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Synthesis of polyhydroxylated α-nitrocyclohexane carboxylic acids derived from D-glucose: a striking case of racemization

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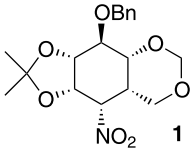
Abstract—The first total synthesis of polyhydroxylated α-nitrocyclohexane carboxylic acids from sugars is reported. A salient aspect of the synthesis is an unexpected Henry-mediated racemization of this new class of highly functionalized cyclohexanes.

1. Introduction

The classical nitroaldol condensation (the Henry reaction) involves reaction between a carbonyl compound and an alkylnitro compound bearing α-hydrogens. This reaction results in the formation of a carbon–carbon bond with concomitant generation of a β-nitroalcohol, from which a wide variety of other organic compounds can be derived by functional transformations of the hydroxy and the nitro functional groups.[1] The intramolecular Henry reaction has also proven to be a powerful method for the preparation of nitro cycloalkanes, and representative examples include synthetic intermediates recently used in the preparation of the natural compound perhydrohistionicotoxin,[2] the lycoricidine alkaloid pancratistatin[3] and the antineoplastic agent taxol.[4] Furthermore, this reaction is of appreciable interest for the synthesis of nitro-containing sugars (nitro sugars), recognized both as novel compounds and as valuable synthetic intermediates for the transformation of sugars into cyclohexane and cyclopentane derivatives[5] such as **1**[6] and **2**,[7] which can also be prepared by reaction of nitromethane with dialdehydes derived from sugars (Fig. 1).



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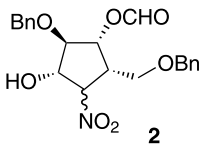

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Figure 1.

2. Results and discussion

Nitroacetic acid and its esters often show a similar reactivity to alkylnitro compounds and they are therefore convenient starting materials for the synthesis of 2-nitroalkanoic acids, which in turn are valuable synthetic intermediates for the synthesis of nitro alcohols, nitro amines, halonitro compounds, nitroacrylates, amino acids, amino alcohols, etc.[8] In fact, methyl nitroacetate has been shown to be a versatile glycine synthetic equivalent in the preparation of non-natural α-amino acids,[9] including cyclic amino acids from dialdehydes,[10] but its chemistry with sugars has received much less attention than the corresponding nitro alkanes. Indeed, despite the fact that a few examples have been reported of intramolecular reactions of methyl nitroacetate with dialdehydes derived from sugars to give 3-nitropyranose derivatives,[11] the nitroacetic acid-mediated transformation of sugars into cycloalkanes has not been carried out.

The work described in this paper concerns preliminary results from a project aimed at the synthesis of sugar-derived cycloalkane α-nitro acid esters, illustrated by the preparation of α-nitro acid esters **10** and **11** (Scheme 1), which were obtained by a synthetic sequence involving two consecutive Henry reactions. The first Henry reaction was performed between ethyl nitroacetate and D-glucose derivative **3**, a process that gave a mixture of epimeric compounds **5**. The second step was an intramolecular Henry reaction of epimeric mixture **6**. Alternatively, compounds **5** were trans

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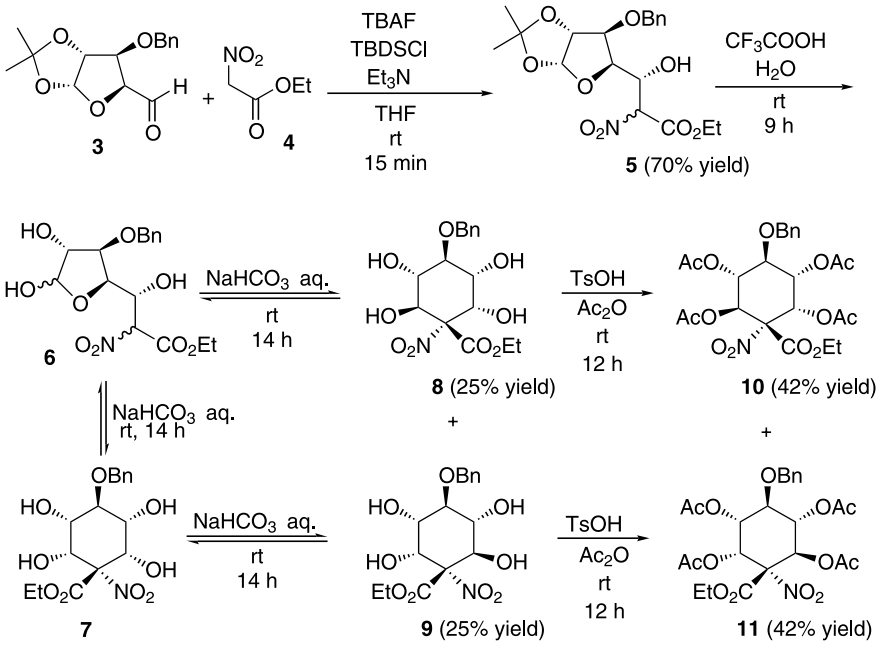
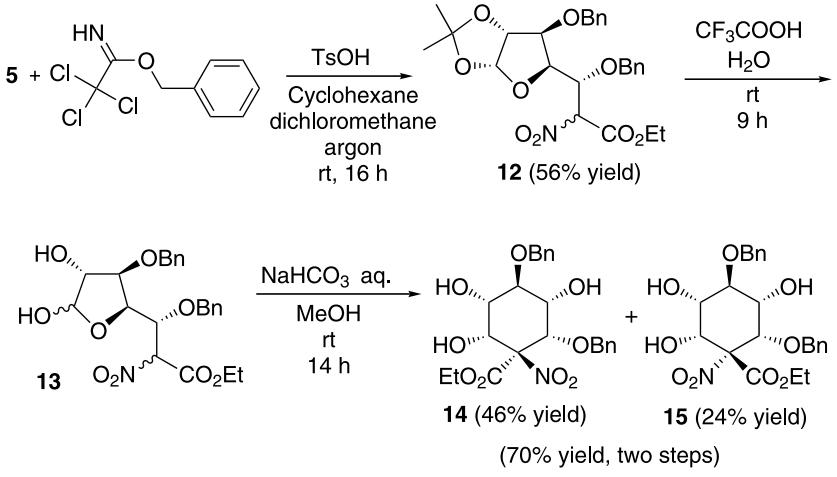


Scheme 1.

formed into the epimeric mixture of compounds **14**+**15** via compounds **12** and **13** (Scheme 2).

In the first experiment, condensation of aldehyde **3**[12] with ethyl nitroacetate under typical Henry reaction conditions gave a 70% yield of a 3:2 mixture of epimers **5**[13] (Scheme 1), which decompose on standing. Subsequent removal of the acetonide protecting group by treatment of **5** with a 1:1 trifluoroacetic acid/water mixture gave an unstable mixture of compounds **6**, which was immediately treated with 2% aqueous sodium bicarbonate solution to give, surprisingly, the racemic mixture of ethyl α-nitrocyclohexane carboxylates **8** and **9** ($[\alpha]_D^{20}$ 0.0). The racemic mixture **8**+**9** was subsequently reacted with acetic anhydride and *p*-toluenesulphonic acid to give the corresponding racemic mixture **10**+**11** (64% overall yield for the three last steps, $[\alpha]_D^{20}$ 0.0). The stereochemistry of these two compounds was firmly established by an X-ray crystallographic study of the mixture **10**+**11**.[14]

The crystallographic study also indicated that the favored chair conformations are, respectively, those represented in Figure 2—both of which have an equatorial disposition of the hydrogen at C_2 and axial dispositions of hydrogens at C_3, C_4, C_5 and C_6. These conformations are also the ones favored in solution, a fact easily established from the ^{1}H NMR spectrum of the mixture **10**+**11**, which includes two doublets at 6.03 and 6.15 ppm due to the highly deshielded protons at C_6 and C_2. The doublet at 6.03 ppm was assigned to the proton at C_6 on the basis of its coupling constant ($J=10.0$ Hz), which indicates a diaxial disposition for both protons at C_6 and at C_5. The coupling constant



Scheme 2.

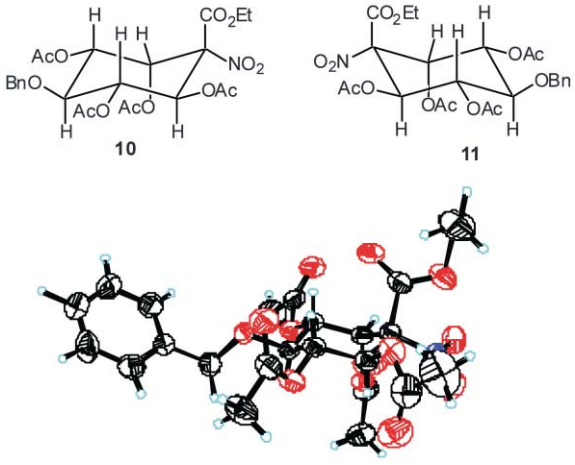


Figure 2. Chair conformation of compounds **10** and **11**, and ORTEP diagram corresponding to an X-ray molecular structure of compound **10**.

for the doublet at 6.15 ppm ($J=3.2$ Hz) allowed us to establish the equatorial disposition of the proton at C_2 and the axial disposition of the proton at C_3.

These results may be explained on the assumption that the intramolecular Henry reaction of compounds **6** gives diastereomers **7** and **8**, and that **8** is a stable compound, but **7** isomerizes to the more stable compound **9** through a retro-Henry reaction followed by a stereoselective intramolecular Henry reaction.[15] The equimolar amounts of enantiomers **8** and **9** resulting from this process may be explained in terms of equilibration based on the reversibility of the Henry reaction.

We next decided to explore the possibility of modifying the process leading to the racemic mixture **8**+**9** by protecting (as the benzyloxy derivative) the strategic hydroxy group at C_5 in compounds **5**, which is implied in the transformation of **7** into **9**. Accordingly, the mixture of nitroesters **5** was reacted with benzyltrichloroacetimidate[16] and the resulting mixture of epimers **12** was then subjected to the same reaction sequence as compounds **5**. This sequence again involved removal of the acetonide group of **12** with trifluoroacetic acid and water, followed by treatment of the resulting mixture of compounds **13** with 2% aqueous sodium bicarbonate solution (Scheme 2). A 2:1 mixture of cyclohexane nitroesters **14** (46% yield, $[\alpha]_D^{17}$ −6.45) and **15** (24% yield, $[\alpha]_D^{17}$ −11.0) resulted from this procedure and both compounds were formed from the expected intramolecular Henry reaction. The stereochemistry of each compound was established from their spectroscopic data.

Compound **14** shows an NOE between the ethyl chain (methyl group) and the hydroxy groups at C_3 (2.4%), C_5 (5.2%) and C_6 (0.7%). Therefore, the relative stereochemistry is that corresponding to a cyclohexane chain conformation where the ethoxy carbonyl substituent is axial, the hydroxy groups at C_3 and C_5 are axial and the hydroxy group at C_6 is equatorial. Additionally, the intense NOE (22%) between protons H_5 and H_6 provides further evidence for the equatorial and the axial disposition proposed for both protons. Moreover, the presence of two singlets at $\delta=5.02$ ppm ($J=10.9$ Hz) and $\delta=5.06$ ($J=11.3$ Hz), due to protons H_6 and H_2, clearly indicates an axial disposition of the two protons (Fig. 3).

Similar ^{1}H NMR experiments for compound **15** allowed us to establish it to be a C_1 epimer of compound **14**. Compound **15** showed an intense NOE (19.1%) between protons H_5 and H_6, a situation consistent with an axial–equatorial disposition or a diequatorial disposition of the two protons. However, the coupling constant values for the signals of both protons H_6 (d, $\delta=4.85$ ppm, $J=10.4$ Hz, 1H) and H_2 (d, $\delta=5.02$, $J=11.5$ Hz, 1H) correspond to an axial–equatorial disposition.

In summary, we describe here the first transformation of a sugar (D-glucose) into polyhydroxylated α-nitrocyclohexane carboxylic acids. A salient aspect of this synthesis was that we unexpectedly obtained the racemic mixture **8**+**9**, as a consequence of the regiospecific β-epimerization of compound **7** to compound **9** (the enantiomer of compound **8**) by a Henry reaction and the subsequent equilibration of compounds **8** an **9** through compounds **6** and **7**. Racemization was efficiently avoided by appropriate protection of the C_5 OH group of compound **6**.

This new chemistry could be used for the transformation of dialdehydes—including sugar-derived dialdehydes—into polyhydroxylated α-nitrocycloalkane

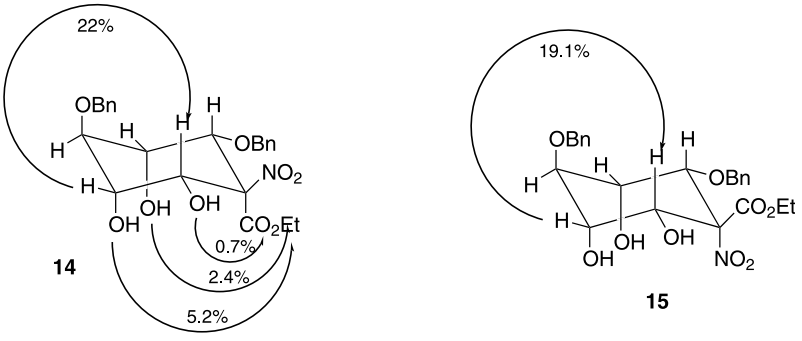


Figure 3.

carboxylic acids, that could in turn be converted into polyhydroxylated cycloalkane α-amino acids, a class of compounds that have not been studied to any great extent.[17] Future efforts will focus on the application of the new method to the synthesis of this amino acids with a view to their incorporation into peptides.

3. Experimental

Melting points were determined using a Kofler Thermogerate apparatus and are uncorrected. Specific rotations were recorded on a JASCO DIP-370 optical polarimeter. Infrared spectra were recorded on a MIDAC FTIR spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Bruker WM-300 apparatus or a Bruker AMX-500, using deuterochloroform solutions containing tetramethylsilane as internal standard. Mass spectra were obtained on a Kratos MS 50 TC mass spectrometer. Elemental analyses were obtained from the Elemental Analysis Service at the University of Santiago de Compostela. Thin-layer chromatography (TLC) was performed using Merck GF-254 type 60 silica gel and ethyl acetate/hexane mixtures as eluants; the TLC spots were visualized with Hanesian mixture. Column chromatography was carried out using Merck type 9385 silica gel. Solvents were purified as per Ref. 18. Solutions of extracts in organic solvents were dried with anhydrous sodium sulfate.

3.1. Ethyl 3-*O*-benzyl-6-deoxy-6-nitro-1,2-*O*-isopropyl-D,L-glycero-α-D-glucoheptofuronate 5

Ethyl nitroacetate (0.91 g, 6.87 mmol), a solution of compound **3** (1.27 g, 4.58 mmol) in THF (5 ml), triethylamine (0.47 g, 4.58 mmol) and a solution of *tert*-butyldimethylsilyl chloride (1.04 g, 6.87 mmol) in THF (7 ml) were sequentially added to a solution of tetrabutylammonium fluoride (0.55 g, 1.74 mmol) in THF (6 ml) at 0°C. The reaction mixture was stirred at rt for 15 min and then filtered. The solvent was evaporated in vacuo and the solid residue was dissolved in dichloromethane (125 ml). The resulting solution was washed with water (3×100 ml) and the organic layer was dried with anhydrous sodium sulphate, filtered and evaporated in vacuo. The residue was submitted to flash column chromatography (eluant: 2:7 ethyl acetate/hexane) to yield ethyl 3-*O*-benzyl-6-deoxy-6-nitro-1,2-*O*-isopropyl-D,L-glycero-α-D-glucoheptofuronate **5** (1.31 g, 70%) as a 3:2 mixture of epimers: IR (NaCl, cm^{-1}) 3390 (–OH), 1694 (C=O), 1567 ($–NO_2$), 1381 ($–NO_2$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.32 (s, 3H, $–CH_3$), 1.33 (s, 3H, $–CH_3$), 1.45 (s, 3H, $–CH_3$), 1.48 (s, 3H, $–CH_3$), 1.32 (t, 6H, $J=7.2$ Hz, 2×–OCH_2CH_3), 3.26 (d, 1H, $J=6.3$ Hz, 1×–OH), 3.27 (d, 1H, 8.8 Hz, 1×–OH), 4.12–4.19 (m, 2H), 4.19–4.21 (m, 1H), 4.30–4.35 (m, 5H), 4.58–4.72 (m, 7H), 4.78–4.81 (m, 1H), 5.46 (d, 1H, $J=3.4$ Hz, H_6), 5.50 (d, 1H, $J=1.6$ Hz, H_6), 5.88 (d, 1H, $J=3.2$ Hz, H_1), 5.89 (d, 1H, $J=3.2$ Hz, H_1), 7.30–7.38 (m, 10H, 10×H-Ph); ^{13}C NMR (75.3 MHz, $CDCl_3$) δ 13.86, 13.92, 26.45, 26.95, 63.20, 63.39, 68.13, 68.36, 72.65, 79.19, 80.68, 80.99, 82.31, 82.36, 88.40, 88.56, 105.17, 105.32, 127.92, 128.25, 128.67, 137.12, 163.11, 163.39; MS (EI) m/z 354 (M^+–1, 0.1%), 217 (0.3%), 127 (1.2%), 91 (100%).

3.2. Ethyl 3-*O*-benzyl-6-deoxy-6-nitro-D,L-glycero-α-D-glucoheptofuronate 6

A solution of compounds **5** (0.23 g, 0.57 mmol) in a 1:1 mixture of trifluoroacetic acid/water (4 ml) was stirred at rt for 9 h. The solvent was evaporated in vacuo and the residue was coevaporated with toluene (3×1 ml) to remove traces of trifluoroacetic acid. The product was used in the next step without further purification.

3.3. (1*R*,2*R*,3*R*,4*R*,5*S*,6*R*)-4-*O*-Benzyl-1-ethoxycarbonyl-2,3,5,6-tetrahydroxy-1-nitrocyclohexane 8 and (1*S*,2*S*,3*R*,4*S*,5*S*,6*S*)-4-*O*-benzyl-1-ethoxycarbonyl-2,3,5,6-tetrahydroxy-1-nitrocyclohexane 9

A 2% aqueous solution of sodium bicarbonate (6 ml) was added to a solution of compound **6** (0.2 g, 0.54 mmol) in methanol (17 ml) and the mixture was stirred at rt for 14 h. The reaction mixture was then acidified with a resin (DOWEX 50W), filtered and the solvent evaporated in vacuo. The residue was submitted to flash column chromatography (eluant: 2:3 ethyl acetate/hexane) and the racemic mixture **8**+**9** (100 mg, 50% yield) was isolated as an unstable white solid: $[\alpha]_D^{20}$ 0.0 (*c* 1.08 in $CHCl_3$); IR (NaCl, cm^{-1}) 3364–3468 (–OH), 1678 (–C=O), 1562 ($–NO_2$), 1380 ($–NO_2$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.42 (t, 3H, $J=7.3$ Hz, $–CH_3$), 3.73–3.85 (m, 2H), 4.33–4.58 (m, 4H), 4.67 (d, $J_{5,6}=9.3$ Hz, 1H), 5.06 (d, $J_{2,3}=2.8$ Hz, 1H), 7.40–7.62 (m, 5H, H–Ph); ^{13}C NMR (75.3 MHz, $CDCl_3$) δ 12.8, 62.66, 70.76, 71.11, 72.99, 73.40, 74.71, 81.01, 98.81, 127.09, 127.78, 139.17, 164.61; MS (EI) m/z 280 (M^+–91, 0.2%), 157 (3%), 145 (5%), 107 (12%), 91 (100%).

3.4. (1*R*,2*R*,3*R*,4*S*,5*S*,6*R*)-2,3,5,6-Tetraacetoxy-4-*O*-benzyl-1-ethoxycarbonyl-1-nitrocyclohexane 10 and (1*S*,2*S*,3*R*,4*R*,5*S*,6*S*)-2,3,5,6-tetraacetoxy-4-*O*-benzyl-1-ethoxycarbonyl-1-nitrocyclohexane 11

p-Toluenesulphonic acid (10 mg, 0.05 mmol) was added to a solution of the racemic mixture **8**+**9** (41 mg, 0.11 mmol) in acetic anhydride (6 ml) and the mixture was stirred at rt for 12 h. The reaction mixture was then evaporated in vacuo and coevaporated with toluene (3×1 ml) to remove traces of acetic acid. The residue was submitted to flash column chromatography (eluant: 2:7 ethyl acetate/hexane) to give the racemic mixture **10**+**11** (12.2 mg, 84%). Spectroscopic data for the racemic mixture: mp 115–118°C (EtOH); $[\alpha]_D^{20}$ 0.0 (*c* 1 in $CHCl_3$); IR (NaCl, cm^{-1}) 2925 (–CH–), 1754 ($–CO_2Et$, –OAc), 1574 ($–NO_2$), 1374 ($–NO_2$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.37 (t, $J=7.23$ Hz, 3H, $–CH_3$), 1.96, 1.97, 2.04, 2.07 (4×s, 12H, $–COCH_3$), 3.95–4.02 (m, 1H), 4.36–4.72 (m, 4H), 5.43–5.49 (m, 1H), 5.77 (dd, 1H, $J=3.2$ Hz, $J=10.4$ Hz), 6.03 (d, 1H, $J_{5,6}=10$ Hz), 6.15 (d, 1H, $J_{2,3}=3.2$ Hz), 7.23–7.38 (m, 5H, H-Ph); ^{13}C NMR (75.3 MHz, $CDCl_3$) δ 13.92, 20.41, 20.49, 20.61, 64.70, 69.38, 70.82, 72.05, 76.61, 77.46, 93.28, 127.42, 127.95, 128.46, 137.60, 161.64, 168.08, 168.66, 169.53, 169.56; MS (CI, NH_3) m/z 540 (M^++1,

12%), 432 (12%), 390 (18%), 91 (100%). Anal. calcd for $C_{24}H_{29}NO_{13}$: C, 53.43; H, 5.42; N, 2.60. Found C, 53.45; H, 5.40; N, 2.65.

3.5. Ethyl 3,5-di-*O*-benzyl-6-deoxy-6-nitro-1,2-*O*-isopropyl-D,L-glycero-α-D-glucoheptofuronate 12

A mixture of benzyl-2,2,2-trichloroacetimidate (1.5 ml, 8.04 mmol) and trifluoromethanesulphonic acid (0.009 ml) in dry cyclohexane (32 ml) was added to a solution of **5** (1.65 g, 4.02 mmol) in dry dichloromethane (16 ml). The mixture was stirred at rt for 16 h under argon, filtered and the filtrate washed with saturated aqueous sodium bicarbonate solution (1×60 ml) and water (1×60 ml). The organic layers were dried, filtered and the solvent evaporated in vacuo. The residue was submitted to flash column chromatography (eluant: 1:6 ethyl acetate/hexane) to give ethyl 3,5-di-*O*-benzyl-6-deoxy-6-nitro-1,2-*O*-isopropyl-D,L-glycero-α-D-glucoheptofuronate (**12**) (1.14 g, 56% yield) as a yellow oil: IR (NaCl, cm^{-1}) 1754 (–C=O), 1565 ($–NO_2$), 1375 ($–NO_2$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.24–1.35 (m, 12H, 2×–$CO_2CH_2CH_3$), 1.52, 1.57 (2×s, 6H, 2×–CH_3), 4.12–4.93 (m, 16H), 5.59 (d, 1H, $J_{5,6}=4.2$ Hz, H-6), 5.63 (s, 1H, H-6), 5.90, 5.91 (2×d, 2H, $J_{1,2}=3.8$ Hz, $J_{1,2}=4.2$ Hz, 2×H_1), 7.11–7.37 (m, 20H, H–Ph); ^{13}C NMR (75.3 MHz, $CDCl_3$) δ 13.78, 13.93, 26.52, 26.94, 62.89, 63.07, 71.70, 71.86, 74.21, 78.96, 79.04, 80.91, 81.17, 82.54, 81.74, 89.11, 89.29, 104.89, 127.38, 127.72, 127.79, 128.17, 128.30, 128.35, 128.45, 128.56, 128.65, 136.92, 137.51, 137.69, 162.74, 163.13; MS (CI, NH_3) m/z 501 (M^+, 0.1), 500 [$(M+H)^+$, 0.25], 271 (2), 181 (22), 129 (14), 91 (100). HRMS: calcd for $C_{26}H_{31}NO_9$ (M^+) 501.1954. Found 501.1948.

3.6. Ethyl 3,5-di-*O*-benzyl-6-deoxy-6-nitro-D,L-glycero-α-D-glucoheptofuronate 13

A solution of compounds **12** (0.51 g, 1.03 mmol) in a 1:1 mixture of trifluoroacetic acid/water (18 ml) was stirred at rt for 21 h. The solvent was evaporated in vacuo, coevaporated with toluene (3×10 ml) in order to remove traces of trifluoroacetic acid, and the solid residue was used in the next step without further purification.

3.7. (1*S*,2*R*,3*R*,4*R*,5*S*,6*S*)-2,4-Di-*O*-benzyl-1-ethoxycarbonyl-3,5,6-trihydroxy-1-nitrocyclohexane 14 and (1*R*,2*R*,3*R*,4*R*,5*S*,6*S*)-4-di-*O*-benzyl-1-ethoxycarbonyl-3,5,6-trihydroxy-1-nitrocyclohexane 15

A 2% aqueous solution of sodium bicarbonate (12 ml) was added to a solution of **13** (0.46 g, 9.98 mmol) in methanol (36 ml) and the mixture was stirred at rt for 14 h. The reaction mixture was then acidified with a resin (DOWEX 50W), filtered and the solvent evaporated in vacuo. The residue was submitted to flash column chromatography (eluant: 4:9 ethyl acetate/hexane) to give compound **14** (0.22 g, 46% over the last two steps) and compound **15** (0.10 g, 24% over the last two steps) as yellow oils. **Data for compound 14**: $[\alpha]_D^{17}$ −6.45 (*c*, 1.10 in CH_2Cl_2); IR (NaCl, cm^{-1}) 3539–3472 (–OH), 1748 (–C=O), 1554 ($–NO_2$), 1370 ($–NO_2$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.26 (t, 3H, $J=7.3$ Hz, –OCH_2CH_3), 2.45 (bs, 1H, –OH), 2.83 (bs, 1H, –OH), 3.38 (bs, 1H, –OH), 3.74–3.77 and 3.83–3.87 (m, 2H, –OCH_2Ph), 4.11–4.18 and 4.30–4.37 (m, 2H, –OCH_2CH_3), 4.47–4.54 (m, 4H), 4.75 (d, 1H, $J=11.3$ Hz), 5.02 (d, 1H, $J=10.9$ Hz), 5.06 (d, $J=11.3$ Hz, 1H), 7.16–7.41 (m, 10H, H-Ph); ^{13}C NMR (75.3 MHz, $CDCl_2$) δ 13.72, 64.48, 71.39, 71.61, 72.60, 75.04, 77.05, 77.84, 80.27, 95.68, 127.22, 127.90, 128.01, 128.21, 128.42, 128.64, 137.41, 138.35, 164.36; MS (EI) m/z 460 (M^+−1, 0.03%), 370 (1.6%), 264 (3%), 181 (5%), 107 (10%), 91 (100%), 65 (10%). HRMS calcd for: $C_{23}H_{26}NO_9$ (M^+−1) 460.1607. Found 460.1608. **Data for compound 15**: $[\alpha]_D^{17}$ −11.0 (*c*, 1.60 in $CHCl_3$); IR (NaCl, cm^{-1}) 3549–3453 (2×–OH), 1741 (–C=O), 1564 ($–NO_2$), 1371 ($–NO_2$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.29 (t, $J=7.1$ Hz, 3H, –OCH_2CH_3), 2.32 (d, 1H, –OH), 2.76 (bs, $J=3.0$ Hz, 1H, –OH), 3.26 (d, $J=3.4$ Hz, 1H, –OH), 3.75–3.84 (m, 2H, –OCH_2Ph), 4.30 (q, 2H, –OCH_2CH_3), 4.45–4.49 (m, 2H), 4.57–4.60 (m, 2H), 4.76 (d, $J=11.5$ Hz, 1H), 4.85 (d, $J=10.4$ Hz, 1H), 5.02 (d, $J=11.5$ Hz, 1H), 7.17–7.40 (m, 10H, H-Ph); ^{13}C NMR (75.3 MHz, $CDCl_3$) δ 13.85, 63.75, 71.63, 71.95, 73.05, 74.86, 76.59, 79.62, 79.91, 97.43, 128.00, 128.03, 128.21, 128.37, 128.65, 137.22, 138.38, 163.33; MS (EI) m/z 460 (M^+−1, 0.13), 370 (6), 264 (4), 181 (4), 107 (10), 91 (100). HRMS calcd for: $C_{23}H_{26}NO_9$ (M^+−1) 460.1607. Found 461.1603.

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14. **Crystal structure determination**: A suitable crystal of the racemic mixture (**10**+**11**) (block, colorless, dimensions $0.45\times0.40\times0.35$ mm^3) was used for the structure determination. X-Ray data were collected using a Bruker SMART CCD area detector single-crystal diffractometer with graphite-monochromatized Mo-Kα radiation ($\lambda=$ 0.71073 Å) by the phi-omega scan method at 298(2) K. A total of 1271 frames of intensity data were collected for each compound. The first 50 frames were recollected at the end of data collection to monitor for decay. The crystal used for the diffraction study showed slight decomposition during data collection (0.1%). The integration process yielded a total of 16807 reflections, of which 5648 [R(int) = 0.0192] were independent. Absorption corrections were applied using the SADABS[19] program (maximum and minimum transmission coefficients, 0.9637 and 0.9536). The structure was solved using the Bruker SHLXTL-PC[20,21] software by direct methods and refined by full-matrix least-squares methods on F^2. Hydrogen atoms were located on residual density maps except those of the methyl groups that were included in calculated positions, then fixed their positions and refined in the riding mode. For **10**+**11** convergence was reached at a final $R_1 = 0.0489$ [for $I>2\sigma(I)$], $wR_2 = 0.01588$ [for all data], 434 parameters, with allowance for the thermal anisotropy for all non-hydrogen atoms. The weighting scheme employed was $w=[\sigma^2(F_0^2+(0.0812P)^2+(0.4066P)]$ and $P=(|F_0|^2+2|F_c|^2)/3$ and the goodness-of-fit on F^2 was 1.008 for all observed reflections. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC 205855 (**10**+**11**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk). Crystallographic data for (**10**+**11**): $C_{24}H_{29}NO_{13}$, $M=539.48$. Monoclinic, space group $P2(1)/c$ with $a=13.444(1)$, $b=14.710(1)$, $c=14.261(1)$ Å, $\alpha=90°$, $\beta=101.440(2)°$, $\gamma=90°$, $V=2764.2(4)$ Å^3, D_{calcd} ($Z=4$) = 1.296 g cm^{-3}. $F(000)=1136$. Absorption coefficient = 0.0107 cm^{-1}.
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