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Studies on the reactivity of (pentitol-1-yl)nitrocyclohexadienes with acetyl chloride in methanol

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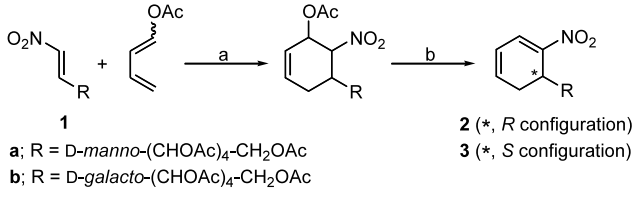
Abstract—(Pentitol-1-yl)nitrocyclohexadienes with pentaacetylated D-*galacto* and D-*manno* sugar side-chains react in different ways when they are subjected to transesterification with acetyl chloride in methanol. Although both processes should commence with a deacetylation, subsequent intramolecular nucleophilic attack from the resulting hydroxyl groups on electrophilic carbons on the cyclohexadiene ring was dependant on the nature of the sugar side-chain, as well as on the configuration at the stereogenic carbon of the cyclohexadiene ring. Thus, D-*manno* nitrocyclohexadiene led to a complex mixture from which we could either isolate or identify products with dioxatricyclodecane dimethyl ketal, benzofuran, chromane-3,4-diol, bicyclic or tricyclic oximes, nitrobenzene, and nitrocyclohexenol structures. In contrast, D-*galacto* nitrocyclohexadiene led exclusively to a bicyclic oxime.

1. Introduction

The design of novel dienes, together with the study of their reactivity and applications, has continued to be an important challenge in synthetic organic chemistry.[1] In particular, conjugated dienes bearing electron-withdrawing substituents such as a nitro group, play a prominent role in both Diels–Alder and Michael reactions. As a part of our continuing interest in this field,[2] we have reported[2c] that asymmetric Diels–Alder reactions between the sugar-derived D-*manno*- or D-*galacto*-1-nitroalkenes **1a** or **1b** and 1-acetoxy-1,3-butadiene produced adducts which, by subsequent elimination of acetic acid, led to (pentitol-1-yl)nitrocyclohexadienes **2a** and **3b**, respectively (Scheme 1). It is noteworthy that these two dienes showed high stability and could be stored in a dessicator for prolonged periods without any appreciable decomposition. In contrast, their analogue, 1-nitrocyclohexa-1,3-diene, suffers rapid oxidation to nitrobenzene on exposure to air.[3] Furthermore, Seebach et al. have described[4] that trisubstituted chiral 1-nitrocyclohexa-1,3-dienes are unstable materials, such that neither their elemental analyses nor their specific rotations could be described. Hence, because of their stability and structure, we think that **2a** and **3b** could constitute useful materials for the study of the relatively unexplored chemistry on this type of cyclic diene.[3–5]



Scheme 1. *Reagents and conditions*: (a) Ph-Me, hydroquinone (cat.), 105°C, 96 h; (b) NaOAc/THF, reflux, 3.5 h.

Although less widely applied than the more classical deacetylation reactions with alkaline or mineral acid catalysis, non-aqueous acid transesterification conditions such as the use of acetyl chloride in methanol have been utilized for selective removal of *O*-acetyl and *O*-formyl groups,[6] being an alternative when other methods are unsuccessful.[7] In this paper, we report a detailed analysis of the results we have achieved by application of this acidic transesterification process to peracetylated (pentitol-1-yl)nitrocyclohexadienes **2a** and **3b**. We have found that product distributions and reaction mechanisms appear to be dependent on both the configuration of the sugar side-chain and that of the stereogenic carbon to which the chain is attached.

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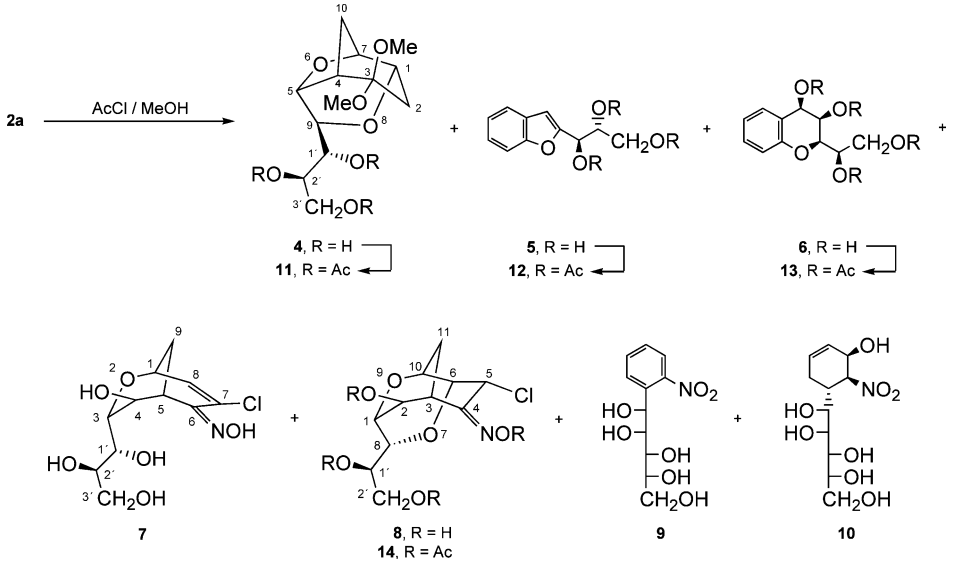
2. Results and discussion

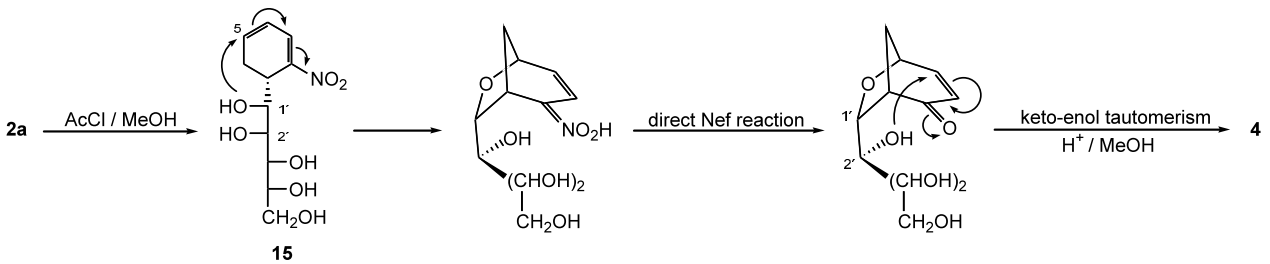
Treatment of 1′,2′,3′,4′,5′-penta-*O*-acetyl-1′-*C*-[(1*R*)-2-nitrocyclohexa-2,4-dienyl]-D-*manno*-pentitol[8] **2a** with acetyl chloride in methanol (methanolic hydrogen chloride[6]) at 0°C for 10 min, followed by warming at 50–55°C for 4.5 h, afforded a complex mixture which was subjected to flash column chromatography on silica gel. As a result, we collected several fractions in which the products **4**–**10** either could be detected or isolated (Scheme 2).

From the first fraction to be eluted, we isolated a pure compound (TLC R_f 0.88, 10:1 AcOEt–EtOH) whose ^{1}H and ^{13}C NMR data agree with the tricyclic ketalic structure **4**. As shown in Scheme 3, formation of the latter could be justified through a process involving deacetylation of the sugar side-chain of **2a**, followed by conjugate intramolecular nucleophilic addition from OH-1′ on the spatially close olefinic C-5 carbon of the intermediate **15**. Then, a direct Nef reaction,[9] and a second conjugate nucleophilic addition from OH-2′ on the resulting α,β-unsaturated carbonyl system, would led to an enol which, by tautomerization and ketalization of the carbonyl group in the presence of methanol, would give the product **4**. It should be noted that if the sequence of additions from hydroxyl groups to C-5 were reversed; i.e. first from OH-2′, inspection of molecular models suggests that OH-1′ would be situated in a position in which the second cyclization could not occur. Furthermore, although geometrically possible, the second cyclization would also be precluded in a mechanism through first addition of OH-1′ on C-3 of the nitroalkenic double bond; in this case, the resulting product would contain an isolated and little polarized carbon–carbon double bond with no tendency to react with any hydroxyl group.

Compound **4** yielded an acetyl derivative **11**, whose HRMS and ^{1}H NMR spectrum indicate the existence of only three acetate groups; this finding agrees with the proposed mechanism, since it implies that two hydroxyl groups were involved in the overall process leading to **4**. Furthermore, the ring-closures through OH-1′ and OH-2′ of **15** are supported by the small changes (ca. 0.1 ppm) that have been observed on comparison of the chemical shifts of H-5 and H-9 in **4** with those of the same protons in its acetyl derivative **11**. Neither ^{1}H nor ^{13}C NMR spectra from both **4** or **11** showed resonances for olefinic protons or carbons; instead, a signal at ca. 110 ppm that disappeared in DEPT experiments was attributed to C-3, being the methoxy group near 3.3 and 53 ppm. Methylenic C-2 and C-10 appeared as high-field signals (35.0–27.8 ppm) that were inverted in



Scheme 2.



Scheme 3.

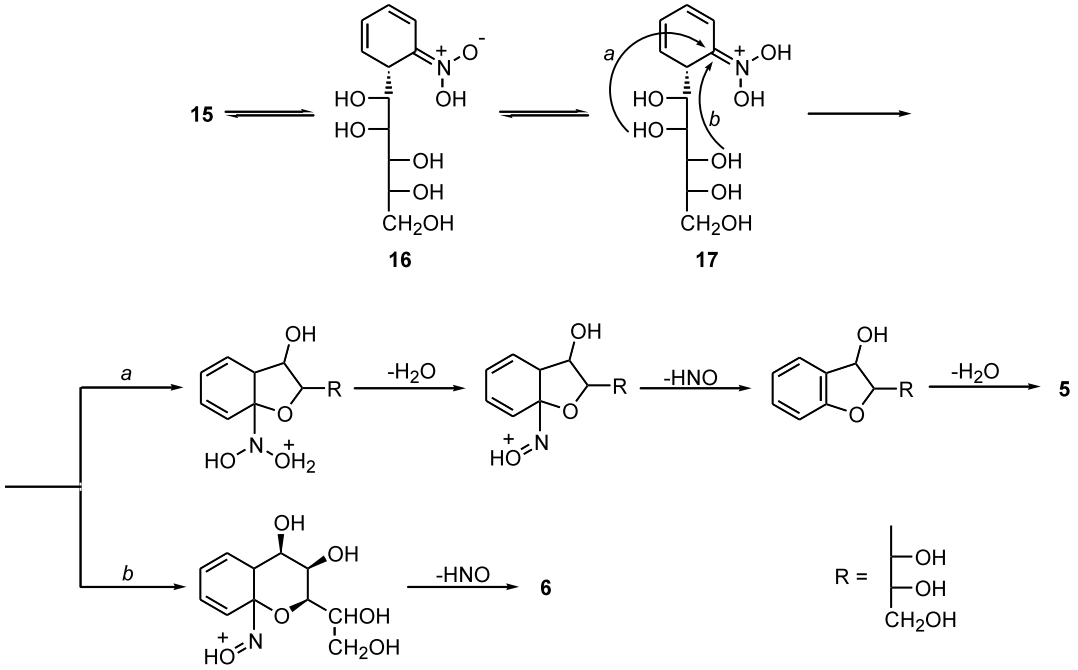
^{13}C NMR DEPT experiments, whereas the two ring-carbons that suffered the nucleophilic attacks (bridge-head C-1 and C-7 in **4** and **11**) appeared at values (85–79 ppm) that are consistent with cyclic carbons bonded to oxygen. Finally, the coupling constants $J_{1,7}$ (ca. 1 Hz), that were observed for these two compounds indicate the vicinity of H-1 and H-7, thus supporting conjugate additions from hydroxyl groups on the C-1 and C-7 carbons.

The fractions with TLC characteristics R_f 0.69 and 0.61 (10:1 AcOEt–EtOH) were shown to contain benzofuran **5** and chromane-3,4-diol **6**, respectively, being characterized by their spectroscopic data (HMRS, IR, ^{1}H and ^{13}C NMR), as well as by the preparation of their corresponding peracetyl derivatives 2-[(1′*R*,2′*R*)-1′,2′,3′-triacetoxypropyl]benzofuran **12** and 2(*R*)-2-[(1′*R*)-1′,2′-diacetoxyethyl]-(3*R*,4*R*)-3,4-diacetoxychromane **13**. Coupling constants and chemical shifts for proton and carbon atoms in each pair of compounds **5** and **12**, or **6** and **13**, closely match with those have been described for benzofuran[10] or related *cis*-3,4-dihydroxychromanes.[11] The location of the sugar side-chain at C-2 in **5** and **12** is consistent with the small value (<1 Hz) we have observed for the long-range coupling between H-3 and H-7.[10] Absolute configurations at C-2, C-3 and C-4 in chromanes **6** and **13** follows from their provenance from compound **2a** with D-*manno* configuration in its sugar side-chain. The values of $J_{2,3}$ (<1 Hz) and $J_{3,4}$ (4.0 Hz) were similar to those that have been described in flavonoids[12] and substituted chromanes[10,13] with *all-cis* relationships between substituents in analogous positions.

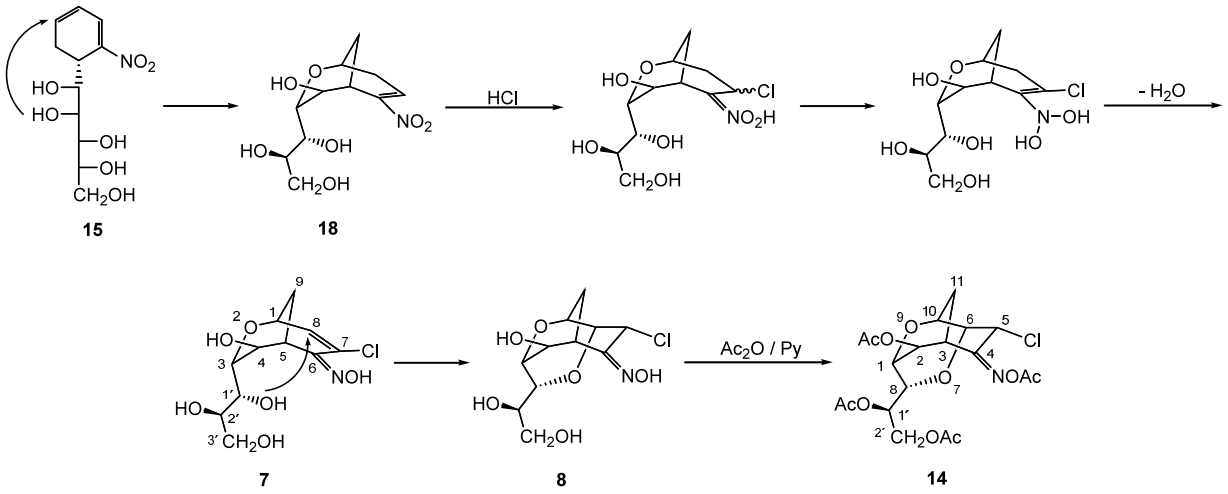
The formation of both **5** and **6** could occur via deacetylated nitrodiene **15** which, under the acid conditions that we have used, isomerizes to the *aci*-nitro tautomer **16** (Scheme 4),[14] in equilibrium with its protonated form **17**. Then, an intramolecular nucleophilic attack[15] from the second hydroxyl group of the sugar side-chain at C-2 (path *a*), sequential loss of water and nitroxyl, followed by aromatic stabilization would give the benzofuran **5**. Pathway *b*, leading to chromane **6**, follows a similar mechanism to that described above; however, the final dehydration would be less favourable, since aromatic stabilization in the heterocyclic moiety cannot occur in this case.

Evaporation of the fourth fraction from the column yielded an oil which contained (^{1}H NMR) the α,β-unsaturated oxime **7** (TLC R_f 0.45, 10:1 AcOEt-EtOH), together with unidentified minor inseparable impurities (Scheme 5). As proof for its structure, compound **7** exhibited a sharp singlet at 10.76 ppm, thus supporting the presence of a hydroxyl oxime proton. Furthermore, a careful study of the chemical shifts and coupling constants in this compound showed a complete similarity with those corresponding to the α,β-unsaturated chloro-oxime **20**, prepared from 1-(D-*galacto*)-2-nitrocyclohexa-2,4-diene **3b** (see Scheme 7 below). On irradiation of the signal of H-1 (4.42 ppm), a doublet at 6.58 ppm (H-8) collapsed, as well as in multiplets at 2.40 and 1.59 ppm (H-9a and H-9b, respectively); these two latter protons were also altered by irradiation at 3.57 ppm (H-5). The magnitude of the coupling constant between H-1 and H-8 ($J_{1,8}$ = 6.4 Hz), too large for an allylic constant, agrees with the position the chlorine atom at C-7, a consequence of a 1,4-addition of hydrogen chloride on the protonated α-nitroalkenic system in **18**. This fact eliminates a possible mechanism in which the former cyclization indicated in Scheme 5 had occurred by conjugate addition from the second hydroxyl group on the sugar side chain.

The next fraction in order of elution (TLC R_f 0.39, 10:1 AcOEt–EtOH) afforded an oil which was acetylated in



Scheme 4.



Scheme 5.

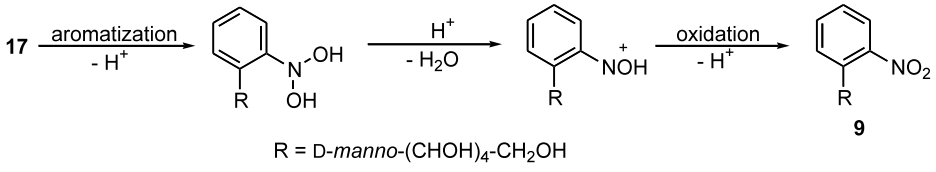
the conventional manner, and purified by preparative thin layer chromatography; thus, we isolated a compound whose IR, NMR and HRMS data agree with tetraacetylated tricyclic oxime **14** (Scheme 5). As distinguished from tricyclic ketal **11**, the ^{1}H NMR spectrum of **14** showed only two sets of methylene protons (at C-11 and C-2′), whereas four singlets corresponding to the methyls of acetates were present. By irradiation of the signal of H-1′ (ddd, 5.27 ppm) the double doublets at 4.63, 4.15 and 4.03 ppm, collapsed to doublets and hence were assigned to H-2′, H-2″ and H-8, respectively. In a similar way, H-8 showed coupling with H-1′, as well as with a broad singlet appearing at 4.20 ppm (H-1). Cyclization through hydroxyl groups on the second and the third carbon atoms of the sugar side-chain in **15** is supported by the chemical shifts of H-1 and H-8 in **14**; the values do not agree with those expected for protons on carbon bearing acetate groups, but rather with hydrogens bonded to carbons involved in ether groups. At 4.83 ppm appeared a multiplet in which the resonances of H-2 and H-5 were superimposed; on irradiation of this signal, H-3 (4.39 ppm) and H-1, as well as in a doublet at 3.87 ppm, which was attributed to H-6 collapsed. As the most significant signals in the ^{13}C NMR spectrum of **14**, we note those for the oxime carbon and C-5 (159.0 and 56.8 ppm, respectively), the latter being at a chemical shift which is characteristic of carbon atoms in α-chlorine chlorocyclohexane systems.[10b]

The formation of tricyclic oxime **14** could be explained by an intramolecular cyclization, in which the first hydroxyl group in the sugar side-chain of **7** adds on the unsaturated C-8 carbon, this product then being acetylated (Scheme 5). The resulting *cis*-relationship between substituents at C-5 and C-6 in **14** is consistent with the coupling constant $J_{5,6}$ (3.8 Hz).

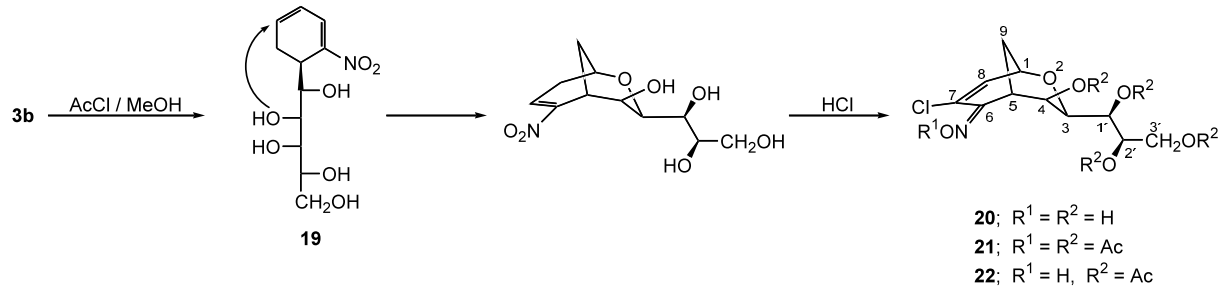
Evaporation of the two latter fractions of the column yielded oils, one each containing the previously synthesized nitrobenzene **9**[16] and nitrocyclohexenol **10**[2c] (TLC R_f 0.30 and 0.20, respectively, 10:1 AcOEt:EtOH), together with some minor inseparable and unidentified impurities. As proposed in Scheme 6, compound **9** would result from aromatization and loss of water of protonated nitronic acid **17**, followed by oxidation[3,17] of the resulting nitroso derivative. Nitrocyclohexanol **10** could arise from acetic acid addition on the nitroalkenic bond of **15**, followed by deacetylation;[6] in this way, the remaining and isolated double bond in the product would be slightly polarized and hence with no tendency to react with hydroxyl groups in the sugar side-chain.

On the other hand, the reaction of 1′,2′,3′,4′,5′-penta-*O*-acetyl-1′-*C*-[(1*S*)-2-nitrocyclohexa-2,4-dienyl]-D-*galacto*-pentitol **3b** with acetyl chloride in methanol took place in a different way to what we have described above for its D-*manno* isomer. In this case, evaporation of the solvent after the reaction time led to an oil which contained, nearly pure, 7-chloro-7-en-(4*S*)-4-hydroxy-(3*R*)-[(1′*S*,2′*R*)-1′,2′,3′-trihydroxypropyl]-2-oxabicyclo-[3.3.1]nonane-6-one oxime **20**[18] (Scheme 7).

Compound **20** exhibited hydroxyl IR bands at 3600-3200 cm^{-1}, as well as those characteristic[19a] of C=C, C=N and N–O bonds of the α,β-unsaturated oxime



Scheme 6.



Scheme 7.

system (weak; 1647, 1600 and 960 cm^{-1}). A deuterium oxide exchangeable singlet that appeared at 10.62 ppm in the ^1H NMR spectrum of **20** was assigned to the oxime proton; also, double resonance experiments proved that H-3 (dd, 3.39 ppm) did not show any coupling with hydroxyl protons, thus indicating the nucleophile involved in the cyclization had been OH-2′ of intermediate **19**.

Treatment of **20** with acetic anhydride in pyridine yielded a product **21**, in which the ^1H NMR signal attributable to acidic =N–O*H* proton was absent; instead, we found five singlets at 2.29–2.03 ppm, that were assigned to methyl protons of acetates. On standing in ethanolic solution at room temperature for 2 weeks, the pentaacetate **21** suffered conversion into a new compound whose data agree with structure **22**; thus, four singlet signals of methyl groups of acetates were present, whereas a deuterium oxide exchangeable singlet was found at 10.00 ppm (N=O–*H*); also, a broad IR band of medium intensity, appearing at 3370 cm^{-1}, could be assigned to stretching of hydroxyl oxime group.

As common characteristics, each one of the ^1H NMR spectra of **20**–**22** showed a broad doublet at 6.28-6.47 ppm, which was assigned to their respective olefinic H-8 protons. The values of $J_{1,8}$ couplings (ca. 6.6 Hz) are decisive to elucidate the structures, since they indicate a vicinal relationship between H-1 and H-8, and support chlorine atoms being placed at C-7. Concerning the connection between the sugar side-chain and the cyclic system, the couplings $J_{1',3}$ (9.0–9.7 Hz) indicate that, in the three cases, protons H-1′ and H-3 are *anti*-periplanar. As can be deduced from the Karplus equation,[20] the values of $J_{3,4}$ (1.6–2.0 Hz) and $J_{4,5}$ (<1 Hz) agree with dihedral angles H-3–C-3–C-4–H-4 and H-4–C-4–C-5–H-5 of ca. 60 and 90°, respectively, thus evidencing the conformation of the pyranoid rings correspond to slightly distorted chairs, where the substituents at C-4 should not be completely axial. On comparing chemical shifts between **20** and their acetylated derivatives, we found that H-4, H-1′, H-2′, H-3′and H-3″ in **21** and **22** showed characteristic downfield α-acylation shifts[21] by 1.9-0.6 ppm, whereas smaller downfield β-acylation effects[21] (ca. 0.35 ppm) were observed for H-5 and H-3.

In agreement with the proposed structures, ^{13}C NMR spectra of **20**–**22** exhibited resonances for their respective oxime carbons at 151.4, 157.2 and 151.2 ppm.[19] Olefinic C-7 and C-8 appeared between 132.9 and 128.4 ppm, being deduced from DEPT experiments that the latter was at higher field in the three cases. For compound **21**, signals of the acetate group on the nitrogen (167.2 and 19.2 ppm) were assigned[19b,c] at somewhat higher field than those of the other carbonyl groups (170.4–169.6 and 20.9–20.4 ppm); since the former two were the unique absent in tetraacetate **22**, this fact supported that only *N*-deacylation had occurred when **21** was dissolved in ethanol. Finally, C-1, C-3, C-4, C-1′, C-2′ and C-3′ were found at the expected range for oxygen-bonded carbons (69.3–62.1 ppm), being bridgehead C-5 and methylenic C-9 (DEPT inverted) those appearing at highest field.

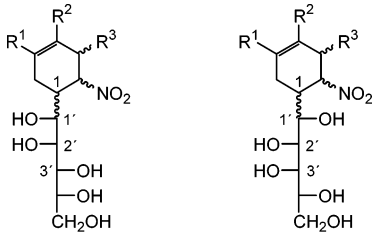
As shown in Scheme 7, the mechanism justifying the formation of **20** should be similar to that has been proposed for oxime **7** in Scheme 5. In this case, a subsequent intramolecular cyclization leading to a tricyclic compound, as occurred from **7** to yield **8**, would be precluded, since the *exo*-orientation of the sugar side-chain causes that its hydroxyl groups are too far from electrophilic centres at the bicyclic framework.

2.1. Discussion on the different reactivity of 1-glyco-2-nitrocyclohexa-2,4-dienes 2a and 3b with acetyl chloride in methanol

Being diastereoisomers, the only differences between the structures of **2a** and **3b** are those that arise from the opposite configurations of stereogenic centers C-1, C-1′ and C-3′. These changes should be the reason that hydroxyl groups could be in the appropriate positions to attack on electrophilic carbons of the nitrocyclohexadiene ring; hence, our goal here is concerning on conformations which could adopt each one of the starting compounds.

Since the deacetylated derivatives of **2a** and **3b** (**15** and **19**, respectively) are not isolable under the reaction conditions, we have no experimental data available about their preferred conformations. However, we have ^1H NMR data for closely related glyconitrocyclohexene systems **23** and **24**, which could be valid as compounds of reference.[2c,22] In the case of **15**, the related compounds would be those of D-*manno* series **23**, in which the coupling constants $J_{1,1'}$ (1.0–4.4 Hz) indicate that protons H-1 and H-1′ mainly present a *gauche* relationship, with slight conformational rigidity for the bond

C-1–C-1′. Furthermore, as the values for $J_{1',2'}$ (ca. 9 Hz) and $J_{2',3'}$ (ca. 2 Hz) indicate *anti*-periplanar and *gauche* relationships between H-1′/H-2′ and H-2′/H-3′, respectively, we assume that conformational possibilities for **15** would be those depicted as **15A**–**15D** in Fig. 1. Assuming that the avoidance of parallel 1,3-interactions between substituents is a major factor in establishing the favoured conformations,[23] led us to consider that arrangements **15A** and **15C** would be preponderant. In the former, proximity between the hydroxyl group at C-1′ and C-5 allows the attack *a*, thus leading to ketal **4** (see Scheme 3), isolated in 10% yield. By considering **15C**, the most feasible attacks would be from OH-2′ on either C-2 (*b*) or, in a lesser degree, on C-5 (*d*), thus leading to benzofuran **5** or oxime **7**, isolated in 39% and 4%, respective yields; finally, it is also possible the reaction of OH-3′ with C-2 (*c*), from which chromane **6** (5%) would arise.



R^1, R^2 = H, Me; R^3 = H, OH, $OSiMe_3$

Concerning (D-*galacto*)nitrocyclohexadiene **3b**, the reference compounds for its deacetylated derivative **19** would be those of the series **24**. Here, the coupling constants $J_{1,1'}$ and $J_{2',3'}$ (both of ca. 9 Hz) and $J_{1',2'}$ (ca. 1 Hz) indicate *anti*-relationships between protons H-1/H-1′ and H-2′/H-3′, as well as a *gauche*-relationship between H-1′ and H-2′. From the inspection of the resulting dispositions for **19** (**19A** and **19B**, Fig. 2), it can be deduced that, in both, only the hydroxyl group at C-2′ is in a favourable position to effect a nucleophilic attack on C-5, thus leading exclusively to oxime **20** (Scheme 7). The absence of products as **9** and **10** in Scheme 2 could be justified because in **3b**, nucleophilic

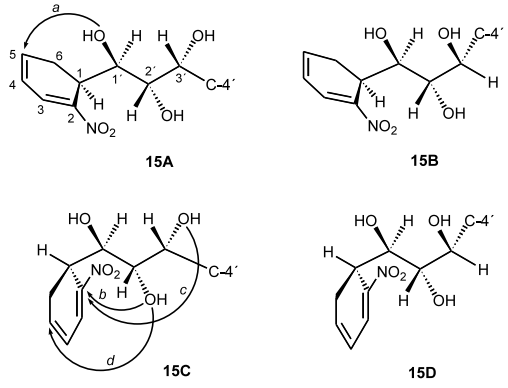


Figure 1. Conformations and attacks from hydroxyl groups on the cyclohexadiene ring of **15**.

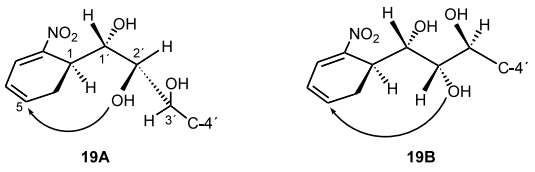


Figure 2. Conformations and attacks from hydroxyl groups on the cyclohexadiene ring of **19**.

attack from OH-2′ should be more favoured (shorter reaction time) than any nucleophilic attack from hydroxyl groups in **2a**.

As conclusion, we have shown that the result of the deacetylation of **2a** and **3b** follows a pathway, which is a consequence from configurational and conformational differences between their respective sugar side-chains, as well as of the configuration of the carbon on the cyclohexadiene ring bearing that sugar side-chain. In each case, the mechanism of the reaction would be mainly determined by the proximity of the internal nucleophile (an hydroxyl group) and the electrophilic carbon of the unsaturated system.

3. Experimental

3.1. General

Silica gel 60 (Merck, 230–400 mesh ASTM for flash chromatography) was used for column chromatography, which was carried out using the flash mode. Preparative TLC was performed using silica gel (Merck 60 GF_{254}). TLC was performed on precoated Merck Kieselgel 60 GF_{254} aluminum backed plates; spots were visualized by UV light or iodine vapour. NMR spectra were taken either on a Bruker AC/PC instruments (400.13 MHz for ^1H and 100.62 MHz for ^{13}C) with tetramethylsilane as internal reference and deuteriochloroform or hexadeuteriodimethyl sulfoxide as solvent. Coupling constant values are recorded in Hz. When reported, characterization of NMR signals is based on addition of deuterium oxide, homonuclear double-resonance and DEPT experiments. High resolution mass spectra were recorded on a VG Autospec spectrometer. Infrared spectra were recorded on a Perkin-Elmer 399 or on a FT-IR MIDAC Corporation spectrophotometers. Melting points were determined with an Electrothermal 8100 apparatus and are uncorrected. Optical rotations were obtained at 20±2°C with a Perkin–Elmer 241 polarimeter; $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}.

3.2. Reaction of 1′,2′,3′,4′,5′-penta-*O*-acetyl-1′-*C*-[(1*R*)-2-nitrocyclohexa-2,4-dienyl]-D-*manno*-pentitol 2a with acetyl chloride in methanol

To a stirred suspension of 1′,2′,3′,4′,5′-penta-*O*-acetyl-1′-*C*-[(1*R*)-2-nitrocyclohexa-2,4-dienyl]-D-*manno*-pentitol **2a** (1.0 g, 2.06 mmol) in methanol at 0°C (25 mL) was added acetyl chloride (0.55 mL). After 10 min at

0°C, the reaction mixture was stirred at 50–55°C for 4.5 h and then the resulting solution was neutralized with saturated aqueous sodium hydrogencarbonate. Evaporation of the solvent afforded an oily residue, which was chromatographed through a column of silica gel (10:1 AcOEt:EtOH). Thus, from the successive fractions, the following compounds could be isolated:

3.2.1. (1′*R*,2′*R*)-1′,2′,3′-Trihydroxy-3,3-dimethoxy-(1*R*,4*S*,5*R*,7*S*,9*R*)-6,8-dioxatricyclo[3.2.2.1^{4,7}]decane 4. Oil (0.06 g, 10%): R_f 0.88 (10:1 AcOEt:EtOH); ^{1}H NMR (DMSO-d_6) δ 4.24 (d, 1H, $J_{4,5}$=4.2 Hz, $J_{5,9}$<1 Hz, H-5), 4.09 (d, 1H, $J_{1',9}$=2.0 Hz, H-9), 4.02 (dd, 1H, $J_{1,7}\sim$1 Hz, $J_{7,10b}$=5.1 Hz, H-7), 3.57 (br d, 1H, $J_{2',3'}$= 2.0 Hz, H-3′), 3.38 (dd, 1H, $J_{3',3''}$=11.3 Hz, $J_{2',3''}$=5.6 Hz, H-3″), 3.36 (m, 1H, H-2′), 3.29 (dd, 1H, $J_{1',2'}$=8.5 Hz, H-1′), 3.23 (s, 6H, 2×OCH$_3$), 3.09 (m, 1H, $J_{1,2a}\sim J_{1,2b}$=8.0 Hz, H-1), 2.77 (br t, 1H, $J_{4,10b}$=4.0 Hz, $J_{4,10a}$<1 Hz, H-4), 2.28 (dd, 1H, $J_{2a,2b}$=13.3 Hz, H-2a), 1.83 (br d, 1H, $J_{10a,10b}$=12.1 Hz, $J_{7,10a}$<1 Hz, H-10a), 1.71 (dt, 1H, H-10b), 1.18 (dd, 1H, H-2b); ^{13}C NMR (DMSO-d_6) δ 109.4 (C-3), 85.2, 84.0, 79.0, 75.2 (C-1, C-5, C-7, C-9), 71.4, 71.3 (C-1′, C-2′), 63.5 (C-3′), 56.2, 49.1 (OCH$_3$), 46.3 (C-4), 35.1 (C-2), 27.8 (C-10).

To a solution of **4** (0.01 g, 0.034 mmol) in dry pyridine (0.2 mL) was added acetic anhydride (0.1 mL). After 6 h at 0°C, the reaction mixture was poured onto ice cold water, extracted with chloroform (3×25 mL) and washed successively with 1 M hydrochloric acid (2×25 mL), saturated aqueous sodium hydrogencarbonate (2× 25 mL) and water (2×25 mL). The organic layer was dried ($MgSO_4$) and the solvent evaporated to yield (1′*R*,2′*R*)-1′,2′,3′-triacetoxy-3,3-dimethoxy-(1*R*,4*S*,5*R*, 7*S*,9*R*)-6,8-dioxatricyclo[3.2.2.1^{4,7}]decane **11** as an oil (0.011 g, 78%): R_f 0.12 (1:1 AcOEt:hexane); $[\alpha]_D$= +23.5 (*c* 0.26, $CHCl_3$); *v* (film) 1740 (C=O), 1215 and 1050 (C-O-C, C-O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.21 (m, 2H, H-1′, H-2′), 4.41 (dd, 1H, $J_{3',3''}$=12.9 Hz, $J_{2',3'}$=2.3 Hz, H-3′), 4.28 (d, 1H, $J_{4,5}$=4.1 Hz, H-5), 4.20 (m, 1H, H-9), 4.20 (dd, 1H, $J_{2',3''}$=5.4 Hz, H-3″), 4.16 (dd, 1H, $J_{1,7}\sim$1 Hz, H-7), 3.37 (s, 3H, OCH$_3$), 3.35 (s, 3H, OCH$_3$), 3.23 (m, 1H, $J_{1,2a}\sim J_{1,2b}$=7.9 Hz, H-1), 2.60 (br t, 1H, $J_{4,10b}$=3.8 Hz, $J_{4,10a}$<1 Hz, H-4), 2.54 (dd, 1H, $J_{2a,2b}$=13.1 Hz, H-2a), 2.13 (s, 3H, 1 OAc), 2.09 (s, 3H, 1 OAc), 2.06 (s, 3H, 1 OAc), 2.04 (br d, 1H, H-10a), 1.85 (dt, 1H, $J_{10a,10b}$=12.5 Hz, $J_{7,10b}$=5.3 Hz, H-10b), 1.22 (dd, 1H, H-2b); ^{13}C NMR ($CDCl_3$) δ 170.7, 169.9 (O*C*OCH$_3$), 110.0 (C-3), 84.5, 82.4, 79.0, 76.2 (C-1, C-5, C-7, C-9), 70.7, 70.4 (C-1′, C-2′), 61.6 (C-3′), 56.9, 50.0 (OCH$_3$), 48.9 (C-4), 33.7 (C-2), 28.4 (C-10), 20.9, 20.7 (OCO*C*H$_3$). CI HRMS: calcd for $C_{19}H_{28}O_{10}$-H 415.1604. Found $(M-H)^+$ 415.1585. Calcd for $C_{19}H_{28}O_{10}$-CH_3 401.1447. Found $(M-CH_3)^+$ 401.1388.

3.2.2. 2-[(1′*R*,2′*R*)-1′,2′,3′-Trihydroxypropyl]benzofuran 5. Oil (0.16 g, 39%): R_f 0.69 (10:1 AcOEt:EtOH); $[\alpha]_D$=−1.0 (*c* 0.60, MeOH); *v* (film) 3400–3200 (OH), 1550 (C=C) and 1040 (C–O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.56 (d, 1H, $J_{4,5}$=6.9 Hz, H-4), 7.50 (br s, 1H, $J_{6,7}$=7.4 Hz, $J_{3,7}$<1 Hz, H-7), 7.21 (m, 2H, H-5, H-6), 6.71 (br s, 1H, H-3), 4.56 (d, 1H, $J_{1',2'}$=6.6 Hz, H-1′), 3.75 (m, 1H, H-2′), 3.58 (dd, 1H, $J_{3',3''}$=11.1 Hz, $J_{2',3'}$= 3.5 Hz, H-3′), 3.50 (dd, 1H, H-3″); ^{13}C NMR (DMSO-d_6) δ 154.0 (C-7a), 151.8 (C-2), 128.3 (C-3a), 123.6 (C-6), 122.5 (C-5), 120.8 (C-4), 111.0 (C-7), 103.7 (C-3), 73.4 (C-1′), 68.0 (C-2′), 62.9 (C-3′). CI HRMS: calcd for $C_{11}H_{12}O_4$+H 208.0735. Found $(M+H)^+$ 208.0732.

As described in Section 3.2.1, treatment of **5** (0.45 g, 2.16 mmol) with dry pyridine (4.5 mL) and acetic anhydride (2.25 mL), led to 2-[(1′*R*,2′*R*)-1′,2′,3′-triacetoxypropyl]benzofuran **12** as an oil which crystallized from ethanol (0.5 g, 69%): mp 69–70°C, R_f 0.72 (1:1 AcOEt:hexane); $[\alpha]_D$=+73.0 (*c* 0.33, $CHCl_3$); *v* (KBr) 1740 (C=O), 1210 and 1020 (C–O–C) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.56 (d, 1H, $J_{4,5}$=7.6 Hz, H-4), 7.49 (br d, 1H, $J_{6,7}$=8.2 Hz, $J_{3,7}$<1 Hz, H-7), 7.31 (td, 1H, $J_{5,6}$= $J_{6,7}$=8.5 Hz, $J_{4,6}$=1.4 Hz, H-6), 7.24 (br t, 1H, $J_{5,7}$<1 Hz, H-5), 6.80 (br s, 1H, H-3), 6.23 (d, 1H, $J_{1',2'}$=6.1 Hz, H-1′), 5.65 (td, 1H, H-2′), 4.43 (dd, 1H, $J_{3',3''}$=12.3 Hz, $J_{2',3'}$=3.1 Hz, H-3′), 4.35 (dd, 1H, $J_{2',3''}$=6.1 Hz, H-3″), 2.14 (s, 3H, 1 OAc), 2.05 (s, 3H, 1 OAc), 2.03 (s, 3H, 1 OAc); ^{13}C NMR ($CDCl_3$) δ 170.5, 169.7, 169.3 (O*C*OCH$_3$), 154.8 (C-7a), 151.2 (C-2), 127.4 (C-3a), 124.9 (C-6), 123.0 (C-5), 121.3 (C-4), 111.4 (C-7), 106.5 (C-3), 70.3 (C-1′), 67.0 (C-2′), 61.7 (C-3′), 20.7, 20.6 (OCO*C*H$_3$). Anal. calcd for $C_{17}H_{18}O_7$: C, 61.07; H, 5.42. Found: C, 60.75; H, 5.57.

3.2.3. 2(*R*)-2-[(1′*R*)-1′,2′-Dihydroxyethyl]-(3*R*,4*R*)-chromane-3,4-diol 6. Oil (0.023 g, 5%): R_f 0.61 (10:1 AcOEt:EtOH); $[\alpha]_D$=−1.0 (*c* 0.55, MeOH); *v* (film) 3400–3200 (OH), 1650 and 1560 (C=C) and 1070 (C–O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.34 (d, 1H, $J_{5,6}$=7.4 Hz, H-5), 7.07 (t, 1H, $J_{6,7}$=7.3 Hz, $J_{7,8}$=8.1 Hz, H-7), 6.86 (t, 1H, H-6), 6.64 (d, 1H, H-8), 5.20 (d, 1H, $J_{4,OH}$=6.7 Hz, 4-OH), 4.86 (d, 1H, $J_{1',OH}$=5.9 Hz, 1′-OH), 4.69 (dd, 1H, $J_{3,4}$=4.0 Hz, H-4), 4.65 (d, 1H, $J_{3,OH}$=4.0 Hz, 3-OH), 4.53 (t, 1H, $J_{2',OH}$=$J_{2'',OH}$=5.5 Hz, 2′-OH), 4.11 (t, 1H, $J_{2,3}$<1 Hz, H-3), 3.88 (d, 1H, $J_{1',2}$=8.6 Hz, H-2), 3.77 (m, 1H, H-1′), 3.70 (dd, 1H, $J_{2',2''}$=11.4 Hz, $J_{1',2'}$= 2.8 Hz, H-2′), 2.51 (dd, 1H, $J_{1',2''}$=5.6 Hz, H-2″); ^{13}C NMR (DMSO-d_6) δ 153.7 (C-8a), 127.9, 125.9 (C-5, C-7), 120.3 (C-6), 115.5, 115.2 (C-4a, C-8), 76.5, 69.5, 66.9, 63.9 (C-2, C-3, C-4, C-1′), 62.9 (C-2′). CI HRMS: calcd for $C_{11}H_{14}O_5$+H 226.0841. Found $(M+H)^+$ 226.0842.

As described in Section 3.2.1, treatment of **6** (0.05 g, 0.22 mmol) with dry pyridine (0.5 mL) and acetic anhydride (0.25 mL), led to 2(*R*)-2-[(1′*R*)-1′,2′-diacetoxyethyl]-(3*R*,4*R*)-3,4-diacetoxychromane **13** as an oil which crystallized from ethanol (0.065 g, 73%): mp 79–80°C; R_f 0.65 (1:1 AcOEt:hexane); $[\alpha]_D$=+119.4 (*c* 0.17, $CHCl_3$); *v* (KBr) 1740 (C=O), 1600 (C=C), 1215 and 1030 (C–O–C) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.26 (t, 1H, $J_{6,8}$=7.3 Hz, H-8), 7.19 (d, 1H, $J_{5,7}$=7.6 Hz, H-5), 7.00 (t, 1H, H-7), 6.90 (d, 1H, H-6), 6.19 (d, 1H, $J_{3,4}$=4.0 Hz, H-4), 5.64 (br d, 1H, $J_{2,3}$<1 Hz, H-3), 5.29 (m, 1H, H-1′), 4.63 (dd, 1H, $J_{2',2''}$=12.3 Hz, $J_{1',2'}$=2.0 Hz, H-2′), 4.47 (br d, 1H, $J_{1',2}$=9.6 Hz, H-2), 4.33 (dd, 1H, $J_{1',2''}$=4.4 Hz, H-2″), 2.14 (s, 3H, 1 OAc), 2.07 (s, 3H, 1 OAc), 2.05 (s, 3H, 1 OAc), 2.03 (s, 3H, 1 OAc);

^{13}C NMR ($CDCl_3$) δ 170.5, 170.0 ($OCOCH_3$), 152.9 (C-8a), 129.5 (C-4a), 126.7 (C-5), 121.6 (C-6), 118.4 (C-7), 116.5 (C-8), 72.2 (C-4), 67.7 (C-3), 66.3 (C-1′), 62.1 (C-2′), 61.9 (C-2), 20.8, 20.6 ($OCOCH_3$). FAB HRMS: calcd for $C_{19}H_{22}O_9$+Na 417.1161. Found $(M+Na)^+$ 417.1166.

3.2.4. 7-Chloro-7-en-(4*R*)-4-hydroxy-(3*R*)-3-[(1′*R*,2′*R*)-1′,2′,3′-trihydroxypropyl]-2-oxabicyclo[3.3.1]nonan-6-one oxime 7. Oil (0.020 g, 4%): R_f 0.45 (10:1 AcOEt:EtOH). Although some minor inseparable impurities were present in this fraction, the following ^{1}H NMR signals (DMSO-d_6) could be safely assigned: δ 10.76 (s, 1H, C=N–O*H*), 6.58 (d, 1H, $J_{1,8}=6.4$ Hz, H-8), 4.42 (m, 1H, H-1), 3.57 (m, 1H, H-5), 2.40 (br d, 1H, $J_{9a,9b}=11.8$ Hz, H-9a), 1.59 (br d, 1H, H-9b). By comparison of these data with those of unsaturated oxime **20** (prepared from D-*galacto*-nitrocyclohexadiene **3b**), we assigned tentatively the structure **7** for the title compound.

3.2.5. (2*S*,5*R*,8*R*)-2-Acetoxy-8-[(1′*R*)-1′,2′-diacetoxyethyl] - 5 - chloro - (1*R*,3*R*,6*S*,10*S*) - 7,9 - dioxatricyclo-[4.2.2.1^{3,10}]undecane-4-one oxime acetate 14. The title compound (oil; 3% yield from **2a**) was obtained by conventional acetylation of the oily residue left by evaporation of the solvent from fraction with TLC R_f 0.39 (10:1 AcOEt: EtOH), followed by purification through preparative TLC (1:1 AcOEt:hexane). $[\alpha]_D=+15.0$ (*c* 0.16, $CHCl_3$); *v* (KBr) 1780 (N–O–C=O), 1745, 1735 (C=O), 1635 (C=N), 1225 and 1060 (C–O–C) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.27 (ddd, 1H, H-1′), 4.83 (d, 1H, $J_{5,6}=3.8$ Hz, H-5), 4.82 (m, 1H, H-2), 4.63 (dd, 1H, $J_{2',2''}=12.3$ Hz, $J_{1',2'}=2.3$ Hz, H-2′), 4.39 (m, 1H, H-3), 4.23 (m, 1H, H-10), 4.20 (br s, 1H, H-1), 4.15 (dd, 1H, $J_{1',2''}=4.6$ Hz, H-2″), 4.03 (dd, 1H, $J_{8,1'}=10.0$ Hz, $J_{1,8}=1.7$ Hz, H-8), 3.87 (d, 1H, H-6), 2.37 (br d, 1H, $J_{11a,11b}=13.7$ Hz, H-11a), 2.26 (s, 3H, CH_3COON), 2.22 (m, 1H, H-11b), 2.19 (s, 3H, 1 OAc), 2.07 (s, 3H, 1 OAc), 2.05 (s, 3H, 1 OAc); ^{13}C NMR ($CDCl_3$) δ 170.7, 170.0, 169.6, 167.6 ($OCOCH_3$), 159.0 (C-4), 78.6, 78.0, 72.2, 69.7, 69.0, 68.7 (C-1′, C-1, C-2, C-6, C-8, C-10), 62.2 (C-2′), 56.8 (C-5), 30.2 (C-3), 29.7 (C-11), 21.2, 20.9, 20.8, 19.6 ($OCOCH_3$). CI HRMS: calcd for $C_{19}H_{24}NO_{10}$-Cl 426.1400. Found $(M-Cl)^+$ 426.1343. Calcd for $C_{17}H_{21}ClNO_8$-OAc 402.0955. Found $(M-OAc)^+$ 402.0954.

3.2.6. 2-Nitro-1-(D-*manno*-pentitol-1′-yl)benzene 9.[16] Oil (0.022 g, 4%): R_f 0.30 (10:1 AcOEt:EtOH); $[\alpha]_D=-2.2$ (*c* 0.50, pyridine); *v* (film) 3600–3200 (OH), 1560, 1400 (NO_2), 1020 (C–O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.83 (d, 1H, $J_{3,4}=7.8$ Hz, H-3), 7.75 (d, 1H, $J_{5,6}=8.0$ Hz, H-6), 7.65 (t, 1H, H-4), 7.44 (t, 1H, H-5), 5.49 (d, 1H, $J_{1,1'}=1.0$ Hz, H-1′), 5.0–3.0 (m, 5H, 5× OH), 3.8–3.2 (m, 5H, H-2′, H-3′, H-4′, H-5′, H-5″); ^{13}C NMR (DMSO-d_6) δ 150.0 (C-2), 139.6 (C-1), 132.6, 128.9, 127.7, 123.4 (C-3, C-4, C-5, C-6), 73.6 (C-1′), 71.4, 69.6, 67.1 (C-2′, C-3′, C-4′), 64.0 (C-5′).

3.2.7. 1′-*C*-[(1*R*,5*R*,6*S*)-5-Hydroxy-6-nitrocyclohex-3-enyl]-D-*manno*-pentitol 10[2c]. Oil (0.090 g, 15%): R_f 0.20 (10:1 AcOEt:EtOH); $[\alpha]_D=-23.6$ (*c* 0.50, pyridine); *v* (film) 3600–3200 (OH), 1555, 1385 (NO_2), 1026 (C–O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 5.90 (m, 1H, H-3), 5.74 (dd, 1H, $J_{3,4}=10.0$ Hz, $J_{4,5}=3.1$ Hz, H-4), 4.89 (dd, 1H, $J_{5,6}=4.3$ Hz, $J_{1,6}=11.1$ Hz, H-6), 4.5–4.1 (m, 6H, 6×OH), 4.37 (t, 1H, H-5), 3.8–3.2 (m, 6H, H-1′, H-2′, H-3′, H-4′, H-5′, H-5″), 2.73 (m, 1H, H-1), 2.37 (br d, 1H, $J_{2a,2b}=18.1$ Hz, H-2a), 2.07 (br d, 1H, H-2b); ^{13}C NMR (DMSO-d_6) δ 129.4 (C-4), 126.8 (C-3), 88.6 (C-6), 71.4, 69.9, 69.6, 69.1, 65.2, 63.9 (C-5, C-1′, C-2′, C-3′, C-4′, C-5′), 35.2 (C-1), 26.8 (C-2).

3.3. Reaction of 1′,2′,3′,4′,5′-penta-*O*-acetyl-1′-*C*-[(1*S*)-2-nitrocyclohexa-2,4-dienyl]-D-*galacto*-pentitol 3b with acetyl chloride in methanol. Synthesis of 7-chloro-7-en-(4*S*)-4-hydroxy-(3*R*)-3-[(1′*S*,2′*R*)-1′,2′,3′-trihydroxypropyl]-2-oxabicyclo[3.3.1]nonane-6-one oxime 20

To a stirred suspension of 1′,2′,3′,4′,5′-penta-*O*-acetyl-1′-*C*-[(1*S*)-2-nitrocyclohexa-2,4-dienyl]-D-*galacto*-pentitol (**3b**; 1.0 g, 2.06 mmol) in methanol at 0°C (25 mL) was added acetyl chloride (0.55 mL). After 10 min at 0°C, the reaction mixture was stirred at 50–55°C for 2 h, the solvent evaporated, and the resulting residue was passed through a short column of silica gel (10:1 AcOEt:EtOH). Evaporation of the solvent yielded the title compound as a chromatographically pure oil which crystallized from methanol–ethyl ether (0.53 g, 83%): mp 92–93°C; R_f 0.42 (10:1 AcOEt:EtOH); $[\alpha]_D=+168.6$ (*c* 0.43, MeOH); *v* (KBr) 3600–3200 (OH), 1647, 1600 (C=C, C=N), 1038 (C–O), 960 (N–O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 10.62 (s, 1H, C=N–O*H*), 6.31 (br d, 1H, $J_{1,8}=6.7$ Hz, $J_{8,9a}<1$ Hz, H-8), 4.89 (d, 1H, OH-4), 4.38 (t, 1H, OH-3′), 4.38 (m, 1H, $J_{1,5}<1$ Hz, H-1), 4.08 (d, 1H, OH-1′), 4.00 (d, 1H, OH-2′), 3.71 (br d, 1H, $J_{4,OH}=5.0$ Hz, $J_{3,4}=1.6$ Hz, $J_{4,9s}<1$ Hz, H-4), 3.68 (br d, 1H, $J_{1',OH}=8.0$ Hz, $J_{1',2'}<1.0$ Hz, H-1′), 3.58 (m, 1H, $J_{4,5}<1$ Hz, H-5), 3.50 (m, 1H, $J_{2',3'}=J_{2',3''}=7.0$ Hz, $J_{2',OH}=6.9$ Hz, H-2′), 3.39 (dd, 1H, $J_{1',3}=9.0$ Hz, H-3), 3.31 (m, 2H, H-3′, H-3″), 2.29 (br d, 1H, $J_{1,9a}=3.5$ Hz, $J_{5,9a}=1.6$ Hz, H-9a), 1.41 (br d, 1H, $J_{9s,9a}=12.8$ Hz, $J_{5,9s}=3.5$ Hz, $J_{1,9s}<1$ Hz, H-9s); ^{13}C NMR (DMSO-d_6) δ 151.4 (C-6), 132.0 (C-7), 128.4 (C-8), 69.3, 69.2, 67.5 (C-1, C-3, C-4), 65.8, 62.8 (C-1′, C-2′, C-3′), 34.8 (C-5), 24.4 (C-9). FAB HRMS: calcd for $C_{11}H_{16}ClNO_6$+Na 316.0563. Found $(M+Na)^+$ 316.0559.

3.4. 7-Chloro-7-en-(4*S*)-4-acetoxy-(3*R*)-3-[(1′*S*,2′*R*)-1′,2′,3′-triacetoxypropyl]-2-oxabicyclo[3.3.1]nonane-6-one oxime acetate 21 and 7-chloro-7-en-(4*S*)-4-acetoxy-(3*R*)-3-[(1′*S*,2′*R*)-1′,2′,3′-triacetoxypropyl]-2-oxabicyclo-[3.3.1]nonane-6-one oxime 22

As described in Section 3.2.1 for **11**, acetylation of oxime **20** (0.069 g, 0.22 mmol) with pyridine (7.0 mL) and acetic anhydride (3.5 mL), led to compound **21** as an oil which crystallized from ethanol (0.070 g, 61%):

mp 189–190°C; R_f 0.32 (1:1 AcOEt:hexane); $[\alpha]_D$ = +49.1 (*c* 0.42, $CHCl_3$); *v* (KBr) 3050 (=C–H), 1785 (N–O–C=O), 1740, 1730 (C=O), 1600, 1582 (C=N, C=C), 1225 and 1040 (C–O–C), 1007, 940 (N–O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.47 (br d, 1H, $J_{1,8}$ = 6.6 Hz, $J_{8,9a}$ < 1 Hz, H-8), 5.45 (ddd, 1H, H-2′), 5.32 (dd, 1H, $J_{1',2'}$ = 1.7 Hz, H-1′), 4.80 (m, 1H, $J_{4,9s}$ < 1 Hz, H-4), 4.59 (m, 1H, H-1), 4.22 (dd, 1H, $J_{3',3''}$ = 11.6 Hz, $J_{2',3'}$ = 5.2 Hz, H-3′), 3.88 (dd, 1H, $J_{2',3''}$ = 7.3 Hz, H-3″), 3.85 (m, 1H, $J_{4,5}$ < 1 Hz, H-5), 3.79 (dd, 1H, $J_{1',3}$ = 9.6 Hz, $J_{3,4}$ = 2.0 Hz, H-3), 2.33 (br d, 1H, $J_{9s,9a}$ = 13.4 Hz, $J_{1,9a}$ = 3.2 Hz, $J_{5,9a}$ = 1.6 Hz, H-9a), 2.29 (s, 3H, N-OAc), 2.12 (s, 3H, 1 OAc), 2.09 (s, 3H. 1 OAc), 2.05 (s, 3H, 1 OAc), 2.03 (s, 3H, 1 OAc), 1.72 (br d, 1H, $J_{5,9s}$ = 3.2 Hz, $J_{1,9s}$ < 1 Hz, H-9s); ^{13}C NMR ($CDCl_3$) δ 170.4, 170.0, 169.6 (O*C*OCH$_3$), 167.2 (NO*C*OCH$_3$), 157.2 (C-6), 132.4, 132.3 (C-7, C-8), 68.3, 68.2, 66.3, 66.2, 64.2 (C-1, C-3, C-4, C-1′, C-2′), 62.1 (C-3′), 33.9 (C-5), 24.9 (C-9), 20.9, 20.6, 20.4, 19.2 (OCO*C*H$_3$). FAB HRMS: calcd for $C_{21}H_{27}ClNO_{11}$+H 504.1273. Found $(M+H)^+$ 504.1261. Anal. calcd for $C_{21}H_{26}ClNO_{11}$: C, 50.06; H, 5.21; N, 2.78. Found: C, 49.89; H, 5.30; N, 2.78.

When compound **21** was dissolved in ethanol, TLC (1:1 AcOEt:hexane) showed its progressive conversion into a more-mobile product that showed to be the oxime tetraacetate **22**. After 15 days, the mixture was stabilized (**21**:**22** ratio, 2:1), being isolated an analytical sample of **22** by preparative TLC (2:1 AcOEt–hexane). Crystallized from EtOH: mp 193–195°C, R_f 0.45 (1:1 AcOEt:hexane); $[\alpha]_D$ = +92.2 (*c* 0.33, $CHCl_3$); *v* (KBr) 3370 (OH), 3050 (=C–H), 1745, 1735 and 1710 (C=O), 1610, 1590 (C=N, C=C), 1220, 1030 (C–O–C), 1005, 960 (N–O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.00 (br s, 1H, C=N–O*H*), 6.28 (br d, 1H, $J_{1,8}$ = 6.6 Hz, $J_{8,9a}$ < 1 Hz, H-8), 5.46 (ddd, 1H, H-2′), 5.31 (dd, 1H, $J_{1',2'}$ = 1.9 Hz, H-1′), 4.95 (m, 1H, $J_{4,9s}$ < 1 Hz, H-4), 4.55 (m, 1H, H-1), 4.24 (dd, 1H, $J_{3',3''}$ = 11.6 Hz, $J_{2',3'}$ = 5.1 Hz, H-3′), 3.89 (m, 1H, $J_{4,5}$ < 1 Hz, H-5), 3.88 (dd, 1H, $J_{2',3''}$ = 7.3 Hz, H-3″), 3.82 (dd, 1H, $J_{1',3}$ = 9.7 Hz, $J_{3,4}$ = 1.9 Hz, H-3), 2.34 (br d, 1H, $J_{9s,9a}$ = 13.3 Hz, $J_{1,9a}$ = 2.7 Hz, $J_{5,9a}$ = 1.6 Hz, H-9a), 2.11 (s, 3H, 1 OAc), 2.09 (s, 3H, 1 OAc), 2.05 (s, 3H, 1 OAc), 2.03 (s, 3H, 1 OAc), 1.65 (br d, 1H, $J_{5,9s}$ = 2.7 Hz, $J_{1,9s}$ < 1 Hz, H-9s); ^{13}C NMR ($CDCl_3$) δ 170.5, 169.8, 169.6 (O*C*OCH$_3$), 151.2 (C-6), 132.9 (C-7), 128.4 (C-8), 68.4, 68.3, 66.7, 66.4, 64.1 (C-1, C-3, C-4, C-1′, C-2′), 62.2 (C-3′), 32.0 (C-5), 24.9 (C-9), 21.0, 20.7, 20.6, 20.5 (OCO*C*H$_3$). FAB HRMS: calcd for $C_{19}H_{25}ClNO_{10}$+H 462.1166. Found $(M+H)^+$ 462.1160.

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References

1. (a) Fringelli, F.; Taticchi, A. *Dienes in the Diels–Alder Reaction*; Wiley: New York, 1990; (b) *The Chemistry of Dienes and Polyenes*, Rappoport, Z., Ed.; Wiley: New York; Vol. 2, 2000.
2. (a) Román, E.; Serrano, J. A.; Cuéllar, M. E.; Marfil, A.; Galbis, J. A. *J. Carbohydr. Chem.* **1992**, *11*, 1; (b) Areces, P.; Román, E.; Pozo, M. C.; Serrano, J. A. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1939; (c) Serrano, J. A.; Cáceres, L. E.; Román, E. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1863; (d) Román, E.; Baños, M.; Higes, F. J.; Serrano, J. A. *Tetrahedron: Asymmetry* **1998**, *9*, 449; (e) Areces, P.; Pozo, M. C.; Román, E.; Serrano, J. A. *Heterocycles* **2000**, *53*, 81; (f) Areces, P.; Jiménez, J. L.; Pozo, M. C.; Román, E.; Serrano, J. A. *J. Chem. Soc., Perkin Trans. 1* **2001**, 754; (g) Ballini, R.; Bosica, G.; Gil, M. V.; Román, E.; Serrano, J. A. *Tetrahedron: Asymmetry* **2002**, *13*, 1773.
3. Bloom, A. J.; Mellor, J. M. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2737.
4. Seebach, D.; Missbach, M.; Caderari, G.; Eberte, M. *J. Am. Chem. Soc.* **1990**, *112*, 7625.
5. Alston, P. V.; Ottenbrite, R. M.; Newby, J. *J. Org. Chem.* **1979**, *44*, 4939.
6. Byramova, N. E.; Ovchinnikov, M. V.; Backinowsky, L. V.; Kochetkov, N. K. *Carbohydr. Res.* **1983**, *124*, C8.
7. Horton, D.; Usui, T. *Carbohydr. Res.* **1991**, *216*, 33.
8. To clarify the discussion, the original numbering which was given in Ref. 2c for compounds **2a**, **3b** and **10** has been maintained.
9. Feuer, H.; Nielsen, A. T. *J. Am. Chem. Soc.* **1962**, *84*, 688.
10. (a) Bird, C. W.; Cheeseman, G. W. H. *Comprehensive Heterocyclic Chemistry*; Pergamon Press: New York, 1984; Vol. 4, p. 1; (b) Pretsch, E.; Buehlmann, P.; Affolter, C. *Structure Determination of Organic Compounds*; 3rd ed.; Berlin: Springer, 2000.
11. (a) Boyd, D. R.; Sharma, N. D.; Boyle, R.; Evans, T. A.; Malone, J. F.; McCombe, K. M.; Dalton, H.; Chima, J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1757; (b) Jennings, R. L.; Ottridge, A. P. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1733.
12. (a) Clark-Lewis, J. W.; Jackman, L. M.; Williams, L. R. *J. Chem. Soc.* **1962**, 3858; (b) Halpin, R. A.; El-Naggar, S. F.; McCombe, K. M.; Vyas, K. P.; Boyd, D. R.; Jerina, D. M. *Tetrahedron Lett.* **1982**, *23*, 1655.
13. Booth, H.; Huckle, D.; Lockhart, I. M. *J. Chem. Soc., Perkin Trans. 2* **1973**, 227.
14. This type of intermediate has been proposed in the conversion of secondary nitroalkanes to carbonyl compounds under acid media. See Ref. 8.
15. A similar intramolecular nucleophilic attack in the formation of acylfurans has been proposed: (a) Yanami, T.; Ballatore, A.; Miyashita, M.; Kato, M.; Yoshikoshi, A. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1144; (b) Yoshikoshi, A.; Miyashita, M. *Acc. Chem. Res.* **1985**, *18*, 284.
16. Cáceres, L. E. Ph.D. Thesis, University of Extremadura, 1993.
17. Coombes, R. G. *Comprehensive Organic Chemistry*; Pergamon Press: New York, 1979; Vol. 2, p. 305.

18. A structurally related oxime has been obtained from 1,2,3,4,5-penta-*O*-acetyl-1-*C*-[(4*S*,5*S*)-1,2-dimethyl-4-nitro-1-cyclohexen-5-yl]-D-*galacto*-pentitol: Gil, M. V.; Román, E.; Serrano, J. A.; Hursthouse, M. B.; Light, M. E. *Tetrahedron: Asymmetry* **2001**, *12*, 1673.
19. (a) Tkachev, A. V.; Chibiryaev, A. M.; Denisov, A. Y.; Gatilov, Y. V. *Tetrahedron* **1995**, *51*, 1789; (b) Nesi, R.; Giomi, D.; Papaleo, S.; Turchi, S. *Heterocycles* **1991**, *32*, 1913; (c) Chiacchio, U.; Corsaro, A.; Librando, V.; Rescifina, A.; Romeo, R.; Romeo, G. *Tetrahedron* **1996**, *52*, 14323.
20. (a) Karplus, M. *J. Chem. Phys.* **1959**, *30*, 11; (b) Karplus, M. *J. Am. Chem. Soc.* **1963**, *30*, 2870.
21. Lerch, U.; Burdon, M. G.; Moffatt, J. G. *J. Org. Chem.* **1971**, *36*, 1507.
22. (a) Moreno, M. Ch.; Plumet, J.; Román, E.; Serrano, J. A.; Rodríguez, M. L.; Ruíz-Pérez, C. *Tetrahedron Lett.* **1989**, *30*, 3179; (b) Serrano, J. A.; Moreno, M. Ch.; Román, E.; Arjona, O.; Plumet, J.; Jiménez, J. *J. Chem. Soc., Perkin Trans. 1* **1991**, 3207; (c) Román, E.; Baños, M.; Gutiérrez, J. I.; Serrano, J. A. *J. Carbohydr. Chem.* **1995**, *14*, 703.
23. Blanc-Muesser, M.; Defaye, J.; Horton, D. *Carbohydr. Res.* **1980**, *87*, 71.