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Enantioselective synthesis of 1-nitrotricyclo[5,2,2,$0^{2,6}$]undeca-3,8-dienes via tandem consecutive asymmetric Diels–Alder reaction–Cope rearrangement

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Abstract

The 1-glyco-2-nitrocyclohexa-2,4-dienes **1a** and **5a** react with cyclopentadiene to yield, almost exclusively, the 10-glyco-1-nitrotricyclo[5,2,2,$0^{2,6}$]undeca-3,8-dienes **4a** and **8a**. Formation of these products is explained as the result of a tandem consecutive asymmetric Diels–Alder reaction–Cope rearrangement. Periodate oxidation of deprotected sugar side-chains, followed by sodium borohydride reduction yielded enantiomerically pure 10-formyl- and 10-hydroxymethyl-1-nitrotricyclo[5,2,2,$0^{2,6}$]undeca-3,8-dienes. Structures have been determined by X-ray crystallographic and spectroscopic analyses, and chemical correlation.

1. Introduction

The development of new and highly enantioselective processes constitutes one of the areas in chemical synthesis that has been more intensely studied in the last years. In particular, the most attractive methodology in this field is focused towards those reactions where several stereogenic centres can be constructed in one step, thus opening the way to enantiomerically pure complex molecules. With this objective in mind, we have reported[1] on the enantioselective syntheses of some norbornene or cyclohexene nitroaldehydes, by means of asymmetric Diels–Alder reactions with sugar-derived nitroalkenes as chiral dienophiles and cyclic or acyclic dienes. As a consequence of this work, we also described[1] the preparation of the 1-D-*manno*- and 1-D-*galacto*-2-nitrocyclohexa-2,4-dienes **1a** and **5a** as the result of the cycloadditions between the suitable dienophiles and 1-acetoxybuta-1,3-diene, followed by acetic acid elimination. In contrast with the instability of 1-nitrocyclohexa-1,3-diene (which on exposure to air is rapidly converted

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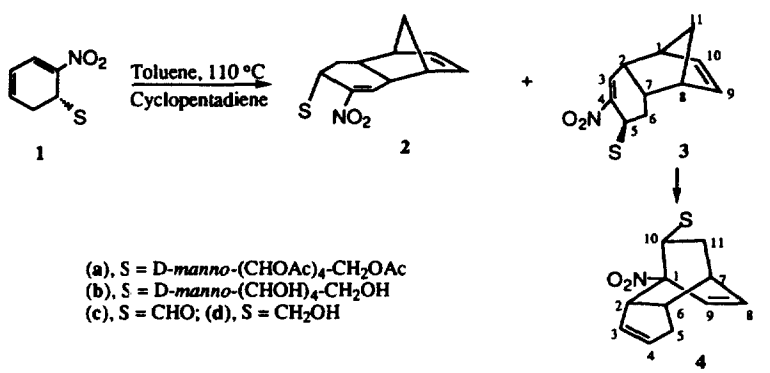
into nitrobenzene),[2] both compounds **1a** and **5a** were very stable on storage at room temperature, thus becoming useful synthons to study the scarcely explored[2,3] chemistry of 1-nitrocyclo-1,3-dienes, as well as their possible facial stereoselectivity.[4]

In this paper, we wish to describe the results of the reactions between **1a** or **5a** and cyclopentadiene. The major products that were isolated (**4a** and **8a**, respectively), are actually the consequence of sigmatropic Cope rearrangements of the initially formed norbornenic adducts **3a** and **7a**.

2. Results and discussion

The reactions of nitrocyclohexadienes **1a** and **5a** with 4.0 equiv. of cyclopentadiene were carried out in toluene at 110°C, for 96 h, to produce the 10-glyco-1-nitrotricyclo[5,2,2,$0^{2,6}$]undeca-3,8-dienes **4a** and **8a**, respectively, in fairly good yields. It is noteworthy that the ^{1}H NMR spectra of both reaction mixtures — at the end of the heating time — practically superimposed those of **4a** or **8a**, once purified. However, through a careful chromatographic analysis, we could also isolate (PTLC) the norbornenic adducts **2a** and **3a** (from the reaction mixture of **1a**) or **6a** and **7a** (from the reaction mixture of **5a**). These substances were present in very small quantities, showing chromatographic mobilities nearly identical to those of the major products **4a** or **8a**.

Treatment of **4a** with potassium carbonate in a methanol:water (9:1) solution afforded the penta-hydroxylated compound **4b** which, by oxidative cleavage of its sugar side-chain with sodium metaperiodate, led to 1-nitrotricyclo[5,2,2,$0^{2,6}$]undeca-3,8-diene-10-carbaldehyde **4c**; reduction of this compound with sodium borohydride yielded the alcohol **4d** (Scheme 1).



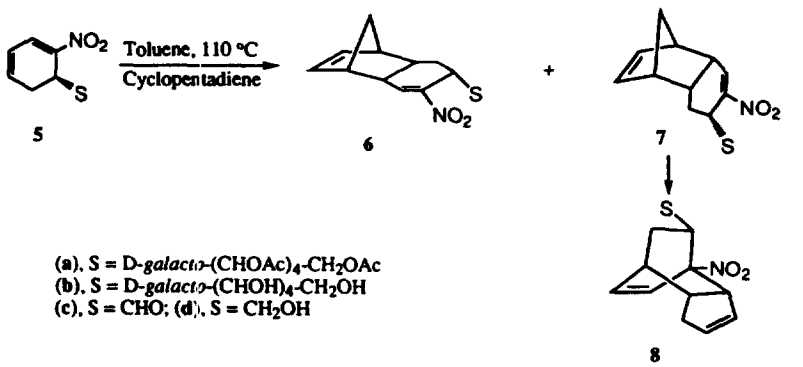
1 2 3 4

Scheme 1.

Through a similar pathway, **8a** led to **8b**, **8c** and **8d** (Scheme 2). The structures assigned to new compounds are based on elemental analyses, and spectroscopic evidence (IR, HRMS, ^{1}H and ^{13}C NMR), including X–H correlation for **4a** and **8a**. The location of the olefinic double bond in the cyclopentene ring, as well as the absolute configurations of the chiral centers in **4a** was unambiguously determined by X-ray crystallographic analysis, whose perspective view is shown in Fig. 1.

The stereochemical relationship between **4a** and **8a** was deduced from comparison between their respective derivatives without the sugar side-chain, thus compounds **4c** and **4d** showed specific rotations with nearly equal value but opposite sign to those of **8c** and **8d** (i.e. the tricyclic portion of compounds of series **4** and **8** are not superimposable mirror images).

The *cis* arrangement between the sugar side-chain and the proton that appears at the higher field in the ^{1}H NMR spectrum of **8a** (namely H-11b) was ascertained on the basis of NOE difference experiments: a significant enhancement (6.6%) was observed on the signal of H-11b when the first proton in the sugar



Scheme 2.

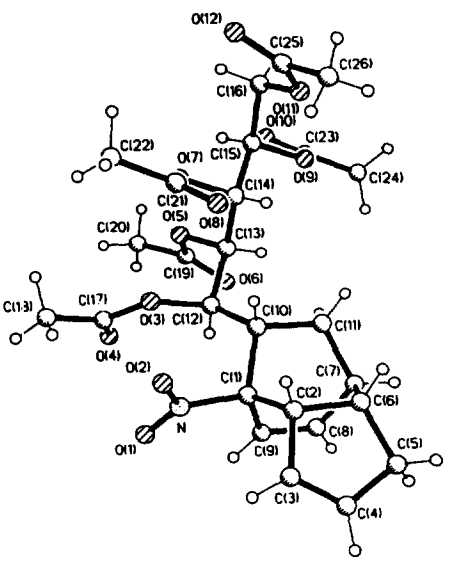


Fig. 1. X-Ray crystal structure of compound **4a**

moiety (H-1′) was selectively irradiated. This fact is also supported because in aldehyde **8c**, with H-11b close to the formyl group, this proton is 0.62 ppm downfield from that in **8a**, whereas for H-11a the same shift was only of 0.12 ppm. When **8c** is reduced to alcohol **8d**, both H-11 protons again showed similar shifts to **8a**. Similar correlations were made between **4a**, **4c** and **4d**.

On inspection of NMR spectra of norbornene derivatives, we have observed that, as expected,[5] the *endo* H-2 and H-7 protons in **2a** and **6a** appear at higher field (2.0–2.3 ppm) than the same protons in **3a** and **7a** (2.7–2.9 ppm), where they are *exo*. Furthermore, C-3 and C-6 carbon atoms appear at higher field in the *endo* compounds than in their *exo* isomers.

Compounds **4a** and **8a** may appear as the corresponding Diels–Alder cycloadducts from reactions where the cyclopentadiene dienophile interacts, in an *endo* mode, with the less hindered faces of nitrocyclohexadienes **1a** or **5a** (i.e., the sugar side-chain exerts a stereofacial *anti* directing effect). However, PM3 semiempirical calculations performed with a simplified model (S=–CHOH–CH_3) of the starting nitrocyclohexadienes gave the frontier orbital energies and coefficients showed in Fig. 2; in this way, by applying Frontier Molecular Orbital Theory, our cycloadditions would be of the normal electron-demand type (HOMO diene–LUMO dienophile interaction), where the smaller energy separation occurs between the HOMO of the cyclopentadiene and the LUMO of the compound **1a** or **5a**. As the values of

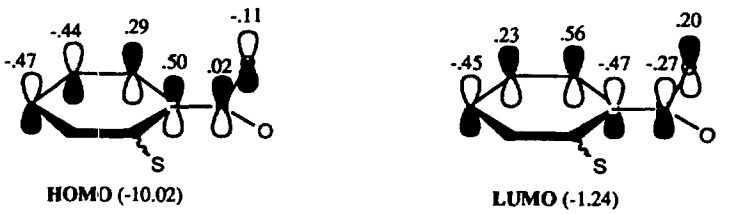
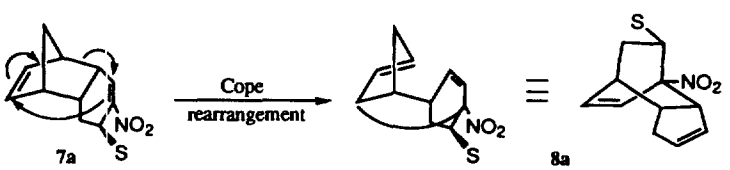


Fig. 2.

the calculated coefficients indicate, the preferred regioisomers would arise from a reaction involving the double bond that supports the nitro group.

Furthermore, when, as in our case, each component in the Diels–Alder system is in principle capable of acting either as diene or dienophile, cycloaddition may be followed by Cope rearrangement[6] of the initially formed *endo*-adduct. If the ring fused to the norbornenic system is larger than five, the special facility of this process is presumably derived from the relief of strain.[7–9] On the other hand, if compounds **4a** and **8a** were actually Diels–Alder adducts, their isomers with the double bond at C-4 would be also formed.

To demonstrate that Cope rearrangement operates, each one of compounds **2a**, **3a**, **4a**, **6a**, **7a**, and **8a** was heated in toluene at 110°C. After 4 days, **3a** and **7a** were converted into **4a** and **8a**, respectively, through Cope rearrangements (Scheme 3). On the contrary, compounds **2a** and **6a** remained unchanged because of the *exo* orientation of their nitrocyclohexene-ring double bonds. In contrast, *exo* and *endo* mixtures of Diels–Alder adducts from acyclic 2-nitro-1,3-butadienes have been completely transformed into Cope products.[10,11] We think that this difference could be due to the absence of *exo–endo* interconversion in our conditions; furthermore, compounds **4a** and **8a** remained unchanged, thus showing the irreversibility of the Cope rearrangement.



Scheme 3.

Our results indicate that the reaction proceeds through an asymmetric Diels–Alder cycloaddition between cyclopentadiene, as the diene, and the double bond at C-4 of either **1a** or **5a**, as the dienophilic counterparts. The approach of the cyclopentadiene would occur with complete facial stereoselectivity and almost exclusively (a small quantity of the *exo* adducts **2a** and **6a** was also formed) in the *endo* mode, on the opposite face to that which is occupied by the sugar side-chain. Subsequently, each of the *endo* adducts **3a** or **7a** undergoes Cope rearrangement via a 'boat transition state' to yield the corresponding tricyclic compounds **4a** or **8a** (Scheme 3). The lack of reactivity of the double bond adjacent to the nitro group may be explained as a consequence of its major degree of substitution, as well as the greater steric hindrance caused by the proximity of the sugar chain. This behaviour is in contrast with that observed for the reaction between cyclopentadiene and the acyclic dienophile (1*E*,3*E*)-5,6,7-tri-*O*-acetyl-1,2,3,4-tetradeoxy-1-nitro-D-*erythro*-hepta-1,3-dienitol.[12] Since the intermediate *endo* adducts are isolable entities, the overall process could be classified (following the terminology of Denmark and Thorarensen[13]) as a *tandem consecutive* Diels–Alder reaction–Cope rearrangement.

Because the position of the final equilibrium in the Cope rearrangement is governed by the relative stability of the starting materials and the products, we have performed semiempirical calculations[14,15]

for simplified model compounds of **7a** and **8a** (S=–CHOH–CH_3), finding that the second compound was more stable by about 3.4 Kcal/mol.

In summary, we have developed an efficient stereoselective synthesis of enantiomerically pure 10-formyl- or 10-hydroxymethyl-1-nitrotricyclo[5,2,2,$0^{2,6}$]undeca-3,8-dienes, demonstrating that the overall process is a tandem consecutive Diels–Alder reaction–Cope rearrangement.

3. Experimental

Solvents were evaporated under reduced pressure below 40°C bath temperature. 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. Infrared spectra were recorded in the range 4000–600 cm^{-1} with Perkin–Elmer 399 or Midac FT-IR spectrophotometers. NMR spectra were recorded at 20°C on Bruker spectrometers AM 400 (400.13 MHz for ^1H, 100.62 MHz for ^{13}C) with TMS or residual $CHCl_3$/$(CH_3)_2SO$ as internal standard. NMR assignments were confirmed by homonuclear double resonance experiments, and DEPT. Chemical shifts are reported in ppm and coupling constants are reported in Hz. Mass spectra were recorded on a VG Autospec spectrometer. TLC was performed on precoated plates of silica gel 60 GF_{254} (Merck), with visualisation of spots by UV light or iodine vapour, and the solvent systems specified. Column chromatography was performed in the flash mode using silica gel 60 (particle size 0.2–0.063 mm, Merck). Elemental analyses were determined by the Servicio de Microanálisis, CSIC, Barcelona. Calculations have been performed by using the semiempirical method[14,15] MNDO-PM3, based on the NDDO approach (Neglect of Diatomic Differential Overlap) from MOPAC programs,[16] implemented in the Convex 210 computer of the University of Extremadura.

*3.1. X-Ray crystal structure determination of **4a***

3.1.1. Crystal data

$C_{26}H_{33}NO_{12}$, *M* 551.5. Crystal size 0.48×0.42×0.22 mm. *T*=298(2) K. Crystal system: orthorhombic, space group $P2_12_12_1$, *a*=8.338(2) Å, *b*=15.2881(2) Å, *c*=22.277(2) Å. *V*=2838.4(8) $Å^3$, *Z*=4; D_c=1.291 Mg/m^3. μ=0.103 mm^{-1}, F(000)=1168.

3.1.2. Data collection

X-Ray measurements were made with a Siemens P4 diffractometer and graphite monochromatized Mo-K_α radiation (λ=0.71073 Å). 3618 reflections were scanned in the range $1<\theta<25°$, by the $\omega-2\theta$ scan mode, and of these 3412 were independent (R_{int}=0.030). Index ranges $-1\leq h\leq 9$, $-1\leq k\leq 18$, $-1\leq l\leq 26$. Examination of three standard reflections, monitored after 97 scans, showed no sign of crystal deterioration.

3.1.3. Structure determination and refinement

The structure was solved by direct methods and subsequent Fourier differences and refined by full-matrix least-squares using anisotropic thermal parameters for non-hydrogen atoms. The hydrogen atoms were located from a differential Fourier synthesis and placed in idealized position (C–H=0.96 Å) riding on their respective bonded atoms. The final refinement was carried out with a weighting scheme of $w=[1/\sigma^2(F_0)+0.0003F_0^2]$ and converged to $R(F)$=0.049 and $R_W(F)$=0.057 for 2894 reflections with $F_0>2\sigma(F_0)$ and 352 refined parameters. The goodness of fit on F^2 was 1.58. The largest negative and

positive peaks in the final difference map were 0.19 and −0.21 e $Å^{-3}$. All calculations were performed on a Silicon Graphics Iris Indigo XS24 computer using the SHELXTL-IRIS program package.[17]

Additional material is available from the Cambridge Crystallographic Centre, which comprises hydrogen atom coordinates, atomic thermal motion parameters, bond lengths and angles and a list of the observed and calculated structure factors.

*3.2. (1R,2S,6S,7R,10R)-1-Nitrotricyclo[5,2,2,$0^{2,6}$]-10-(1′,2′,3′,4′,5′-penta-*O*-acetyl-*D*-manno-pentitol-1′-yl)undeca-3,8-diene (**4a**), (1S,2R,5R,7S,8R)-3-nitrotricyclo[6,2,1,$0^{2,7}$]-5-(1′,2′,3′,4′,5′-penta-*O*-acetyl-*D*-manno-pentitol-1′-yl)undeca-3,8-diene (**3a**) and (1S,2S,5R,7S,8R)-3-nitrotricyclo[6,2,1,$0^{2,7}$]-5-(1′,2′,3′,4′,5′-penta-*O*-acetyl-*D*-manno-pentitol-1′-yl)undeca-3,8-diene (**2a**)*

To a solution of 1′,2′,3′,4′,5′-penta-*O*-acetyl-1′-*C*-[(1*R*)-2-nitrocyclohexa-2,4-dienyl]-*D*-*manno*-pentitol[1] **1a** (1.0 g, 2.06 mmol) in dry toluene (10 mL) was added cyclopentadiene (0.68 mL, 8.24 mmol). After the reaction mixture had been heated at 110°C for 96 h in a closed glass container, its NMR spectra showed disappearance of the starting nitrodiene and formation of **4a** as the only appreciable product. Evaporation of the solvent led to an oily residue, which was chromatographed through a column of silica gel (ethyl acetate:hexane=1:2), to afford 0.79 g (70%) of compound **4a**: m.p.=163–164°C (from MeOH); R_F (ethyl acetate:hexane=1:1) 0.56; $[\alpha]_D$ +100.2 (c 0.43, $CHCl_3$); ν_{max} (KBr) cm^{-1} 3040 (=C–H), 1740 (C=O), 1535 and 1365 (NO_2), 1205 and 1035 (C–O–C); ^1H NMR ($CDCl_3$) δ 6.57 (brd, 1H, $J_{8,9}$=9.0 Hz, $J_{2,9}$=$J_{9,10}$=$J_{7,9}$<1 Hz, H-9), 6.22 (dd, 1H, $J_{7,8}$=6.4 Hz, H-8), 5.72 (dc, 1H, $J_{3,4}$=5.7 Hz, $J_{4,5a}$=$J_{4,5b}$=$J_{2,4}$=1.9 Hz, H-4), 5.49 (dd, 1H, $J_{2',3'}$=2.2 Hz, $J_{3',4'}$=8.5 Hz, H-3′), 5.15 (m, 1H, $J_{2,3}$=$J_{3,5b}$=$J_{3,5a}$=2.1 Hz, H-3), 5.14 (dd, 1H, H-2′), 5.08 (ddd, 1H, H-4′), 4.81 (dd, 1H, $J_{1',10}$=10.9 Hz, $J_{1',2'}$=4.4 Hz, H-1′), 4.22 (dd, 1H, $J_{4',5'}$=2.6 Hz, $J_{5',5''}$=12.6 Hz, H-5′), 4.02 (dd, 1H, $J_{4',5''}$=5.6 Hz, H-5″), 3.48 (brd, 1H, $J_{2,6}$=9.2 Hz, H-2), 3.09 (td, 1H, $J_{10,11b}$=3.4 Hz, $J_{10,11a}$=10.9 Hz, H-10), 2.80 (m, 1H, H-7), 2.68 (m, 1H, $J_{6,7}$=$J_{5b,6}$=4.0 Hz, H-6), 2.48 (m, 1H, $J_{5a,5b}$=17.4 Hz, $J_{5a,6}$=9.8 Hz, H-5a), 1.98 (ddd, 1H, $J_{7,11a}$=1.8 Hz, H-11a), 1.88 (brd, 1H, H-5b), 1.26 (brd, 1H, $J_{7,11b}$=3.6 Hz, $J_{11a,11b}$=12.7 Hz, H-11b), 2.13, 2.06, 2.0, 1.99, 1.93 (each 3H, each s, 5×OAc); ^{13}C NMR ($CDCl_3$) δ 170.6–169.7 (*O*COMe), 136.0 (C-4), 131.5 (C-8), 127.0 (C-3), 126.2 (C-9), 90.0 (C-1), 72.8 (C-1′), 68.7, 68.6 (C-2′,3′), 67.2 (C-4′), 61.8 (C-5′), 58.4 (C-2), 41.8 (C-10), 40.3 (C-6), 39.2 (C-5), 35.2 (C-7), 30.2 (C-11), 20.8–20.3 (OCO*Me*); Anal. calcd for $C_{26}H_{33}NO_{12}$: C, 56.62; H, 6.03; N, 2.54; found: C, 56.69; H, 6.07; N, 2.54.

From mother liquors of crystallization of **4a**, the norbornenic adducts *endo*-**3a** (23 mg) and *exo*-**2a** (8 mg) were isolated, by preparative thin layer chromatography (PTLC) (ether:hexane=1:1; four elutions). **3a**: R_F (ethyl acetate:hexane=1:1) 0.63; ^1H NMR ($CDCl_3$) δ 7.22 (d, 1H, $J_{2,3}$=2.1 Hz, H-3), 6.08 (m, 2H, H-9,10), 5.54 (dd, 1H, $J_{3',4'}$=8.7 Hz, H-3′), 5.46 (dd, 1H, $J_{1',2'}$=9.2 Hz, $J_{2',3'}$=2.4 Hz, H-2′), 5.13 (dd, 1H, $J_{1',5}$=6.4 Hz, H-1′), 5.12 (ddd, 1H, H-4′), 4.26 (dd, 1H, $J_{4',5'}$=2.6 Hz, H-5′), 4.09 (dd, 1H, $J_{4',5''}$=7.2 Hz, $J_{5',5''}$=12.5 Hz, H-5″), 3.65 (brd, 1H, $J_{5,6b}$=2.1 Hz, H-5), 3.03 (m, 1H, H-1), 2.97 (m, 1H, H-8), 2.86 (brd, 1H, $J_{1,2}$=2.1 Hz, $J_{2,7}$=9.4 Hz, H-2), 2.77 (m, 1H, $J_{6a,7}$=12 Hz, $J_{6b,7}$=6.5 Hz, $J_{7,8}$=2.6 Hz, H-7), 1.94 (m, 1H, H-6b), 1.59 (brd, 1H, $J_{11s,11a}$=8.5 Hz, H-11a), 1.56 (brd, 1H, H-11s), 1.11 (td, 1H, $J_{6a,6b}$=12.0 Hz, $J_{5,6a}$=4.6 Hz, H-6a), 2.14, 2.10, 2.09, 2.07, 1.92 (each 3H, each s, 5×OAc); ^{13}C NMR ($CDCl_3$) δ=170.6–169.6 (*O*COMe), 151.1 (C-4), 138.6, 136.5, 135.1 (C-3,9,10), 70.9, 70.2, 68.4, 67.2 (C-1′,2′,3′,4′), 61.8 (C-5′), 50.0 (C-11), 47.2, 46.5 (C-1,8), 40.1, 36.3, 35.4 (C-2,5,7), 29.7 (C-6), 20.9–20.5 (OCO*Me*); HRMS (FAB) calcd for $C_{26}H_{33}NO_{12}$: 574.1900 $(M+Na)^+$; found: 574.1900. **2a**: R_F (ethyl acetate:hexane=1:1) 0.65; ^1H NMR ($CDCl_3$) δ 7.32 (d, 1H, $J_{2,3}$=2.4 Hz, H-3), 6.22 (m, 2H, H-9,10), 5.52 (dd, 1H, $J_{3',4'}$=8.5 Hz, H-3′), 5.47 (dd, 1H, $J_{1',2'}$=8.7 Hz, $J_{2',3'}$=2.4 Hz, H-2′), 5.09 (ddd, 1H, H-4′), 5.08 (dd, 1H, $J_{1',5}$=6.7 Hz, H-1′), 4.25 (dd, 1H, $J_{4',5'}$=2.8 Hz, H-5′), 4.07 (dd, 1H, $J_{4'5''}$=5.3 Hz,

$J_{5',5''}$=12.5 Hz, H-5''), 3.75 (brd, 1H, $J_{5,6b}$=2.5 Hz, H-5), 2.75 (m, 1H, H-1), 2.57 (m, 1H, H-8), 2.21 (brd, 1H, $J_{2,7}$=8.1 Hz, H-2), 2.11 (m, 1H, H-6b), 2.02 (m, 1H, H-7), 1.38 (brd, 1H, $J_{11s,11a}$=9.1 Hz, H-11a), 1.32 (m, 1H, $J_{6a,6b}$=$J_{6a,7}$=11.9 Hz, $J_{5,6a}$=4.2 Hz, H-6a), 1.23 (brd, 1H, H-11s), 2.10 (s, 6H, 2×OAc), 2.09, 2.06, 1.88 (each 3H, each s, 3×OAc); ^{13}C NMR ($CDCl_3$) δ 170.1–169.6 (O*C*OMe), 151.8 (C-4), 139.1, 137.1, 136.7 (C-3,9,10), 70.5, 70.2, 68.4, 67.3 (C-1',2',3',4'), 61.8 (C-5'). 49.8 (C-11) 46.9, 46.3 (C-1,8), 39.9, 36.5, 33.9 (C-2,5,7), 29.4 (C-6), 20.5–20.0 (OCO*Me*); HRMS (FAB) calcd for $C_{26}H_{33}NO_{12}$: 574.1900 $(M+Na)^+$; found: 574.1902.

3.3. (1R,2S,6S,7R,10R)-1-Nitrotricyclo[5,2,2,$0^{2,6}$]-10-(D-manno-pentitol-1'-yl)undeca-3,8-diene (4b)

To a solution of **4a** (1.0 g, 1.81 mmol) in 90% methanol (25 mL) was added potassium carbonate (0.63 g, 4.53 mmol), and the mixture was stirred for 45 min at room temperature. TLC (ethyl acetate:ethanol=6:1) then showed the complete absence of starting material (R_F 0.90) and the presence of only one product with R_F 0.47. The reaction mixture was neutralized with Amberlite IR-120 (H^+) resin, and evaporated, to give **4b** as a chromatographically pure oil (0.48 g, 78%), that crystallized from methanol; m.p.=202–203°C, R_F (ethyl acetate:ethanol=6:1) 0.9; $[\alpha]_D$ +98.9 (c 0.46, MeOH); ν_{max} (KBr) cm^{-1} 3500–3200 (OH), 3040 (=C–H), 1530 and 1360 (NO_2), and 1025 (C–O); ^{1}H NMR (DMSO-d_6) δ 6.65 (d, 1H, $J_{8,9}$=8.9 Hz, H-9), 6.16 (dd, 1H, $J_{7,8}$=6.7 Hz, H-8), 5.73 (brd, 1H, $J_{3,4}$=4.1 Hz, $J_{4,5a}$=$J_{4,5b}$=$J_{2,4}$<1.0 Hz, H-4), 5.09 (brd, 1H, $J_{2,3}$=$J_{3,5a}$=$J_{3,5b}$<1.0 Hz, H-3), 4.87 (d, 1H, $J_{1',OH}$=6.3 Hz, 1'-OH), 4.43 (d, 1H, $J_{4',OH}$=6.9 Hz, 4'-OH), 4.34 (t, 1H, 5'-OH), 4.26 (d, 1H, $J_{H,OH}$=6.9 Hz, OH), 4.23 (d, 1H, $J_{H,OH}$=6.2 Hz, OH), 3 55 (m, $J_{5',OH}$=$J_{5'',OH}$=5 6 Hz, H-5'), 3.49 (m, 2H, H-2',3'), 3.43 (m, 1H, $J_{3',4'}$=8.3 Hz, $J_{4',5'}$=3.0 Hz, H-4'), 3.37 (m, 1H, H-5''), 3.28 (brd, 1H, $J_{2,6}$=8.3 Hz, H-2), 3.15 (m, 1H, J $_{1',10}$=8.9 Hz, $J_{1',2'}$=4.8 Hz, H-1'), 2.84 (t, 1H, $J_{10,11a}$=8.9 Hz, $J_{10,11b}$<1.0 Hz, H-10), 2.66 (m, 1H, H-7), 2.62 (m, 1H, H-6), 2.38 (brdd, 1H, $J_{5a,5b}$=17.3 Hz, $J_{5a,6}$=8.8 Hz, H-5a), 1.85 (brdd, 1H, $J_{7,11a}$<1.0 Hz, H-11a), 1.81 (brd, 1H, H-5b), 1.08 (brd, 1H, H-11b); ^{13}C NMR (DMSO-d_6) δ 135.9 (C-4), 130.3 (C-8), 127.6, 127.4 (C-3,9), 90.5 (C-1), 76.7 (C-1'), 71.3, 70.5, 69.9 (C-2',3',4'), 63.6 (C-5'), 58.6 (C-2), 45.4 (C-10), 40.3 (C-6), 38.8 (C-5), 34.9 (C-7), 32.1 (C-11); Anal. calcd for $C_{16}H_{23}NO_7$: C, 56.30; H, 6.79; N, 4.10; found: C, 56.03; H, 6.95; N, 4.12.

3.4. (1R,2S,6S,7R,10R)-1-Nitrotricyclo[5,2,2,$0^{2,6}$]undeca-3,8-diene-10-carbaldehyde (4c)

To a solution of **4b** (71 mg, 0.21 mmol) in water (12 mL) at 0°C was added a solution of sodium metaperiodate (0.21 g, 1.0 mmol) in water (1.3 mL), and the mixture was stirred for 15 min at 0°C. TLC (ethyl acetate:ethanol=6:1) then showed complete conversion of the starting material (R_F 0.47) into only one product with R_F 0.86. The solution was then extracted with chloroform (4×15 mL), and the extracts were washed with water, dried ($MgSO_4$), and evaporated to yield the aldehyde **4c** as a chromatographically pure, colourless oil (35 mg, 77%); R_F (ethyl acetate:ethanol=6:1) 0.86; $[\alpha]_D$+72.7 (c 0.36, $CHCl_3$); ν_{max} (film) cm^{-1} 3045 (=C–H), 2850 and 2715 (C–H aldehyde), 1725 (C=O), 1530 and 1360 (NO_2); ^{1}H NMR ($CDCl_3$) δ 9.34 (s, 1H, C*H*O), 6.71 (d, 1H, $J_{8,9}$=8.8 Hz, J $_{7,9}$=J $_{2,9}$<1.0 Hz, H-9), 6.22 (dd, 1H, $J_{7,8}$=6.5 Hz, H-8), 5.78 (dc, 1H, $J_{3,4}$=6.1 Hz, $J_{4,5a}$=2.2 Hz, $J_{4,5b}$=2.4 Hz, $J_{2,4}$=3.0 Hz, H-4), 5.39 (dc, 1H, $J_{3,5a}$=2.2 Hz, $J_{2,3}$=3.1 Hz, $J_{3,5b}$=2.4 Hz, H-3), 3.56 (dd, 1H, $J_{10,11a}$=11.0 Hz, $J_{10,11b}$=4.8 Hz, H-10), 3.48 (brd, 1H, $J_{2,6}$=9.2 Hz, $J_{2,5b}$=2.4 Hz $J_{2,5a}$=2.2 Hz, H-2), 2.86 (m, 1H, J $_{7,11a}$=3.5 Hz, $J_{7,11b}$=2.2 Hz, H-7), 2.77 (m, 1H, $J_{5a,6}$=9.9 Hz, $J_{5b,6}$=3.8 Hz, $J_{6,7}$=3.1 Hz, $J_{6,8}$<1.0 Hz, H-6), 2.54 (m, 1H, $J_{5a,5b}$=16.8 Hz, H-5a), 2.09 (ddd, 1H, $J_{11a,11b}$=12.9 Hz, H-11a), 1.92 (brd, 1H, H-5b), 1.74 (ddd, 1H, H-11b); ^{13}C NMR ($CDCl_3$) δ 198.4 (CHO), 136.0 (C-4), 131.6 (C-8), 128.0, 126.8 (C-3,9), 88.8 (C-1), 57.7 (C-2), 53.6 (C-10), 40.7 (C-6), 39.1 (C-5), 35.2 (C-7), 27.0 (C-11).

3.5. (1R,2S,6S,7R,10R)-1-Nitrotricyclo[5,2,2,$0^{2,6}$]-10-hydroxymethyl-undeca-3,8-diene (4d)

A solution of compound **4c** (46 mg, 0.21 mmol) in methanol (3 mL) at 0°C was treated with sodium borohydride (7.6 mg, 0.20 mmol). After being stirred for 15 min at 0°C, the reaction mixture was diluted with water (10 mL) and extracted with methylene dichloride (4×10 mL). The combined extracts were dried ($MgSO_4$) and evaporated to give **4d** as a chromatographically pure, colourless oil (40 mg, 86%), which was crystallized from ether:light petroleum; m.p.=128–129°C; R_F (ethyl acetate:ethanol=1:1) 0.45; $[\alpha]_D$ +76.1 (c 0.41, $CHCl_3$); ν_{max} (KBr) cm^{-1} 3400–3200 (OH), 3040 (=C–H), 1530 and 1370 (NO_2); ^1H NMR ($CDCl_3$) δ 6.72 (d, 1H, $J_{8,9}$=8.6 Hz, H-9), 6.24 (dd, 1H, $J_{7,8}$=6.6 Hz, H-8), 5.74 (dc, 1H, $J_{3,4}$=6.2 Hz. $J_{4,5a}$=$J_{4,5b}$=$J_{2,4}$=2.2 Hz, H-4), 5.26 (dc, 1H, $J_{2,3}$=$J_{3,5a}$=$J_{3,5b}$=2.2 Hz, H-3), 3.61 (brd, 1H, $J_{2,6}$=9.1 Hz, H-2), 3.41 (dd, 1H, $J_{Ha,Hb}$=11.1 Hz, $J_{Ha,10}$=7.4 Hz, CH_aH_bOH), 3.30 (dd, 1H, $J_{Hb,10}$=6.1 Hz, CH_aH_bOH), 2.75 (m, 3H, H-6,7,10), 2.52 (brdd, 1H, $J_{5a,5b}$=17.2 Hz, $J_{2,5b}$=1.7 Hz, H-5a), 1.96 (ddd, 1H, $J_{11a,11b}$=12.8 Hz, $J_{7,11a}$=2.2 Hz, H-11a), 1.90 (brd, 1H, H-5b). 1.61 (brs, 1H, OH), 1.07 (ddd, 1H, $J_{10,11b}$=4.4 Hz, $J_{7,11b}$=3.5 Hz, H-11b); ^{13}C NMR ($CDCl_3$) δ 135.5 (C-4), 131.6 (C-8), 127.2, 126.5 (C-3,9), 91.1 (C-1), 64.3 (CH_2OH), 58.2 (C-2), 44.7 (C-10), 40.5 (C-6), 39.2 (C-5), 35.6 (C-7), 29.4 (C-11); Anal. calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33; found: C, 65.04; H, 7.02; N, 6.26.

3.6. (1S,2R,6R,7S,10S)-1-Nitrotricyclo[5,2,2,$0^{2,6}$]-10-(1′,2′,3′,4′,5′-*penta*-O-*acetyl*-D-galacto-*pentitol-1′-yl*)*undeca-3,8-diene* (8a), (1R,2S,5S,7R,8S)-3-nitrotricyclo[6,2,1,$0^{2,7}$]-5-(1′,2′, 3′,4′,5′-*penta*-O-*acetyl*-D-galacto-*pentitol-1′-yl*)*undeca-3,8-diene* (7a) *and* (1R,2R,5S,7R,8S)-3-nitrotricyclo[6,2,1,$0^{2,7}$]-5-(1′,2′,3′,4′,5′-*penta*-O-*acetyl*-D-galacto-*pentitol-1′-yl*)*undeca-3,8-diene* (6a)

To a solution of 1′,2′,3′,4′,5′-penta-*O*-acetyl-1′-*C*-[(1*S*)-2-nitrocyclohexa-2,4-dienyl]-D-*galacto*-pentitol[1] **5a** (1.0 g, 2.06 mmol) in dry toluene (10 mL) was added cyclopentadiene (0.68 mL, 8.24 mmol). After the reaction mixture had been heated at 110°C for 96 h in a closed glass container, its NMR spectra showed disappearance of the starting nitrodiene and formation of **8a** as the only appreciable product. Evaporation of the solvent led to an oily residue, which was chromatographed through a column of silica gel (ethyl acetate:hexane=1:1), to afford 0.75 g (67%) of compound **8a**: m.p.=144–145°C (from MeOH); R_F (ethyl acetate:hexane=1:1) 0.59; $[\alpha]_D$ −25.2 (c 0.49, $CHCl_3$); ν_{max} (KBr) cm^{-1} 3040 (=C–H), 1735 (C=O), 1525 and 1360 (NO_2), 1205 and 1020 (C–O–C); ^1H NMR ($CDCl_3$) δ 6.56 (d, 1H, $J_{8,9}$=9.1 Hz, H-9), 6.18 (dd, 1H, $J_{7,8}$=6.6 Hz, H-8), 5.71 (dc, 1H, $J_{3,4}$=5.8 Hz, $J_{4,5a}$=$J_{4,5b}$=$J_{2,4}$=1.7 Hz, H-4), 5.21 (dd, 1H, H-2′), 5.19 (ddd, 1H, H-4′), 5.14 (dc, 1H, $J_{2,3}$=$J_{3,5a}$=$J_{3,5b}$=1.8 Hz, H-3), 4.96 (dd, 1H, $J_{2',3'}$=10.1 Hz, $J_{3',4'}$=1.5 Hz, H-3′), 4.72 (dd, 1H, $J_{1',10}$=10.8 Hz, $J_{1',2'}$=1.0 Hz, H-1′), 4.27 (dd, 1H, $J_{4',5'}$=4.3 Hz, $J_{5',5''}$=11.9 Hz, H-5′), 3.74 (dd, 1H, $J_{4',5''}$=7.7 Hz, H-5″), 3.39 (brd, 1H, $J_{2,6}$=9.3 Hz, H-2), 2.77 (m, 1H, H-7), 2.74 (td, 1H, $J_{10,11a}$=10.8 Hz, H-10), 2.63 (m, 1H, $J_{6,7}$=$J_{5b,6}$=4.2 Hz, H-6), 2.44 (brdd, 1H, $J_{5a,5b}$=17.3 Hz, $J_{5a,6}$=9.7 Hz, H-5a), 1.97 (m, 1H, H-11a), 1.88 (brd, 1H, H-5b), 1.12 (dt, 1H, $J_{7,11b}$=$J_{10,11b}$=3.4 Hz, $J_{11a,11b}$=13.1 Hz, H-11b), 2.18, 2.07, 2.04, 1.98, 1.94 (each 3H, each s, 5×OAc); ^{13}C NMR ($CDCl_3$) δ 170.3–169.8 (*O*COMe), 136.1 (C-4), 130.3 (C-8), 126.9 (C-3), 126.7 (C-9), 89.9 (C-1), 71.3 (C-1′), 68.1 (C-4′), 67.6 (C-3′), 67.1 (C-2′), 62.6 (C-5′), 58.8 (C-2), 41.9 (C-10), 40.5 (C-6), 39.0 (C-5), 35.0 (C-7), 30.7 (C-11), 20.8–20.2 (OCO*Me*); Anal. calcd for $C_{26}H_{33}NO_{12}$: C, 56.62; H, 6.03; N, 2.54; found: C, 56.56; H, 6.01; N, 2.49.

From the mother liquors of crystallization of **8a**, the norbornenic adducts *endo*-**7a** (11 mg) and *exo*-**6a** (18 mg) were isolated, by preparative thin layer chromatography (PTLC) (ether:hexane=1:1; four elutions). **7a**: R_F (ethyl acetate:hexane=1:1) 0.66; ^1H NMR ($CDCl_3$) δ 7.20 (d, 1H, $J_{2,3}$=2.1 Hz, H-3), 6.06 (m, 2H, H-9,10), 5.41 (dd, 1H, $J_{1',2'}$=1.6 Hz, $J_{2',3'}$=9.9 Hz, H-2′), 5.31 (ddd, 1H, H-4′), 5.27 (dd, 1H, $J_{3',4'}$=2.1 Hz, H-3′), 5.17 (dd, 1H, $J_{1',5}$=10.5 Hz, H-1′), 4.27 (dd, 1H, $J_{4',5'}$=5.0 Hz, H-5′), 3.84 (dd,

1H, $J_{4',5''}$=7.3 Hz, $J_{5',5''}$=11.5 Hz, H-5''), 3.34 (brd, 1H, H-5), 3.03 (m, 1H, H-1), 2.99 (m, 1H, H-8), 2.90 (brd, 1H, $J_{1,2}$=2.8 Hz, $J_{2,7}$=3.5 Hz, H-2), 2.71 (m, 1H, H-7), 2.05 (m, 1H, H-6b), 1.61 (brd, 1H, $J_{11s,11a}$=8.4 Hz, H-11a), 1.57 (brd, 1H, H-11s), 1.00 (td, 1H, $J_{6a,7}$=$J_{6a,6b}$=12.0 Hz, $J_{5,6a}$=5.0 Hz, H-6a), 2.22, 2.12, 2.11, 2.02, 1.91 (each 3H, each s, 5×OAc); ^{13}C NMR ($CDCl_3$) δ 170.3–170.0 (*O*COMe), 150.5 (C-4), 138.7, 136.2, 134.9 (C-3,9,10), 69.8, 67.7, 67.5, 66.9 (C-1',2',3',4'), 61.9 (C-5'), 49.8 (C-11), 46.9, 46.3 (C-1,8), 39.9, 36.5, 33.9 (C-2,5,7), 29.4 (C-6), 20.5–20.0 (OCO*Me*); HRMS (FAB) calcd for $C_{26}H_{33}NO_{12}$: 574.1900 $(M+Na)^+$; found: 574.1914. **6a**: R_F (ethyl acetate:hexane=1:1) 0.70; ^{1}H NMR ($CDCl_3$) δ 7.29 (d, 1H, $J_{2,3}$=2.3 Hz, H-3), 6.25, 6.23 (each dd, 2H, $J_{9,10}$=5.6 Hz, $J_{8,9}$=$J_{1,10}$=2.8 Hz, H-9,10), 5.39 (dd, 1H, $J_{1',2'}$=1.3 Hz, $J_{2',3'}$=10.0 Hz, H-2'), 5.30 (ddd, 1H, H-4'), 5.25 (dd, 1H, $J_{3',4'}$=2.0 Hz, H-3'), 5.13 (dd, 1H, $J_{1',5}$=10.5 Hz, H-1'), 4.25 (dd, 1H, $J_{4',5'}$=5.0 Hz, H-5'), 3.82 (dd, 1H, $J_{4',5''}$=7.3 Hz, $J_{5',5''}$=11.7 Hz, H-5''), 3.50 (brd, 1H, $J_{5,6b}$=2.0 Hz, H-5), 2.76 (m, 1H, H-1), 2.61 (m, 1H, H-8), 2.27 (m, 2H, H-2, 6b), 2.00 (m, 1H, $J_{2,7}$=7.6 Hz, H-7), 1.38 (brd, 1H, $J_{11s,11a}$=9.1 Hz, H-11a), 1.22 (brd, 1H, H-11s), 1.21 (m, 1H, $J_{5,6a}$=4.5 Hz, H-6a), 2.23, 2.12, 2.06, 2.02, 1.90 (each 3H, each s, 5×OAc); ^{13}C NMR ($CDCl_3$) δ 170.6–169.6 (*O*COMe), 151.5 (C-4), 139.4, 137.2, 136.7 (C-3,9,10), 69.3, 67.9, 67.7, 67.3 (C-1',2',3',4'), 62.2 (C-5'), 47.7, 46.3 (C-1,8), 43.6 (C-11), 39.8, 34.3, 34.2 (C-2,5,7), 30.3 (C-6), 20.8–20.3 (OCO*Me*); HRMS (FAB) calcd for $C_{26}H_{33}NO_{12}$: 574.1900 $(M+Na)^+$; found: 574.1901.

*3.7. (1S,2R,6R,7S,10S)-1-Nitrotricyclo[5,2,2,0^{2,6}]-10-(*D-galacto-*pentitol-1'-yl)undeca-3,8-diene (8b)*

Following the same procedure described for the base-catalyzed deacetylation of **4a**, the adduct **8a** (1.0 g, 1.81 mmol) yielded crystalline **8b** (0.45 g, 73%): m.p.=229–230°C (desc.)(from MeOH); R_F (ethyl acetate:ethanol=3:1) 0.64; $[\alpha]_D$ −84.4 (c 0.46, MeOH); ν_{max} (KBr) cm^{-1} 3500–3200 (OH), 3040 (=C–H), 1530 and 1355 (NO_2), and 1025 (C–O); ^{1}H NMR (DMSO-d_6) δ 6.69 (d, 1H, $J_{8,9}$=9.0 Hz, H-9), 6.19 (dd, 1H, $J_{7,8}$=6.5 Hz, H-8), 5.74 (dc, 1H, $J_{3,4}$=5.7 Hz, $J_{4,5a}$=$J_{4,5b}$=$J_{2,4}$=1.8 Hz, H-4), 5.10 (dc, 1H, $J_{2,3}$=$J_{3,5a}$=$J_{3,5b}$=2.0 Hz, H-3), 4.41 (t, 1H, $J_{5',OH}$=$J_{5'',OH}$=5.5 Hz, 5'-OH), 4.27 (d, 1H, $J_{2',OH}$=7.8 Hz, 2'-OH), 4.11 (d, 1H, $J_{4',OH}$=6.5 Hz, 4'-OH), 4.00 (d, 1H, $J_{3',OH}$=7.3 Hz, 3'-OH), 3.64 (c, $J_{3',4'}$<1.0 Hz, $J_{4',5'}$=$J_{4',5''}$=6.5 Hz, H-4'), 3.57 (d, 1H, $J_{1',OH}$=8.8 Hz, 1'-OH), 3.35 (m, 2H, H-5',5''), 3.35 (m, 1H, H-2), 3.26 (m, 3H, H-1',2',3'), 2.89 (td, 1H, $J_{1',10}$=$J_{10,11a}$=9.8 Hz, H-10), 2.68 (m, 1H, H-7), 2.65 (m, 1H, H-6), 2.41 (brdd, 1H, $J_{5a,5b}$=17.5 Hz, $J_{5a,6}$=9.5 Hz, H-5a), 1.82 (brd, 1H, H-5b), 1.79 (brdd, 1H, $J_{7,11a}$<1.0 Hz, H-11a), 0.88 (dt, 1H, $J_{11a,11b}$=12.6 Hz, $J_{10,11b}$=$J_{7,11b}$=3.2 Hz, H-11b); ^{13}C NMR (DMSO-d_6) δ 135.8 (C-4), 130.7 (C-8), 127.4, 126.7 (C-3,9), 90.5 (C-1), 72.1 (C-1'), 69.1, 68.7, 68.1 (C-2',3',4'), 63.2 (C-5'), 58.5 (C-2), 44.1 (C-10), 40.1 (C-6), 38.7 (C-5), 34.9 (C-7), 29.3 (C-11); Anal. calcd for $C_{16}H_{23}NO_7$: C. 56.30; H, 6.79; N, 4.10; found: C, 56.49; H, 6.85; N, 4.21.

3.8. (1S,2R,6R,7S,10S)-1-Nitrotricyclo[5,2,2,0^{2,6}]undeca-3,8-diene-10-carbaldehyde (8c)

Using the same procedure as for the preparation of **4c**, degradation of pentahydroxypentyl side-chain of **8b** (0.18 g, 0.53 mmol) gave aldehyde **8c** (93 mg, 80%) as a chromatographically pure, colourless oil; $[\alpha]_D$ −70.2 (c 0.54, $CHCl_3$); IR, ^{1}H and ^{13}C NMR spectra were identical with those described for **4c**.

3.9. (1S,2R,6R,7S,10S)-1-Nitrotricyclo[5,2,2,0^{2,6}]-10-hydroxymethyl-undeca-3,8-diene (8d)

Following the procedure described for the preparation of **4d**, compound **8c** (83 mg, 0.38 mmol) led to alcohol **8d** (72 mg, 86%): $[\alpha]_D$ −71.2 (c 0.51, $CHCl_3$); IR, ^{1}H and ^{13}C NMR spectra were identical with those described for **4d**.

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