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Three-step assembly of 4-aminotetrahydropyran-2-ones from isoxazoline-2-oxides†

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Tetrahydropyran-2-ones with a 4-amino function connected to a tertiary carbon atom – a widely naturally occurring fragment – are constructed by a three step protocol from easily available isoxazoline 2-oxides. In the first stage, the carbon skeleton of the target product is formed upon a C,C-coupling of a silyl ketene acetal with a nitronate function, under silyl triflate catalysis. The key step of the assembly consists of the oxidative cleavage of an endocyclic N–O bond of intermediate cyclic nitroso acetals with *m*CPBA, accompanied with lactone ring closure, and gives rise to β-nitro-δ-lactones in 63–85% yields. The latter are reduced with amalgamated aluminium, to furnish the target scaffold.

Introduction

The 4-aminosubstituted six-membered lactone scaffold (marked as structure **1** in Fig. 1), derived from β-amino acids, occurs in different classes of natural products, like stephadiamine,[1] kopsihainin D[2] and the tetrodotoxin (TTX) family[3,4] (Fig. 1), exhibiting various biological activities. In particular, TTX and its congeners constitute the key components of the puffer fish fugu poison[5] and due to their complex structure are considered as classical objects for total synthesis.[6] However, few syntheses of these compounds have succeeded.[7–10] Difficulties usually arise from the construction of the stereogenic quaternary carbon center connected with an amine (further guanidine) function. For this purpose, non-trivial or indirect methods such as Beckmann[7b] and Overman[8] rearrangements, asymmetric transferring Strecker synthesis[9] or chiral Rh-catalyzed C–H nitrene insertion[10] have to be employed. Therefore, the development of simple, direct methods for the construction of lactones **1** is an urgent task.

In this manuscript a convenient strategy for the synthesis of the scaffold **1** is suggested, which is based on a detailed investigation of the transformations of cyclic nitronates.[11]

A common retrosynthetic analysis for the β-amino acid moiety in lactones **1** employs a Mannich-type disconnection with the γ-imino alcohol cations **A** as key precursors for the generation of amines **1** (Scheme 1). However, this type of reaction is not generally applied, due to the complexity of the Mannich reaction with ketimines,[12] although the approach could provide the fast and simple assembly of the target molecule **1**.

Our recent results in the area of five-membered cyclic nitronates chemistry[13] suggest that the easily available five-membered nitronates **2** (isoxazoline 2-oxides)[11] can serve as useful synthetic equivalents for ketiminium cations **A** (Scheme 1) in the reaction with a silyl ketene acetal, but this approach requires an additional step for the reduction of both of the N–O bonds and the cyclization of the resulting products

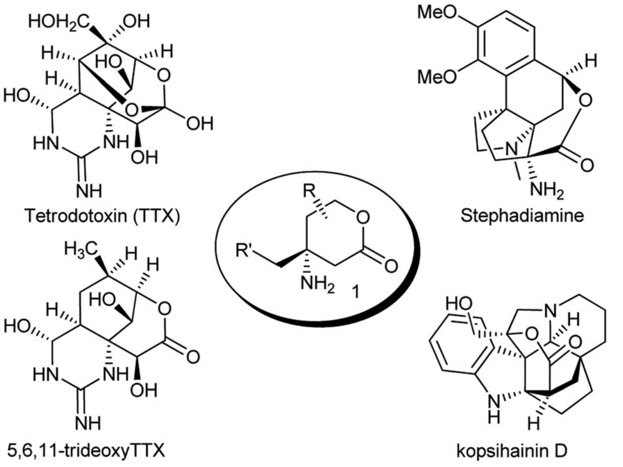

Fig. 1 Selected natural products containing β-alkyl-β-amino-δ-valerolactone moiety **1**.

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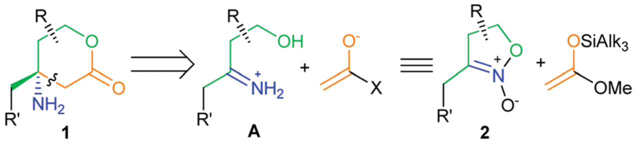
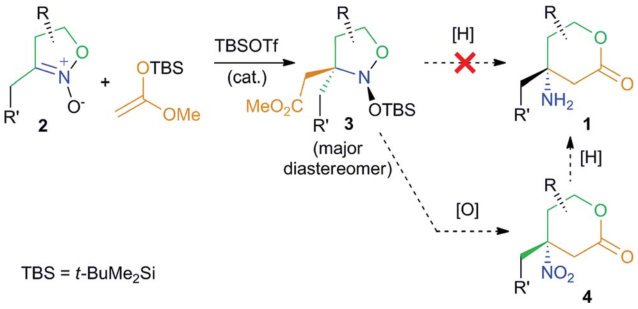
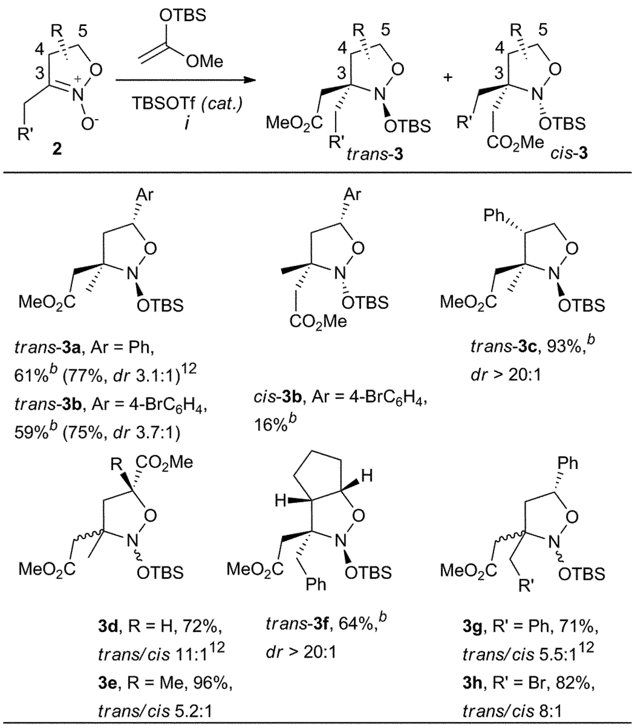


Scheme 1 Retrosynthesis *via* Mannich-disconnection of scaffold **1**.



Scheme 2 Three-step protocol for synthesis of the target amines **1** *via* intermediacy of nitro lactones **4**.

Table 1 Silyl ketene acetal addition to five-membered cyclic nitronates **2**[a]



trans-**3a**, Ar = Ph, 61%[b] (77%, *dr* 3.1:1)[12]
trans-**3b**, Ar = 4-BrC$_6$H$_4$, 59%[b] (75%, *dr* 3.7:1)

cis-**3b**, Ar = 4-BrC$_6$H$_4$, 16%[b]

trans-**3c**, 93%,[b] *dr* > 20:1

3d, R = H, 72%, *trans*/*cis* 11:1[12]
3e, R = Me, 96%, *trans*/*cis* 5.2:1

trans-**3f**, 64%,[b] *dr* > 20:1

3g, R′ = Ph, 71%, *trans*/*cis* 5.5:1[12]
3h, R′ = Br, 82%, *trans*/*cis* 8:1

[a] *Conditions i*: CH$_2$Cl$_2$ (0.2 M), TBSOTf (0.1–1.0 eq.), 2,6-dimethylpyridine (0.25 eq.), −78 °C, 1–24 h; see Experimental section for details. [b] Isolated yield of pure isomer.

into lactones **1** (Scheme 2). It should be noted that this method employs reagents with their usual polarities, with the configuration of the C-4 stereocenter of the target product being set at the stage of the C–C bond forming reaction.

Thus, the suggested strategy starts with the coupling of nitronates **2** with silyl ketene acetals. This transformation, like other Mukaiyama–Mannich reactions, requires a Lewis acid catalyst – *tert*-butyldimethylsilyl triflate (TBSOTf), in particular – for the production of nitroso acetals **3** (Scheme 2) in a rather highly diastereoselective fashion.[13,14] The products **3** contain the complete carbon skeleton of the target amines **1** and for their transformation into lactones **1**, only the transformations of the functional groups is required. However, the direct reduction of compounds **3** into amines **1** with both N–O bonds cleavage and lactone ring closure, within a one step protocol turned out to be ineffective.[13] A more convenient approach seems to employ two steps (Scheme 2): (1) lactone cycle formation *via* oxidation of isoxazolidines **3** into nitro compounds **4**; (2) selective nitro group reduction in lactones **4**. This modified scheme is supported with our recent research on the six-membered analogues of nitroso acetals **3** which are effectively oxidized with *m*CPBA into the corresponding nitro compounds with the retention of the relative configuration of all the stereocenters.[15,16]

A nitro group connected to a tertiary carbon in lactones **4** can be *a priori* regarded as a latent amine function, due its inertness to common reagents.[17] Therefore, in this manuscript, the main accent was on the preparation of the nitroso acetals **3** (step **2** → **3**) and their oxidation to nitro lactones **4**.

Results and discussion

Starting from the available nitronates **2** (ref. 11), a representative series of functionalized nitroso acetals **3a–h** was obtained *via* silyl ketene acetal addition, according to a well-known protocol,[13] or its modified version (Table 1, see the Experimental section for details). Only three of these: compounds *trans*-**3a**, **3g** (inseparable mixture of isomers *trans*/*cis* 5.5 : 1) and *trans*-**3d** (containing 8% of the *cis*-isomer) have been obtained previously.[13] The synthesis of the derivatives *trans*-**3b** and *cis*-**3b** proceeded in a rather similar way, although for **3e** the *trans*-selectivity was apparently decreased in comparison with the analogous **3d**.

To the best of our knowledge, no 4-substituted nitronates **2** were introduced in this type of reaction beforehand. These compounds were found to exhibit nearly a 100% *trans*-selectivity in coupling with the silyl ketene acetal, but required prolonged reaction times. The synthesis of the 4-phenyl-substituted *trans*-**3c** was completed in only 24 h with 0.2 equivalents of TBSOTf. The synthesis of the even more bulky bicyclic *trans*-**3f** required a full equivalent of the promoter within 8 h exposure at −78 °C. The *trans*-position of the substituent at C-4 and the introduced ketene acetal residue was proved by NOE NMR experiments (see Fig. 3).

The electrophilic activity of the nitronate **2h**, containing a halomethyl group at C-3, might appear in two different fashions – nucleophile addition at the C=N bond, or its halogenation.[18] Fortunately, the nitronate **2h** (R′ = Br) reacted with the silyl

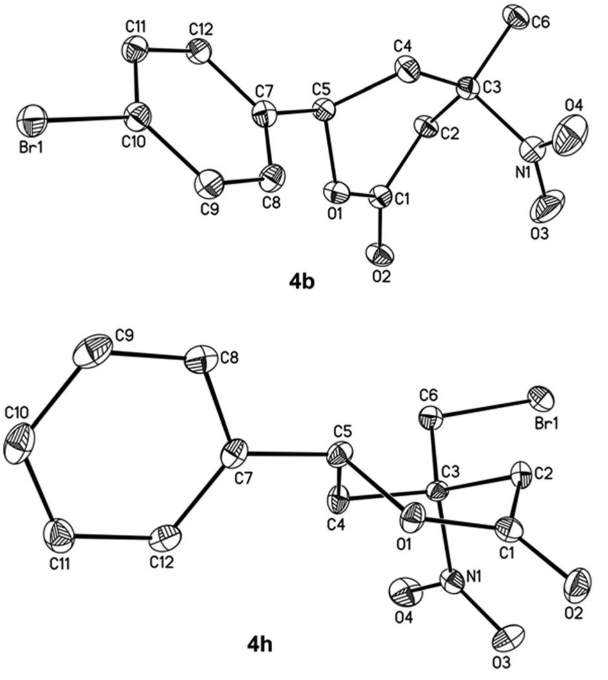
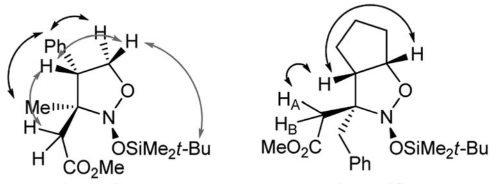
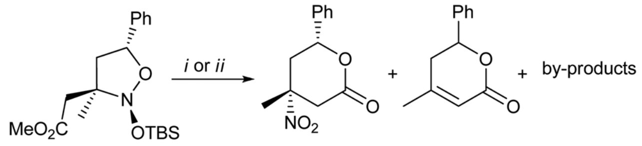


Fig. 2 Molecular structures of **4b** and **4h** presented in thermal ellipsoids at 50% probability. Hydrogen atoms are omitted for clarity.



trans-**3c** *trans*-**3f**

Fig. 3 Key NOE correlations for *trans*-**3c** and *trans*-**3f**.



trans-**3a** **4a** **5a**

Conditions:	4a	5a	by-products
i (standard):[15] *m*CPBA (1.1 eq), AcOH (2.0 eq), CH_2Cl_2, 24h	55%	8%	~30%
ii (optimized): *m*CPBA (1.1 eq), CH_2Cl_2, 72h	85%	7%	<5%

Scheme 3 Optimization of nitroso acetal **3** oxidation.

ketene acetal in a usual fashion, to give the respective nitroso acetal **3h** (*trans*/*cis* = 8 : 1).

For the elaboration of the second stage of the suggested protocol (Scheme 2, **3** → **4**) the oxidation was optimized on the model nitroso acetal **3a**. When the conditions, previously reported for 6-membered cyclic analogues of **3**,[15] were applied to **3a** (Scheme 3), protocol (i), the target nitro lactone **4a** was obtained in only a 55% yield, along with the nitrous acid elimination product **5a** (8%) and a mixture of unidentified linear by-products. The best result (Scheme 3), conditions (ii), achieved with sole *m*CPBA utilization and prolongation of the reaction time up to 3 days, accomplished the lactone ring-closure step. With the latter process in hand, this increased the isolated yield of the nitro lactone **4a** to 85%.

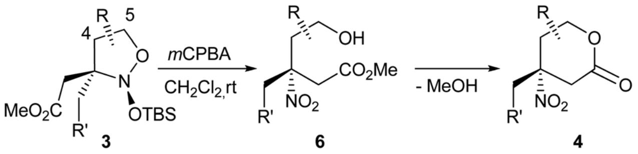
The optimized oxidation conditions were applied to the whole nitroso acetal **3** series. The individual diastereomers of the 5- or 4-aryl substituted nitroso acetals *trans*-**3a–c** and *cis*-**3b** were smoothly oxidized to give the desired lactones **4a–c** and **4b′** in moderate to high yields with the retention of configuration of all the stereocenters (Table 2, entries 1–4). The $R'CH_2$-substituted at C-3 nitroso acetals **3f–h** (R′ = Ph, Br, entries 7–9), that were usually used as diastereomeric mixtures, also gave the target nitro lactones **4f–h**, but a longer reaction time was required. When the nitroso acetals **3d,e**, with the electron-withdrawing CO_2Me group at C-5 were employed (entries 5–6), only the formation of acyclic γ-nitro alcohols **6d,e** – the proposed precursors of lactones **4** – was observed, reasonably due to the lower nucleophilicity of the alcohol function in these substrates. Even more acidic conditions (Amberlyst-15®), did not manage to achieve the cyclization of **6d** and **6e** into the corresponding lactones, **4d** and **4e**.

The configurations of compounds **4b** and **4h** were supported by X-ray diffraction analysis (Fig. 2). The stereochemistry of the other nitro lactones **4** was assigned by the similarity of their coupling constants with those of **4b** and **4h** in the ^{1}H NMR spectra. The nitro group formation in all of the compounds **4** was proven by ^{14}N NMR.

The last step of the lactones **1** preparation – selective reduction of the nitro group – despite many precedents in the literature for tertiary nitro compounds[17,19] – turned out to be rather capricious. The standard hydrogenation conditions, like Pd/C in MeOH performed on **4a** gave only the acyclic product **7** in almost a quantitative yield as the result of the hydrogenolysis of the CH(Ph)–OC(O) fragment (Scheme 4). The other screened reagents ($NaBH_4/NiCl_2$,[20] Fe/AcOH,[19] Fe/NH_4Cl[19] and even H_2/Ni_{Ra}[17,19]) gave mainly the "HNO_2" elimination product **5a**, along with by-products, of unknown structures. [A more convenient protocol for the synthesis of enones **5** from lactones **4** was developed with the utilization *t*-BuOK in THF. It furnished compounds **5a** and **5c** with 94% and 95% yields, within 15–30 minutes, respectively (Scheme 4)].

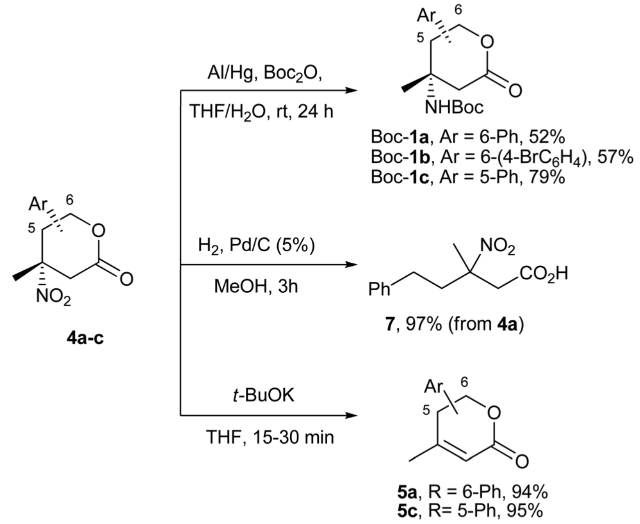
In these circumstances, we managed to reduce the nitro group with the rarely used amalgamated aluminium.[21] The most complicated intermediates – nitro compounds **4a** and **4b** with the benzyl carboxylate function – gave the protected derivatives **Boc-1a** and **Boc-1b** of target amines in 52 and 57% yields, respectively (Scheme 4). For the extremely sterically hindered lactone **4c**, a slightly modified procedure was applied, when the reduction and protection were divided into two technical steps. By this methodology and the utilization of a catalytic amount of DMAP for the Boc_2O activation, the desired product Boc-**1c** was obtained in a 79% yield.

Table 2 Oxidation of nitroso acetals **3** series



#	Nitroso acetal **3** (substituents)	Reaction time, days	Product, yield, % (*trans*/*cis dr*[a])
1	*trans*-**3a** (R = 5-Ph, R′ = H)	3	**4a**, 85
2	*trans*-**3b** (R = 5-(4-BrC$_6$H$_4$), R′ = H)	3	**4b**, 79
3	*cis*-**3b** (R = 5-(4-BrC$_6$H$_4$), R′ = H)	3	**4b′**, 63
4	*trans*-**3c** (R = 4-Ph, R′ = H)	2	**4c**, 76
5	**3d**, *trans*/*cis*, 11/1 (R = 5-CO$_2$Me, R′ = H)	1	**6d**/**6d′**, 95 (15 : 1)
6	**3e**, *trans*/*cis*, 5.2/1 (R = 5-CO$_2$Me and 5-Me, R′ = H)	1	**6e**/**6e′**, 92 (6.3 : 1)
7	*trans*-**3f** (R = *cis*-4,5-(CH$_2$)$_3$-, R′ = Ph)	7	**4f**, 64
8	**3g**, *trans*/*cis*, 5.5/1 (R = 5-Ph, R′ = Ph)	5	**4g**/**4g′**, 79 (6.5 : 1)
9	**3h**, *trans*/*cis*, 8/1 (R = 5-Ph, R′ = Br)	5	**4h**, 85 (>20 : 1)

[a] Determined by ^{1}H NMR spectra.



Scheme 4 Reduction and accompanying reactions of nitro lactones 4a–c.

Conclusions

In summary, we have demonstrated that the target β-amino-δ-lactones **1**, or more precisely, their *N*-Boc derivatives, can be obtained from the five-membered cyclic nitronates **2**, according to the suggested three-step protocol. The novelty of the approach consists of the combination of three transformations (C,C-coupling, oxidation and selective reduction of the NO$_2$ group). This procedure was applied to the synthesis of scaffolds **1** for the first time. In our opinion, there are no obstacles for the accomplishment of this strategy in an asymmetric manner.

Experimental section

General remarks

Reactions with TBSOTf were performed in oven-dried (150 °C) glassware under an argon atmosphere. The NMR spectra were recorded on a Bruker AM-300 (^{1}H: 300.13 MHz, ^{13}C: 75.47 MHz, ^{14}N: 21.69 MHz, ^{29}Si: 59.63 MHz) and Bruker AMX-400 (^{1}H: 400.1 MHz, ^{13}C: 100.6 MHz) and referenced to a residual solvent peak. The chemical shifts are reported in ppm (*δ*); multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). The ratios of the stereoisomers were derived from the relative integral intensities of the characteristic signals in the ^{1}H NMR spectra. Coupling constants, *J*, are reported in Hertz. Key NOESY correlations are shown with arrows (Fig. 2). The IR spectra were recorded on a Bruker VEKTOR-22 in the range 400–4000 cm^{-1} (resolution 2 cm^{-1}) as a thin layer. The melting points were determined on Kofler melting point apparatus and are uncorrected. The elemental analyses were performed by the Analytical Laboratory of the N. D. Zelinsky Institute of Organic Chemistry. The HR mass spectra were recorded on a Bruker MicroTOFF spectrometer with electrospray ionization (ES-I).

The X-ray diffraction measurements were carried out using SMART 1000 CCD and Smart APEX II diffractometers at 100 K.

The frames were integrated and corrected for absorption by the APEX 2 program package [APEX2 Software Package, Bruker AXS Inc., 5465, East Cheryl Parkway, Madison, WI 5317, 2005]. The details of crystallographic data and experimental conditions are given in Table SI1 in the ESI.† The structures were solved by a direct method and refined by the full-matrix least-squares technique against F2 in the anisotropic–isotropic approximation. The hydrogen atoms were located from the difference Fourier maps and refined in a rigid body model. All the calculations were performed using the APEX 2 program package [APEX2 Software Package, Bruker AXS Inc., 5465, East Cheryl Parkway, Madison, WI 5317, 2005].

The analytical thin-layer chromatography was performed on silica gel plates, with the QF-254 indicator. The visualization of the TLC plates was accomplished with a UV light and/or anisaldehyde/$\mathrm{H_2SO_4}$. The preparative liquid chromatography was performed on columns with "Merck"-silica (Kieselgel 60, 230–400 mesh). All the solvents for the chromatography and extractions were of technical grade and distilled prior to use. The following solvents and reagents were distilled from the indicated drying agents: $\mathrm{CH_2Cl_2}$, $\mathrm{CHCl_3}$, $\mathrm{Et_3N}$ ($\mathrm{CaH_2}$), MeOH (Mg), THF, dioxane ($\mathrm{LiAlH_4}$).

Synthesis of nitroso acetals 3 (first step, see Scheme 3)

Nitroso acetals *trans*-3b and *cis*-3b. TBSOTf (150 μL, 173 mg, 0.65 mmol) was added at −78 °C to a stirred solution of 5-(4-bromophenyl)-3-methyl-isoxazoline-2-oxide **2b** (837 mg, 3.27 mmol), 1-(*tert*-butyldimethylsilyloxy)-1-methoxyethene (0.93 mL, 788 mg, 3.92 mmol) and 2,6-lutidine (95 μL, 87 mg, 0.82 mmol) in $\mathrm{CH_2Cl_2}$ (10 mL). The reaction mixture was stirred at the same temperature for 1 hour, then quenched with MeOH (33 μL, 26 mg, 0.82 mmol) and poured into a mixture of water (10 mL) and hexane (20 mL). The aqueous layer was separated out and back-extracted with hexane (2 × 5 mL). Combined organic layers were washed successively with sat. $\mathrm{NaHCO_3}$ solution (7 mL) and brine (15 mL) and dried over $\mathrm{Na_2SO_4}$. The residue was subjected to column chromatography (eluent EtOAc–hexane 1/40 → 1/20 → 1/10) to give the separated diastereomers, *trans*-**3b** (852 mg, 59%) and *cis*-**3c** (233 mg, 16%) each as a slowly crystallizing colorless oil (*dr* 3.5 : 1).

Methyl *rel*-((2*S*,3*R*,5*R*)-5-(4-bromophenyl)-(2-*tert*-butyldimethylsilyloxy)-3-methylisoxazolidin-3-yl)acetate *trans*-3b. Mp = 42–43 °C (pentane), TLC: $R_\mathrm{f} = 0.58$ (hexane–EtOAc, 3/1); ^{1}H NMR (300.13 MHz, 299 K, $\mathrm{CDCl_3}$): $\delta = 0.17$ and 0.22 [2s, 6H, $\mathrm{Si(CH_3)_2}$], 0.94 [s, 9H, *t*-Bu], 1.28 [s, 3H, Me], 2.10 [dd, $^2J = 12.3$, $^3J = 5.6$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$], 2.58 [d, $^2J = 15.1$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B(CO_2Me)}$], 2.52–2.67 [m, 2H, $\mathrm{CH_A}H_\mathrm{B}$ and $\mathrm{CH_A}H_\mathrm{B}\mathrm{(CO_2Me)}$], 3.69 [s, 3H, $\mathrm{CO_2Me}$], 5.54 [dd, $^3J = 9.6$, $^3J = 5.6$ Hz, 1H, CH], 7.25 [d, $^3J = 8.7$ Hz, $\mathrm{CH}_{o\text{-}\mathrm{Ar}}$] and 7.48 [d, $^3J = 8.7$ Hz, $\mathrm{CH}_{m\text{-}\mathrm{Ar}}$] ppm; ^{13}C NMR (75.47 MHz, 299 K, $\mathrm{CDCl_3}$): $\delta = -5.0$ and -4.8 [$\mathrm{Si(CH_3)_2}$], 18.0 [$C\mathrm{(CH_3)_3}$], 25.5 [$\mathrm{CH_3}$], 25.9 [$\mathrm{C(}C\mathrm{H_3)_3}$], 42.0 [$C\mathrm{H_2CO_2Me}$], 43.7 [$\mathrm{CH_2}$], 51.6 [$\mathrm{OCH_3}$], 74.4 [CNO], 80.3 [CH], 121.3 [$\mathrm{C_{i\text{-}Ph}}$], 128.1 and 131.5 [$\mathrm{CH}_{o\text{-}\mathrm{Ph}}$ and $\mathrm{CH}_{m\text{-}\mathrm{Ph}}$], 139.5 [CBr], 171.6 [OC = O] ppm; ^{29}Si NMR (300 K, $\mathrm{CDCl_3}$): $\delta = 25.9$ ppm. $\mathrm{C_{19}H_{30}NO_4BrSi}$ (444.44): calcd C, 51.35; H, 6.80; N, 3.15; found: C, 51.57; H, 6.88; N, 3.16%.

Methyl *rel*-((2*R*,3*S*,5*R*)-5-(4-bromophenyl)-(2-*tert*-butyldimethylsilyloxy)-3-methylisoxazolidin-3-yl)acetate *cis*-2b. Mp = 46 °C (pentane), TLC: $R_\mathrm{f} = 0.51$ (hexane–EtOAc, 3/1); ^{1}H NMR (300.13 MHz, 323 K, $\mathrm{CDCl_3}$): $\delta = 0.17$ and 0.19 [2s, 6H, $\mathrm{Si(CH_3)_2}$], 0.91 [s, 9H, *t*-Bu], 1.34 [s, 3H, Me], 2.52 [t, $^2J \approx {}^3J = 12.0$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$], 2.59–2.68 [m, 2H, $\mathrm{CH_A}H_\mathrm{B}$ and $\mathrm{C}H_\mathrm{C}\mathrm{H_D(CO_2Me)}$], 2.90 [d, $^2J = 14.9$ Hz, 1H, $\mathrm{CH_C}H_\mathrm{D}\mathrm{(CO_2Me)}$], 3.70 [s, 3H, $\mathrm{CO_2Me}$], 5.25 [dd, $^3J \approx {}^3J = 7.8$ Hz, 1H, CH], 7.36 [d, $^3J = 8.3$ Hz, 2H, $\mathrm{CH}_{o\text{-}\mathrm{Ar}}$] and 7.44 [d, $^3J = 8.3$ Hz, 2H, $\mathrm{CH}_{m\text{-}\mathrm{Ar}}$] ppm; ^{13}C NMR (75.47 MHz, 323 K, $\mathrm{CDCl_3}$): $\delta = -4.9$ and -4.6 [$\mathrm{Si(CH_3)_2}$], 17.8 [$C\mathrm{(CH_3)_3}$], 21.9 [$\mathrm{CH_3}$], 26.0 [$\mathrm{C(}C\mathrm{H_3)_3}$], 41.5 [$C\mathrm{H_2CO_2Me}$], 43.7 [$\mathrm{CH_2}$], 51.4 [$\mathrm{OCH_3}$], 74.6 [$\mathrm{CNO_2}$], 84.6 [CH], 121.4 [$\mathrm{C_{i\text{-}Ph}}$], 129.1 and 131.1 [$\mathrm{CH}_{o\text{-}\mathrm{Ph}}$ and $\mathrm{CH}_{m\text{-}\mathrm{Ph}}$], 135.5 [CBr], 171.3 [OC = O] ppm; ^{29}Si NMR (300 K, $\mathrm{CDCl_3}$): $\delta = 25.4$ ppm.

$\mathrm{C_{19}H_{30}NO_4BrSi}$ (444.44): calcd C, 51.35; H, 6.80; N, 3.15; found C, 51.66; H, 7.05; N, 3.38%.

Methyl *rel*-((2*S*,3*R*,5*R*)-(2-*tert*-butyldimethylsilyloxy)-3-methyl-4-phenylisoxazolidin-3-yl)acetate *trans*-3c. Obtained by the same procedure as **3b**. The reaction was performed on 2.0 mmol scale with 24 h exposure. Yield 681 mg (93%); *dr* > 20:1; mp = 26 °C (pentane); TLC: $R_\mathrm{f} = 0.49$ (hexane–EtOAc, 5/1); ^{1}H NMR (400.1 MHz, 305 K, $\mathrm{CDCl_3}$): $\delta = 0.15$ and 0.23 [2s, 6H, $\mathrm{Si(CH_3)_2}$], 0.95 [s, 9H, *t*-Bu], 1.09 [s, 3H, Me], 2.56 [d, $^2J = 14.9$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B(CO_2Me)}$], 2.77 [d, $^2J = 14.9$ Hz, 1H, $\mathrm{CH_A}H_\mathrm{B}$-$\mathrm{(CO_2Me)}$], 3.55 [s, 3H, $\mathrm{CO_2Me}$], 4.07 [dd, $^3J = 9.9$, $^3J = 7.9$ Hz, 1H, CH], 4.26 [t, $^2J \approx {}^3J = 7.9$ Hz, 1H, $\mathrm{C}H_\mathrm{C}\mathrm{H_D}$], 4.59 [dd, $^3J = 9.9$, $^2J = 7.9$ Hz, 1H, $\mathrm{CH_C}H_\mathrm{D}$], 7.27–7.35 [m, 5H, Ph] ppm; ^{13}C NMR (100.6 MHz, 305 K, $\mathrm{CDCl_3}$): $\delta = -5.1$ and -4.7 [$\mathrm{Si(CH_3)_2}$], 18.1 [$C\mathrm{(CH_3)_3}$], 20.4 [$\mathrm{CH_3}$], 26.0 [$\mathrm{C(}C\mathrm{H_3)_3}$], 40.3 [$C\mathrm{H_2CO_2Me}$], 51.2 [$\mathrm{OCH_3}$], 52.1 [CH], 73.0 [$\mathrm{OCH_2}$], 76.6 [CN], 127.3 [$\mathrm{CH}_{p\text{-}\mathrm{Ph}}$], 128.4 and 129.3 [$\mathrm{CH_{Ph}}$], 136.7 [$\mathrm{C_{i\text{-}Ph}}$], 170.7 [OC = O] ppm; ^{29}Si NMR (300 K, $\mathrm{CDCl_3}$): $\delta = 26.1$ ppm. $\mathrm{C_{19}H_{31}NO_4Si}$ (365.54): calcd C, 62.43; H, 8.55; N, 3.83; found C, 62.53; H, 8.38; N, 3.84%.

Methyl 2-(((*tert*-butyldimethylsilyl)oxy)-3-methoxycarbonyl-3,5-dimethylisoxazolidine-5-carboxylate) 3e. Obtained by the same procedure as **3b** on a 2.0 mmol scale. Yield 691 mg (96%), *dr* 5.2 : 1 (inseparable mixture), colorless oil; TLC: $R_\mathrm{f} = 0.66$ (hexane–EtOAc, 1/1); ^{1}H NMR (400.1 MHz, 305 K, $\mathrm{CDCl_3}$): *rel*-2*S*,3*R*,5*R*-isomer, *trans*-**3e** (major): $\delta = 0.11$ and 0.20 [2s, 6H, $\mathrm{Si(CH_3)_2}$], 0.89 [s, 9H, *t*-Bu], 1.13 [s, 3H, $\mathrm{NCCH_3}$], 1.69 [s, 3H, $\mathrm{OCCH_3}$], 2.50 [d, $^2J = 14.7$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$], 2.51 [d, $^2J = 12.8$ Hz, 1H, $\mathrm{C}H_\mathrm{C}\mathrm{H_D(CO_2Me)}$], 2.82 [d, $^2J = 14.7$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$], 2.85 [d, $^2J = 12.8$ Hz, 1H, $\mathrm{C}H_\mathrm{C}\mathrm{H_D(CO_2Me)}$], 3.66 [s, 3H, $\mathrm{CO_2CH_3}$], 3.73 [s, 3H, $\mathrm{CH_2CO_2}C\!H_3$]; *rel*-2*R*,3*S*,5*R*-isomer, *cis*-**3e** (minor): $\delta = 0.08$ and 0.17 [2s, 6H, $\mathrm{Si(CH_3)_2}$], 0.84 [s, 9H, *t*-Bu], 1.27 [s, 3H, $\mathrm{NCCH_3}$], 1.53 [s, 3H, $\mathrm{OCCH_3}$], 2.50 [d, $^2J = 14.7$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$], 2.51 [d, $^2J = 12.8$ Hz, 1H, $\mathrm{C}H_\mathrm{C}\mathrm{H_D(CO_2Me)}$], 2.82 [d, $^2J = 14.7$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$], 2.85 [d, $^2J = 12.8$ Hz, 1H, $\mathrm{C}H_\mathrm{C}\mathrm{H_D(CO_2Me)}$], 3.66 [s, 3H, $\mathrm{CH_2CO_2}C\!H_3$], 3.68 [s, 3H, $\mathrm{CO_2CH_3}$] ppm; ^{13}C NMR (100.6 MHz, 305 K, $\mathrm{CDCl_3}$): *rel*-2*S*,3*R*,5*R*-isomer, *trans*-**3e** (major): $\delta = -5.0$ and -4.4 [$\mathrm{Si(CH_3)_2}$], 17.8 [$C\mathrm{(CH_3)_3}$], 22.8 [$\mathrm{NC}C\mathrm{H_3}$], 26.8 [$\mathrm{C(}C\mathrm{H_3)_3}$], 28.5 [$\mathrm{OC}C\mathrm{H_3}$], 42.1 [$C\mathrm{H_2CO_2Me}$], 46.5 [$\mathrm{CH_2}$], 51.7 [$\mathrm{CH_2CO_2}C\mathrm{H_3}$], 52.6 [$\mathrm{CO_2}C\mathrm{H_3}$], 74.4 [N–*C*], 88.6 [N–O–*C*], 171.4 [$\mathrm{CH_2}C\mathrm{O_2Me}$], 174.0 [$C\mathrm{O_2Me}$]; *rel*-2*R*,3*S*,5*R*-isomer, *cis*-**3e** (minor): $\delta = -4.9$ and -4.4 [$\mathrm{Si(CH_3)_2}$], 17.9 [$C\mathrm{(CH_3)_3}$], 24.3 [$\mathrm{NC}C\mathrm{H_3}$], 25.2 [$\mathrm{C(}C\mathrm{H_3)_3}$], 25.8 [$\mathrm{OC}C\mathrm{H_3}$], 42.3 [$C\mathrm{H_2CO_2Me}$], 44.1

[CH_2], 51.7 [$CH_2CO_2CH_3$], 52.3 [CO_2CH_3], 74.8 [N–*C*], 86.4 [N–O–*C*], 171.5 [CH_2CO_2Me], 175.1 [CO_2Me] ppm. ^{29}Si NMR (305 K, $CDCl_3$, INEPT): *rel*-2*S*,3*R*,5*R*-isomer, *trans*-**3e** (major): $\delta = 26.0$; *rel*-2*R*,3*S*,5*R*-isomer, *cis*-**3e** (minor): $\delta = 26.2$ ppm. HRMS (ES-I) calcd for $C_{16}H_{31}NO_6SiH$ $[M + H]^+$ 362.1993; found 362.1990.

Methyl 2-(*rel*-(2*S*,3*S*,3a*S*,6a*S*)-3-benzyl-(2-*tert*-butyldimethylsilyloxy)-hexahydro-2*H*-cyclopenta[*d*]isoxazol-3-yl)acetate *trans*-3f. Obtained by the same procedure as **3b** with 1.0 eq. of TBSOTf and 8 h exposure. Performed on a 1.20 mmol scale. Yield 307 mg (64%), *dr* > 20 : 1, slightly greenish oil, TLC: $R_f = 0.85$ (hexane–EtOAc, 1/1); ^{1}H NMR (300.13 MHz, 300 K, $CDCl_3$): $\delta = -0.21$ and 0.09 [2s, 6H, $Si(CH_3)_2$], 0.87 [s, 9H, *t*-Bu], 1.66–1.80 [m, 4H, $CH_{2Cyc.}$], 1.90–2.00 and 2.11–2.21 [2m, 2H, $CH_{2Cyc.}$] 2.27 [d, $^2J = 16.3$ Hz, 1H, CH_AH_B], 2.73 [d, $^2J = 16.3$ Hz, 1H, CH_AH_B], 2.83 [d, $^2J = 13.7$ Hz, 1H, CH_CH_DPh], 3.02 [d, $^2J = 13.7$ Hz, 1H, CH_CH_DPh], 3.06 [t, $^3J \approx {}^3J = 7.3$ Hz, 1H, CH], 3.71 [s, 3H, CO_2Me], 5.16 [dd, $^3J = 6.4$, $^3J = 5.3$ Hz, 1H, OCH], 7.16–7.31 [m, 5H, Ph] ppm. ^{13}C NMR (75.47 MHz, 300 K, $CDCl_3$): $\delta = -5.2$ and -5.0 [$Si(CH_3)_2$], 17.8 [$C(CH_3)_3$], 25.9 [$C(CH_3)_3$], 26.6, 27.9, 30.6, 37.4 and 38.9 [CH_2], 51.4 [OCH_3], 53.3 [CH], 79.0 [C–N], 87.4 [OCH], 126.2 [$CH_{p\text{-}Ph}$], 127.5 and 128.5 [$CH_{o\text{-}Ph}$ and $CH_{m\text{-}Ph}$], 137.9 [$C_{i\text{-}Ph}$], 172.0 [OC = O] ppm; ^{29}Si NMR (300 K, $CDCl_3$): $\delta = 25.1$ ppm; HRMS (ES-I) calcd for $C_{22}H_{35}NO_4SiNa$ $[M + Na]^+$ 428.2228; found 428.2208.

Methyl 3-bromomethyl-5-phenyl-(2-*tert*-butyldimethylsilyloxy)-isoxazolidin-3-ylacetate 3h. Obtained by the same procedure as **3b** except with a 3 h exposure. The reaction was performed on a 1.50 mmol scale; yield 570 mg (86%), *dr* 8.0 : 1 (inseparable mixture), TLC: $R_f = 0.76$ (hexane–EtOAc, 1/1); ^{1}H NMR (300.13 MHz, 302 K, $CDCl_3$): *rel*-2*S*,3*R*,5*R*-isomer, *trans*-**3h** (major): $\delta = 0.22$ and 0.26 [2s, 6H, $Si(CH_3)_2$], 0.97 [s, 9H, *t*-Bu], 2.65 [dd, $^2J = 13.2$, $^3J = 10.2$ Hz, 1H, CH_AH_B], 2.92 [dd, $^2J = 13.2$, $^3J = 8.8$ Hz, 1H, CH_AH_B], 3.00 [d, $^2J = 16.9$ Hz, 1H, $CH_CH_D(CO_2Me)$], 3.12 [d, $^2J = 16.9$ Hz, 1H, $CH_CH_D(CO_2Me)$], 3.64 [d, $^2J = 11.0$ Hz, 1H, CH_EH_FBr], 3.72 [s, 3H, CO_2Me], 3.78 [d, $^2J = 11.0$ Hz, 1H, CH_EH_FBr], 5.63 [dd, $^3J = 8.8$, $^3J = 6.6$, 1H, CH], 7.28–7.48 [m, 5H, Ph]; *rel*-2*R*,3*S*,5*R*-isomer, *cis*-**3h** (minor): $\delta = 0.04$ and 0.20 [2s, 6H, $Si(CH_3)_2$], 0.90 [s, 9H, *t*-Bu], 2.32 [dd, $^2J = 13.2$, $^3J = 6.6$ Hz, 1H, CH_AH_B], 2.87–3.01 [m, 2H, CH_AH_B and $CH_CH_D(CO_2Me)$, overlaps with major isomer], 3.14 [d, $^2J = 16.9$ Hz, 1H, $CH_CH_D(CO_2Me)$], 3.67 [d, $^2J = 17.6$ Hz, 1H, CH_EH_FBr], 3.72 [s, 3H, CO_2Me], 3.78 [d, $^2J = 17.6$ Hz, 1H, CH_EH_FBr], 5.63 [dd, $^3J = 10.2$, $^3J = 8.1$ Hz, 1H, CH], 7.28–7.48 [m, 5H, Ph] ppm; ^{13}C NMR (75.47 MHz, 302 K, $CDCl_3$): *rel*-2*S*,3*R*,5*R*-isomer, *trans*-**3h** (major): $\delta = -5.2$ and -4.8 [$Si(CH_3)_2$], 18.0 [$C(CH_3)_3$], 25.9 [$C(CH_3)_3$], 37.8 and 37.9 [CH_2CO_2Me and CH_2Br], 42.3 [CH_2], 51.7 [OCH_3], 77.3 [C–N], 80.3 [OCH], 126.4 [$CH_{p\text{-}Ph}$], 128.0 and 128.7 [$CH_{o\text{-}Ph}$ and $CH_{m\text{-}Ph}$], 139.1 [$C_{i\text{-}Ph}$], 171.0 [OC = O]; *rel*-2*R*,3*S*,5*R*-isomer, *cis*-**3h** (minor): $\delta = -4.9$ and -4.5 [$Si(CH_3)_2$], 17.8 [$C(CH_3)_3$], 25.7 [$C(CH_3)_3$], 35.1 [CH_2Br], 37.4 [CH_2CO_2Me], 41.8 [CH_2], 51.7 [OCH_3], 76.5 [C–N], 84.7 [OCH], 127.3, 127.7 and 128.2 [CH_{Ph}], 140.1 [$C_{i\text{-}Ph}$], 170.8 [OC = O] ppm; HRMS (ES-I) calcd for $C_{19}H_{30}BrNO_4SiNa$ $[M + Na]^+$ 466.1020 and 466.1000; found 466.1023 and 466.1002.

Nitro lactone 4 formation (second step, see Scheme 3)

General procedure. The nitroso acetal **3** (1.00 mmol) and *m*CPBA (70%, 271 mg, 1.10 mmol) as a solution in CH_2Cl_2 (3.0 mL) were kept, with occasional shaking, at room temperature for 1–7 days (a green or blue color of reaction mixture after *m*CPBA addition was observed in several cases, due to the intermediacy of nitroso compounds). The reaction mixture was poured into a mixture of EtOAc (15 mL)/$NaHCO_3$ (12 mL, saturated aqueous solution). The aqueous layer was back-extracted with EtOAc (2 × 5 mL). The combined organic phase was washed with H_2O (10 mL), brine (10 mL) and dried over Na_2SO_4. The solvents were evaporated *in vacuo*. The residue was subjected to column chromatography (eluent EtOAc–hexane 1/5 → 1/3 → 1/2), or to recrystallization from $CHCl_3$–hexane or Et_2O to give the nitro compound **4** or **6** as colorless crystals.

***rel*-(4*R*,6*R*)-4-Methyl-4-nitro-6-phenyltetrahydro-2*H*-pyran-2-one, 4a.** Yield 199 mg (85%), mp = 92–95 °C (Et_2O), TLC: $R_f = 0.43$ (hexane–EtOAc, 1/1). IR (thin layer from CCl_4): 1753 (br *νs.*, νC═O), 1547 (*νs.*, $\nu_{as}NO_2$), 1354 (s, ν_sNO_2); ^{1}H NMR (300.13 MHz, 299 K, $CDCl_3$): $\delta = 1.87$ [s, 3H, CH_3], 2.56 [dd, $^2J = 15.5$, $^3J = 3.7$ Hz, 1H, CH_AH_B], 2.63 [dd, $^2J = 15.5$, $^3J = 11.4$ Hz, 1H, CH_AH_B], 2.98 [d, $^2J = 16.9$ Hz, 1H, CH_CH_D], 3.35 [d, $^2J = 16.9$ Hz, 1H, CH_CH_D)], 5.32 [dd, $^3J = 11.4$, $^3J = 3.7$ Hz, 1H, CH], 7.33–7.45 [m, 5H, Ph] ppm; ^{13}C NMR (75.47 MHz, 299 K, $CDCl_3$): $\delta = 25.8$ [CH_3], 40.0 [CH_2], 42.0 [$CH_2C{=}O$], 77.2 [CH], 84.4 [CNO_2], 126.0 and 128.6 [$CH_{o\text{-}Ph\ and\ m\text{-}Ph}$], 129.1[($CH_{p\text{-}Ph}$], 137.2 [$C_{i\text{-}Ph}$], 167.6 [OC═O] ppm; ^{14}N NMR (299 K, $CDCl_3$): $\delta = 16$ ($\nu_{1/2} \approx 100$ Hz) ppm. $C_{12}H_{13}NO_4$ (235.24): calcd C, 61.27; H, 5.57; N, 5.95; found C, 61.36; H, 5.72; N, 5.85%.

rel-(4*R*,6*R*)-6-(4-Bromophenyl)-4-methyl-4-nitrotetrahydro-2*H*-pyran-2-one 4b. Yield 249 mg (79%), mp = 162–165 °C (Et_2O), TLC: $R_f = 0.33$ (hexane–EtOAc, 1/1); ^{1}H NMR (300.13 MHz, 312 K, $CDCl_3$): $\delta = 1.88$ [s, 3H, CH_3], 2.55–2.64 [m, 2H, CH_2], 2.97 [d, $^2J = 17.2$ Hz, 1H, CH_AH_B], 3.35 [d, $^2J = 17.2$ Hz, 1H, CH_AH_B], 5.29 [dd, $^3J = 10.5$, $^3J = 3.5$ Hz, 1H, CH], 7.25 [d, $^3J = 8.0$ Hz, 2H, CH_{Ar}], 7.56 [d, $^3J = 8.0$ Hz, 2H, CH_{Ar}] ppm; ^{13}C NMR (75.47 MHz, 312 K, $CDCl_3$): $\delta = 25.7$ [CH_3], 40.1 [CH_2], 41.6 [CH_2], 76.5 [CH], 83.9 [CNO_2], 123.2 [CBr], 127.5 [C_{Ar}], 132.2 and 136.3 [CH_{Ar}], 166.6 [OC═O] ppm; ^{14}N NMR (312 K, $CDCl_3$): $\delta = 13$ ($\nu_{1/2} \approx 150$ Hz) ppm; $C_{12}H_{12}BrNO_4$ (314.13): calcd C, 45.88; H, 3.85; N, 4.46; found C, 45.62; H, 3.77; N, 4.21%.

***rel*-(4*S*,6*R*)-6-(4-Bromophenyl)-4-methyl-4-nitrotetrahydro-2*H*-pyran-2-one 4b′.** Yield 198 mg (63%), mp = 111–112 °C (Et_2O), TLC: $R_f = 0.57$ (hexane/EtOAc, 1/1). ^{1}H NMR (300.13 MHz, 323 K, $CDCl_3$): $\delta = 1.77$ [s, 3H, CH_3], 2.08 [dd, $^2J = 14.5$, $^3J = 11.7$ Hz, 1H, CH_AH_B], 2.79 [d, $^2J = 17.7$ Hz, 1H, CH_CH_D], 2.86 [dd, $^2J = 14.5$, $^3J = 1.7$ Hz, 1H, CH_AH_B], 3.63 [d, $^2J = 17.7$ Hz, 1H, CH_CH_D], 5.27 [dd, $^3J = 11.7$, $^3J = 1.7$ Hz, 1H, CH], 7.25 [d,$^3J = 8.1$ Hz, 2H, CH_{Ar}], 7.54 [d, $^3J = 8.1$ Hz, 2H, CH_{Ar}] ppm; ^{13}C NMR (75.47 MHz, 323 K, $CDCl_3$): $\delta = 27.1$ [CH_3], 39.6 [CH_2], 41.7 [CH_2], 76.7 [CH], 85.3 [CNO_2], 123.0 [CBr], 127.3 [C_{Ar}], 132.0 and 136.5 [C_{Ar}], 166.2 [OC = O] ppm. ^{14}N NMR (323 K, $CDCl_3$): $\delta = 13$ ($\nu_{1/2} \approx 150$ Hz) ppm; $C_{12}H_{12}BrNO_4$ (314.13): calcd C, 45.88; H, 3.85; N, 4.46; found C, 45.91; H, 3.62; N, 4.48%.

***rel*-(4*S*,5*S*)-4-Methyl-4-nitro-5-phenyltetrahydro-2*H*-pyran-2-one 4c.** Yield 179 mg (76%), mp = 122–124 °C ($CHCl_3$–hexane, 2/1), TLC: $R_f = 0.36$ (hexane–EtOAc, 1/1); ^{1}H NMR (400.1 MHz, 305 K, $CDCl_3$): $\delta = 1.59$ [s, 3H, CH_3], 2.80 [d, $^2J = 17.8$ Hz, 1H, CH_AH_B], 3.35 [d, $^2J = 17.8$ Hz, 1H, CH_AH_B], 3.38 [dd, $^3J = 11.0$, $^3J = 5.3$ Hz, 1H, CH], 4.51 [dd, $^2J = 12.1$, $^3J = 5.3$ Hz, 1H, CH_AH_B], 4.78 [t, $^2J \approx {}^3J = 11.7$ Hz, 1H, $\mathrm{CH_A}H_\mathrm{B}$], 7.04 [d, $^3J = 7.7$ Hz, 2H, $\mathrm{CH}_{o\text{-Ph}}$], 7.30–7.42 [m, 3H, $\mathrm{CH}_{m\text{-Ph}}$ and $\mathrm{CH}_{p\text{-Ph}}$] ppm; ^{13}C NMR (100.6 MHz, 305 K, CDCl$_3$): $\delta = 24.4$ [CH$_3$], 40.9 [$C\mathrm{H_2C{=}O}$], 48.4 [CH], 68.5 [OCH$_2$], 87.7 [CNO$_2$], 128.5 and 129.2 [$\mathrm{CH}_{o\text{-Ph}}$ and $\mathrm{CH}_{m\text{-Ph}}$], 129.4 [$\mathrm{CH}_{p\text{-Ph}}$], 132.4 [$\mathrm{C}_{\text{i-Ph}}$], 166.7 [OC=O] ppm; ^{14}N NMR (28.9 MHz, 299 K, CDCl$_3$): $\delta = 7$ ($\nu_{1/2} \approx 100$ Hz) ppm; $C_{12}H_{13}NO_4$ (235.24): calcd C, 61.27; H, 5.57; N, 5.95; found C, 60.99; H, 5.56; N, 5.96%.

Dimethyl *rel*-(2*R*,4*R*)-2-hydroxy-4-methyl-4-nitrohexanediolate 6d. Yield 237 mg (95%), oil, TLC: $R_f = 0.30$ (hexane–EtOAc, 1/1); ^{1}H NMR (300.13 MHz, 299 K, CDCl$_3$): $\delta = 1.75$ [s, 3H, CH$_3$], 2.43 [dd, $^2J = 14.7$, $^3J = 10.4$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$], 2.58 [dd, $^2J = 14.7$, $^3J = 2.6$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$], 3.09–3.24 [m, 3H, CH$_2$ and OH], 3.67 [s, 3H, CO$_2$Me], 3.79 [s, 3H, CO$_2$Me], 4.27 [dd, $^3J = 10.4$, $^3J = 2.4$ Hz, 1H, CH] ppm; ^{13}C NMR (75.47 MHz, 299 K, CDCl$_3$): $\delta = 24.1$ [CH$_3$], 41.7 and 41.8 [CH$_2$], 52.0 and 53.1 [OCH$_3$], 67.3 [CH], 87.1 [CNO$_2$], 169.7 and 174.3 [OC=O] ppm; ^{14}N NMR (299 K, CDCl$_3$): $\delta = 14$ ($\nu_{1/2} \approx 200$ Hz) ppm; HRMS (ES-I) calcd for $C_9H_{15}NO_7Na$ [M + Na]$^+$ 272.0741; found 272.0747.

Dimethyl 2-hydroxy-2,4-dimethyl-4-nitrohexanediolate 6e/6e′. Yield 235 mg (89%), *dr* 6.3 : 1 (inseparable mixture), oil, TLC: $R_f = 0.32$ (hexane–EtOAc, 1/1); ^{1}H NMR (300.13 MHz, 299 K, CDCl$_3$): *rel*-2*R*,4*R*-isomer **6e** (major): $\delta = 1.41$ [s, 3H, CH$_3$], 1.68 [s, 3H, CH$_3$], 2.67 [s, 2H, CH$_2$], 2.95 [d, $^2J = 16.4$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$], 3.09 [d, $^2J = 16.4$ Hz, 1H, $\mathrm{CH_A}H_\mathrm{B}$], 3.20 [br s, 1H, OH], 3.68 [s, 3H, CO$_2$Me], 3.79 [s, 3H, CO$_2$Me]; *rel*-4*S*,6*R*-isomer **6e′** (minor): $\delta = 1.42$ [s, 3H, CH$_3$], 1.64 [s, 3H, CH$_3$], 2.64 [d, $^2J = 15.2$ Hz, 1H, $\mathrm{C}H_\mathrm{C}\mathrm{H_D}$], 2.74 [d, $^2J = 15.2$ Hz, 1H, $\mathrm{CH_C}H_\mathrm{D}$], 3.12 [d, $^2J = 17.2$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$], 3.20 [br s, 1H, OH], 3.25 [d, $^2J = 17.2$ Hz, 1H, $\mathrm{CH_A}H_\mathrm{B}$], 3.68 [s, 3H, CO$_2$Me], 3.80 [s, 3H, CO$_2$Me] ppm; ^{13}C NMR (75.47 MHz, 299 K, CDCl$_3$): *rel*-4*R*,6*R*-isomer **6e** (major): $\delta = 23.0$ and 29.7 [CH$_3$], 43.1 and 45.8 [CH$_2$], 52.0 and 53.2 [OCH$_3$], 73.0 [C], 86.6 [CNO$_2$], 169.4 and 176.9 [OC=O]; *rel*-4*S*,6*R*-isomer **6e′** (minor): $\delta = 23.9$ and 29.6 [CH$_3$], 41.9 and 45.3 [CH$_2$], 51.9 and 53.2 [OCH$_3$], 72.9 [C], 87.4 [CNO$_2$], 169.9 and 176.9 [OC=O] ppm; ^{14}N NMR (299 K, CDCl$_3$): $\delta = 19$ ($\nu_{1/2}$, *ca.* 200 Hz) ppm; HRMS (ES-I) calcd for $C_{10}H_{17}NO_7Na$ [M + Na]$^+$ 286.0897; found 286.0900.

***rel*-(4*R*,4a*S*,7a*S*)-4-Benzyl-4-nitrohexahydrocyclapenta[*b*]-pyran-2(3*H*)-one 4f.** Yield 178 mg (64%), mp = 105–107 °C (hexane–EtOAc, 10/1), TLC: $R_f = 0.66$ (hexane–EtOAc, 1/1); ^{1}H NMR (300.13 MHz, 301 K, CDCl$_3$): $\delta = 1.52$ [ddd, $^2J = 17.7$, $^3J = 12.3$, $^2J = 7.4$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$(1)], 1.73–1.97 [m, 3H, CH$_2$(2), $\mathrm{CH_A}H_\mathrm{B}$(1)], 2.03–2.16 [m, 2H, CH$_2$(3)], 2.94 [dt, $^3J = 9.1$, $^3J \approx {}^3J = 5.7$, Hz 1H, CH], 2.99 [s, 2H, CH$_2$Ph], 3.10 [d, $^2J = 14.3$ Hz, 1H, $\mathrm{C}H_\mathrm{C}\mathrm{H_D}$CO], 3.10 [d, $^2J = 14.3$ Hz, 1H, $\mathrm{CH_C}H_\mathrm{D}$CO], 5.00 [dd, $^3J = 7.3$, $^3J = 4.9$ Hz, 1H, OCH], 7.03 [dd, $^3J = 6.5$, $^4J = 2.9$ Hz, 2H, $\mathrm{CH}_{o\text{-Ph}}$], 7.29–7.37 [m, 3H, $\mathrm{CH}_{m\text{-Ph}}$, $\mathrm{CH}_{p\text{-Ph}}$] ppm; ^{13}C NMR (75.47 MHz, 301 K, CDCl$_3$): $\delta = 22.2$ [CH$_2$-2], 26.2 [CH$_2$-1], 32.7 [CH$_2$Ph], 34.3 [CH$_2$-3], 44.9 [$C\mathrm{H_2CO}$], 45.6 [CH], 82.3 [OCH], 90.0 [CNO$_2$], 128.3 [$\mathrm{CH}_{p\text{-Ph}}$], 129.1 and 130.1 [$\mathrm{CH}_{m\text{-Ph}}$ and $\mathrm{CH}_{o\text{-Ph}}$], 132.2 [$\mathrm{C}_{\text{i-Ph}}$], 167.3 [OC=O] ppm; ^{14}N NMR (299 K, CDCl$_3$): $\delta = 8$ ($\nu_{½} \approx 230$ Hz) ppm; HRMS (ES-I) calcd for $C_{15}H_{17}NO_4Na$ [M + Na]$^+$ 298.1050; found 298.1050.

4-Benzyl-4-nitro-6-phenyltetrahydro-2*H*-pyran-2-one 4g/4g′. Yield 245 mg (79%), *dr* 6.5 : 1 (inseparable mixture), mp = 129–135 °C (Et$_2$O), TLC: $R_f = 0.47$ (hexane–EtOAc, 1/1); ^{1}H NMR (300.13 MHz, CDCl$_3$): *rel*-4*R*,6*R*-isomer **4g** (major): $\delta = 2.65$ [dd, $^2J = 15.4$, $^3J = 11.7$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$], 2.78 [dd, $^2J = 15.4$, $^3J = 3.7$ Hz, 1H, $\mathrm{CH_A}H_\mathrm{B}$], 3.07 [d, $^2J = 16.9$ Hz, 1H, $\mathrm{C}H_\mathrm{C}\mathrm{H_D}$], 3.26 [d, $^2J = 16.9$ Hz, 1H, $\mathrm{CH_C}H_\mathrm{D}$], 3.41 [d, $^2J = 14.0$ Hz, 1H, $\mathrm{C}H_\mathrm{E}\mathrm{H_F}$], 3.52 [d, $^2J = 14.0$ Hz, 1H, $\mathrm{CH_E}H_\mathrm{F}$], 5.12 [dd, $^3J = 11.7$, $^3J = 3.7$ Hz, 1H, CH], 7.11–7.19 [m, 2H, $\mathrm{CH_{Ph}}$], 7.25–7.44 [m, 8H, Ph]; *rel*-4S,6*R*-isomer **4g′** (minor): δ (selected signals) = 2.86 [d, $^2J = 14.0$ Hz, 1H, $\mathrm{C}H_\mathrm{C}\mathrm{H_D}$], 3.50 [d, $^2J = 14.0$ Hz, 1H, $\mathrm{CH_E}H_\mathrm{F}$], 5.22 [dd, $^3J = 12.5$, $^3J = 2.0$ Hz, 1H, CH] ppm; ^{13}C NMR (75.47 MHz, CDCl$_3$): *rel*-4*R*,6*R*-isomer **4g** (major): $\delta = 37.6$, 40.3, 44.8, [3 CH$_2$], 77.0 [CH], 87.9 [CNO$_2$], 125.8, 128.6, 129.0, 129.1, 129.2 and 129.9 [$\mathrm{CH_{Ph}}$], 132.4 and 137.5 [$\mathrm{C}_{\text{i-Ph}}$], 167.4 [OC = O], *rel*-4*S*,6*R*-isomer **4g′** (minor): $\delta = 37.1$, 40.4 and 45.8 [3 CH$_2$], 77.3 [CH], 87.9 [CNO$_2$], 126.0, 127.3, 128.4, 128.9, 129.0 and 129.9 [$\mathrm{CH_{Ph}}$], 132.0 and 138.1 [$\mathrm{C}_{\text{i-Ph}}$], 166.7 [OC=O] ppm; ^{14}N NMR (299 K, CDCl$_3$): $\delta = 15$ ($\nu_{1/2}$, *ca.* 200 Hz) ppm; HRMS (ES-I) calcd for $C_{18}H_{17}NO_4Na$ [M + Na]$^+$ 334.1050; found 334.1050.

***rel*-(4*R*,6*R*)-4-Bromomethyl-4-nitro-6-phenyltetrahydro-2*H*-pyran-2-one 4h.** Yield 85%, *dr* > 20 : 1, mp = 92–95 °C (Et$_2$O), TLC: $R_f = 0.43$ (hexane–EtOAc, 1/1); ^{1}H NMR (300.13 MHz, 299 K, CDCl$_3$): $\delta = 2.70$–2.84 [m, 2H, CH$_2$], 3.20 [d, $^2J = 16.9$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$], 3.41 [d, $^2J = 16.9$ Hz, 1H, $\mathrm{CH_A}H_\mathrm{B}$], 3.95–4.09 [m, 2H, CH$_2$Br], 5.32 [dd, $^3J = 9.5$, $^3J = 5.2$ Hz, 1H, CH], 7.32–7.49 [m, 5H, Ph] ppm; ^{13}C NMR (75.47 MHz, 299 K, CDCl$_3$): $\delta = 35.2$ [CH$_2$Br], 37.2 and 40.1 [CH$_2$ and $C\mathrm{H_2C{=}O}$], 77.1 [CH], 86.4 [CNO$_2$], 125.9 and 129.0 [$\mathrm{CH}_{o\text{-Ph}}$ and $\mathrm{CH}_{m\text{-Ph}}$], 129.3 [$\mathrm{CH}_{p\text{-Ph}}$], 136.4 [$\mathrm{C}_{\text{i-Ph}}$], 168.6 [OC=O] ppm; ^{14}N NMR (21.69 MHz, 299 K, CDCl$_3$): $\delta = 6$ ($\nu_{1/2}$, *ca.* 170 Hz) ppm; $C_{12}H_{12}BrNO_4$ (314.13): calcd C, 45.88; H, 3.85; N, 4.46; found: C, 46.00; H, 3.87; N, 4.27%.

Reduction of nitro lactones 4 into carbamates Boc-1 (third step, see Scheme 3)

General procedure. Aluminum foil was cut into strips (8 pieces, 20 × 5 mm, 120 mg, 5.2 mmol, 20 eq.). The clean meal surface was washed with hexane and Et$_2$O. After that, it was poured into a 2% HgCl$_2$ solution in water (10 mL) for 15 s, then washed with MeOH, and Et$_2$O without drying. After all these preliminary preparations[22] the foil was added to nitro lactone **4a** or **b** (0.26 mmol, 1.0 eq.) as a solution in THF/H$_2$O (9/1, 5 mL) with water bath cooling (**Caution**! exothermic reaction and hydrogen evaluation). The reaction mixture was stirred for 1 hour and Boc$_2$O (40 mg, 0.18 mmol, 1.5 eq.) was added. After an additional 18 hours, the reaction mixture was poured into a EtOAc (15 mL)/H$_2$O (10 mL) mixture. The water layer was back-extracted with EtOAc (2 × 3 mL). The combined organic layers were washed with H$_2$O (7 mL), brine (10 mL) and dried over Na$_2$SO$_4$. The solvents were evaporated *in vacuo*. The residue was subjected to column chromatography (eluent EtOAc–hexane, 1/5 → 1/3 → 1/1), to give the protected amine **Boc-1a** or **1b**, as a colorless solid.

***tert*-Butyl [*rel*-(2*R*,4*R*)-4-methyl-6-oxo-2-phenyltetrahydro-2*H*-pyran-4-yl]carbamate Boc-1a.** Yield: 41.3 mg (52%); mp = 99–101 °C (CDCl$_3$); TLC: $R_f = 0.35$ (hexane–EtOAc, 1/1); ^{1}H NMR (400 MHz, 305 K, CDCl$_3$): $\delta = 1.44$ [s, 9H, C(CH$_3$)$_3$], 1.54 [s, 3H, CH$_3$], 2.21 [dd, $^2J = 15.6$, $^3J = 3.4$ Hz, 1H, $\mathrm{C}H_\mathrm{A}\mathrm{H_B}$], 2.48 [t, $^2J \approx {}^3J = 14.0$ Hz, 1H, $\mathrm{CH_A}H_\mathrm{B}$], 2.72 [d, $^2J = 16.9$ Hz, 1H, $\mathrm{C}H_\mathrm{C}\mathrm{H_D}$], 3.08

[d, ${}^2J = 16.9$ Hz, 1H, $\mathrm{CH_C}\mathit{H}_\mathrm{D}$], 4.61 [br s, 1H, NH], 5.29 [dd, ${}^3J = 12.1$, ${}^3J = 3.4$ Hz, 1H, CH], 7.26–7.42 [m, 5H, Ph] ppm; ^{13}C NMR (75.47 MHz, 305 K, $CDCl_3$): $\delta = 26.6$ [CH_3], 28.5 [$C(\mathit{C}H_3)_3$], 42.5 [CH_2], 42.8 [CH_2], 77.1 and 77.3 [C–N and $\mathit{C}(CH_3)_3$], 78.4 [OCH], 126.0 and 128.8 [$CH_{m\text{-}Ph}$ and $CH_{o\text{-}Ph}$], 128.6 [$CH_{p\text{-}Ph}$], 139.0 [$C_{i\text{-}Ph}$], 154.2 [$C{=}O_{Boc}$], 170.3 [OC = O] ppm; HRMS (ES-I) calcd for $C_{17}H_{23}NO_4Na$ $[M + Na]^+$ 328.1519; found 328.1513.

***tert*-Butyl [*rel*-(2*R*,4*R*)-2-(4-bromophenyl)-4-methyl-6-oxo-tetrahydro-2*H*-pyran-4-yl]carbamate Boc-1b.** Yield 55 mg (55%); mp = 172–173 °C (hexane–Et_2O, 1/1),TLC: $R_f = 0.39$ (hexane–EtOAc, 1/1); ^{1}H NMR (300.13 MHz, 300 K, $CDCl_3$): $\delta = 1.43$ [s, 9H, $C(CH_3)_3$], 1.53 [s, 3H, CH_3], 2.20 [dd, ${}^2J = 14.0$, ${}^3J = 2.5$ Hz, 1H, $\mathit{C}H_AH_B$], 2.49 [t, ${}^2J \approx {}^3J = 14.0$ Hz, 1H, $CH_A\mathit{H}_B$], 2.71 [d, ${}^2J = 16.9$ Hz, 1H, $\mathit{C}H_CH_D$], 3.10 [d, ${}^2J = 16.9$ Hz, 1H, $CH_C\mathit{H}_D$], 4.63 [br s, 1H, NH], 5.27 [dd, ${}^3J = 12.0$, ${}^3J = 2.5$ Hz, 1H, CH], 7.27 [d, ${}^3J = 8.4$ Hz, 2H, CH_{Ar}], 7.53 [d, ${}^3J = 8.4$ Hz, 2H, CH_{Ar}] ppm; ^{13}C NMR (75.47 MHz, 300 K, $CDCl_3$): $\delta = 26.6$ [CH_3], 28.3 [$C(\mathit{C}H_3)_3$], 37.0 [CH_2], 42.3 [CH_2], 77.5 [OCH], 78.2 and 80.2 [C–N and $\mathit{C}(CH_3)_3$] 122.4 [CBr], 125.9 [C_{Ar}], 127.5 and 131.8 [CH_{Ar}], 154.1 [$C{=}O_{Boc}$], 169.7 [OC=O] ppm; HRMS (ES-I) calcd for $C_{17}H_{22}BrNO_4Na$ $[M + Na]^+$ 406.0624; found 406.0619.

Reduction of nitro lactone 4c. Aluminum foil was cut into strips (8 pieces, 20 × 5 mm, 120 mg, 4.4 mmol). The clean meal surface was washed with hexane and Et_2O. After that, it was poured into a 2% $HgCl_2$ solution in water (10 mL) for 15 s, then washed with MeOH, and Et_2O without drying. After all these preliminary preparations[22] the foil was added to dioxane (4.5 mL). Then, the nitro lactone **4c** (69 mg, 0.29 mmol) and water (0.5 mL) were added successively with water bath cooling (**Caution**! exothermic reaction and hydrogen evaluation). The reaction mixture was stirred for 1 hour and additional water (0.5 mL) was added. After an additional 18 hours, the reaction mixture was filtered through Celite® and washed with MeOH (3 × 7 mL). The solvents were evaporated *in vacuo.* The residue was dissolved in $CHCl_3$ (5 mL) and poured into a mixture of brine (5 mL) and $CHCl_3$ (5 mL). The organic layer was separated and the aqueous phase was extracted with $CHCl_3$ (2 × 5 mL). The combined organic phase was dried over Na_2SO_4, and the solvents were evaporated, to give the crude amine **1c** (~60 mg), which was dissolved in CH_2Cl_2 (2.0 mL).

***rel*-(4*S*,5*S*)-4-Amino-4-methyl-5-phenyltetrahydro-2*H*-pyran-2-one 1c.** TLC: $R_f = 0.19$ (hexane–EtOAc, 1/1); ^{1}H NMR (300.1 MHz, 300 K, $CDCl_3$): $\delta = 1.25$ [br s, 2H, NH_2], 1.40 [s, 3H, CH_3], 2.32 [d, ${}^2J = 17.3$ Hz, 1H, $\mathit{C}H_AH_B$], 2.79 [d, ${}^2J = 17.3$ Hz, 1H, $CH_A\mathit{H}_B$], 3.13 [dd, ${}^3J = 8.2$, ${}^3J = 5.5$ Hz, 1H, CH], 3.96 [dd, ${}^2J = 11.1$, ${}^3J = 5.5$ Hz, 1H, $\mathit{C}H_CH_D$], 4.24 [dd, ${}^2J = 11.1$, ${}^3J = 8.2$ Hz, 1H, $CH_C\mathit{H}_D$], 7.20 [dd, ${}^3J = 8.8$, ${}^4J = 1.5$ Hz, 2H, $CH_{o\text{-}Ph}$], 7.19–7.40 [m, 3H, $CH_{m\text{-}Ph}$ and $CH_{p\text{-}Ph}$] ppm.

***tert*-Butyl *rel*-(4*S*,5*S*)-4-methyl-2-oxo-5-phenyltetrahydro-2*H*-pyran-4-ylcarbamate Boc-1c.** To furnish the protected amine, Boc_2O (59 mg, 0.31 mmol) along with DMAP (2 mg, cat.) was added to the **1c** solution and the reaction mixture was stirred for 2.5 hours. The solvents were evaporated *in vacuo*. The residue was subjected to preparative thin layer chromatography (eluent hexane–EtOAc, 1/1) chromatography to give 70 mg (79%) of pure **Boc-1c** as a colorless oil, crystallized from a CH_2Cl_2–pentane mixture. Mp = 106–107 °C (pentane–Et_2O, 2/1), TLC: $R_f = 0.31$ (hexane–EtOAc, 1/1); ^{1}H NMR (400.1 MHz, 305 K, $CDCl_3$): $\delta = 1.36$ [s, 3H, CH_3], 1.42 [s, 9H, *t*-Bu], 2.29 [d, ${}^2J = 17.2$ Hz, 1H, $\mathit{C}H_AH_B$], 2.80 [d, ${}^2J = 17.2$ Hz, 1H, $CH_A\mathit{H}_B$], 3.24 [t, ${}^3J \approx {}^3J = 6.8$ Hz, 1H, CH], 4.48 [dd, ${}^2J = 11.2$, ${}^3J = 7.8$ Hz, 1H, $\mathit{C}H_CH_D$], 4.57 [dd, ${}^3J = 11.2$, ${}^3J = 6.7$ Hz, 1H, $CH_C\mathit{H}_D$], 6.52 [br s, 1H, NH], 7.23 [dd, ${}^3J = 7.8$, ${}^4J = 1.4$ Hz, 2H, $CH_{o\text{-}Ph}$], 7.28–7.34 [m, 3H, $CH_{m\text{-}Ph}$ and $CH_{p\text{-}Ph}$] ppm. ^{13}C NMR (100.6 MHz, 305 K, $CDCl_3$): $\delta = 21.8$ [CH_3], 27.8 [*t*-Bu], 41.5 [$CH_2C = O$], 50.8 [CH], 69.7 [OCH_2], 69.7 [C–N], 82.7 [C–O], 128.2 [$CH_{p\text{-}Ph}$], 129.0 and 129.2 [$CH_{o\text{-}Ph\text{ and }m\text{-}Ph}$], 136.8 [$\mathit{C}_{i\text{-}Ph}$], 153.2 [$C{=}O_{Boc}$], 176.9 [OC=O] ppm; HRMS (ES-I) calcd for $C_{17}H_{23}NO_4Na$ $[M + Na]^+$ 328.1519; found 328.1523.

Other transformations of nitro lactones 4

3-Methyl-3-nitro-5-phenylpentanoic acid 7. A solution of nitro compound **4a** (94 mg, 0.4 mmol) and suspended 5% Pd/C (15 mg) in MeOH (2.0 mL) was stirred in a H_2 atmosphere (from a balloon) for 8 hours. After that, the catalyst was separated out on a filter paper, washed 5 times with MeOH (5 × 2 mL). The solvents were evaporated *in vacuo*. The residue was subjected to column chromatography (eluent MeOH–$CHCl_3$, 1/25) to give 92 mg (97%) of the nitro acid **7** as colorless prisms; mp = 76–77 °C (hexane–EtOAc, 1/20), TLC: $R_f = 0.38$ ($CHCl_3/CH_3OH$, 25/1); ^{1}H NMR (300.13 MHz, 299 K, $CDCl_3$): $\delta = 1.81$ [s, 3H, CH_3], 2.19–2.37 [m, 2H, CH_2], 2.63–2.69 [m, 2H, CH_2], 2.94 [d, ${}^2J = 16.9$ Hz, 1H, $\mathit{C}H_AH_B$], 3.30 [d, ${}^2J = 16.9$ Hz, 1H, $CH_A\mathit{H}_B$], 6.00–7.10 [br s, 1H, COOH], 7.13–7.35 [m, 5H, Ph] ppm; ^{13}C NMR (75.47 MHz, 299 K, $CDCl_3$): $\delta = 22.9$ [CH_3], 30.2, 41.8 and 41.9 [3 CH_2], 81.78 [CNO_2], 126.5, 128.3 and 128.7 [CH_{Ph}], 139.7 [$C_{i\text{-}Ph}$], 174.0 [COOH] ppm; $C_{12}H_{15}NO_4$ (237.25): calcd C, 60.75; H, 5.90; N, 6.37; found C, 60.88; H, 5.92; N, 6.33.

4-Methyl-6-phenyl-5,6-dihydropyran-2-one 5a. ^{t}BuOK (21 mg, 0.187 mmol) was added to a precooled to 0 °C solution of the nitro lactone **4a** (40 mg, 0.170 mmol) in THF (1.0 mL). The reaction mixture was stirred for 15 min and poured into a Et_2O (5 mL)/H_2O (4 mL) mixture. The water layer was back-extracted with Et_2O (2 × 2 mL). The combined organic layers were washed with H_2O (4 mL), brine (4 mL) and dried over Na_2SO_4. The solvents were evaporated *in vacuo*. The residue was subjected to column chromatography (eluent EtOAc–hexane, 1/3) to give 30.1 mg (94%) of the enone **5a**[23] as a colorless solid; mp = 58–60 °C (Et_2O), TLC: $R_f = 0.29$ (hexane–EtOAc, 1/1); ^{1}H NMR (300.13 MHz, 299 K, $CDCl_3$): $\delta = 2.03$ [s, 3H, CH_3], 2.46 [dd, ${}^2J = 17.9$, ${}^3J = 3.8$ Hz, 1H, $CH_A\mathit{H}_B$], 2.65 [dd, ${}^2J = 17.9$, ${}^3J = 12.1$ Hz, 1H, $\mathit{C}H_AH_B$], 5.41 [dd, ${}^3J = 12.1$, ${}^3J = 3.8$ Hz, 1H, CH], 5.92 [s, 1H, =CH], 7.27–7.55 [m, 5H, Ph] ppm; ^{13}C NMR (75.47 MHz, 299 K, $CDCl_3$): $\delta = 22.9$ [CH_3], 36.9 [CH_2], 78.6 [OCH], 116.8 [=CH], 126.1, 128.6 and 128.7 [CH_{Ph}], 138.7 [$C_{i\text{-}Ph}$], 157.0 [=C], 164.9 [OC=O] ppm.

4-Methyl-5-phenyl-5,6-dihydropyran-2-one 5c. Obtained by the same procedure as **5a**; yield 30.5 mg (95%), mp = 49–50 °C (Et_2O), TLC: $R_f = 0.38$ (hexane–EtOAc, 1/1); ^{1}H NMR (400.1 MHz, 305 K, $CDCl_3$): $\delta = 1.85$ [d, ${}^4J = 0.6$ Hz, 3H, CH_3], 3.49 [t, ${}^3J \approx {}^3J = 4.8$ Hz, 1H, $\mathit{CH}Ph$], 4.38 [dd, ${}^2J = 11.2$, ${}^3J = 4.8$ Hz, 1H, $\mathit{C}H_AH_B$], 4.58 [dd, ${}^2J = 11.2$, ${}^3J = 4.8$ Hz, 1H, $CH_A\mathit{H}_B$], 5.98 [q, ${}^4J = 0.6$ Hz, 1H, =CH], 7.19 [dd, ${}^3J = 7.9$, ${}^4J = 1.5$ Hz, 2H, $CH_{o\text{-}Ph}$], 7.26–7.36

[m, 3H, Ph] ppm; ^{13}C NMR (100.3 MHz, 305 K, $CDCl_3$): $\delta = 21.7$ [CH_3], 45.1 [CH], 78.6 [OCH_2], 117.7 [=CH], 128.0 [$CH_{p\text{-}Ph}$], 128.1 and 129.1 [CH_{Ph}], 137.1 [$C_{i\text{-}Ph}$], 159.2 [=C], 164.2 [OC=O]; HRMS (ES-I) calcd for $C_{12}H_{12}O_2$ $[M + Na]^+$ 211.0730; found 211.0731.

X-Ray data

Single crystals, suitable for X-ray diffraction analysis, were obtained by the slow cooling and slow evaporation of $CHCl_3$ solutions of **4b**, **4h**, saturated at reflux.

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