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One-pot synthesis of highly functionalized morphans from C-glycosides

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ABSTRACT

Highly functionalized morphan derivatives were synthesized from nitroalkene 2′-(oxoalkyl)-C-glycosides by a tandem reaction that created three (two C–N and one C–C) new bonds and four stereogenic centers in a one-pot procedure under very mild conditions without the use of expensive reagents. The transformation was achieved from a β-elimination/Michael addition cascade, followed by Michael addition of the amine and intramolecular enamination. In the presence of sodium cyanoborohydride the iminium intermediate was reduced in situ to afford the desired morphans.

1. Introduction

Morphine, with a morphan substructure, is the best-known opioid analgesic. Subtle changes in substitutions on morphan ring and *N*-alkyl group may lead to dramatic differences in binding specificity to μ, κ, and δ opioid receptors, consequently providing different pharmacologic effects.[1] Much effort has been made in the synthesis of a variety of compounds including 5-phenylmorphan and other morphan analogues to discover effective opioid receptor agonists as analgesics that do not produce physical dependence and antagonists to treat such dependence.[2] New efficient synthetic methods to access novel morphan derivatives with diverse ring and N-substitutions are still desirable to advance structure–activity relationship studies.

Because various azabicyclic compounds such as hydroxylated quinolizidines,[3] indolines, and oxindoles[4] have been synthesized from C-glycosides by tandem β-elimination and intramolecular Michael additions, we envisioned that a morphan ring system could be constructed by reaction of nitroalkene 2′-(oxoalkyl)-C-glycosides (e.g., **1** and **12**) with amines. As a base, an amine may instigate β-elimination leading to a conjugated ketone,[5] and as a nucleophile an amine may attack the nitroalkene at C5 via Michael addition.[6] These reactions might occur spontaneously or stepwise, and could be followed by an intramolecular Michael addition of the nitroalkyl anion to conjugated ketone to form highly functionalized cyclohexane derivatives. These intermediates may allow an intramolecular cyclization to form an enamine between amino and carbonyl groups when proper conformation and stereo configuration are present. Although there were other potential competing reactions, we report here the chemo- and stereoselective reaction of nitroalkene C-glycosides **1** and **12** with various amines leading to a class of highly functionalized morphan analogues.

2. Results and discussion

Nitroalkene C-glycosides **1** and **12** were synthesized from the respective allyl-C-glycoside intermediates of D-ribose and D-arabinose by performing 2′-oxidation prior to β-elimination at C5.[7] The ribosyl substrate **1** was anomerically pure in the α-configuration and the arabinosyl substrate **12** was an anomeric mixture (α/β 1:1). As the Michael addition of amines has been reported under non-solvent conditions (NSCs),[8] nitroalkene **1** was first treated with allylamine at room temperature for two days, which gave bridged azabicycle **2a** (65%), an enamine possessing a morphan skeleton as the major product (Scheme 1). Additionally, small amounts of nitrocyclohexene **4** and cyclohexylamine **5a** (R = allyl) were also isolated as intermediates. In contrast to the reaction with allylamine, when **1** was similarly treated with benzylamine and cyclohexylamine the respective bridged azabicycles **2b** and **2c** were obtained as minor products (ca. 10%) and the cyclohexylamine intermediates (**5b** R = Bn and **5c** R = C_6H_{11}) were isolated as the major products (50–70%), which could be converted to **2b** and **2c**, respectively, upon base treatment.

Two possible reaction pathways are illustrated in Scheme 1. The first involves a tandem sequence of β-elimination, concurrent Michael addition of the alkoxide anion to the nitroalkene (epoxidation to **3**), an intramolecular Michael addition of the nitroalkyl anion to the α,β-unsaturated ketone followed by base catalyzed β-elimination and epoxide ring opening to give cyclic nitroalkene

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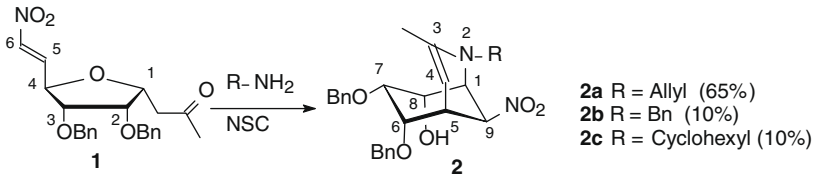
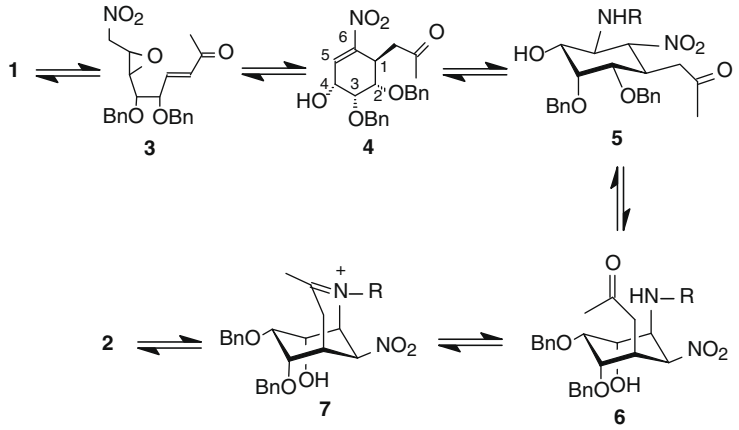
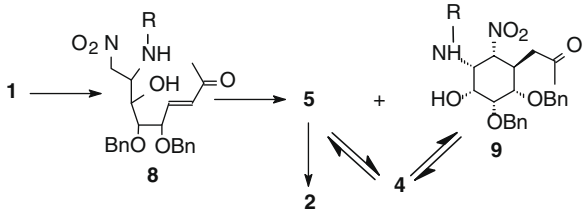


Pathway A



Pathway B



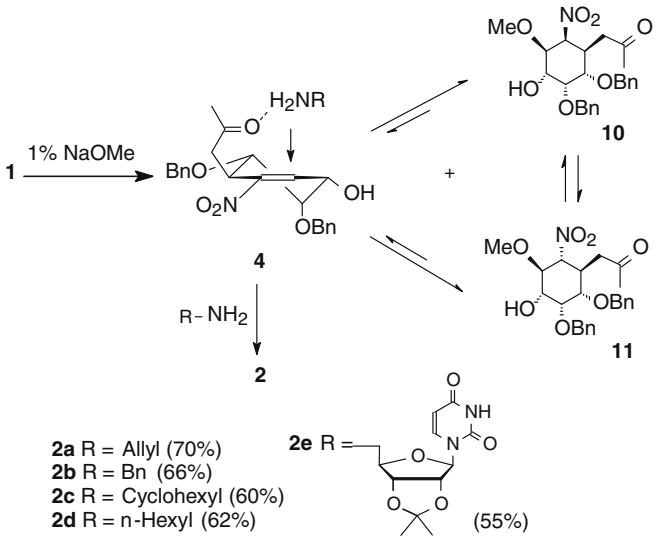
Scheme 1.

4. Addition of an amine to **4** then produced **5** in the $^4C_1$ conformation. The subsequent conformational change may be initiated or followed immediately by C6-epimerization, leading to **6** with a highly strained 1,5-diaxial configuration stabilized by an equatorial 6-nitro group. Reaction of the imino and carbonyl groups of **6** produced iminium **7** that was followed by isomerization to enamine **2**. The second pathway involves initial Michael addition of the amine to nitroalkene followed by β-elimination to produce **8**. Because nitroalkanes have a pK_a around 8.6, lower than that of secondary amines (9.5–11),[9] and the nitroalkyl anion is a softer nucleophile than the secondary amine, thus an intramolecular Michael addition of a nitroalkyl anion to the conjugated ketone is likely favored to produce two diastereomers, **5** and **9**. The former can be converted to **2** directly while the latter has to go through a retro-Michael addition to **4** en route to **2**.

The limited conversion to **2b** and **2c** from **1** under NSC suggests that benzylamine and cyclohexylamine behaved more like a nucleophile and to less extent a base, because of their inability to induce a C6-epimerization to stabilize the 1,5-diaxial conformation (**6**) needed for enamine formation. Thus, we reasoned out, regardless of the reaction pathways, that the addition of base should facilitate the formation of **4** and the subsequent transformation.

In fact, when **1** was treated with base (1% sodium methoxide) overnight in the absence of amine, we were able to isolate 5-*O*-methyl-6-nitrocyclohexanes,[10] **10** and **11**, as major products together with small amount of cyclohexene **4**. Further experiments revealed that **4**, **10**, and **11** were in equilibrium under basic conditions through β-elimination of nitroalkane and addition of methoxide to the nitroalkene. The reversible reaction between diastereomers **10** and **11** also indicates that these basic conditions (1% sodium methoxide) are able to facilitate the C6-epimerization. Consequently, we treated **1** with 1% sodium methoxide–methanol prior to the addition of representative amines, including allylamine, cyclohexylamine, benzylamine, hexylamine and uridine amine, as expected the respective azabicycles (**2a**–**e**) were obtained overnight in consistent yield (Scheme 2).

To demonstrate the generality of this reaction, D-arabinosyl substrate **12** was also treated with allylamine and benzylamine in 1% sodium methoxide. In addition to the expected bridged azabicycles (**13a** and **13b**, see Scheme 3), caged compounds, **14a** and **14b** were also isolated as minor products. Apparently, two C1-isomers (**4**-like cyclohexenes) were obtained from Michael addition, which is in agreement with the previous observation of a similar intramolecular Michael addition of amine[3] and nitroalkyl anion[4] to conjugated ketones. Complete stereoselectivity was achieved on D-ribosyl substrates giving 1,4-*trans* configured products, whereas a mixture of 1,4-*trans* (major) and 1,4-*cis* (minor) diastereoisomers was produced from D-arabinosyl substrates. It was hypothesized that steric hindrance, disfavored 1,3-diaxial interactions and a proposed 4-hydroxy group directing effect were all



Scheme 2.

contributing factors to the stereoselectivities.[4] The subsequent addition reaction of the amine to the two nitrocyclohexene diastereomers was highly stereoselective and could be directed by the ketone functionality via amino/carbonyl H-bonding,[11] which overcame steric hindrance of the neighboring hydroxyl group. During the final enamination reaction, the azabicyclic compounds **13a** and **13b** were synthesized through 1,4-*trans* configured intermediates, whereas iminium intermediates from 1,4-*cis* configured nitrocyclohexene underwent an intramolecular addition of the 4-hydroxy group to the iminium moiety giving respective caged *N*/*O*-acetals **14a** and **14b**.

The above-mentioned mechanism was supported by the fact that we were able to isolate pure 1,4-*trans* and 1,4-*cis* 5-*O*-methyl-6-nitrocyclohexanes (**15** and **16**) by treatment of **12** with 1% sodium methoxide (see Scheme 3). Furthermore, reaction of **15** and **16** with allylamine under 1% sodium methoxide produced **13a** and **14a** via nitrocyclohexene intermediates as illustrated in Scheme 3.

Because the iminium moiety in intermediate **7** can be reduced in situ, treatment of nitroalkene **1** with amines in 1% sodium methoxide–methanol in the presence of sodium cyanoborohydride was attempted. As expected, morphans **17a–c** were obtained stereoselectively in good yield. Similarly, reaction of **12** with amines (allylamine and benzylamine) also gave respective morphans **18a** and **18b** as the major products, but the respective caged derivatives **14a** and **14b** remained (see Scheme 4). Although **18** and **14** were inseparable by chromatography, but pure **18a** was obtained from **15** and allylamine under basic conditions.

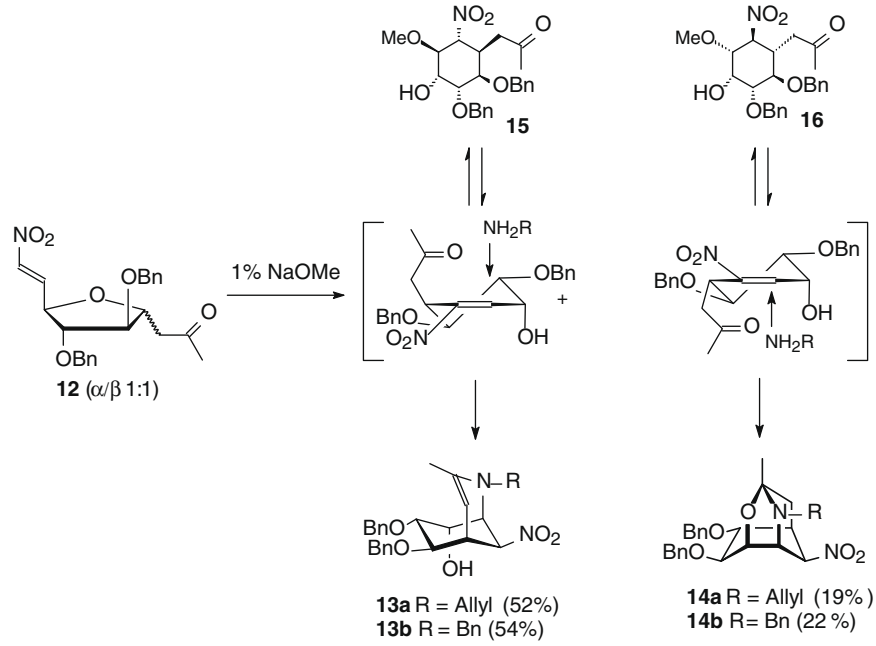
The stereochemistry and conformation of morphan derivatives (**17** and **18**) and caged derivatives **14a–b** were established based on the NOEs observed from NOESY experiments (see Fig. 1). For example, NOEs between H7/H6 and H4a, H3 and H4b, H4b and H5 were observed in **17a** but not between H7 and C3–Me or H3. Therefore, the piperidine ring of **17** and **18** likely adopts a boat conformation in which the methyl group is equatorially attached to C3. The conformation of **14** was proposed based on the diagnostic NOE between H7 and H9.

In summary, we have developed a tandem reaction that allowed quick access to morphan analogues with structural diversity from C-glycosides. The reaction of nitroalkene 2′-(oxopropyl)-C-glycosides with variety of primary amines was achieved under basic conditions involving β-elimination/Michael addition cascade, followed by Michael addition of the amine and intramolecular enamination. In addition to flexibility of choosing different sugar substrates and amines, various other modifications on the enamine,[12] nitro,[13] and *N*/*O*-acetal[14] functionalities can further provide molecular complexity. The chemistry described here should thus be very useful for morphan scaffold based drug development for pain and addiction treatment.

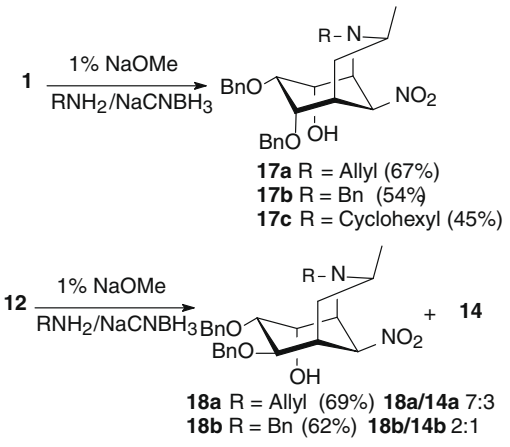
3. Experimental

3.1. General method

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 400 MHz and 100 MHz, respectively, with a Varian instrument at 298 K. Chemical shifts were given in ppm downfield to the signal of internal TMS, and were assigned on the basis of 2D ^{1}H–^{1}H COSY and



Scheme 3.



Scheme 4.

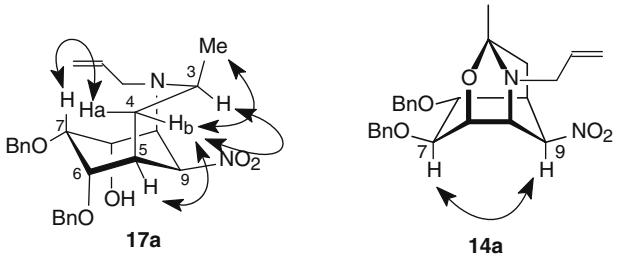


Figure 1.

^{1}H–^{13}C chemical-shift correlated experiments. For high resolution mass spectroscopic analysis, samples in CH_2Cl_2–CH_3OH 1:1 were mixed with Agilent ES tuning mix for internal mass calibration and infused into a QSTAR mass spectrometer at a flow rate of 4 μL/min. Optical rotations were measured on a Perkin–Elmer spectrometer. All chemicals were used without further purification.

3.2. General synthetic procedures

(a) Substrate (**1** or **12**, 50–100 mg) was dissolved in 1% $NaOCH_3$–CH_3OH (1–2 mL) at room temperature. To the solution after 2 h was added amine (50–100 μL) and the reaction solution was kept overnight. EtOAc was added and the organic solution was washed with water, dried, and purified by column chromatography to give product(s) (**2**, **13**, and **14**). (b) Substrate (**1** or **12**, 50–100 mg) was dissolved in 1% $NaOCH_3$–CH_3OH (1–2 mL) at room temperature. To the solution after 2 h were added amine (50–100 μL) and sodium cyanoborohydride (5–10 equiv) and the mixture was kept at room temperature for 16 h. EtOAc was added and the organic solution was washed with water, dried, and purified by column chromatography to give product(s) (**17**, **18**, and **14**).

3.3. (1*R*,2*S*,3*R*,4*R*)-1-Acetylmethyl-2,3-di-*O*-benzyl-4-hydroxy-6-nitrocyclohex-5-ene (4)

Syrup, $[\alpha]_D$ −2 (*c* 2.0, $CHCl_3$); ^{1}H NMR: δ 2.03 (s, 3H, 3′-Me), 2.23 (dd, 1H, H1′b, $J_{1'b,1}$ = 9.6 Hz, $J_{1'b,1'a}$ = 18.4 Hz), 2.69 (dd, 1H, H1′a, $J_{1'a,1}$ = 2.4 Hz, $J_{1'a,1'b}$ = 18.4 Hz), 3.45 (d, 1H, OH, *J* = 10.4 Hz), 3.60 (d, 1H, H3, *J* = 3.6 Hz), 3.77 (br d, 1H, H1, *J* = 9.6 Hz), 3.89 (br s, 1H, H2), 4.45 (m, 1H, H4), 4.60 and 4.65 (d and d, 1H each, Bn, *J* = 12.0 Hz), 4.70 (s, 2H, Bn), 7.22–7.39 (m, 11H, H5, Bn); ^{13}C NMR: δ 30.1 (C3′), 35.1 (C1), 42.4 (C1′), 64.4 (C4), 71.4 (Bn), 72.2 (C3), 72.6 (Bn), 78.3 (C2), 128.1 (Bn), 128.30 (Bn), 128.32 (Bn), 128.36 (Bn), 128.76 (Bn), 128.79 (Bn), 133.2 (C5), 137.4 (Bn), 137.6 (Bn), 150.0 (C6), 205.1 (C2′). ESIMS: calcd for $C_{23}H_{26}NO_6$ $[M+H]^+$ 412.1760, found 412.1732.

3.4. (1*R*,2*S*,3*R*,4*R*,5*S*,6*R*)-1-Acetylmethyl -5-allylamino-2,3-di-*O*-benzyl-4-hydroxy-6-nitrocyclohexane (5a)

Syrup, $[\alpha]_D$ −61 (*c* 1.5, $CHCl_3$); ^{1}H NMR: δ 2.01 (s, 3H, 3′-Me), 2.30 (dd, 1H, H1′b, $J_{1'b,1}$ = 5.2 Hz, $J_{1'b,1'a}$ = 18.4 Hz), 2.79 (dd, 1H, H1′a, $J_{1'a,1}$ = 3.2 Hz, $J_{1'a,1'b}$ = 18.4 Hz), 2.94 (m, 1H, H1), 3.23 (d, 1H, N–CH_2, *J* = 6.0 Hz), 3.40 (dd, 1H, H4, $J_{3,4}$ = 2.0 Hz, $J_{4,5}$ = 10.0 Hz), 3.50 (dd, 1H, H5, $J_{4,5}$ = $J_{5,6}$ = 10.0 Hz), 3.73 (dd, 1H, H2, $J_{2,3}$ = 2.0 Hz, $J_{1,2}$ = 11.2 Hz), 4.18 (br s, 1H, H3), 4.32 (d, 1H, Bn, *J* = 11.6 Hz), 4.56 (d, 1H, Bn, *J* = 11.6 Hz), 4.72–4.78 (m, 2H, H6, Bn) 4.95 (d, 1H, Bn, *J* = 11.6 Hz), 5.06 (m, 2H, CH_2=), 5.79 (m, 1H, CH=), 7.22–7.39 (m, 10H, Ph); ^{13}C NMR: δ 30.7 (C3′), 38.0 (C1), 39.1 (C1′), 48.4 (N–CH_2), 59.6 (C5), 70.7 (C4), 72.2 (Bn), 74.8 (Bn), 75.1 (C3), 77.1 (C2), 88.9 (C6), 116.6 (CH_2=), 128.0 (Bn), 128.2 (Bn), 128.3 (Bn), 128.7 (Bn), 128.8 (Bn), 136.5 (CH=), 137.4 (Bn), 137.6 (Bn), 207.4 (C2′). ESIMS: calcd for $C_{26}H_{33}N_2O_6$ $[M+H]^+$ 469.2338, found 469.2333.

3.5. (1*R*,2*S*,3*R*,4*R*,5*S*,6*R*)-1-Acetylmethyl-5-benzylamino-2,3-di-*O*-benzyl-4-hydroxy-6-nitrocyclohexane (5b)

Crystals, mp 114–115 °C; $[\alpha]_D$ −16 (c 2.0, $CHCl_3$); ^{1}H NMR: δ 1.98 (s, 3H, 3′-Me), 2.30 (dd, 1H, H1′b, $J_{1'b,1}$ = 4.8 Hz, $J_{1'b,1'a}$ = 18.4 Hz), 2.67 (d, 1H, OH, *J* = 6.4 Hz), 2.78 (dd, 1H, H1′a, $J_{1'a,1}$ = 3.2 Hz, $J_{1'a,1'b}$ = 18.4 Hz), 2.93 (m, 1H, H1), 3.40 (m, 1H, H4), 3.53 (dd, 1H, H5, $J_{4,5}$ = $J_{5,6}$ = 10.8 Hz), 3.71 (s, 2H, N–CH_2), 3.73 (dd, 1H, H2, $J_{2,3}$ = 2.0 Hz, $J_{1,2}$ = 11.2 Hz), 4.14 (dd, 1H, H3, $J_{2,3}$ = $J_{3,4}$ = 2.4 Hz), 4.30 (d, 1H, Bn, *J* = 11.2 Hz), 4.55 (d, 1H, Bn, *J* = 11.2 Hz), 4.68 (d, 1H, Bn, *J* = 11.6 Hz), 4.80 (dd, 1H, H6, $J_{1,6}$ = $J_{5,6}$ = 10.8 Hz), 4.92 (d, 1H, Bn, *J* = 11.6 Hz), 7.20–7.36 (m, 15H, Ph); ^{13}C NMR: δ 30.7 (C3′), 37.9 (C1), 39.1 (C1′), 50.1 (N–CH_2), 59.8 (C5), 70.7 (C4), 72.2 (Bn), 74.8 (Bn), 75.3 (C3), 77.5 (C2), 88.8 (C6), 127.5 (Bn), 127.97 (Bn), 128.01(Bn), 128.2 (Bn), 128.3 (Bn), 128.5 (Bn), 128.7(Bn), 128.8 (Bn), 137.4 (Bn), 138.6 (Bn), 139.8 (Bn), 207.4 (C2′). ESIMS: calcd for $C_{30}H_{35}N_2O_6$ $[M+H]^+$ 519.2495, found 519.2474.

3.6. (1*R*,2*S*,3*R*,4*R*,5*S*,6*R*)-1-Acetylmethyl-5-cyclohexylamino-2,3-di-*O*-benzyl-4-hydroxy-6-nitrocyclohexane (5c)

Crystals, mp 105–106 °C; $[\alpha]_D$ −21 (c 1.7, $CHCl_3$); ^{1}H NMR: δ 0.82–1.30 (m, 5H, CH_2 cyclohexyl), 1.50–1.89 (m, 5H, CH_2 cyclohexyl), 1.98 (s, 3H, 3′-Me), 2.26 (dd, 1H, H1′b, $J_{1'b,1}$ = 5.2 Hz, $J_{1'b,1'a}$ = 18.4 Hz), 2.37 (m, 1H, N–CH), 2.76 (dd, 1H, H1′a, $J_{1'a,1}$ = 3.2 Hz, $J_{1'a,1'b}$ = 18.0 Hz), 2.97 (m, 1H, H1), 3.19 (dd, 1H, H4, $J_{3,4}$ = 1.2 Hz, $J_{4,5}$ = 10.4 Hz), 3.53 (dd, 1H, H5, $J_{4,5}$ = $J_{5,6}$ = 10.4 Hz), 3.69 (dd, 1H, H2, $J_{2,3}$ = 2.0 Hz, $J_{1,2}$ = 11.6 Hz), 4.18 (br s, 1H, H3), 4.27 (d, 1H, Bn, *J* = 11.6 Hz), 4.52 (d, 1H, Bn, *J* = 11.6 Hz), 4.60 (dd,1H, H6, $J_{1,6}$ = $J_{5,6}$ = 10.8 Hz) 4.81 (d, 1H, Bn, *J* = 11.6 Hz), 4.92 (d, 1H, Bn, *J* = 11.6 Hz), 7.20–7.41 (m, 10H, Ph); ^{13}C NMR: δ 24.8 (CH_2), 25.1 (CH_2), 26.0 (CH_2), 30.7 (C3′), 34.6 (CH_2), 35.0 CH_2), 38.2 (C1), 39.2 (C1′), 54.7 (N–CH), 58.0 (C5), 72.0 (Bn), 72.5 (C4), 74.6 (C3), 74.7 (Bn), 77.0 (C2), 90.7 (C6), 127.9 (Bn), 128.0 (Bn), 128.1(Bn), 128.2 (Bn), 128.6 (Bn), 128.7 (Bn), 128.8(Bn), 137.5 (Bn), 138.9 (Bn), 139.8, 207.5 (C=O). ESIMS: calcd for $C_{29}H_{39}N_2O_6$ $[M+H]^+$ 511.2808, found 511.2791.

3.7. (1*R*,2*S*,3*R*,4*R*,5*S*,6*S*)-1-Acetylmethyl-2,3-di-*O*-benzyl-4-hydroxy-5-methoxy-6-nitrocyclohexane (10)

Syrup, $[\alpha]_D$ −15 (*c* 0.8, MeOH); ^{1}H NMR: δ 2.09 (s, 3H, 3′-Me), 2.16 (m, 1H, H1′b), 2.41 (d, 1H, OH, $J_{OH,4}$ = 6 Hz), 2.92 (d, 1H,

H1′a, $J_{1,1'b}$ = 18.8 Hz), 3.03 (m, 1H, H1), 3.52 (s, 3H, OCH_3), 3.71 (m, 1H, H5), 3.89 (d, 1H, H2, $J_{1,2}$ = 11.6 Hz), 4.23 (m, 2H, H3, H4), 4.42 (d, 1H, Bn, J = 11.6 Hz), 4.62 and 4.66 (d and d, 1H each, Bn, J = 11.6 Hz), 4.90 (d, 1H, Bn, J = 11.6 Hz), 5.42 (br s, 1H, H6) 7.20–7.39 (m, 10H, Ph); ^{13}C NMR: δ 30.6 (C3′), 33.8 (C1), 41.1 (C1′), 58.9 (OCH_3), 70.3 (C4), 72.3 (Bn), 75.3 (Bn), 76.1 (Bn), 77.4 (C2), 78.6 (C5), 86.2 (C6),128.0 (Bn), 128.1 (Bn), 128.3 (Bn), 128.6 (Bn), 128.8 (Bn), 137.5 (Bn), 138.6 (Bn), 206.6 (C=O). ESIMS: calcd for $C_{24}H_{30}NO_7$ $[M+H]^+$ 444.2022, found 444.2020.

3.8. (1*R*,2*S*,3*R*,4*R*,5*S*,6*R*)-1-Acetylmethyl-2,3-di-*O*-benzyl-4-hydroxy-5-methoxy-6-nitrocyclohexane (11)

Syrup, $[\alpha]_D$ −24 (*c* 0.5, $CHCl_3$); ^{1}H NMR: δ 1.99 (s, 3H, 3′-Me), 2.26–2.35 (m, 2H, H1′b,OH), 2.73 (dd, 1H, H1′a, $J_{1'a,1'a}$ = 3.6 Hz, $J_{1,1'a}$ = 18.4 Hz), 2.89 (m, 1H, H1), 3.45 (s, 3H, OCH_3), 3.51 (dd, 1H, H4, $J_{4,5}$ = 7.2 Hz, $J_{4,OH}$ = 5.2 Hz), 3.74 (d, 1H, H2, $J_{1,2}$ = 11.2 Hz), 3.96 (dd, 1H, H5, $J_{4,5}$ = $J_{5,6}$ = 10.0 Hz), 4.08 (br s, 1H, H3), 4.33 (d, 1H, Bn, J = 11.6 Hz), 4.58 and 4.64 (d and d, 1H each, Bn, J = 11.6 Hz), 4.65 (s, 1H, H6) 4.97 (d, 1H, Bn, J = 11.6 Hz), 7.20–7.39 (m, 10H, Ph); ^{13}C NMR: δ 30.7 (C3′), 37.1 (C1), 39.0 (C1′), 61.2 (OCH_3), 72.5 (Bn), 73.0 (C4), 75.0 (Bn), 76.2 (Bn), 77.6 (C2), 82.0 (C5), 88.6 (C6),128.1 (Bn), 128.2 (Bn), 128.4 (Bn), 128.8 (Bn), 128.9 (Bn), 137.3 (Bn), 138.4 (Bn), 206.9 (C=O). ESIMS: calcd for $C_{24}H_{30}NO_7$ $[M+H]^+$ 444.2022, found 444.2025.

3.9. (1*S*,5*R*,6*S*,7*R*,8*R*,9*S*)-2-Allyl-6,7-di-*O*-benzyl-8-hydroxy-3-methyl-9-nitro-2-azabicyclo[3,3,1]nonan-3-ene (2a)

Syrup, $[\alpha]_D$ −61 (*c* 1.5 , $CHCl_3$); ^{1}H NMR: δ 1.71 (s, 3H, Me), 3.43 (m, 1H, H5), 3.49 (d, 1H, OH, J = 6.0 Hz), 3.60 (dd, 1H, H7, $J_{6,7}$ = $J_{7,8}$ = 3.2 Hz), 3.65 (dd, 1H, N–CH_2, J = 7.2 Hz, J = 16.0 Hz), 3.84 (dd, 1H, N–CH_2, J = 4.8 Hz, J = 16.0 Hz), 3.93–3.99 (m, 2H, H4, H6), 4.16 (m, 1H, H8), 4.20 (br s, 1H, H1), 4.51 (d, 1H, Bn, J = 11.6 Hz), 4.62 (d, 1H, Bn, J = 11.6 Hz), 4.69 and 4.73 (d and d, 1H each, Bn, J = 12.4 Hz), 5.12–5.21 (m, 3H, CH_2=, H9), 5.74 (m, 1H, CH=), 7.26–7.39 (m, 10H, Ph); ^{13}C NMR: δ 19.8 (Me), 37.0 (C5), 54.2 (N–CH_2), 59.8 (C1), 70.8 (Bn), 72.9 (C8), 73.2 (C7), 73.3 (C9), 73.5 (Bn), 81.2 (C6), 87.4 (C4), 117.5 (CH_2=), 127.9 (Bn), 128.01 (Bn), 128.03 (Bn), 128.2 (Bn), 128.6 (Bn), 128.7 (Bn), 135.7 (CH=), 137.8 (Bn), 138.1 (Bn), 141.4 (C3). ESIMS: calcd for $C_{26}H_{31}N_2O_5$ $[M+H]^+$ 451.2233, found 451.2225.

3.10. (1*S*,5*R*,6*S*,7*R*,8*R*,9*S*)-2-Benzyl-6,7-di-*O*-benzyl-8-hydroxy-3-methyl-9-nitro-2-azabicyclo[3,3,1]nonan-3-ene (2b)

Syrup, $[\alpha]_D$ −43 (*c* 1.6, $CHCl_3$); ^{1}H NMR: δ 1.78 (s, 3H, Me), 3.39 (d, 1H, OH, J = 5.6 Hz), 3.46 (m, 1H, H5), 3.65 (dd, 1H, H7, $J_{6,7}$ = $J_{7,8}$ = 3.2 Hz), 3.76 (m, 1H, H8) 3.96 (m, 1H, H6), 4.07 (d, 1H, H4, $J_{4,5}$ = 6.8 Hz), 4.10 (d, 1H, N–Bn, J = 15.6 Hz), 4.20 (m, 1H, H1), 4.42 (d, 1H, Bn, J = 11.6 Hz), 4.52 (d, 1H, Bn, J = 11.6 Hz), 4.56 (d, 1H, N–Bn, J = 15.6 Hz), 5.14 (br s, 1H, H9), 7.18–7.40 (m, 15H, Ph); ^{13}C NMR: δ 20.5 (Me), 37.2 (C5), 55.5 (N–Bn), 60.4 (C1), 70.5 (Bn), 72.6 (C8), 72.8 (C7), 73.3 (C9), 73.5 (Bn), 81.1 (C6), 88.3 (C4), 127.8 (Bn), 127.9 (Bn), 128.0 (Bn), 128.2 (Bn), 128.6 (Bn), 128.7 (Bn), 128.9 (Bn), 137.8 (Bn), 138.1 (Bn), 139.4 (Bn), 141.7 (C3). ESIMS: calcd for $C_{30}H_{33}N_2O_5$ $[M+H]^+$ 501.2389, found 501.2400.

3.11. (1*S*,5*R*,6*S*,7*R*,8*R*,9*S*)-2-Cyclohexyl-6,7-di-*O*-benzyl-8-hydroxy-3-methyl-9-nitro-2-azabicyclo[3,3,1]nonan-3-ene (2c)

Syrup, $[\alpha]_D$ −92 (*c* 2.0, $CHCl_3$); ^{1}H NMR: δ 0.80–1.94 (m, 13H, cyclohexyl CH_2, Me), 3.24 (m, 1H, N–CH), 3.34 (m, 1H, H5), 3.56 (d, 1H, OH, J = 5.6 Hz), 3.60 (dd, 1H, H7, $J_{6,7}$ = $J_{7,8}$ = 3.6 Hz), 3.93 (m, 1H, H6), 3.98 (d, 1H, H4, $J_{4,5}$ = 6.0 Hz), 4.10 (m, 1H, H8), 4.38 (m, 1H, H1), 4.50 (d, 1H, Bn, J = 11.2 Hz), 4.61 (d, 1H, Bn, J = 11.2 Hz), 4.69 (s, 2H, Bn), 5.18 (br s, 1H, H9), 7.26–7.36 (m, 10H, Ph); ^{13}C NMR: δ 20.4 (Me), 25.6 (CH_2), 26.0 (CH_2), 26.7 (CH_2), 30.9 (CH_2), 33.1 (CH_2), 35.8 (C5), 55.2 (C1), 57.3 (N–Bn), 70.8 (Bn), 73.42 (C9), 73.45 (Bn), 73.48 (C8), 74.9 (C7), 81.2 (C6), 87.9 (C4), 127.87 (Bn), 127.96 (Bn), 128.01 (Bn), 128.1 (Bn), 128.6 (Bn), 128.7 (Bn), 137.8 (Bn), 138.1 (Bn), 140.7 (C3). ESIMS: calcd for $C_{29}H_{37}N_2O_5$ $[M+H]^+$ 493.2702, found 493.2679.

3.12. (1*S*,5*R*,6*S*,7*R*,8*R*,9*S*)-2-Hexyl-6,7-di-*O*-benzyl-8-hydroxy-3-methyl-9-nitro-2-azabicyclo[3,3,1]nonan-3-ene (2d)

Syrup, $[\alpha]_D$ +3 (*c* 1, $CHCl_3$); ^{1}H NMR: δ 0.90 (t, 3H, *n*-hex–CH_3, J = 7.2 Hz), 1.18–1.36 (m, 6H, CH_2), 1.40–1.57 (m, 2H, CH_2), 1.67 (s, 3H, Me), 3.05 (t, 2H, N–CH_2, J = 8.4 Hz), 3.42 (m, 1H, H5), 3.53 (br s, 1H, OH), 3.59 (dd, 1H, H7, $J_{6,7}$ = $J_{7,8}$ = 3.2 Hz), 3.91–3.96 (m, 2H, H4, H6), 4.16 (br s, 1H, H8), 4.21 (m, 1H, H1), 4.50 (d, 1H, Bn, J = 11.6 Hz), 4.63 (d, 1H, Bn, J = 11.6 Hz), 4.68 and 4.72 (d and d, 1H each, Bn, J = 14.4 Hz), 5.15 (dd, 1H, H9, J = 2.4 Hz, J = 4.0 Hz), 7.26–7.38 (m, 10H, Ph); ^{13}C NMR: δ 14.2 (CH_3 *n*-hex), 19.9 (Me), 22.9 (CH_2), 26.6 (CH_2), 30.0 (CH_2), 31.8 (CH_2), 36.8 (C5), 51.0 (N–CH_2), 59.7 (C1), 70.8 (Bn), 73.2 (C8), 73.3 (C7), 73.39 (C9), 73.44 (Bn), 81.4 (C6), 86.6 (C4), 127.9 (Bn), 128.99 (Bn), 128.03 (Bn), 128.1 (Bn), 128.6 (Bn), 128.7 (Bn), 137.8 (Bn), 138.1 (Bn), 141.5 (C3). ESIMS: calcd for $C_{29}H_{39}N_2O_5$ $[M+H]^+$ 495.2858, found 495.2851.

3.13. (1*S*,5*R*,6*S*,7*R*,8*R*,9*S*)-2-(Uridine 2′,3′-di-*O*-isopropylidene-5′-deoxy-5′-amino)-6,7-di-*O*-benzyl-8-hydroxy-3-methyl-9-nitro-2-azabicyclo[3,3,1]nonan-3-ene (2e)

Syrup, $[\alpha]_D$ +24 (*c* 2, $CHCl_3$); ^{1}H NMR: δ 1.32 (s, 3H, U-Me), 1.55 (s, 3H, U-Me), 1.60 (s, 3H, Me), 3.36 (br s, 1H, H5), 3.40 (dd, 1H, U-H5, $J_{4,5}$ = 3.2 Hz, J_{gem} = 15.5 Hz), 3.53–3.62 (m, 2H, H7, U-H5), 3.88 (dd, 1H, H6, $J_{5,6}$ = $J_{6,7}$ = 4.0 Hz), 3.95 (d, 1H, H4, J = 6.4 Hz), 4.17 (m, 1H, U-H4), 4.25 (br s, 2H, H1, H8), 4.45 (d, 1H, Bn, J = 11.6 Hz), 4.60 (d, 1H, Bn, J = 11.6 Hz), 4.64 and 4.68 (d and d, 1H each, Bn, J = 13.2 Hz), 4.70 (dd, 1H, U-H3, J = 4.8 Hz, J = 6.4 Hz), 5.05 (d, 1H, U-H2, J = 6.4 Hz), 5.14 (br s, 1H, H9), 5.44 (br s, 1H, U-H1), 5.69 (d, 1H, U-H7, $J_{6,7}$ = 8.0 Hz), 7.14 (d, 1H, U-H6, $J_{6,7}$ = 8.0 Hz), 7.23–7.34 (m, 10H, Ph); ^{13}C NMR: δ 20.4 (Me), 25.4 (U-Me), 27.3 (U-Me), 36.9 (C5), 53.9 (U-C5), 60.4 (C1), 70.7 (Bn), 72.7 (C9), 73.1 (Bn), 73.2 (C7), 73.4 (C8), 81.0 (C6), 82.5 (U-C3), 84.4 (U-C2), 87.6 (U-C4), 88.5 (C4), 96.4 (U-C1), 102.8 (U-C7), 114.9 (*C*-Me_2), 127.9 (Bn), 128.0 (Bn), 128.1 (Bn), 128.6 (Bn), 128.7 (Bn), 137.7 (Bn), 138.1 (Bn), 141.4 (C3), 143.6 (U-C6), 150.0 (C=O), 163.3 (C=O). ESIMS: calcd for $C_{35}H_{41}N_4O_{10}$ $[M+H]^+$ 677.2822, found 677.2818.

3.14. (1*S*,5*R*,6*R*,7*R*,8*R*,9*S*)-2-Allyl-6,7-di-*O*-benzyl-8-hydroxy-3-methyl-9-nitro-2-azabicyclo[3,3,1]nonan-3-ene (13a)

Syrup, $[\alpha]_D$ −139 (*c* 0.6, $CHCl_3$); ^{1}H NMR: δ 1.78 (s, 3H, Me), 2.60 (s, 1H, OH), 3.48 (m, 1H, H5), 3.59 (dd, 1H, H7, $J_{6,7}$ = 8.8 Hz, $J_{7,8}$ = 4.0 Hz), 3.62 (dd, 1H, N–CH_2, J = 7.6 Hz, J = 16.0 Hz), 3.77 (dd, 1H, H6, $J_{5,6}$ = 3.6 Hz, $J_{6,7}$ = 8.8 Hz), 3.86 (dd, 1H, N–CH_2, J = 5.2 Hz, J = 16.0 Hz), 3.97 (dd, 1H, H8, $J_{7,8}$ = $J_{1,8}$ = 4.0 Hz), 4.10 (dd, 1H, H1, $J_{1,8}$ = 2.8 Hz, $J_{1,9}$ = 6.0 Hz), 4.22 (d, 1H, H4, J = 6.4 Hz), 4.62 (d, 1H, Bn, J = 11.2 Hz), 4.66 (d, 1H, Bn, J = 11.6 Hz), 4.73 (br s, 1H, H9), 4.77 (d, 1H, Bn, J = 11.6 Hz), 4.80 (d, 1H, Bn, J = 11.2 Hz), 5.14 (m, 2H, CH_2=), 5.74 (m, 1H, CH=), 7.26–7.42 (m, 10H, Ph); ^{13}C NMR: δ 19.9 (Me), 35.6 (C5), 54.0 (N–CH_2), 57.8 (C1), 71.6 (C8), 72.1 (Bn), 73.7 (Bn), 74.9 (C9), 79.2 (C7), 81.7 (C6), 87.9 (C4), 117.3 (CH_2=), 127.77 (Bn), 127.83 (Bn), 127.9 (Bn), 128.0 (Bn), 128.4 (Bn), 128.5 (Bn), 135.7 (CH=), 138.1 (Bn), 138.2 (Bn), 140.3 (C3). ESIMS: calcd for $C_{26}H_{31}N_2O_5$ $[M+H]^+$ 451.2232, found 451.2212.

3.15. (1*S*,5*R*,6*R*,7*R*,8*R*,9*S*)-2-Benzyl-6,7-di-*O*-benzyl-8-hydroxy-3-methyl-9-nitro-2-azabicyclo[3,3,1]nonan-3-ene (13b)

Syrup, $[\alpha]_D$ −6 (*c* 0.8, $CHCl_3$); ^1H NMR: δ 1.86 (s, 3H, Me), 3.49 (m, 1H, H5), 3.58–3.63 (m, 2H, H7, H8), 3.72 (dd, 1H, H6, $J_{5,6}$ = 2.8 Hz, $J_{6,7}$ = 8.0 Hz), 4.06 (m, 1H, H1), 4.09 (d, 1H, N–CH_2, *J* = 15.6 Hz), 4.29 (d, 1H, H4, *J* = 6.4 Hz), 4.50 (d, 1H, Bn, *J* = 11.6 Hz), 4.54 (d, 1H, N–CH_2, *J* = 15.6 Hz), 4.64 (d, 1H, Bn, *J* = 11.6 Hz), 4.70 (d, 1H, Bn, *J* = 11.6 Hz), 4.72 (br s, 1H, H9), 4.76 (d, 1H, Bn, *J* = 11.6 Hz), 7.19–7.38 (m, 15H, Ph); ^{13}C NMR: δ 20.7 (Me), 35.9 (C5), 54.4 (N–CH_2), 58.5 (C1), 71.4 (C8), 72.3 (Bn), 73.6 (Bn), 75.0 (C9), 79.2 (C7), 81.8 (C6), 89.0 (C4), 127.7 (Bn), 127.9 (Bn), 128.0 (Bn), 128.1 (Bn), 128.2 (Bn), 128.65 (Bn), 128.67 (Bn), 128.8 (Bn), 138.2 (Bn), 138.4 (Bn), 139.6 (Bn), 140.7 (C3). ESIMS: calcd for $C_{30}H_{33}N_2O_5$ $[M+H]^+$ 501.2389, found 501.2370.

3.16. (1*R*,3*R*,5*S*,6*R*,7*R*,8*S*,9*R*)-2-Allyl-6,7-di-*O*-benzyl-3-methyl-9-nitro-3,8-oxy-2-azabicyclo[3,3,1]nonane (14a)

Syrup, $[\alpha]_D$ +19 (*c* 0.5, $CHCl_3$); ^1H NMR: δ 1.40 (s, 3H, Me), 1.68 (d, 1H, H4a, $J_{4a,4b}$ = 14 Hz), 2.31 (dd, 1H, H4b, $J_{4b,5}$ = 6.4 Hz), 2.82–2.90 (m, 2H, H5, NCH_2), 3.36–3.46 (m, 2H, H7, NCH_2), 3.94 (d, 1H, H6, $J_{5,6}$ = 5.6 Hz), 4.18 (m, 1H, H1), 4.38 (d, 1H, H8, $J_{1,8}$ = 6.4 Hz), 4.60–4.66 (m, 3H, H9, Bn), 4.63 and 4.72 (d and d, 1H each, Bn, *J* = 12.4 Hz), 5. 14 (m, 2H, CH_2=), 5.70 (m, 1H, CH=), 7.21–7.38 (m, 10H, Ph); ^{13}C NMR: δ 20.9 (Me), 36.2 (C5), 40.8 (C4), 52.0 (NCH_2), 62.2 (C1), 71.8 (Bn), 72.0 (Bn), 73.6 (C8), 79.4 (C9), 80.3 (C7), 85.2 (C6), 98.0 (C3), 118.5 (CH_2=), 127.9 (Bn), 128.1 (Bn), 128.2 (Bn), 128.6 (Bn), 128.7 (Bn), 135.5 (CH=), 137.7 (Bn), 138.0 (Bn). ESIMS: calcd for $C_{26}H_{31}N_2O_5$ $[M+H]^+$ 451.2232, found 451.2259.

3.17. (1*R*,3*R*,5*S*,6*R*,7*R*,8*S*,9*R*)-2-Benzyl-6,7-di-*O*-benzyl-3-methyl-9-nitro-3,8-oxy-2-azabicyclo[3,3,1]nonane (14b)

Syrup, $[\alpha]_D$ +37 (*c* 0.5, $CHCl_3$); ^1H NMR: δ 1.39 (s, 3H, Me), 1.71 (d, 1H, H4a, $J_{4a,4b}$ = 14 Hz), 2.43 (dd, 1H, H4b, $J_{4b,5}$ = 6.4 Hz), 2.82 (d, 1H, H5, $J_{4b,5}$ = 6.4 Hz), 3.28 (d, 1H, NCH_2, *J* = 13.2 Hz), 3.41 (d, 1H, H7, $J_{7,8}$ = 5.2 Hz), 3.92–3.98 (m, 2H, H1, H6), 4.02 (d, 1H, NCH_2, *J* = 13.2 Hz), 4.42–4.51 (m, 3H, H9, H8, Bn), 4.62 (d, 1H, Bn, *J* = 12 Hz), 4.64 and 4.72 (d and d, 1H each, Bn, *J* = 12 Hz), 7.18–7.37 (m, 15H, Ph); ^{13}C NMR: δ 21.5 (Me), 36.1 (C5), 40.8 (C4), 53.6 (NCH_2), 63.6 (C1), 71.8 (Bn), 72.1(Bn), 73.5 (C9), 79.3 (C8), 80.2 (C7), 85.2 (C6), 98.6 (C3), 127.6 (Bn), 127.9 (Bn), 128.0 (Bn), 128.1 (Bn), 128.2 (Bn), 128.5 (Bn), 128.6 (Bn), 128.7 (Bn), 128.9 (Bn), 137.7 (Bn), 138.0 (Bn), 138.1 (Bn). ESIMS: calcd for $C_{30}H_{33}N_2O_5$ $[M+H]^+$ 501.2389, found 501.2389.

3.18. (1*R*,2*R*,3*R*,4*R*,5*S*,6*R*)-1-Acetylmethyl-2,3-di-*O*-benzyl-4-hydroxy-5-methoxy-6-nitrocyclohexane (15)

Syrup, $[\alpha]_D$ −60 (*c* 1.5, $CHCl_3$); ^1H NMR: δ 1.87 (s, 3H, Me), 2.11 (m, 1H, H1′a), 2.37 (d,1H, OH, $J_{OH,4}$ = 8.4 Hz), 2.63 (dd, 1H, H1′b, $J_{1'a,1'b}$ = 10.8 Hz, $J_{1,1'b}$ = 18.4 Hz), 2.97 (m, 1H, H1), 3.47 (s, 3H, OCH_3), 3.80–3.92 (m, 4H, H2, H3, H4, H5), 4.18 (d, 1H, Bn, *J* = 12.0 Hz), 4.40 (dd, 1H, H6, $J_{5,6}$ = 9.6 Hz, $J_{1,6}$ = 12.4 Hz), 4.46, 4.54 and 4.73 (d, d and d, 1H each, Bn, *J* = 11.6 Hz), 7.18 (m, 2H, Ph), 7.27–7.33 (m, 8H, Ph); ^{13}C NMR: δ 30.2 (Me), 35.0 (C1), 39.9 (C1′), 61.3 (OCH_3), 71.9 (C4), 73.0 (Bn), 73.6 (C3), 75.8 (C2), 82.2 (C5), 89.2 (C6),128.5 (Bn), 128.6 (Bn), 128.7 (Bn), 128.9 (Bn), 137.2 (Bn), 137.3 (Bn), 205.8 (C=O). ESIMS: calcd for $C_{24}H_{30}NO_7$ $[M+H]^+$ 444.2022, found 444.2016.

3.19. (1*S*,2*R*,3*R*,4*R*,5*R*,6*S*)-1-Acetylmethyl-2,3-di-*O*-benzyl-4-hydroxy-5-methoxy-6-nitrocyclohexane (16)

Crystals, mp 166–168 °C; $[\alpha]_D$ +33 (*c* 2, $CHCl_3$); ^1H NMR: δ 1.92 (s, 3H, Me), 2.32–2.42 (m, 2H, H1, H1′a), 2.45 (s, 1H, OH), 2.57 (m, 1H, H1′b), 3.34 (s, 3H, OCH_3), 3.50 (dd, 1H, H3, $J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 9.2 Hz), 3.67 (dd, 1H, H2, $J_{1,2}$ = 10.0 Hz, $J_{2,3}$ = 2.4 Hz), 3.96 (dd, 1H, H5, $J_{4,5}$ = $J_{5,6}$ = 9.2 Hz), 4.38 (m, 1H, H4), 4.48 (d, 1H, Bn, *J* = 11.6 Hz), 4.70 (m, 2H, Bn), 4.87 (d, 1H, H6, $J_{1,6}$ = 11.6 Hz), 4.93 (d, 1H, Bn, *J* = 11.6 Hz), 7.20–7.38 (m, 10H, Ph); ^{13}C NMR: δ 30.2 (Me), 39.0 (C1), 40.9 (C1′), 58.0 (OCH_3), 65.8 (C4), 72.7 (Bn), 75.5 (Bn), 77.4 (C5), 80.3 (C2), 82.4 (C3), 87.6 (C6), 128.0 (Bn), 128.1 (Bn), 128.3 (Bn), 128.6 (Bn), 128.8 (Bn), 137.5 (Bn), 138.6 (Bn), 206.6 (C=O). ESIMS: calcd for $C_{24}H_{30}NO_7$ $[M+H]^+$ 444.2022, found 444.2053.

3.20. (1*S*,3*S*,5*R*,6*S*,7*R*,8*R*,9*S*)-2-Allyl-6,7-di-*O*-benzyl-8-hydroxy-3-methyl-9-nitro-2-azabicyclo[3,3,1]nonane (17a)

Syrup, $[\alpha]_D$ −30 (*c* 1, $CHCl_3$); ^1H NMR: δ 0.85 (d, 3H, Me, $J_{3,Me}$ = 5.6 Hz), 0.91 (d, 1H, H4a, $J_{4a,4b}$ = 12.4 Hz), 2.04 (m, 1H, H4b), 2.51 (m, 1H, H3), 3.09–3.32 (m, 4H, H5, OH, NCH_2), 3.74 (br s, 1H, H6), 3.99 (m, 2H, H1, H8), 4.09 (br s, 1H, H7), 4.50 and 4.65 (d and d, 1H each, Bn, *J* = 12 Hz), 4.67 (s, 2H, Bn), 4.89 (br s, 1H, H9), 5.15 (m, 2H, CH_2=), 5.80 (m, 1H, CH=), 7.27–7.39 (m, 10H, Ph); ^{13}C NMR: δ 22.0 (Me), 32.8 (C5), 33.1 (C4), 45.8 (C3), 57.0 (NCH_2), 60.3 (C1), 70.7 (Bn), 71.1 (C7), 71.9 (C8), 73.5 (Bn), 78.0 (C9), 81.5 (C6), 118.3 (CH_2=), 127.9 (Bn), 128.1 (Bn), 128.2 (Bn), 128.6 (Bn), 128.7 (Bn), 134.8 (CH=), 137.7 (Bn), 138.1 (Bn). ESIMS: calcd for $C_{26}H_{33}N_2O_5$ $[M+H]^+$ 453.2389, found 453.2380.

3.21. (1*S*,3*S*,5*R*,6*S*,7*R*,8*R*,9*S*)-2-Benzyl-6,7-di-*O*-benzyl-8-hydroxy-3-methyl-9-nitro-2-azabicyclo[3,3,1]nonane (17b)

Syrup, $[\alpha]_D$ −44 (*c* 1, $CHCl_3$); ^1H NMR: δ 0.91 (d, 3H, Me, $J_{3,Me}$ = 5.6 Hz), 1.38 (m, 1H, H4a), 1.94 (m, 1H, H4b), 2.60 (m, 1H, H3), 3.00 (m, 1H, H5), 3.06 (d, 1H, OH, $J_{OH,8}$ = 3.6 Hz), 3.56 (d, 1H, NCH_2, *J* = 14.8 Hz), 3.81 (d, 1H, *J* = 14.8 Hz, NCH_2), 3.83–3.90 (m, 3H, H6, H7, H1), 4.36 (d, 1H, H8, $J_{7,8}$ = 3.2 Hz), 4.56 and 4.68 (d and d, 1H each, Bn, *J* = 11.6 Hz), 4.66 (s, 2H, Bn), 5.05 (br s, 1H, H9), 7.20–7.40 (m, 15H, Ph); ^{13}C NMR: δ 23.7 (Me), 30.6 (C4), 34.4 (C5), 51.9 (C3), 55.7 (NCH_2), 60.2 (C1), 66.2 (C8), 71.0 (Bn), 73.5 (Bn), 74.9 (C7), 77.8 (C9), 80.2 (C6), 127.2 (Bn), 127.9 (Bn), 128.0 (Bn), 128.1 (Bn), 128.2 (Bn), 128.3 (Bn), 128.4 (Bn), 128.6 (Bn), 128.8 (Bn), 137.7 (Bn), 137.9 (Bn), 139.5(Bn). ESIMS: calcd for $C_{30}H_{35}N_2O_5$ $[M+H]^+$ 503.2545, found 503.2549.

3.22. (1*S*,3*S*,5*R*,6*S*,7*R*,8*R*,9*S*)-2-Cyclohexyl-6,7-di-*O*-benzyl-8-hydroxy-3-methyl-9-nitro-2-azabicyclo[3,3,1]nonane (17c)

Syrup, $[\alpha]_D$ −31 (*c* 1, $CHCl_3$); ^1H NMR: δ 0.83 (d, 3H, Me, $J_{3,Me}$ = 5.6 Hz), 0.89 (m, 1H, H4a), 1.02–1.84 (m, 10H, CH_2), 2.06 (m, 1H, H4b), 2.58–2.73 (m, 2H, H3, NCH), 3.17 (m, 1H, H5), 3.28 (d, 1H, OH, $J_{OH,8}$ = 5.2 Hz), 3.73 (m, 1H, H6), 3.96 (m, 1H, H1), 4.01 (m, 1H, H8), 4.15 (dd, 1H, H7, $J_{6,7}$ = $J_{7,8}$ = 3.6 Hz), 4.47 and 4.63 (d and d, 1H each, Bn, *J* = 11.6 Hz), 4.65 (s, 2H, Bn), 4.91 (m, 1H, H9), 7.27–7.39 (m, 10H, Ph); ^{13}C NMR: δ 21.8 (Me), 23.5, 25.7, 26.1, 26.9, 32.2, 33.2 (C4), 33.5 (C5), 43.0 (C3), 56.0 (C1), 57.1 (NCH_2), 64.0 (C8), 70.5 (C7), 70.9 (Bn), 73.3 (Bn), 74.9 (C7), 78.2 (C9), 81.4 (C6), 127.2 (Bn), 127.8 (Bn), 127.9 (Bn), 128.4 (Bn), 128.5 (Bn), 137.6 (Bn), 137.9 (Bn). ESIMS: calcd for $C_{29}H_{39}N_2O_5$ $[M+H]^+$ 495.2858, found 495.2837.

3.23. (1*S*,3*S*,5*R*,6*R*,7*R*,8*R*,9*S*)-2-Allyl-6,7-di-*O*-benzyl-8-hydroxy-3-methyl-9-nitro-2-azabicyclo[3,3,1]nonane (18a)

Syrup, ^{1}H NMR: δ 0.94 (d, 3H, Me, $J_{3,Me}$ = 5.6 Hz), 1.67 (m, 1H, H4a), 1.83 (m, 1H, H4b), 2.53 (m, 1H, H3), 3.13 (dd, 1H, NCH, J = 8.4, 14.8 Hz), 3.30 (m, 2H, H5, NCH), 3.66 (dd, 1H, H6, $J_{5,6}$ = 9.2, $J_{6,7}$ = 4.4 Hz), 3.83 (dd, 1H, H8, $J_{7,8}$ = 4.0, $J_{1,8}$ = 4.4 Hz), 3.90–3.97 (m, 2H, H1, H7), 4.55–4.79 (m, 4H, Bn, H9), 4.80 (d, 1H, Bn, J = 11.2 Hz), 5.16 (m, 2H, CH_2=), 5.77 (m, 1H, CH=), 7.27–7.39 (m, 10H, Ph); ^{13}C NMR: δ 21.9 (Me), 29.8 (C4), 31.5 (C5), 45.8 (C3), 56.9 (NCH_2), 58.7 (C1), 70.1 (C8), 71.8 (Bn), 73.7 (Bn), 77.7 (C9), 79.3 (C7), 79.6 (C6), 118.2 (CH_2=), 127.8 (Bn), 128.0 (Bn), 128.1 (Bn), 128.2 (Bn), 128.6 (Bn), 128.7 (Bn), 134.9 (CH=), 137.9 (Bn), 138.4 (Bn). ESIMS: calcd for $C_{26}H_{33}N_2O_5$ $[M+H]^+$ 453.2389, found 453.2352.

3.24. (1*S*,3*S*,5*R*,6*R*,7*R*,8*R*,9*S*)-2-Benzyl-6,7-di-*O*-benzyl-8-hydroxy-3-methyl-9-nitro-2-azabicyclo[3,3,1]nonane (18b)

Syrup, ^{1}H NMR: δ 1.03 (d, 3H, Me, $J_{3,Me}$ = 5.6 Hz), 1.74 (m, 1H, H4a), 1.89 (m, 1H, H4b), 2.61 (m, 1H, H3), 3.33 (m, 1H, H5), 3.46 (d, 1H, NCH_2, J = 13.6 Hz), 3.63 (dd, 1H, H6, $J_{6,7}$ = 4.8 $J_{5,6}$ = 9.6 Hz), 3.85–4.05 (m, 4H, H7, H8, H1, NCH_2), 4.42–4.75 (m, 5H, Bn, H9), 7.17–7.38 (m, 10H, Ph); ^{13}C NMR: δ 23.2 (Me), 29.6 (C4), 31.7 (C5), 47.5 (C3), 59.8 (NCH_2), 60.0 (C1), 70.1 (C8), 71.8 (Bn), 73.2 (Bn), 77.0 (C7), 79.2 (C9), 79.4 (C6), 127.8 (Bn), 127.9 (Bn), 128.0 (Bn), 128.1 (Bn), 128.4 (Bn), 128.5, 128.6 (Bn), 138.4, 140.2 (Bn). ESIMS: calcd for $C_{30}H_{35}N_2O_5$ $[M+H]^+$ 503.2545, found 503.2546.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2009.08.028.

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