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Indium-Mediated Reaction of 1-Bromo-1-nitroalkanes with Aldehydes: Access to 2-Nitroalkan-1-ols

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A novel method for the preparation of 2-nitroalkan-1-ols by an indium-promoted reaction of bromonitromethane with a variety of aldehydes is reported. The reaction was also performed with 2-bromo-2-nitropropanes to afford 2,2-dialkyl-2-nitroalkan-1-ols. The use of chiral sugar-derived aldehydes furnished the corresponding 2-nitroalkan-1-ols with excellent stereoselectivity. The utility of the novel sugar-derived 2,2-dialkyl-2-nitroalkan-1-ols for the preparation of branched iminosugar derivatives was demonstrated by the preparation of a hydroxymethyl branched polyhydroxylated azepane.

Introduction

The nitro-aldol reaction, often known as the Henry reaction, has received a great deal of attention from the synthetic community, as it is a powerful carbon–carbon bond-forming reaction that proceeds under mild basic conditions.[1] The reaction couples a carbonyl compound to a nitroalkane bearing an α hydrogen atom, thereby creating a β-nitroalkanol that can result in the formation of one or two chiral centers. The classical Henry reaction, which involves the base-catalyzed reaction of nitroalkanes and aldehydes, has been widely used in synthesis.[2] Moreover, the true synthetic utility lies in further transformations of the resulting β-nitroalkanols, including reduction, oxidation, or dehydration.[3]

Nevertheless, the classical nitro-aldol reaction does suffer from some important drawbacks. For example, the reversibility of the reaction means that the β-nitroalkanols are often obtained with poor stereochemical control.[3a] Although several methods have been developed to avoid this problem, they are often experimentally complex and in most cases very specific conditions are required.[4] In addition, when either the starting carbonyl compound or the resulting 2-nitro alcohols are base sensitive, the nitro-aldol conditions can give rise to undesired side reactions that furnish the target 2-nitroalkane-1-ols in low yields. On the other hand, it is known that the nitro-aldol reaction is very sensitive to steric factors and "becomes less and less satisfactory the more substituents there are attached to the C atoms to be linked together".[5] Hence, sterically hindered nitroalkanes are less reactive and usually fail to give the desired nitro-aldol products in good yields. Thus, the nitro-aldol condensation of α,α-dialkylnitroalkanes[6] has not been widely used in organic synthesis, despite the usefulness of the resulting 1,1-alkyl-1-nitroalkan-2-ols.[7]

To circumvent these limitations, it is of great interest to develop alternative procedures for the preparation of 2-nitroalkan-1-ols that obviate the use of bases and allow β-nitroalkanols derived from hindered nitroalkanes to be obtained in good yields. A recent contribution by Concellon et al.[8] consists of the SmI_2-promoted reaction of bromonitromethane with aldehydes,[9] an approach that allows 2-nitroalkanols to be obtained in high yield and with good stereoselectivity under very mild reaction conditions. On other hand, the tin(II) chloride mediated addition of bromonitromethane to aldehydes was also recently described.[10]

In connection with this work, we decided to investigate an alternative approach based on an indium-promoted addition of α-bromo-α-nitroalkanes to aldehydes. Our aim was to take advantage of the very low first ionization energy of indium(0), which makes it an ideal candidate for use in SET reactions. This property, together with its stability to oxygen and water, prompted exhaustive studies focused on the chemistry of indium with organic molecules in the past several years.[11] The most common uses of indium in organic synthesis are in allylation reactions in Barbier-type processes[12] and in metal-mediated Reformatsky reactions between α-halocarbonyl compounds and aldehydes or ketones.[13]

Results and Discussion

In our preliminary studies, the reaction of bromonitromethane with aldehyde **1a** was assessed at room tem-

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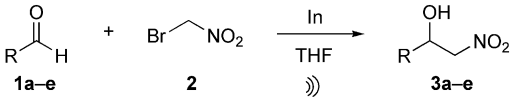
perature, under reflux, or under sonication, by using indium (1–4 equiv.) and DMF, THF, and 75% aqueous methanol or 75% aqueous THF as the solvent (Scheme 1). The best results were achieved with solutions of aldehyde **1a** (1 equiv.), indium (1 equiv.), and bromonitromethane (1.5 equiv.) in THF under sonication.



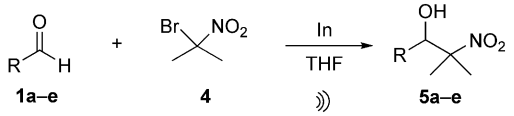
Scheme 1. Indium-mediated reaction of aldehydes **1a**–**e** and bromonitromethane **2**.

As shown by the results compiled in Table 1, under these conditions linear aldehyde **1d**, alicyclic aldehyde **1e**, and aromatic aldehydes **1a**–**c** were efficiently converted into their corresponding 2-nitroalkanols **3d**, **3e**, and **3a**–**c**, respectively. High yields were obtained, except for electron-rich aryl aldehyde **1c**, which as expected, proved to be substantially less reactive and yielded the corresponding adduct **3c** (Table 1, Entry 3) in only 39% yield (together with 51% of recovered starting material).

Table 1. Synthesis of 2-nitroalkan-1-ols **3a**–**e**.

Entry	1	R	3	Yield [%]
1	**1a**	C_6H_5	**3a**	80
2	**1b**	*p*-$NO_2C_6H_4$	**3b**	91
3	**1c**	*p*-$MeOC_6H_4$	**3c**	39
4	**1d**	$CH_3(CH_2)_6$	**3d**	78
5	**1e**	C_6H_{11}	**3e**	81

In subsequent experiments aimed at extending these studies to include hindered 1-bromo-1-nitroalkanes, the case of 2-bromo-2-nitropropane (**4**) was considered first (Scheme 2).



Scheme 2. Indium-mediated reaction of aldehydes **1a**–**e** and 2-bromo-2-nitropropane (**4**).

As shown in Table 2, the reaction of aldehydes **1a**–**e** with **4** under the same reaction conditions as above gave mixtures of 2-nitroalkanols **5a**–**e** and the corresponding starting aldehydes **1a**–**e** in all cases.

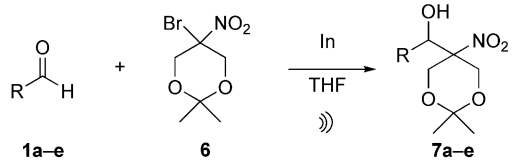
Table 2. Synthesis of 1-substituted 2-methyl-2-nitropropan-1-ols **5a**–**e**.

Entry	1	R	5	Yield[a] [%]
1	**1a**	C_6H_5	**5a**	48 (89)
2	**1b**	*p*-$NO_2C_6H_4$	**5b**	71 (94)
3	**1c**	*p*-$MeOC_6H_4$	**5c**	23 (90)
4	**1d**	$CH_3(CH_2)_6$	**5d**	55 (88)
5	**1e**	C_6H_{11}	**5e**	52 (91)

[a] Yield of isolated product (column chromatography). The yield with respect to the recovered starting material is given in parentheses.

These satisfactory results prompted us to extend these studies to conformationally restricted bromonitroalkane **6**, which proved to be a suitable reagent for the preparation of 1-substituted 2-(hydroxymethyl)-2-nitropropane-1,3-diols recently used as highly valuable intermediates for access to branched-chain iminosugars of biological interest.[14]

Thus, reaction of 5-bromo-2,2-dimethyl-5-nitro-1,3-dioxane (**6**), easily prepared from the cheap, commercially available insecticide bronopol[15] (2-bromo-2-nitropropane-1,3-diol), with aldehydes **1a**–**e** (Scheme 3) gave the corresponding substituted (2,2-dimethyl-5-nitro-1,3-dioxan-5-yl)methanols **7a**–**e** in moderate to good yields based on the recovered starting material (Table 3).



Scheme 3. Indium-mediated reaction of aldehydes **1a**–**e** and 5-bromo-2,2-dimethyl-5-nitro-1,3-dioxane (**6**).

Table 3. Synthesis of 1-substituted (2,2-dimethyl-5-nitro-1,3-dioxan-5-yl)methanols **7a**–**e**.

Entry	1	R	7	Yield[a] [%]
1	**1a**	C_6H_5	**7a**	55 (91)[b]
2	**1b**	*p*-$NO_2C_6H_4$	**7b**	70 (94)
2	**1c**	*p*-$MeOC_6H_4$	**7c**	24 (83)
2	**1d**	$CH_3(CH_2)_6$	**7d**	49 (82)
5	**1e**	C_6H_{11}	**7e**	51 (88)

[a] Yield of isolated product (column chromatography) and yield with respect to the recovered starting material (in brackets). [b] Contaminated with 2,2-dimethyl-5-nitro-1,3-dioxane.

Regarding the mechanism of these indium-mediated transformations, it should be noted that in contrast to the SmI_2-mediated reaction of bromonitromethane with aldehydes, which is promoted by the iodide released by the trace amounts of SmI_3, the synthesis of nitro alcohols **3a**–**e**, **5a**–**e**, and **7a**–**e** by using indium (1.0 equiv.) is consistent with the typical role of indium as a monoelectronic reducing agent in Barbier-type processes.[11] The satisfactory results obtained in the synthesis of racemic nitro alcohols **3a**–**e**, **5a**–**e**, and **7a**–**e** prompted us to test the usefulness of this methodology for the synthesis of enantiopure 1-nitroalkan-2-ols.

Our preliminary studies were carried out with a panel consisting of chiral aldehydes **1f**–**i** (Figure 1), which upon reaction with bromonitromethane (**2**), under the same reaction conditions as before, provided the corresponding 1-nitroalkan-2-ols **3f**–**i** (Scheme 4) in high yields and good diastereomeric ratios (Table 4). The major diastereomers were always *anti*, as predicted by the Felkin–Anh model (Figure 2).

Better stereochemical results were obtained in the reactions of aldehydes **1f**–**i** with bromonitroalkanes **4** and **6** (Scheme 5). Good yields of a single diastereomer were obtained in all cases, although, as in previous similar cases,

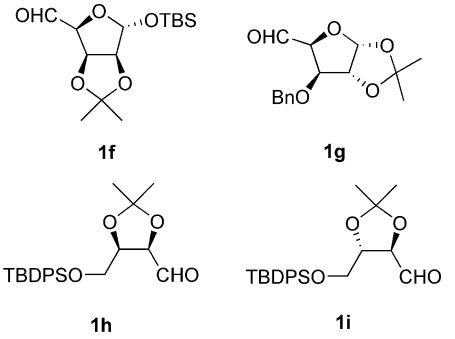
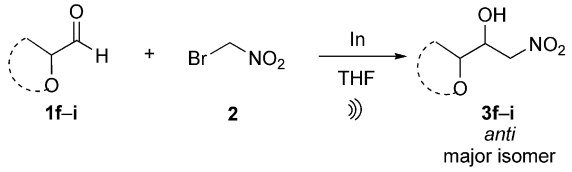


Figure 1. Chiral aldehydes **1f–i**.



Scheme 4. Indium-mediated reaction of aldehydes **1f–i** and bromonitromethane (**2**).

Table 4. Synthesis of enantiopure 2-nitroalkan-1-ols **3f–i**.

Entry	Aldehyde	2-Nitroalkan-1-ol	Yield [%]	*dr*[a]
1	**1f**	**3f**	80	8:1, 5*R*/5*S*
2	**1g**	**3g**	78	9:1, 5*R*/5*S*
3	**1h**	**3h**	81	12:1, 2*S*/2*R*
4	**1i**	**3i**	71	12:1, 2*S*/2*R*

[a] Calculated by ^{1}H NMR spectroscopy.

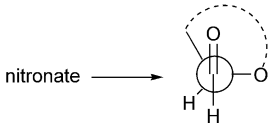
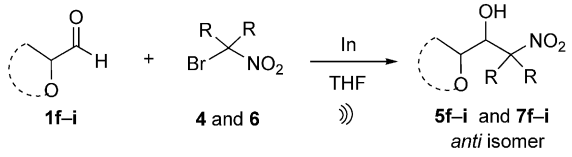


Figure 2. Felkin–Anh model for the attack on sugar aldehydes **1f–i**.

some starting material was always recovered (Table 5). Mannose derivative **7f** was unambiguously characterized by X-ray diffraction (Figure 3).



Scheme 5. Indium-mediated reaction of aldehydes **1f–i** and 2-bromo-2-nitropropane (**4**) or 5-bromo-2,2-dimethyl-5-nitro-1,3-dioxane (**6**).

The excellent diastereoselectivity obtained in the addition of bromonitromethane (**2**) to aldehydes **1f–i** and the total stereocontrol achieved in the addition of the more hindered nitrobromoalkanes **4** and **6** to aldehydes **1f–i**, which can easily be explained in terms of the Felkin–Anh model, constitute clear advantages for the reported indium-mediated access to 2-nitro-1-alkanols with respect to the classical Henry reaction. In fact, it is assumed that the classical

Table 5. Synthesis of enantiopure 1-substituted 2-methyl-2-nitropropan-1-ols **5f–i** and 1-substituted (2,2-dimethyl-5-nitro-1,3-dioxan-5-yl)methanols **7f–i**.

Entry	Aldehyde	Bromonitroalkane	2-Nitroalkan-1-ol	Yield [%]
1	**1f**	**4**	**5f**	70
2	**1g**	**4**	**5g**	68
3	**1h**	**4**	**5h**	66
4	**1i**	**4**	**5i**	71
5	**1f**	**6**	**7f**	70
6	**1g**	**6**	**7g**	75
7	**1h**	**6**	**7h**	69
8	**1i**	**6**	**7i**	71

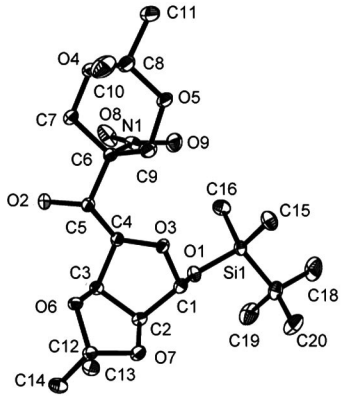
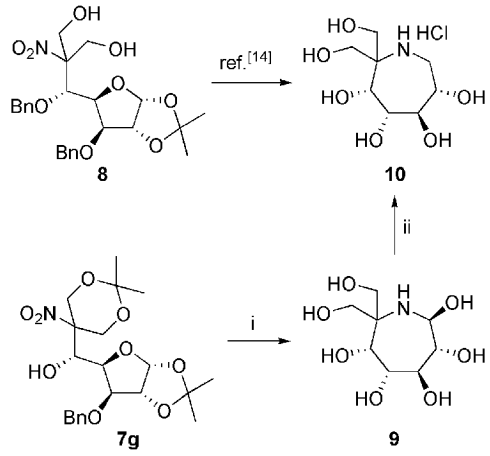


Figure 3. ORTEP diagram for **7f**.

Henry reaction conditions would mainly lead to the Felkin–Anh diastereomer, but due to the reversibility of the reaction in basic media, this major component undergoes partial epimerization at its stereogenic center bearing the hydroxy group, thereby affording a diastereomeric mixture.

Nitrosugar **8**, a derivative of sugar-derived 1-substituted 2-(hydroxymethyl)-2-nitropropane-1,3-diol (**7g**), has recently been reported as a highly valuable intermediate in the synthesis of the branched-chain polyhydroxylated



Scheme 6. Reagents and conditions: (i) 1. Ammonium formate, palladium black, methanol, 50 °C, 20 h, 89%; 2. TFA/H_2O, 1:1, room temp., 16 h; 3. $NaHCO_3$, THF, 40 °C, 24 h, 83%; (ii) 1. $NaCNBH_3$, AcOH, MeOH, room temp., 30 h; 2. AcCl, MeOH, room temp., 30 min, 78%.

azepane **10**, which was prepared in a global 15% yield from D-glucose by a route involving 11 steps.[14] This azepane has now been obtained in a shorter and more efficient way, directly from derivative **7g**, in the five-step sequence depicted in Scheme 6. Thus, catalytic hydrogenation of **7g** provided the corresponding amine by reduction of the nitro group to an amino and the removal of its benzyl group at the C-3 position. Once the isopropylidene groups were removed, the resulting amino derivative was treated with base to afford azepane **9**, which was finally reduced to expected azepane **10**. This compound was now obtained in 38% global yield from D-glucose in a six-step sequence.

Conclusions

In conclusion, we report here novel access to 2-nitroalkanols that consists of the indium-mediated addition of 1-bromo-1-nitroalkanes to aldehydes. This strategy constitutes a promising and convenient alternative to the classical nitro-aldol (Henry) reaction. The approach is very simple from an experimental point of view, and as bases are not required, it is not subject to the limitations of the classical Henry reaction. In addition, this approach may have many advantages with respect to a previously reported samarium-mediated Henry reaction of aldehydes with bromonitromethane, which has not yet been described for more hindered bromonitroalkanes and is more complex from an experimental point of view.

Regarding the stereoselective version of this novel approach to 2-nitroalkanols, promising results were achieved when a panel of chiral sugar-derived aldehydes **1f–j** was treated with bromonitroalkanes **2**, **4**, and **6**. The stereochemistry results were strongly influenced by steric factors. Thus, when the reaction was performed with bulky bromonitroalkanes **4** and **6**, the only diastereoisomeric 2-nitroalkanols obtained were those predicted by the Felkin–Anh model.

As a first practical application of the indium chemistry reported here, and in connection with our present interest in novel synthetic applications of nitrosugars, a new route to branched-chain polyhydroxylated azepane **9** was developed. This approach is shorter and more efficient than the previously reported synthetic route.

Work is now in progress aimed at developing a systematic study of the mechanistic and stereochemical aspects of this novel and highly promising route to 2-nitroalkan-1-ols. The use of this method as a key step in the synthesis of a family of branched-chain iminosugars is also under investigation.

Experimental Section

General: Reactions under sonication were carried out with a Selecta cleaning bath (320 W) at 20 °C. Melting points were determined by using a Kofler Thermogerate apparatus. Specific rotations were recorded with a JASCO DIP-370 optical polarimeter. Nuclear magnetic resonance spectra were recorded with a Varian Mercury plus 200 spectrometer (200 and 50 MHz for ^{1}H and ^{13}C nuclei, respectively). Mass spectra were obtained with a Hewlett Packard 5988A mass spectrometer. Thin-layer chromatography (TLC) was performed by using Merck GF-254 type 60 silica gel and ethyl acetate/hexane mixtures as eluents; the TLC spots were visualized with Hanessian mixture. Column chromatography was carried out by using Merck type 9385 silica gel. CCDC-785480 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

General Procedure for the Reaction of Bromonitroalkanes and Aldehydes: To a suspension of indium powder (0.5 mmol) in THF (1 mL) was added the bromonitroalkane (0.6 mmol), and the mixture was sonicated for 20 min. The corresponding aldehyde (0.5 mmol) was added, and sonication was continued for a further 4 h. The reaction mixture was neutralized with saturated aqueous sodium hydrogen carbonate, diluted with water (10 mL), and extracted with diethyl ether (3 × 25 mL). The combined organic layer was dried with magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (ethyl acetate/hexane) to give the pure compounds shown in Tables 1–3 and 5.

2-Nitro-1-phenylethanol (3a): Aqueous workup gave **3a** as a yellow oil (66.8 mg, 80%). ^{1}H NMR ($CDCl_3$): δ = 2.87 (br. s, 1 H,OH), 4.53–4.61 (m, 2 H, 2-H), 5.29–5.50 (m, 1 H, 1-H), 7.41–7.43 (m, 5 H, Ar-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 71.2, 81.3, 126.1, 129.0, 136.3 ppm.

2-Nitro-1-(4-nitrophenyl)ethanol (3b): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:5) afforded **3b** (96.5 mg, 91%) as a white solid. ^{1}H NMR ($CDCl_3$): δ = 3.19 (br. s, 1 H,OH), 4.55–4.65 (m, 2 H, 2-H), 5.63 (m, 1 H, 1-H), 7.63 (d, J = 8.7 Hz, 2 H, 2 Ar-H), 8.28 (d, J = 8.7 Hz, 2 H, 2 H-Ar) ppm. ^{13}C NMR ($CDCl_3$): δ = 75.3, 80.5, 124.1, 127.07, 143.2, 143.3 ppm.

1-(4-Methoxyphenyl)-2-nitroethanol (3c): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:3) afforded **3c** (38.4 mg, 39%) as a yellow oil. ^{1}H NMR ($CDCl_3$): δ = 2.94 (br. s, 1 H, OH), 3.80 (s, 3 H, OCH_3), 4.45 (dd, $J_{2,1}$ = 3.5 Hz, $J_{2,2'}$ = 13.1 Hz, 1 H, 2-H), 4.59 (dd, $J_{2,1}$ = 9.3 Hz, $J_{2,2'}$ = 13.1 Hz, 1 H, 2′-H), 5.36–5.40 (m, 1 H, 1-H), 6.90 (d, J = 8.8 Hz, 2 H, 2 H-Ar), 7.30 (d, J = 8.8 Hz, 2 H, 2 H-Ar) ppm. ^{13}C NMR ($CDCl_3$): δ = 55.5, 70.8, 81.4, 114.6, 127.5, 130.4, 160.2 ppm.

1-Nitrononan-2-ol (3d): After aqueous workup, **3d** was obtained as a yellow oil (73.7 mg, 78%). ^{1}H NMR ($CDCl_3$): δ = 0.84 (t, J = 6.6 Hz, 3 H, CH_3), 1.19–1.54 (m, 12 H), 4.22–4.29 (m, 1 H), 4.32–4.39 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.0, 22.5, 25.0, 28.9, 29.9, 33.4, 72.0, 80.9 ppm.

1-Cyclohexyl-2-nitroethanol (3e): After aqueous workup, **3e** was obtained as a yellow oil (70.0 mg, 81%). ^{1}H NMR ($CDCl_3$): δ = 0.90–1.73 (m, 11 H), 4.03–4.11, 4.33–4.45 (2 m, 3 H, 1-H, 2-H, 2′-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 25.7, 25.9, 26.1, 27.9, 28.8, 41.4, 72.8, 79.3 ppm.

2-Methyl-2-nitro-1-phenylpropan-1-ol (5a): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:7) afforded **5a** (41.5 mg, 48%) as a yellow oil, together with some starting aldehyde (21.7 mg, 41%). ^{1}H NMR ($CDCl_3$): δ = 1.41 and 1.55 (2 s, 6 H, 2 CH_3), 2.64 (d, J = 1.4 Hz, 1 H, OH), 5.27 (d, J = 1.4 Hz, 1 H, 1-H), 7.32–7.36 (m, 5 H, 5 H-Ar) ppm. ^{13}C NMR ($CDCl_3$): δ = 18.8, 24.9, 71.2, 81.3, 126.1, 129.0, 129.5, 136.3 ppm.

2-Methyl-2-nitro-1-(4-nitrophenyl)propan-1-ol (5b): Purification of the crude material by flash column chromatography (ethyl acetate/

hexane, 1:6) afforded **5b** (85.2 g, 71%) as a white solid, together with some starting aldehyde (15.6 mg, 23%). ^{1}H NMR (acetone): δ = 1.48 and 1.55 (2 s, 6 H, 2 CH_3), 5.49 (d, J = 4.6 Hz, 1 H), 5.59 (d, J = 4.6 Hz, 1 H), 7.64 (d, J = 8.8 Hz, 2 H, 2 H-Ar), 8.25 (d, J = 8.8 Hz, 2 H, 2 H-Ar) ppm. ^{13}C NMR (acetone): δ = 19.7, 24.1, 77.6, 92.6, 123.8, 129.9, 148.2 ppm.

1-(4-Methoxyphenyl)-2-methyl-2-nitropropan-1-ol (5c): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:6) afforded **5c** (28.9 mg, 23%) as a yellow oil, together with some starting aldehyde (50.6 mg, 67%). ^{1}H NMR ($CDCl_3$): δ = 1.41 and 1.55 (2 s, 6 H, 2 CH_3), 3.79 (s, 3 H, OCH_3), 5.23 (br. s, 1 H, OH), 5.28 (s, 1 H, 1-H), 6.88 (d, 2 H, 2 H-Ar), 7.28 (d, 2 H, 2 H-Ar) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.2, 24.4, 55.4, 77.9, 92.4, 113.7, 128.8, 130.6, 159.9 ppm.

2-Methyl-2-nitrodecan-3-ol (5d): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:3) afforded **5d** (59.7 mg, 55%) as a yellow oil, together with some starting aldehyde (21.1 mg, 33%). ^{1}H NMR ($CDCl_3$): δ = 0.86 (t, J = 5.6 Hz, 3 H, CH_3), 1.26–1.54 (m, 18 H), 3.95–4.00 (m, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.3, 20.5, 24.0, 22.8, 26.6, 29.4, 29.6, 31.7, 32.0, 76.2, 92.4 ppm.

1-Cyclohexyl-2-methyl-2-nitropropan-1-ol (5e): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:7) afforded **5e** (52.2 mg, 52%) as a yellow oil, together with some starting aldehyde (21.8 mg, 39%). ^{1}H NMR ($CDCl_3$): δ = 1.15–1.71 (m, 17 H), 3.40–3.51 (m, 1 H, 1-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 22.4, 23.8, 26.1, 26.6, 27.0, 28.9, 32.3, 39.8, 79.8, 92.0 ppm.

(2,2-Dimethyl-5-nitro-1,3-dioxan-5-yl)(phenyl)methanol (7a): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:3) afforded an inseparable 2:1 mixture of **7a** and 2,2-dimethyl-5-nitro-1,3-dioxane (73.4 mg, 55%) as a white solid, together with some starting aldehyde (19.1 mg, 36%). ^{1}H NMR ($CDCl_3$): δ = 1.31 (s, 6 H, 2 CH_3), 4.12–4.43 (m, 4 H, 2 CH_2O), 5.09 (s, 1 H, 1-H), 7.22–7.25 (m, 2 H, 2 H-Ar), 7.34–7.37 (m, 3 H, 3 H-Ar) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.8, 26.2, 61.3, 61.8, 75.1, 89.5, 99.3, 126.8, 129.0, 129.6, 137.0 ppm.

(2,2-Dimethyl-5-nitro-1,3-dioxan-5-yl)(4-nitrophenyl)methanol (7b): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:2) afforded **7b** (109 mg, 70%) as a white solid, together with some starting aldehyde (23.1 mg, 34%). ^{1}H NMR (acetone): δ = 1.26 and 1.39 (2 s, 6 H, 2 CH_3), 4.35–4.41 (m, 4 H, 2 CH_2O), 5.39 (d, J = 3.5 Hz, 1 H, 1-H), 5.81 (d, J = 3.5 Hz, 1 H, OH), 7.64 (d, 2 H, 2 H-Ar), 8.22 (d, 2 H, 2 H-Ar) ppm. ^{13}C NMR (acetone): δ = 20.3, 27.3, 62.4, 62.5, 73.5, 90.1, 99.4, 124.1, 129.2, 131.4, 146.7 ppm. MS (ESI): m/z (%) = 313.10 (8) [M + H]$^+$. HRMS: calcd. for $C_{13}H_{17}N_2O_7$ [M + H]$^+$ 313.1030; found 313.1045.

(4-Methoxyphenyl)(2,2-dimethyl-5-nitro-1,3-dioxan-5-yl)methanol (7c): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:2) afforded **7c** (33.5 mg, 24%) as a yellow oil, together with some starting aldehyde (44.5 mg, 59%). ^{1}H NMR ($CDCl_3$): δ = 1.31 and 1.32 (2 s, 6 H, 2 CH_3), 2.58 (br. s, 1 H, OH), 3.79 (s, 3 H, OCH_3), 4.13–4.19 (m, 2 H, CH_2O), 4.37–4.41 (m, 2 H, CH_2O), 5.04 (d, J = 3.1 Hz, 1 H, 1-H), 6.87 (ABq, 2 H, 2 H-Ar), 7.15 (ABq, 2 H, 2 H-Ar) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.8, 26.3, 55.5, 61.3, 61.8, 74.9, 89.6, 99.3, 114.3, 128.0, 128.9, 160.5 ppm. MS (ESI): m/z (%) = 320.11 (6) [M + Na]$^+$. HRMS: calcd. for $C_{14}H_{19}NO_6Na$ [M + Na]$^+$ 320.1104; found 320.1098.

1-(2,2-Dimethyl-5-nitro-1,3-dioxan-5-yl)-1-nitronoan-2-ol (7d): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:3) afforded **7d** (70.8 mg, 49%) as a yellow oil, together with some starting aldehyde (21.1 mg, 33%). ^{1}H NMR ($CDCl_3$): δ = 0.84 (t, J = 4.8 Hz, 3 H, CH_3), 1.23–1.43 (m, 18 H), 2.28 (d, J = 7.8 Hz, 1 H, OH), 3.78–3.87 (m, 1 H, 2-H), 4.08 (d, J = 13.1 Hz, 1 H, CHO), 4.18 (d, J = 13.1 Hz, 1 H, CHO), 4.42–4.49 (m, 2 H, 2 CHO) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.2, 21.0, 22.7, 25.9, 26.1, 29.3, 31.5, 31.9, 61.6, 62.2, 73.0, 90.5, 99.5 ppm. MS (ESI): m/z (%) = 290.20 (81) [M + H]$^+$, 248.09 (62) [M + Na]$^+$. HRMS: calcd. for $C_{14}H_{28}NO_5$ [M + H]$^+$ 290.1967; found 290.1967.

Cyclohexyl(2,2-dimethyl-5-nitro-1,3-dioxan-5-yl)methanol (7e): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:5) afforded **7e** (69.6 mg, 51%) as a yellow oil, together with some starting aldehyde (20.7 mg, 37%). ^{1}H NMR ($CDCl_3$): δ = 1.09–1.22, 1.43–1.70 (m, 11 H), 1.34 and 1.43 (2 s, 6 H, 2 CH_3), 2.32 (br. s, 1 H, OH), 3.67 (d, J = 8.6 Hz, 1 H, 1-H), 4.01–4.24 (m, 2 H, CH_2O), 4.44–4.54 (m, 2 H, CH_2O) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.0, 25.9, 26.0, 26.2, 26.3, 26.5, 32.4, 39.6, 62.4, 62.7, 77.3, 90.3, 99.5 ppm. MS (ESI): m/z (%) = 274.16 (54) [M + H]$^+$, 296.15 (26) [M + Na]$^+$. HRMS: calcd. for $C_{13}H_{24}NO_5$ [M + H]$^+$ 274.1648; found 274.1653.

1-*O*-*tert*-Butyldimethylsilyl-6-deoxy-2,3-di-*O*-isopropylidene-6-nitro-α-D-mannofuranose (3f): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:7) afforded **3f** (145 mg, 80%) as a clear oil. $[\alpha]_D^{24}$ = +33.9 (c = 1.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.04 and 0.07 (2 s, 6 H, $SiMe_2$), 0.84 [s, 9 H, $SiC(CH_3)_3$], 1.31 and 1.46 (2 s, 6 H, 2 CH_3), 3.01 (br. s, 1 H, OH), 3.91–3.95 (m, 1 H), 4.44–4.55 (m, 4 H), 4.82–4.87 (m, 1 H), 5.29 (s, 1 H, 1-H) ppm. ^{13}C NMR ($CDCl_3$): δ = –5.5, –4.5, 18.0, 24.5, 25.5, 25.8, 67.2, 78.4, 79.2, 79.4, 86.5, 101.4, 113.0 ppm. MS (ESI): m/z (%) = 381.21 (100) [M + Na]$^+$, 364.18 (20) [M + H]$^+$. HRMS: calcd. for $C_{15}H_{30}NO_7Si$ [M + H]$^+$ 364.1786; found 364.1787.

3-*O*-Benzyl-6-deoxy-6-nitro-1,2-*O*-isopropylidene-α-D-glucofuranose (3g): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:3) afforded **3g** (132 mg, 78%) as a yellow oil. $[\alpha]_D^{20}$ = –36.2 (c = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.31 and 1.47 (2 s, 6 H, 2 CH_3), 4.06 (d, J = 3.1 Hz, 1 H), 4.21–4.25 (m, 1 H), 3.41–4.82 (m, 6 H), 5.89 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 7.15–7.38 (m, 10 H, 10 H-Ar) ppm. ^{13}C NMR ($CDCl_3$): δ = 26.7, 27.21, 72.22, 73.8, 74.2, 77.9, 79.9, 81.7, 81.9, 105.4, 112.6, 128.0, 128.2, 128.3, 128.4, 128.7, 128.9, 137.3, 137.7 ppm.

5-*O*-*tert*-Butyldimethylsilyl-1-deoxy-1-nitro-3,4-*O*-isopropylidene-D-ribitol (3h): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:7) afforded **3h** (185.9 mg, 81%) as a white solid. M.p. 98–100 °C (Et_2O/hexane). $[\alpha]_D^{22}$ = –14.8 (c = 3.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.04 [s, 9 H, $C(CH_3)_3$], 1.27 and 1.30 (2 s, 6 H, 2 CH_3), 3.66–3.70 (dd, $J_{4,5}$ = 3.6 Hz, $J_{5,5'}$ = 11.0 Hz, 1 H, 5-H), 3.90 (dd, $J_{4,5'}$ = 9.2 Hz, $J_{5,5'}$ = 11.0 Hz, 1 H, 5′-H), 4.08–4.16 (m, 1 H), 4.28–4.39 (m, 2 H), 4.52 (dd, $J_{1,2}$ = 9.6 Hz, $J_{1,1'}$ = 13.0 Hz, 1 H, 5′-H), 4.70–4.76 (m, 1 H), 7.36–7.44 (m, 5 H, 5 H-Ar), 7.60–7.69 (m, 4 H, 4 H-Ar) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.2, 25.3, 26.9, 27.9, 62.5, 67.6, 76.8, 77.52, 78.7, 109.4, 128.2, 130.5, 131.8, 135.6, 135.7 ppm. MS (ESI): m/z (%) = 482.20 (100) [M + Na]$^+$, 460.21 (14) [M + H]$^+$. HRMS: calcd. for $C_{24}H_{34}NO_6Si$ [M + H]$^+$ 460.2149; found 460.2159.

5-*O*-*tert*-Butyldimethylsilyl-1-deoxy-1-nitro-3,4-*O*-isopropylidene-L-lyxitol (3i): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:5) afforded **3i** (162.9 mg, 71%) as a yellow oil. ^{1}H NMR ($CDCl_3$): δ = 1.04 [s, 9 H, $C(CH_3)_3$], 1.33 and 1.36 (2 s, 6 H, 2 CH_3), 3.56–3.58 (m, 1 H), 3.65–4.03 (m, 3 H), 4.29–4.68 (m, 3 H), 7.39–7.42 (m, 5 H, 5 H-Ar), 7.62–7.66 (m, 4 H, 4 H-Ar) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.3, 27.0, 64.7, 70.6, 78.6, 79.5, 80.5, 110.2, 128.1, 128.2, 130.3, 130.4,

132.4, 132.5, 135.8 ppm. MS (ESI): *m/z* (%) = 482.20 (75) [M + Na]$^+$, 460.21 (15) [M + H]$^+$. HRMS: calcd. for $C_{24}H_{34}NO_6Si$ [M + H]$^+$ 460.2149; found 460.2158.

1-*O*-*tert*-Butyldimethylsilyl-2,3-di-*O*-isopropylidene-(5*R*)-(1-methyl-1-nitroethyl)-α-D-lyxofuranose (5f): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:7) afforded **5f** (136.8 mg, 70%) as a yellow oil. $[\alpha]_D^{23}$ = –21.3 (*c* = 0.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.04 and 0.08 (2 s, 6 H, $SiMe_2$), 0.83 [s, 9 H, $SiC(CH_3)_3$], 1.31 and 1.47 (2 s, 6 H, 2 CH_3), 1.61 (s, 6 H, 2 CH_3), 2.85 (d, *J* = 5.6 Hz, 1 H, OH), 3.80–4.48 (m, 2 H), 4.53–4.63 (m, 1 H), 4.84 (dd, *J* = 3.8 Hz, *J* = 5.8 Hz, 1 H), 5.09 (s, 1 H, 1-H) ppm. ^{13}C NMR ($CDCl_3$): δ = –5.5, –4.5, 18.2, 21.0, 24.0, 25.0, 26.3, 69.6, 73.9, 79.3, 81.1, 84.3, 91.1, 106.13, 113.12 ppm. MS (ESI): *m/z* (%) = 392.21 (12) [M + H]$^+$. HRMS: calcd. for $C_{17}H_{34}NO_7Si$ [M + H]$^+$ 392.2105; found 392.2117.

3-*O*-Benzyl-1,2-*O*-isopropylidene-(5*R*)-(1-methyl-1-nitroethyl)-α-D-xylofuranose (5g): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:4) afforded **5g** (124 mg, 68%) as a yellow oil. $[\alpha]_D^{23}$ = –11.3 (*c* = 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.32/1.47/1.60/1.64 (4 s, 12 H, 4 CH_3), 4.03–4.13 (m, 2 H), 4.39–4.43 (m, 1 H), 4.45 (d, *J* = 7.9 Hz, 1 H, CHPh), 4.58 (d, $J_{1,2}$ = 2.5 Hz, 1 H, 2-H), 4.75 (d, *J* = 7.9 Hz, 1 H, CHPh), 5.93 (d, $J_{1,2}$ = 2.5 Hz, 1 H, 1-H), 7.33–7.39 (m, 5 H, 5 H-Ar) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.7, 24.8, 26.4, 26.9, 72.2, 72.3, 79.5, 81.3, 82.3, 91.8, 105.7, 112.0, 128.2, 128.6, 129.0, 137.2 ppm. MS (ESI): *m/z* (%) = 390.15 (100) [M + Na]$^+$. HRMS: calcd. for $C_{18}H_{25}NO_7Na$ [M + Na]$^+$ 390.1523; found 390.1525.

4-*O*-*tert*-Butyldiphenylsilyl-2,3-di-*O*-isopropylidene-(1*S*)-(1-methyl-1-nitroethyl)-D-erythrol (5h): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:4) afforded **5h** (160.7 mg, 66%) as a yellow oil. $[\alpha]_D^{23}$ = –22.9 (*c* = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.04 [s, 9 H, $C(CH_3)_3$], 1.27 and 1.30 (2 s, 6 H, 2 CH_3), 1.41 (s, 6 H, 2 CH_3), 3.72–3.86 (m, 3 H), 3.49–4.50 (m, 2 H), 7.39–7.45 (m, 5 H, 5 H-Ar), 7.64–7.73 (m, 4 H, 4 H-Ar) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.3, 25.0, 25.4, 27.0, 61.3, 72.4, 79.7, 81.0, 91.1, 110.9, 127.9, 120.0, 128.2, 128.3, 130.0, 135.7, 135.8, 135.9 ppm. MS (ESI): *m/z* (%) = 505.27 (100) [M + Na]$^+$, 488.25 (25) [M + H]$^+$. HRMS: calcd. for $C_{26}H_{38}NO_6Si$ [M + H]$^+$ 488.2462; found 488.2471.

4-*O*-*tert*-Butyldiphenylsilyl-2,3-di-*O*-isopropylidene-(1*S*)-(1-methyl-1-nitroethyl)-D-threitol (5i): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:4) afforded **5i** (172.9 mg, 71%) as a yellow oil. ^{1}H NMR ($CDCl_3$): δ = 1.08 [s, 9 H, $C(CH_3)_3$], 1.27 and 1.29 (2 s, 6 H, 2 CH_3), 1.67 and 1.69 (2 s, 6 H, 2 CH_3), 3.66–3.74 (m, 1 H), 3.83–3.90 (m, 2 H), 4.10–4.23 (m, 2 H), 7.35–7.48 (m, 5 H, 5 H-Ar), 7.66–7.73 (m, 4 H, 4 H-Ar) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.3, 21.6, 23.3, 26.6, 26.7, 65.2, 76.3, 79.6, 81.0, 91.3, 110.2, 127.6, 127.7, 127.8, 128.0, 128.1, 135.6, 135.7 ppm. MS (ESI): *m/z* (%) = 505.27 (100) [M + Na]$^+$, 488.25 (20) [M + H]$^+$. HRMS: calcd. for $C_{26}H_{38}NO_6Si$ [M + H]$^+$ 488.2462; found 488.2484.

1-*O*-*tert*-Butyldimethylsilyl-2,3-di-*O*-isopropylidene-(5*R*)-(2,2-dimethyl-5-nitro-1,3-dioxan-5-yl)-α-D-lyxofuranose (7f): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:3) afforded **7f** (162.0 mg, 70%) as a white solid. M.p. 123–125 °C (Et_2O/hexane). $[\alpha]_D^{25}$ = +22.6 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.10/0.11 (2 s, 6 H, $SiMe_2$), 0.86 [s, 9 H, $SiC(CH_3)_3$], 1.29/1.35/1.42/1.46 (4 s, 12 H, 4 CH_3), 3.01 (br. s, 1 H, OH), 4.07–4.29 (m, 4 H), 4.46–4.83 (m, 4 H), 5.30 (s, 1 H, 1-H) ppm. ^{13}C NMR ($CDCl_3$): δ = –5.5, –4.5, 17.8, 19.8, 24.6, 25.5, 25.9, 27.0, 61.5, 62.2, 70.5, 78.3, 80.6, 85.8, 89.2, 98.9, 101.7, 112.7 ppm. MS (ESI): *m/z* (%) = 464.23 (31) [M + H]$^+$, 486.21 (9) [M + Na]$^+$. HRMS: calcd. for $C_{20}H_{38}NO_9Si$ [M + H]$^+$ 464.2310; found 464.2325.

3-*O*-Benzyl-(5*R*)-(2,2-dimethyl-5-nitro-1,3-dioxan-5-yl)-1,2-*O*-isopropylidene-α-D-xylofuranose (7g): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:3) afforded **7g** (164.6 mg, 75%) as a yellow oil. $[\alpha]_D^{24}$ = –39.7 (*c* = 1.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.34/1.39/1.43/1.45 (4 s, 12 H, 4 CH_3), 4.05–4.34 (m, 5 H), 4.42–4.57 (m, 5 H), 5.91 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 7.24–7.36 (m, 5 H, 5 H-Ar) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.6, 21.5, 25.6, 26.5, 61.1, 62.8, 70.4, 72.4, 78.7, 81.3, 82.5, 90.2, 99.5, 105.6, 112.6, 128.3, 128.9, 129.2, 136.8 ppm. MS (ESI): *m/z* (%) = 440.19 (21) [M + H]$^+$, 462.17 (100) [M + Na]$^+$. HRMS: calcd. for $C_{21}H_{30}NO_9$ [M + H]$^+$ 440.1915; found 440.1894.

4-*O*-*tert*-Butyldiphenylsilyl-2,3-di-*O*-isopropylidene-(1*S*)-(2,2-dimethyl-5-nitro-1,3-dioxan-5-yl)-D-erythrol (7h): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 1:5) afforded **7h** (192.8 mg, 69%) as a yellow oil. $[\alpha]_D^{22}$ = –26.9 (*c* = 1.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.03 [s, 9 H, $SiC(CH_3)_3$], 1.26/1.28/1.37/1.43 (4 s, 12 H, 4 CH_3), 3.57 (dd, $J_{4,5}$ = 2.0 Hz, $J_{5,5'}$ = 7.2 Hz, 1 H, 5-H), 3.76 (t, $J_{4,5'}$ = 7.2 Hz, $J_{5,5'}$ = 7.2 Hz, 1 H, 5′-H), 4.24–4.37 (m, 4 H), 4.47–4.68 (m, 3 H), 7.39–7.48 (m, 5 H, Ar-H), 7.58–7.65 (m, 4 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.1, 20.3, 25.3, 26.8, 27.9, 26.8, 61.2, 62.1, 62.5, 69.7, 76.4, 77.3, 89.9, 99.2, 109.6, 128.2, 130.5, 131.6, 131.7, 135.5, 135.6 ppm. MS (ESI): *m/z* (%) = 560.27 (18) [M + H]$^+$, 582.25 (100) [M + Na]$^+$. HRMS: calcd. for $C_{29}H_{41}NO_8NaSi$ [M + Na]$^+$ 582.2493; found 582.2478.

4-*O*-*tert*-Butyldiphenylsilyl-2,3-di-*O*-isopropylidene-(1*S*)-(2,2-dimethyl-5-nitro-1,3-dioxan-5-yl)-D-threitol (7i): Purification of the crude material by flash column chromatography (ethyl acetate/hexane, 2:9) afforded **7i** (170.5 mg, 61%) as a yellow oil. ^{1}H NMR ($CDCl_3$): δ = 1.05 [s, 9 H, $SiC(CH_3)_3$], 1.33/1.36/1.39/1.46 (4 s, 12 H, 4 CH_3), 3.50–3.54 (m, 1 H), 3.54–4.05 (m, 1 H), 4.15–4.31 (m, 2 H), 4.57–4.71 (m, 2 H), 7.40–7.44 (m, 5 H, Ar-H), 7.62–7.65 (m, 4 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.2, 20.1, 26.7, 26.9, 27.1, 61.9, 62.2, 65.0, 73.6, 79.1, 80.4, 89.8, 99.2, 110.5, 128.2, 130.4, 131.9, 135.7 ppm. MS (ESI): *m/z* (%) = 560.27 (22) [M + H]$^+$, 582.25 (100) [M + Na]$^+$. HRMS: calcd. for $C_{29}H_{41}NO_8NaSi$ [M + Na]$^+$ 582.2493; found 582.2481.

(2*R*,3*R*,4*S*,5*R*,6*R*)-7,7-Bis(hydroxymethyl)azepane-2,3,4,5,6-pentaol (9): Palladium black (0.06 g, 20% w/w) and ammonium formate (1.05 g, 16.56 mmol) were added to a degassed solution of **7g** (0.27 g, 0.61 mmol) in methanol (6 mL), and the resulting mixture was stirred under a nitrogen atmosphere at 50 °C for 24 h. The suspension was then filtered through Celite, and the solvent was evaporated in vacuo to give 5(*R*)-(2,2-dimethyl-5-amino-1,3-dioxan-5-yl)-1,2-*O*-isopropylidene-α-D-xylofuranose (0.17 g, 89% yield) as a clear oil. $[\alpha]_D^{24}$ = –33.6 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.29/1.41/1.50 (3 s, 12 H, 4 CH_3), 3.56–3.62 (m, 2 H, CH_2O), 3.79 (d, $J_{4,5}$ = 7.2 Hz, 1 H, 5-H), 3.96–4.04 (m, 3 H, CH_2O, 4-H), 4.31 (d, $J_{3,4}$ = 1.4 Hz, 1 H, 3-H), 4.50 (d, $J_{1,2}$ = 4.0 Hz, 1 H, 2-H), 5.91 (d, $J_{1,2}$ = 4.0 Hz, 1 H, 1-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.1, 26.1, 26.8, 27.9, 52.0, 65.6, 67.7, 70.7, 75.7, 79.5, 84.9, 98.7, 105.0, 111.7 ppm. MS (ESI): *m/z* (%) = 320.17 (100) [M + H]$^+$. HRMS: calcd. for $C_{14}H_{26}NO_7$ [M + H]$^+$ 320.1703; found 320.1698. A solution of 5(*R*)-(2,2-dimethyl-5-amino-1,3-dioxan-5-yl)-1,2-*O*-isopropylidene-α-D-xylofuranose (0.17 g, 0.61 mmol) in a mixture of triuoroacetic acid and water (2:1, 9 mL) was stirred at room temperature for 4 h. The solvents were removed in vacuo, and the was residue coevaporated with toluene (3 × 5 mL) to afford a crude yellow oil that was dissolved in THF (9 mL). Sodium hydrogen carbonate (0.077 g, 0.915 mmol) was added (0.15 g, 0.61 mmol), and the resulting mixture was heated at 40 °C for 24 h, after which

TLC (chloroform/methanol/water/acetic acid, 60:30:5:3) showed that the starting material had been consumed. The solvent was evaporated in vacuo, and the resulting residue was dissolved in acetone. The solution was filtered, and the filtrate was concentrated under reduced pressure. The residue was puried by flash column chromatography (chloroform/methanol/water, 40:10:1) to give **9** (0.12 g, 0.51 mmol, 83% yield) as a yellow oil. $[\alpha]_D^{23}$ = –13.9 (*c* = 1.3, CH_3OH). ^1H NMR (D_2O): δ = 3.39 (s, 1 H, NH), 3.46 (d, 1 H, $J_{5,6}$ = 8.4 Hz, 6-H), 3.57 (dd, 1 H, $J_{2,3}$ = 1.2 Hz, $J_{3,4}$ = 7.3 Hz, 3-H), 3.71 (dd, 1 H, *J* = 2.3 Hz, *J* = 10.4 Hz, C*H*OH), 3.77–3.80 (m, 3 H, 5-H, CH_2OH), 3.87–3.91 (m, 2 H, 4-H, C*H*OH), 4.99 (d, 1 H, $J_{2,3}$ = 1.2 Hz, 2-H) ppm. ^{13}C NMR (D_2O): δ = 61.4, 67.0, 69.0, 69.3, 71.6, 72.2, 77.3, 94.4 ppm. MS (ESI): *m*/*z* (%) = 240 (100) $[M + H]^+$, 222 (34) $[M + H_2O]^+$. HRMS: calcd. for $C_8H_{18}NO_7$ $[M + H]^+$ 240.1083; found 240.1077.

(3*R*,4*R*,5*R*,6*S*)-2,2-Bis(hydroxymethyl)azepane-3,4,5,6-tetraol Hydrochloride (10): Sodium cyanoborohydride (0.045 g, 0.71 mmol) was added to a solution of **9** (0.034 g, 0.14 mmol) in methanol/acetic acid (98:2, 1 mL). The mixture was stirred at room temperature for 24 h. The solvents were removed in vacuo, after which the residue was dissolved in anhydrous methanol (1 mL) and acetyl chloride (0.1 mL) was added dropwise. The mixture was stirred for 30 min, and the resulting white solid was filtered off and washed with diethyl ether (5 mL) to afford **10** (0.028 g, 0.11 mmol, 78% yield). $[\alpha]_D^{23}$ = –5.6 (*c* = 1.1, CH_3OH). ^1H NMR (D_2O): δ = 3.41–3.58 (m, 3 H, 7-H, 7′-H, 6-H), 3.89–4.18 (m, 7 H, 3-H, 4-H, 5-H, 2 CH_2OH) ppm. ^{13}C NMR (D_2O): δ = 44.1, 59.5, 59.9, 66.4, 70.0, 71.8, 72.4, 74.6 ppm. MS (ESI): *m*/*z* (%) = 224 (60) $[M – Cl]^+$, 206 (100) $[M – Cl + H_2O]^+$. HRMS: calcd. for $C_8H_{18}NO_6$ $[M – Cl]^+$ 224.1134; found 224.1133.

Supporting Information (see footnote on the first page of this article): Copies of the ^{13}C NMR spectra for compounds **3**, **5**, and **7**.

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