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Samarium Diiodide Promoted Reduction of 3,6-Dihydro-2*H*-1,2-oxazines: Competition of 1,4-Amino Alcohol Formation and Ring Contraction to Pyrrole Derivatives

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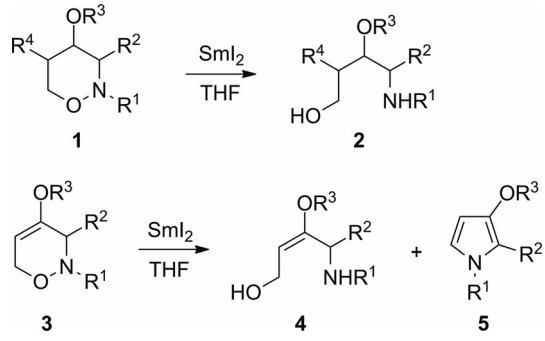
An approach to enantiopure 1,4-amino alcohols of type **4** by samarium diiodide mediated N–O cleavage of 3,6-dihydro-2*H*-1,2-oxazines **3** is presented. In several cases we observed the formation of 3-methoxypyrrole derivatives **5** as byproducts in significant amounts. For 1,2-oxazine derivative *syn*-**3a**, up to 27 % of pyrrole **5a** was isolated. The examples presented show a strong dependence of the chemoselectivity on the structure of the precursor 1,2-oxazines. The formation of pyrroles **5** as side-products is rationalized by a competitive intramolecular hydrogen shift of the initially formed ring cleavage intermediate **B** to **C** and subsequent cyclization of aldehyde **E** to afford **F**. This pathway can be disfavoured when a higher excess of samarium diiodide was employed, which generally provided the 1,4-amino alcohols **4** in good yields.

Introduction

Since the pioneering work of Kagan and co-workers,[1] samarium diiodide has become one of the most important chemoselective reducing agents in organic synthesis. Its extraordinary potential for the formation of challenging scaffolds was exploited in the preparation of various natural products and has recently been reviewed.[2] In addition to the formation of new C–C bonds, the use of SmI_2 often allows smooth transformations of common functional groups. Thus, dehalogenation and deoxygenation,[3] heteroatom/heteroatom bond scission,[3,4] heteroatom/benzyl cleavage, and removal of tosyl groups[5] are possible, depending on the reaction conditions.

In the course of ongoing projects in the synthesis of natural products or their analogues, we studied the chemoselective N–O bond cleavage of various enantiopure 1,2-oxazine derivatives with SmI_2. These versatile heterocycles are easily available by [3+3] cyclization of lithiated alkoxyallenes with nitrones[6] and can be subsequently modified. As disclosed in several reports, smooth SmI_2-mediated ring opening of monocyclic 1,2-oxazine derivatives[4d,4f,7] and bicyclic compounds[8] allow the efficient synthesis of various enantiopure cyclic or acyclic amino polyols. Whereas reactions of samarium diiodide with tetrahydro-2*H*-1,2-oxazine derivatives of type **1** led, in almost all tested examples, exclusively to the desired amino alcohols **2** in excellent yields and purities, in the case of 3,6-dihydro-2*H*-1,2-oxazines **3**, which bear an enol ether moiety, in addition to the expected 1,4-amino alcohols of type **4**, due to competing reactions, the formation of pyrroles **5**[9] was also observed (Scheme 1). Intermediates **4** can also be obtained by alternative reductive processes and are crucial in the stereodivergent syntheses of 3-methoxypyrrolidines and 3-methoxy-2,5-dihydropyrroles.[10] More recently, we studied transformations of 1,4-amino alcohols **4** into polyfunctionalized furan derivatives, which were either isolated or generated as intermediates.[11] In the present report, we demonstrate that SmI_2-promoted reduction of precursors **3** not only provide the expected compounds but also lead to the generation of pyrroles **5**.



Scheme 1. Samarium diiodide induced N–O bond cleavage of tetrahydro-2*H*-1,2-oxazines **1** and of 3,6-dihydro-2*H*-1,2-oxazines **3**.

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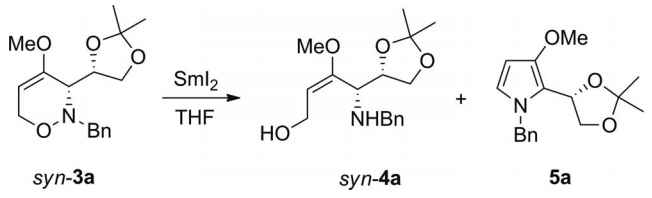
The aim of this report is to call attention to the unexpected formation of this latter product and to discuss a possible mechanism.

Results and Discussion

The unexpected formation of pyrrole **5a** as a side product in fair amounts was discovered during the samarium diiodide promoted reduction of D-glyceraldehyde-derived 3,6-dihydro-2*H*-1,2-oxazine *syn*-**3a**[6c] (Scheme 2). Treatment of *syn*-**3a** with 2.2 equivalents of freshly prepared SmI_2 solution in tetrahydrofuran afforded the expected amino alcohol *syn*-**4a** as the major component (41% yield) and the relatively unstable pyrrole derivative **5a** (21% yield) as the minor product. Small amounts of starting material (23%) were also isolated from the mixture. The ^{1}H NMR spectrum of **5a** showed the characteristic sets of signals attributed to the 1,3-dioxolane, methoxy, and benzyl moieties, and two additional doublets at δ = 5.90 and 6.46 ppm (J = 3.1 Hz each). In the ^{13}C NMR spectrum, the signals at δ = 95.5, 111.1, 120.3, and 147.3 ppm were assigned to the carbon atoms of the newly formed pyrrole ring. All analytical data supported the proposed structure of the hitherto unknown 1-benzyl-3-methoxypyrrole derivative **5a**, bearing the chiral 1,3-dioxolanyl side chain.



Scheme 2. Reaction of D-glyceraldehyde-derived 2*H*-1,2-oxazine *syn*-**3a** with samarium diiodide.

Although compounds such as *syn*-**4a** and **5a** can be easily separated by simple chromatography, we attempted to optimize this transformation to influence the selectivity and possibly obtain hints for the mechanism of the surprising pyrrole formation. The results of these experiments are summarized in Table 1. We examined the effects of the quantities of reducing agent (entries 1–4) and of the temperature (entries 5 and 6) and found that ca. 3.3 equiv. of SmI_2 at room temperature appeared to be optimal for the formation of pyrrole derivative **5a**. The use of a larger excess of samarium diiodide led to a higher *syn*-**4a**/**5a** ratio and enabled isolation of amino alcohol *syn*-**4a** in 74% yield. Neither the use of *tert*-butanol as proton source nor HMPA as a Lewis base resulted in the formation of pyrrole **5a** in significant amounts (entries 7 and 8). Decomposition mainly occurred in the presence of a proton source, whereas addition of HMPA led to no conversion at all. This is rather surprising because the addition of this Lewis base to SmI_2 strongly enhances its reductive power in many reactions.[12]

Examples of 3,6-dihydro-2*H*-1,2-oxazines **3** that were examined under standard conditions (in general with ca. 3 equiv. of SmI_2) are presented in Table 2. Interestingly, the

Table 1. Attempted optimization of the reaction of *syn*-**3a** with SmI_2.

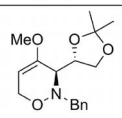
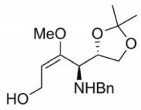
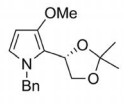
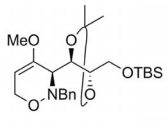
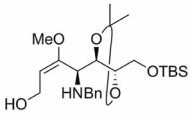
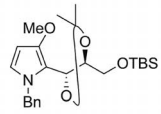
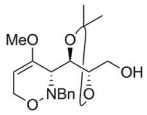
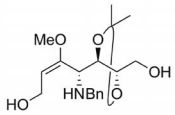
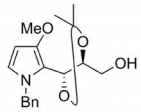
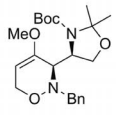
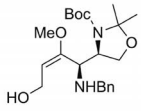
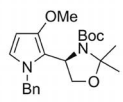
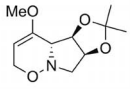
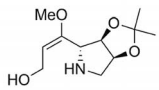
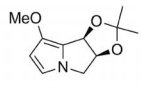
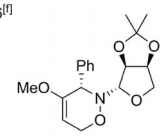
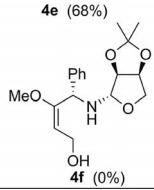
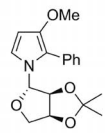
Entry	SmI_2 [equiv.]	Additive	Temp. [°C]	Time [h]	Yield [%] *syn*-**3**	*syn*-**4a**	**5a**
1	0.25	–	r.t.	2	80	0	0
2	2.2	–	r.t.	2	23	41 (ca. 2:1)	21
3	3.3	–	r.t.	2	0	65 (ca. 2.5:1)	27
4	5.5	–	r.t.	2	0	74 (ca. 5:1)	15
5	3.3	–	–78	2	92	0	0
6	2.2	–	66	10 min	0	–[a]	
7	2.2	*t*BuOH (2.0 equiv.)	r.t.	20	8[b]	4[b]	1[b]
8	2.2	HMPA (18.0 equiv.)	r.t.	2	100[b]	0[b]	0[b]

[a] A complex mixture of **4a**, **5a** and unidentified products was formed. [b] Ratio estimated by ^{1}H NMR spectroscopic analysis of the crude reaction mixture.

conversion of diastereomeric 1,2-oxazine *anti*-**3a** was significantly slower under the conditions optimized for *syn*-**3a** (entry 1). After two hours, pyrrole derivative **5a** was obtained in 13% yield only, together with unchanged precursor (38%) and the corresponding amino alcohol *anti*-**4a** (38%). The two L-erythronolactone-derived 1,2-oxazines **3b** and **3c** afforded allylic alcohols **4b** and **4c** as major products and pyrroles **5b** and **5c** were formed only in 18 and 6% yield, respectively (entries 2 and 3). The considerably lower yield of pyrrole **5c** observed in the latter case of *anti*-configured substrate **3c** can be explained by the relative configuration at C-3 (compare reactions of *syn*-**3a** and *anti*-**3a**) and the presence of the free hydroxyl group, which very likely serves as proton source. Whereas *syn*-configured **3b** was fully consumed within two hours (reaction monitored by TLC), in the case of **3c** the starting material could still be detected after this time (similar to *anti*-**3a**), and complete conversion required four hours. The observed dependence of reactivity on the relative configuration of 3,6-dihydro-2*H*-1,2-oxazines has also been observed in other transformations, for example, in hydroborations.[4d,11a]

To our surprise, the reaction of samarium diiodide with 1,2-oxazine **3d** (derived from Garner's aldehyde) provided the corresponding amino alcohol **4d** almost exclusively, and, after purification on silica gel, this product was isolated in 73% yield (Table 2, entry 4). A similar result was noted for fused bicyclic derivative **3e**, which, after 4.5 hours, furnished pyrrolidine derivative **4e** in 68% yield; however, unconsumed starting material (11%) was still present in the crude mixture. Careful analysis of the ^{1}H NMR spectra of the crude reaction mixtures allowed detection of the signals of the respective pyrrole derivatives **5d** and **5e** in very low amounts (less than 1% yield). In the spectra, one typical set of doublets was detected at δ = 5.90 and 6.47 ppm (J = 2.9 Hz), and 5.90 and 6.36 ppm (J = 2.8 Hz), respectively. Due to the low content and limited stability it was not possible to isolate pyrroles **5d** and **5e**.

Table 2. Reductions of 3,6-dihydro-2*H*-1,2-oxazines **3** with SmI_2.[a]

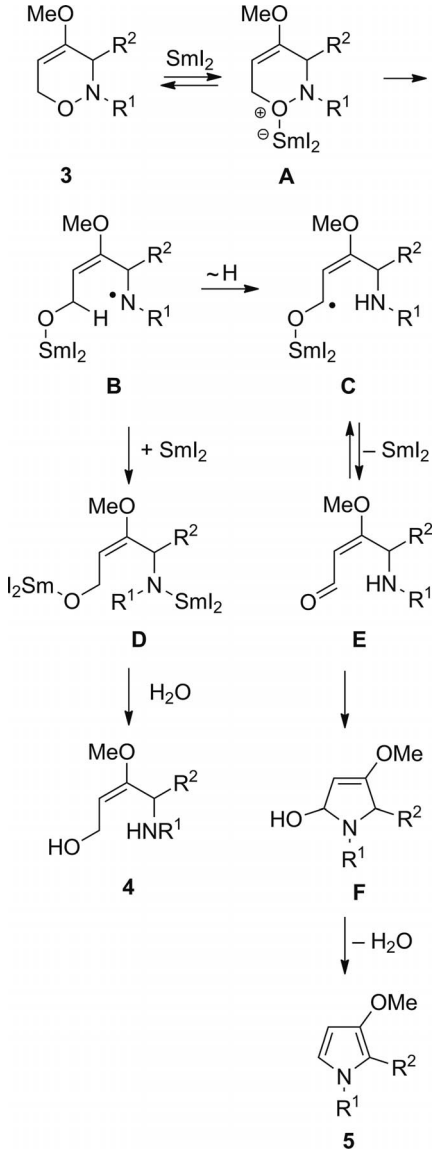
Entry	Substrate	Products	
1[b]	 *anti*-**3a**	 *anti*-**4a** (38%)	 **5a** (13%)
2	 **3b**	 **4b** (60%)	 **5b** (18%)
3[c]	 **3c**	 **4c** (94%)	 **5c** (6%)
4	 **3d**	 **4d** (73%)	 **5d** (<1%)[d]
5[e]	 **3e**	 **4e** (68%)	 **5e** (<1%)[d]
6[f]	 **3f**	 **4f** (0%)	 **5f** (20%)

[a] Reaction conditions (if not stated otherwise): SmI_2 (entry 1: 3.3 equiv.; entries 2–5: ca. 3.0 equiv.; entry 6: ca. 10 equiv.), THF, 2 h. [b] Starting material *anti*-**3a** was recovered in 38% yield. [c] Reaction time 4 h; yields were estimated by ^{1}H NMR spectroscopic analysis of the crude mixture; compound **4c** could be isolated in 79% yield as reported.[11a] [d] Only traces (<1%) of the corresponding pyrrole derivatives were detected in the ^{1}H NMR spectra of the crude mixtures. [e] Reaction time 4.5 h; starting 1,2-oxazine **3e** was recovered in 11% yield. [f] Reaction time 24 h; a complex mixture of very polar compounds derived from the expected amino alcohol **4f** was formed.

In a recent report, a series of 3,6-dihydro-1,2-oxazines such as **3f**, bearing an L-erythronolactone-derived auxiliary at the nitrogen atom, were presented as attractive precursors for the synthesis of highly functionalized hydroxylated compounds.[13] Under all conditions examined, the reaction of **3f** with samarium diiodide furnished only moderate amounts of pyrrole **5f** and numerous highly polar side-products (Table 2, entry 6). The expected allylic alcohol **4f** was not detected, which was probably due to the existence of ring-chain tautomers of this compound allowing a range of destructive subsequent reactions. Only pyrrole **5f** could be isolated by chromatography as a less polar fraction. The first experiment with **3f** was conducted using ca. 6.0 equiv. of SmI_2, and, after five hours, the dark-blue solution became yellow, indicating complete consumption of the reducing agent. However, significant amounts (37%) of starting material **3f** were recovered. Subsequent experiments showed that the use of ca. 10 equiv. SmI_2 was appropriate in this case, leading to full consumption of **3f**. In contrast to model compound *syn*-**3a**, use of the higher amount of SmI_2 did not decrease the amount of pyrrole formation and finally allowed the isolation of **5f** in 20% yield.

A plausible mechanism for the observed SmI_2-mediated transformation of 3,6-dihydro-2*H*-1,2-oxazines **3** into pyrroles is illustrated in Scheme 3. Coordination of the Lewis acidic samarium diiodide to the 1,2-oxazine oxygen forms adduct **A**, which suffers N–O bond cleavage to generate the crucial intermediate **B** bearing an N-centred radical moiety. Depending on the amount of reducing agent, this intermediate can undergo two reactions. A subsequent reduction of intermediate **B** with a second equivalent of samarium diiodide will lead to intermediate **D** and finally to the 1,4-amino alcohol **4**. This pathway is favoured for most compounds studied and is facilitated by the addition of larger amounts of samarium diiodide. Alternatively, several of the compounds investigated also react through a minor pathway involving an intramolecular hydrogen shift as a crucial step, providing samarium ketyl **C** as intermediate. It is well-known that samarium ketyls exist in equilibrium with the corresponding carbonyl compounds and, hence, **C** may deliver α,β-unsaturated aldehyde **E**. This compound can undergo a favourable 5-*exo*-*trig*-cyclization to afford intermediate **F**, which, upon elimination of water, provides pyrrole derivative **5**.[14]

According to the mechanism depicted in Scheme 3, the pathway leading to pyrroles should require only catalytic amounts of SmI_2. However, the result presented in Table 1 (entry 1) reveals that 0.25 equiv. of the reagent is apparently not sufficient to lead to detectable formation of **5a**. Possibly, larger amounts of the Lewis acidic samarium(II) or the generated samarium(III) species are required to trigger the steps leading to the formation of pyrrole **5**. The observation that application of more than 3 equiv. of samarium diiodide considerably disfavours the formation of pyrroles is in agreement with our mechanistic proposal, because intermediate **D** should then be formed faster than samarium ketyl **C**. The failed reaction of *syn*-**3a** with SmI_2 in the presence of HMPA is also significant (Table 1, entry 8). The observation that no conversion at all was observed is in agreement with the mechanism depicted in Scheme 3, in which (reversible) coordination of the 1,2-oxazine oxygen to SmI_2 leading to complex **A** is proposed as the initial step. The presence of the very strong Lewis base HMPA[15] completely prevents this step and, hence, both pathways leading to **4** and **5** are apparently unfavourable. The differences in rates and the dependence of the **4**/**5** ratio on configuration and structure of starting materials **3** cannot be explained by simple assumptions. The formation of pyrroles by ring contraction[16] of 3,6-dihydro-1,2-oxazines has been described in the literature. Conversion under basic[17] or acidic conditions[18] and at elevated temperatures and pressure[19] are known. Nevertheless, all the methods described seem to have limitations. Alternatively, photochemical reactions of certain 3,6-dihydro-2*H*-1,2-oxazines may also furnish pyrroles.[20,21]



Scheme 3. Proposed mechanism for the SmI_2-mediated reaction of 3,6-dihydro-2*H*-1,2-oxazines **3** leading to amino alcohols **4** or pyrroles **5**.

Conclusions

In this report we described samarium diiodide induced reactions of 3,6-dihydro-2*H*-1,2-oxazines **3** leading to the expected 1,4-amino alcohols **4** and the fairly unstable electron-rich pyrrole derivatives **5** as minor components. We present a mechanistic proposal for the formation of the pyrroles that involves an interesting internal redox reaction as a key step. The ability to predict which precursor 1,2-oxazine derivatives will provide the pyrroles in reasonable amount is not yet possible. The reported results again emphasize the versatility (and partial unpredictability) of reactions using 1,2-oxazines as key compounds.[22]

Experimental Section

For general information, see Jasiński et al.;[11a] the NMR and IR spectra of compounds *syn*-**4a**, *anti*-**4a** and **5a** were recorded with Bruker AC 300 and FTIR Nicolet 5SXC instruments, respectively. All reactions were performed under argon in flame-dried flasks with addition of the components by using a syringe.

Reaction of *syn*-3a with SmI_2: 1,2-Oxazine *syn*-**3a** (150 mg, 0.50 mmol) in tetrahydrofuran (5 mL) was treated with a freshly prepared solution of samarium diiodide [obtained by reaction of samarium metal (271 mg, 1.80 mmol) with 1,2-diiodoethane (465 mg, 1.65 mmol) in tetrahydrofuran (10 mL) and stirring at room temp. for 2 h], and stirred at ambient temperature for 2 h. The reaction mixture was quenched with 10% aqueous $Na_2S_2O_3$ (30 mL), extracted with CH_2Cl_2 (3 × 30 mL) and filtered through a pad of Celite. The organic layer was dried with $MgSO_4$, filtered and evaporated to give a pale-yellow oil (140 mg). Purification by column chromatography (silica gel; hexane/ethyl acetate, 3:1 gradient to pure ethyl acetate, then ethyl acetate/methanol, 10:1) afforded unstable **5a** (39 mg, 27%, first eluted) and **4a** (100 mg, 65%, second eluted) as colourless oils.

(*E*)-(4*S*,4′*S*)-4-Benzylamino-4-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-methoxybut-2-en-1-ol (*syn*-4a): $[\alpha]_D^{22}$ = +1.3 (*c* = 0.50, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.34, 1.35 (2 × s, 2 × 3 H, 2 Me), 2.69 (br. s, 2 H, NH, OH), 3.54 (s, 3 H, OMe), 3.57 (d, *J* = 8.0 Hz, 1 H, 4-H), 3.63 (d, *J* = 13.3 Hz, 1 H, C*H*$_2$Ph), 3.76 (dd, *J* = 6.0, 8.5 Hz, 1 H, 5′-H), 3.88 (d, *J* = 13.3 Hz, 1 H, C*H*$_2$Ph), 3.94 (dd, *J* = 6.3, 8.5 Hz, 1 H, 5′-H), 4.04 (d, *J* = 7.4 Hz, 2 H, 1-H), 4.35 (ddd, *J* = 6.0, 6.3, 8.0 Hz, 1 H, 4′-H), 5.02 (t, *J* ≈ 7.4 Hz, 1 H, 2-H), 7.20–7.38 (m, 5 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 25.4, 26.7 (2 × q, Me), 50.9 (t, *C*H$_2$Ph), 54.5 (d, C-4), 57.3 (t, C-1), 59.9 (q, OMe), 66.4 (t, C-5′), 76.6 (d, C-4′), 101.2 (d, C-2), 109.4 (s, C-2′), 127.1, 128.2, 128.4, 139.5 (3 × d, s, Ph), 157.0 (s, C-3) ppm. IR (film): $\tilde{\nu}$ = 3400–3330 (O–H, N–H), 3080–2820 (=C–H, C–H), 1660 (C=C) cm^{-1}. $C_{17}H_{25}NO_4$ (307.4): calcd. C 66.43, H 8.20, N 4.56; found C 66.26, H 8.30, N 4.88.

(4′*S*)-1-Benzyl-2-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-methoxypyrrole (5a): $[\alpha]_D^{22}$ = –0.65 (*c* = 0.30, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.37, 1.43 (2 × s, 2 × 3 H, 2 Me), 3.75 (s, 3 H, OMe), 3.96 (dd, *J* = 6.7, 8.2 Hz, 1 H, 5′-H), 4.17 (t, *J* ≈ 8.2 Hz, 1 H, 5′-H), 5.07 (d, *J* = 16.1 Hz, 1 H, C*H*$_2$Ph), 5.08–5.18 (m, 1 H, 4′-H), 5.19 (d, *J* = 16.1 Hz, 1 H, C*H*$_2$Ph), 5.90, 6.46 (2 × d, *J* = 3.1 Hz, 2 H, 4-H, 5-H), 7.04 (br d, *J* = 6.7 Hz, 2 H, Ph), 7.20–7.36 (m, 3 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 25.5, 26.5 (2 × q, Me), 51.3 (t, *C*H$_2$Ph), 58.5 (q, OMe), 66.6 (t, C-5′), 69.5 (d, C-4′), 95.5 (d, C-4), 108.5 (s, C-2′), 111.1 (s, C-2), 120.3 (d, C-5), 126.5, 127.4, 128.6, 138.4 (3 × d, s, Ph), 147.3 (s, C-3) ppm. IR (film): $\tilde{\nu}$ = 3150–2800 (=C–H, C–H), 1580 (C=C) cm^{-1}. $C_{17}H_{21}NO_3$ (287.4): calcd. C 71.06, H 7.37, N 4.87; found C 71.04, H 7.39, N 5.19.

Reaction of 1,2-Oxazine *anti*-3a with SmI_2: By a procedure similar to that used for *syn*-**3a**, 1,2-oxazine *anti*-**3a** (100 mg, 0.33 mmol) in tetrahydrofuran (4 mL) was added to a freshly prepared solution of samarium diiodide [obtained from samarium metal (177 mg, 1.18 mmol) and 1,2-diiodoethane (304 mg, 1.08 mmol) in tetrahydrofuran (8 mL)]. After workup and purification by column chromatography (silica gel; hexane/ethyl acetate, 3:1 gradient to ethyl acetate, then ethyl acetate/methanol, 10:1) afforded pyrrole derivative **5a** (12 mg, 13%), unconsumed *anti*-**3a** (38 mg, 38%), and amino alcohol *anti*-**4a** (38 mg, 38%) as a brown oil.

(*E*)-(4*R*,4′*S*)-4-Benzylamino-4-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-methoxybut-2-en-1-ol (*anti*-4a): $[\alpha]_D^{22}$ = –3.0 (*c* = 0.50, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.32, 1.38 (2 × s, 2 × 3 H, 2 Me), 2.02 (br. s, 2 H, NH, OH), 3.40 (d, *J* = 9.2 Hz, 1 H, 4-H), 3.51 (d, *J* = 13.1 Hz, 1 H, C*H*$_2$Ph), 3.61 (s, 3 H, OMe), 3.75 (d, *J* = 13.1 Hz, 1 H, C*H*$_2$Ph), 3.82–4.06 (m, 4 H, 1-H, 5′-H), 4.20 (dd, *J* = 6.2, 8.5 Hz, 1 H, 4′-H), 5.18 (t, *J* ≈ 8.2 Hz, 1 H, 2-H), 7.20–7.37 (m, 5

H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 25.3, 26.3 (2 × q, Me), 51.2 (t, *C*H_2Ph), 54.7 (d, C-4), 56.9 (t, C-1), 58.9 (q, OMe), 69.0 (t, C-5′), 75.6 (d, C-4′), 100.9 (d, C-2), 109.5 (s, C-2′), 127.1, 128.2, 128.3, 140.0 (3 × d, s, Ph), 157.5 (s, C-3) ppm. IR (film): $\tilde{\nu}$ = 3450–3340 (O–H, N–H), 3150–2820 (=C–H, C–H), 1660 (C=C) cm^{-1}. $C_{17}H_{25}NO_4$ (307.4): calcd. C 66.43, H 8.20, N 4.56; found C 65.97, H 8.64, N 4.83.

Reaction of 3b with SmI_2: To a solution of samarium diiodide (ca. 0.1 M in THF, 10.5 mL, ca. 10.5 mmol; prepared by the method of Imamoto[23]), a solution of 1,2-oxazine **3b** (161 mg, 0.36 mmol) in degassed tetrahydrofuran (8 mL) was added dropwise at room temp. The mixture was stirred for 2 h, quenched with sat. aqueous sodium potassium tartrate (10 mL) and extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvents removed under reduced pressure. Purification by column chromatography (alumina; hexane/dichloromethane, 3:2) afforded **5b** (28 mg, 18%, >90% purity, first eluted) and amino alcohol **4b** (97 mg, 60%) as colourless oils.

(*E*)-(4*R*,4′*R*,5′*S*)-4-Benzylamino-4-(5′-*tert*-butyldimethylsiloxymethyl-2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-methoxybut-2-en-1-ol (4b): $[\alpha]_D^{22}$ = –15.4 (*c* = 1.30, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.039, 0.042, 0.88 (3 × s, 2 × 3 H, 9 H, TBS), 1.37, 1.45 (2 × s, 2 × 3 H, 2 Me), 3.54 (s, 3 H, OMe), 3.60 (dd, *J* = 5.0, 11.1 Hz, 1 H, C*H*$_2$OTBS), 3.61 (d, *J* = 12.8 Hz, 1 H, C*H*$_2$Ph), 3.72 (dd, *J* = 4.3, 11.1 Hz, 1 H, C*H*$_2$OTBS), 3.84 (d, *J* = 12.8 Hz, 1 H, C*H*$_2$Ph), 3.93 (d, *J* = 8.7 Hz, 1 H, 4-H), 4.06 (dd, *J* = 7.4, 12.6 Hz, 1 H, 1-H), 4.13 (td, *J* ≈ 4.4, 5.9 Hz, 1 H, 5′-H), 4.17 (dd, *J* = 7.6, 12.6 Hz, 1 H, 1-H), 4.64 (dd, *J* = 6.2, 8.7 Hz, 1 H, 4′-H), 5.06 (t, *J* ≈ 7.5 Hz, 1 H, 2-H), 7.21–7.25, 7.29–7.31 (2 × m, 5 H, Ph) ppm; OH and NH signals could not be detected. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = –5.3*, 18.4, 26.0 (q, s, q, TBS), 25.3, 27.6 (2 × q, Me), 48.7 (t, *C*H_2Ph), 54.5 (q, OMe), 56.5 (d, C-4), 57.3 (t, C-1), 62.4 (t, 5′-*C*H_2), 75.1 (d, C-4′), 78.0 (d, C-5′), 100.6 (d, C-2), 108.0 (s, C-2′), 127.1, 128.2, 128.4. 139.6 (3 × d, s, Ph), 158.8 (s, C-3) ppm; * higher intensity. IR (ATR): $\tilde{\nu}$ = 3490–3295 (O–H, N–H), 3090–2830 (=C–H, C–H), 1655 (C=C), 1215, 1090 (C–O) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{24}H_{42}NO_5Si$ [M + H]$^+$ 452.2827; found 452.2849.

(4′*R*,5′*S*)-1-Benzyl-2-(5′-*tert*-butyldimethylsiloxymethyl-2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-methoxypyrrole (5b): $[\alpha]_D^{22}$ = –14.9 (*c* = 1.29, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = –0.04, –0.02, 0.84 (3 × s, 2 × 3 H, 9 H, TBS), 1.34, 1.41 (2 × s, 2 × 3 H, 2 Me), 3.38 (dd, *J* = 4.6, 10.8 Hz, 1 H, C*H*$_2$OTBS), 3.66 (dd, *J* = 7.3, 10.8 Hz, 1 H, C*H*$_2$OTBS), 3.73 (s, 3 H, OMe), 4.30 (td, *J* ≈ 4.6, 7.6 Hz, 1 H, 5′-H), 4.93, 5.22 (2 × d, *J* = 15.8 Hz, 2 H, C*H*$_2$Ph), 5.43 (d, *J* = 7.9 Hz, 1 H, 4′-H), 5.88, 6.35 (2 × d, *J* = 3.1 Hz, 2 H, 4-H, 5-H), 7.04–7.06, 7.21–7.32 (2 × m, 5 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = –5.4*, 18.4, 25.9 (q, s, q, TBS), 23.5, 26.1 (2 × q, Me), 51.8 (t, *C*H_2Ph), 58.2 (q, OMe), 63.8 (t, 5′-*C*H_2), 70.7 (d, C-4′), 78.9 (d, C-5′), 95.4 (d, C-4), 107.7 (s, C-2′), 110.9 (s, C-2), 119.6 (d, C-5), 126.6, 127.3, 128.5, 138.6 (3 × d, s, Ph), 146.9 (s, C-3) ppm; * higher intensity. IR (ATR): $\tilde{\nu}$ = 3065–2835 (=C–H, C–H), 1580 (C=C), 1250, 1090, 1070 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{24}H_{37}NNaO_4Si$ [M + Na]$^+$ 454.2384; found 454.2375.

Reaction of 3c with SmI_2: By a procedure analogous to that used with 1,2-oxazine **3b**, compound **3c** (30 mg, 0.089 mmol) in tetrahydrofuran (1 mL) was treated with samarium diiodide (ca. 0.1 M in THF, 2.7 mL, ca. 0.27 mmol) to quantitatively yield a mixture of crude **4c** and **5c** (30 mg, 94:6 ratio based on the ^{1}H NMR spectrum) after standard workup. Isolation and characterisation data of **4c** was described elsewhere.[11a] Compound **5c** was not isolated but the yield (6%) was estimated from the ^{1}H NMR spectrum of the crude mixture. ^{1}H NMR of **5c** ($CDCl_3$, 500 MHz): δ = 1.25, 1.34 (2 × s, 2 × 3 H, 2 Me), 3.31 (dd, *J* = 4.5, 11.9 Hz, 1 H, 5′-C*H*$_2$), due to overlapping the signals of 5′-C*H*$_2$ (1 H), OMe and 5′-H could not be assigned, 4.97, 5.20 (2 × d, *J* = 15.9 Hz, 2 H, C*H*$_2$Ph), 5.37 (d, *J* = 7.4 Hz, 1 H, 4′-H), 5.91, 6.45 (2 × d, *J* = 3.1 Hz, 2 H, 4-H, 5-H), 7.01–7.04 (m, 2 H, Ph) ppm, 3 H signals of Ph overlapped with other signals.

(*E*)-(4*R*,4′*R*)-4-Benzylamino-4-(3′-*tert*-butoxycarbonyl-2′,2′-dimethyl-1′,3′-oxazolidin-4′-yl)-3-methoxybut-2-en-1-ol (4d): By a procedure similar to that used with 1,2-oxazine **3b**, compound **3d** (85 mg, 0.21 mmol) in tetrahydrofuran (7 mL) was added to a samarium diiodide solution (ca. 0.1 M in THF, 6.3 mL, ca. 0.63 mmol) and stirred for 3 h. After standard workup, the crude product was purified by chromatography (silica gel; dichloromethane/methanol, 40:1) to give amino alcohol **4d** (62 mg, 73%) as a colourless oil. $[\alpha]_D^{22}$ = –37.6 (*c* = 1.28, $CHCl_3$). ^{1}H NMR ([D$_6$]DMSO, 500 MHz, 90 °C): δ = 1.39 (s, 9 H, *t*Bu), 1.40, 1.42 (2 × s, 2 × 3 H, 2 Me), 2.13, 4.09 (2 × br. s, 2 H, NH, OH), 3.51 (d, *J* = 13.6 Hz, 1 H, C*H*$_2$Ph), 3.51 (s, 3 H, OMe), 3.63 (d, *J* = 7.3 Hz, 1 H, 4-H), 3.73 (d, *J* = 13.6 Hz, 1 H, C*H*$_2$Ph), 3.76 (dd, *J* = 5.9, 9.0 Hz, 1 H, 5′-H), 3.88 (dd, *J* = 6.5, 12.2 Hz, 1 H, 1-H), 3.91 (d, *J* = 9.0 Hz, 1 H, 5′-H), 3.97 (dd, *J* = 7.7, 12.2 Hz, 1 H, 1-H), 4.05 (br t, *J* ≈ 6.4 Hz, 1 H, 4′-H), 4.89 (br t, *J* ≈ 7.1 Hz, 1 H, 2-H), 7.17–7.21, 7.25–7.31 (2 × m, 5 H, Ph) ppm. ^{13}C NMR ([D$_6$]DMSO, 126 MHz, 90 °C): δ = 24.3, 27.2 (2 × q, Me), 28.6 (q, *t*Bu), 51.2 (t, *C*H_2Ph), 54.9 (q, OMe), 57.0 (t, C-1), 58.2 (d, C-4), 59.8 (d, C-4′), 64.9 (t, C-5′), 79.6 (s, *t*Bu), 93.6 (d, C-2′), 103.4 (s, C-2), 127.0, 128.4*, 141.5 (2 × d, s, Ph), 152.7 (s, C=O), 155.2 (s, C-3) ppm; * higher intensity. IR (ATR): $\tilde{\nu}$ = 3515–3320 (O–H, N–H), 3085–2820 (=C–H, C–H), 1695 (C=O), 1655 (C=C), 1390, 1250, 1170, 1080 (C–O) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{22}H_{35}N_2O_5$ [M + H]$^+$ 407.2546; found 407.2538.

(*E*)-(3a′*R*,4′*S*,6a′*S*)-3-(2′,2′-Dimethyltetrahydro-[1,3]dioxolo[4,5-*c*]-pyrrol-4′-yl)-3-methoxyprop-2-en-1-ol (4e): By a procedure similar to that used with 1,2-oxazine **3b**, compound **3e** (18.3 mg, 0.080 mmol) in tetrahydrofuran (2 mL) was added to a samarium diiodide solution (ca. 0.1 M in THF, 2.4 mL, ca. 0.24 mmol) and stirred for 4.5 h. After typical workup, the crude mixture was purified by column chromatography (silica gel; dichloromethane/methanol, 15:1) to give unconsumed **3e** (2.0 mg, 11%) and amino alcohol **4e** (12.7 mg, 68%), which was isolated as a colourless oil. $[\alpha]_D^{22}$ = +54.4 (*c* = 1.10, $CHCl_3$). ^{1}H NMR ([D$_6$]DMSO, 500 MHz, 70 °C): δ = 1.24, 1.41 (2 × s, 2 × 3 H, 2 Me), 2.81 (br d, *J* ≈ 12.2 Hz, 1 H, 6′-H), 3.04 (dd, *J* = 4.9, 12.2 Hz, 1 H, 6′-H), 3.44 (s, 3 H, OMe), 3.95 (br d, *J* ≈ 2.0 Hz, 1 H, 4′-H), 3.99 (dd, *J* = 7.3, 12.3 Hz, 1 H, 1-H), 4.03 (dd, *J* = 7.1, 12.3 Hz, 1 H, 1-H), 4.57 (dd, *J* = 2.0, 6.0 Hz, 1 H, 3a′-H), 4.64–4.67 (m, 1 H, 6a′-H), 4.69 (t, *J* ≈ 7.2 Hz, 1 H, 2-H) ppm; OH and NH signals could not be detected. ^{13}C NMR ([D$_6$]DMSO, 126 MHz, 70 °C): δ = 24.3, 26.3 (2 × q, Me), 52.8 (t, C-6′), 53.8 (q, OMe), 56.0 (t, C-1), 62.5 (d, C-4′), 81.4 (d, C-3a′), 83.9 (d, C-6a′), 99.1 (d, C-2), 110.7 (s, C-2′), 157.4 (s, C-3) ppm. IR (ATR): $\tilde{\nu}$ = 3440–3180 (O–H, N–H), 3020–2825 (=C–H, C–H), 1660 (C=C), 1210, 1040 (C–O) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{11}H_{20}NO_4$ [M + H]$^+$ 230.1387; found 230.1385.

(3a′*S*,4′*S*,6a′*S*)-1-(2′,2′-Dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4′-yl)-3-methoxy-2-phenylpyrrole (5f): By a procedure similar to that used with 1,2-oxazine **3b**, compound **3f** (126 mg, 0.38 mmol) in tetrahydrofuran (10 mL) was added to a samarium diiodide solution (ca. 0.1 M in THF, 38 mL, ca. 3.8 mmol) and stirred for 24 h. After typical workup and purification by column chromatography (silica gel; dichloromethane) compound **5f** (24 mg, 20%) was obtained as colourless crystals; m.p. 132–134 °C. $[\alpha]_D^{22}$ = +150.6 (*c* = 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.33, 1.49 (2 × s,

2 × 3 H, 2 Me), 3.73 (s, 3 H, OMe), 4.07–4.14 (m, 2 H, 6′-H), 5.03 (m, 2 H, 3a′-H, 6a′-H), 5.82 (s, 1 H, 4′-H), 6.09, 6.34 (2 × d, J = 3.3 Hz, 2 H, 4-H, 5-H), 7.27–7.31, 7.40–7.44, 7.50–7.53 (3 × m, 5 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 24.7, 26.2 (2 × q, Me), 58.5 (q, OMe), 73.3 (t, C-6′), 80.7 (d, C-6a′), 84.7 (d, C-3a′), 90.3 (d, C-4′), 98.0 (d, C-4), 112.9 (s, C-2′), 115.2 (d, C-5), 119.0 (s, C-2), 126.8, 128.4, 130.0, 130.3 (3 × d, s, Ph), 145.4 (s, C-3) ppm. IR (ATR): $\tilde{\nu}$ = 3065–2830 (=C–H, C–H), 1210, 1080 (C–O) cm^{-1}. ESI-TOF (m/z): calcd. for $C_{18}H_{21}NNaO_4$ $[M + Na]^+$ 338.1363; found 338.1361.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra of compounds prepared.

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