromatography (2 × 15 cm neutral alumina, activity III, *n*-hexane/ethyl acetate, 4:1) afforded in the second fraction 0.252 g (72%) of **11** as a diastereomerically pure, highly viscous, yellow oil. Analytical data of **11** are compiled in Table 4. – ^1H NMR ($CDCl_3$): δ = 7.58–7.51, 7.42–7.33 (2 m, 5H, Ph), 5.77–5.64 (m, 1H, =CH), 5.06–5.03, 5.00 (m, m_c, 2H, $=CH_2$), 4.06–3.96 (m, 2H, 6-H, 4-H_{ax}), 3.12 (m_c, 2H, CH_2N), 2.31 (ddd, J = 13.2, 8.1, 1.9 Hz, 1H, 5-H_{eq}), 1.81 (ddd, J = 13.2, 11.4, 10.1 Hz, 1H, 5-H_{ax}), 1.33 (br. s, 1H, NH), 1.16, 1.04 (2 dd, J = 14.5, 7.4 Hz, J = 14.5, 7.1 Hz, 2H, CH_2Si), 0.10 (s, 9H, $SiMe_3$). – ^{13}C NMR ($CDCl_3$): δ = 158.9 (s, C-3), 134.2, 129.2, 128.6, 126.7 (s, 3 d, Ph), 135.9 (d, =CH), 116.6 (t, $=CH_2$), 74.8 (d, C-6), 48.9 (d, C-4), 47.8 (t, CH_2N), 35.1 (t, C-5), 23.1, –0.5 (t, q, CH_2SiMe_3).

Dehydrohalogenation Reaction of the Dibromo Adduct **7**

4-Bromo-6-ethoxy-3-phenyl-6H-1,2-oxazine (**12**): 0.041 g (0.270 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was added at room temperature to a solution of 0.093 g (0.256 mmol) of **7**. After 3.5 h at room temperature the reaction was quenched with 15 ml of saturated NH_4Cl solution and the resulting mixture was extracted with dichloromethane (3 × 10 ml). Drying of the combined organic phases ($MgSO_4$) and removal of the solvent in vacuo afforded 0.070 g (97%) of crude **12** as a yellow, viscous, oily product. The ^1H-NMR spectrum indicated a **12**/**7** ratio of 95:5. Further purification by chromatography (1 × 18 cm, neutral alumina, activity III, *n*-hexane/ethyl acetate, 4:1) afforded 0.053 g (74%) of **12** as a colourless, highly viscous oil. Analytical data of **12** are compiled in Table 4. – ^1H NMR ($CDCl_3$): δ = 7.61–7.52, 7.47–7.38 (2 m, 5H, Ph), 6.70 (d, J = 5.2 Hz, 1H, 5-H), 5.58 (d, J = 5.2 Hz, 1H, 6-H), 3.95, 3.68, 1.22 (2 m_c, t, J = 7.1 Hz, 2H, 3H, OEt). – ^{13}C NMR ($CDCl_3$): δ = 156.2 (s, C-3), 133.1, 129.7, 128.8, 128.0, 127.8 (s, 4 d, Ph, C-5), 112.9 (s, C-4), 94.7 (d, C-6), 64.3, 14.8 (t, q, OEt).

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