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Tetrahydroisoquinoline alkaloids and 2-deoxyribonolactones from *Aristolochia arcuata*

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Abstract

2-Deoxyribonolactones and four tetrahydroisoquinoline alkaloids were isolated from the acetone extract of the leaves of *Aristolochia arcuata* Mast., together with pinitol, sequoyitol, glycerol, fructose, sucrose, eupomatenoid-7, salsolinol, and 6,7-dihydroxy-1,1-dimethyl-1,2,3,4-tetrahydroisoquinoline. Their structures were determined on the basis of spectroscopic methods, mainly using ^{1}H, ^{13}C, ^{15}N, and ^{31}P NMR.

Keywords: *Aristolochia arcuata*; Aristolochiaceae; Tetrahydroisoquinoline alkaloids; 2-Deoxyribonolactones

1. Introduction

Aristolochia species (Aristolochiaceae) have been used in slimming therapy as a substitute for, or in addition to, traditional Chinese plants. Recently, however, healthcare practitioners have been cautioned against the use of *Aristolochia* species (Therapeutic Goods Administration, 2001). This concern is supported by reports on nephropathy caused by a slimming preparation containing *Aristolochia* species, and by the fact that *Aristolochia* spp. are a source of aristolochic acid, which has been shown to have mutagenic and toxic effects (Violon, 1997; Lopes et al., 2001). Aristolochic acids have not yet been isolated from *Aristolochia arcuata* Mast. (Aristolochiaceae), although we previously isolated 13-oxidodibenzo[*a*,*g*]-quinolizinium alkaloids, aristolane sesquiterpenes, tetrahydrofuran and benzofuran lignans, KNO_3, fructose, sucrose, and sitosterol from this species (Watanabe and Lopes, 1995). As part of our ongoing study of the chemical constituents of *A. arcuata,* the isolation and structural elucidation of eupomatenoid-7, pinitol, sequoyitol, glycerol, fructose, sucrose, salsolinol (**1**), five tetrahydroisoquinoline alkaloids (**2**–**6**), four of them seem to be new, and two 2-deoxyribonolactones (**7** and **8**), one of which appears to be new, are reported here. The structures of the new compounds were determined on the basis of spectroscopic methods (MS, IR, UV, and ^{1}H, ^{13}C, ^{31}P, ^{15}N NMR), mainly using ^{1}H–^{13}C and ^{1}H–^{15}N *g*HMBC NMR experiments. γ-Lactones have been previously identified in plants (Ford, 1984; Ahmed et al., 1995; Kitajima et al., 1999). Endogenous γ-lactones such as 3-hydroxy-4-butanolide and 2-hydroxy-4-hydroxymethyl-4-butanolide have been isolated from rats, and have been shown to enhance satiety and hunger, respectively, by their effects on feeding behavior and the central neurons of rats (Uchikawa et al., 1988). Besides, ^{13}C γ-lactones have been prepared for solid-phase oligonucleotide synthesis (Hayes et al., 2001).

2. Results and discussion

The acetone extract of the leaves of *A. arcuata* was fractionated on chromatographic columns to give pinitol, glycerol, fructose, sucrose, eupomatenoid-7, and salsolinol (**1**), which were identified by comparing their physical and spectroscopic data with those of authentic samples. Tetrahydroisoquinoline alkaloids (**2**–**6**) and 2-deoxyribolactones (**7** and **8**) were also isolated.

The ^{1}H, ^{13}C NMR and *g*HMQC spectra of alkaloid **2** showed signals very similar to those observed for salsolinol

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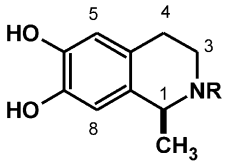
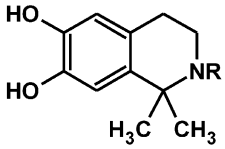
(**1**) and fructose, which were also isolated from this species (Tables 1 and 2). The ESI-MS of alkaloid **2** displayed a *quasi*-molecular ion $[M+H]^+$ at *m*/*z* 342, which was consistent with the molecular formula $C_{16}H_{23}NO_7$. In addition, the base peak at *m*/*z* 194 and the fragment ions at *m*/*z* 205 due to B-ring fragmentation suggested that the fructopyranosyl group was linked to the N atom through C-6′.

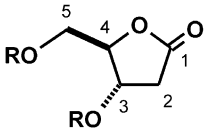
The nOeDS (nOe difference spectroscopy) corroborated this suggestion, since selective irradiation of the



	R
1	H
2	6'-Frc



	R
3	H
4	$CH(CH_2OH)_2$
5	CH_2CH_3
6	6'-Frc



	R
7	H
8	$H(HPO_3)_3$

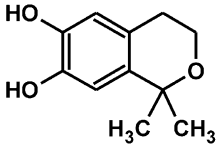


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Table 1
^{1}H NMR spectral data for alkaloids **1**, **2** and **6** (500 MHz, D_2O, δ, *J* in Hz)[a]

H	**1**	**2**	**6**
1	4.33 (*q*, *J* = 6.8)	4.33 (*q*, *J* = 6.9)	
3a	3.40–3.00 (*m*)	3.38–3.32 (*m*)	3.32 (*t*, *J* = 6.5)
3b	3.40–3.00 (*m*)	3.22–3.16 (*m*)	3.32 (*t*, *J* = 6.5)
4	2.85–2.75 (*m*)	2.86–2.72 (*m*)	2.81 (*t*, *J* = 6.5)
5	6.57 (*s*)	6.56 (*s*)	6.56 (*s*)
8	6.60 (*s*)	6.60 (*s*)	6.67 (*s*)
9	1.43 (*d*, *J* = 6.8)	1.43 (*d*, *J* = 6.9)	1.50 (*s*)
10			1.50 (*s*)
2′		3.62 (*d*, *J* = 10.0)	3.62 (*d*, *J* = 10.0)
3′		3.71 (*dd*, *J* = 10.0, 3.5)	3.71 (*dd*, *J* = 10.0, 3.5)
4′		3.86–3.80 (*m*)	3.86–3.82 (*m*)
5′a		3.52 (*dd*, *J* = 12.5, 2.0)	3.52 (*dd*, *J* = 12.5, 2.0)
5′b		3.86–3.80 (*m*)	3.88–3.84 (*m*)
6′a		3.38 (*d*, *J* = 12.0)	3.38 (*d*, *J* = 12.0)
6′b		3.53 (*d*, *J* = 12.0)	3.54 (*d*, *J* = 12.0)

[a] Multiplicities were determined with the assistance of ^{1}H–^{1}H COSY and TOCSY.

Table 2
^{13}C NMR spectral data for alkaloids **1**, **2** and **6** (126 MHz, D_2O, δ)[a]

	1		**2**		**6**	
C	^{13}C (δ)[b]	*g*HMBC	^{13}C (δ)[b]	*g*HMBC and ^{1}H–^{13}C COSY-LR	^{13}C (δ)[b]	*g*HMBC
1	52.0 (*d*)	H-3, H-9	51.1 (*d*)	H-9	57.2 (*s*)	H-8, H-3, H-9,10
3	40.5 (*t*)	H-1	39.6 (*t*)		37.6 (*t*)	H-4
4	25.3 (*t*)	H-3	24.4 (*t*)	H-3a,b	24.6 (*t*)	H-3, H-5
4a	124.7 (*s*)	H-3, H-8	123.7 (*s*)	H-3a, H-3b, H-4, H-8	122.8 (*s*)	H-3, H-4, H-8
5	116.9 (*d*)	H-4	115.9 (*d*)		116.0 (*d*)	H-4
6	145.1 (*s*)	H-8	144.0 (*s*)	H-8	144.0 (*s*)	H-8
7	145.0 (*s*)	H-5	143.3 (*s*)	H-5	143.6 (*s*)	H-5
8	114.4 (*d*)	H-1	113.5 (*d*)	H-1	112.5 (*d*)	
8a	126.4 (*s*)	H-5, H-9	125.5 (*s*)	H-5, H-9	129.9 (*s*)	H-5, H-9,10, H-4
9	19.8 (*q*)	H-1	18.9 (*q*)		27.6 (*q*)	
10					27.6 (*q*)	
1′			98.2 (*s*)	H-2′, H-5′a, H-6′a,b	98.3 (*s*)	H-6′a,b
2′			67.8 (*d*)	H-4′, H-6′a	67.7 (*d*)	
3′			69.9 (*d*)	H-5′a, H-2′	69.9 (*d*)	H-5′a,b
4′			69.4 (*d*)		69.4 (*d*)	
5′			64.1 (*t*)		64.2 (*t*)	
6′			63.5 (*t*)	H-3′	63.5 (*t*)	

[a] Multiplicity was established by DEPT pulse sequence.
[b] Assignments were made with the assistance of *g*HMQC.

Table 3
^{1}H NMR spectral data for alkaloids **3**–**5** (500 MHz, D_2O, δ, J in Hz)[a]

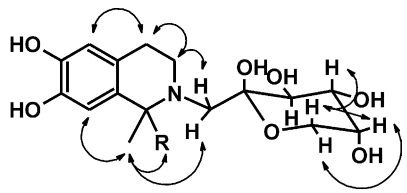
H	**3**	**4**	**5**	**3**	**4**	**5**
	^{1}H (δ)	^{1}H (δ)	^{1}H (δ)	*g*NOESY	*g*NOESY and nOeDS	*g*NOESY and nOeDS
3	3.34 (*t*, *J* = 6.5)	3.36 (*t*, *J* = 6.5)	3.38 (*t*, *J* = 6.5)	H-4	H-1′a, H-1′b, H-4, H-3′	
4	2.83 (*t*, *J* = 6.5)	2.85 (*t*, *J* = 6.5)	2.86 (*t*, *J* = 6.5)	H-3, H-5	H-3, H-5	H-3, H-5
5	6.57 (*s*)	6.60 (*s*)	6.61 (*s*)	H-4	H-4	H-4
8	6.68 (*s*)	6.71 (*s*)	6.72 (*s*)	H-9,10	H-9,10	H-9,10
9,10	1.52 (*s*)	1.55 (*s*)	1.55 (*s*)	H-8	H-3, H-8	H-3, H-8, H-1′
1′						
1′a		3.44 (*dd*, *J* = 12.0, 6.5)	3.52 (*q*, *J* = 7.2)		H-1′b, H-2′, H-3	H-3, H-9,10, H-2′
1′b		3.52 (*dd*, *J* = 12.0, 4.5)			H-1′a, H-2′, H-3	
2′		3.81–3.61 (*m*)	1.05 (*t*, *J* = 7.2)		H-1′a, H-1′b, H-3′a, H-3′b	H-1′
3′a		3.44 (*dd*, *J* = 12.0, 6.5)			H-2′, H-3, H-3′b	
3′b		3.52 (*dd*, *J* = 12.0, 4.5)			H-2′, H-3, H-3′a	

[a] Multiplicities were determined with the assistance of ^{1}H–^{1}H COSY and TOCSY.

methyl hydrogens at δ 1.43 resulted in three nOe enhancements: for H-1 at δ 4.33, H-8 at δ 6.60, and for one of the hydrogens of CH_2-6′ at δ 3.38 (Fig. 1). The *g*HMBC spectrum of **2** was used to assign the quaternary carbons and together with *g*HMQC, *g*NOESY, *J*-resolved, ^{1}H–^{1}H *g*COSY, and *g*TOCSY spectra were used to independently confirm the connectivities among the atoms and establish the relative configuration of **2** (Tables 1 and 2). Thus, alkaloid **2** is 6,7-dihydroxy-1-methyl-*N*-(6′-fructopyranosyl)-1,2,3,4-tetrahydroisoquinoline.

The ESI-MS of alkaloid **3** displayed a *quasi*-molecular ion $[M+H]^+$ at *m*/*z* 194, which was consistent with molecular formula $C_{11}H_{15}NO_2+H$. The IR spectra of **3** showed absorption bands at 3250–3420 cm^{-1}, characteristic of hydroxyl groups. The ^{1}H and ^{13}C NMR spectra showed signals corresponding to one tetrasubstituted aromatic ring, one quaternary carbon, two methylene groups, and two methyl groups (Tables 3 and 4). These data permitted the identification of **3** as 6,7-dihydroxy-1,1-dimethylisochromane **9** (Hsu and Chen, 1993). However, C-1 (δ 57.3) and C-3 (δ 36.5) absorbed at frequencies lower than expected for carbinolic carbons. From a detailed analysis of the *g*NOESY, ^{1}H–^{1}H *g*COSY, ^{1}H–^{13}C *g*COSY, *g*HMQC, and ^{1}H–^{13}C *g*HMBC data (Tables 3 and 4), it was possible to confirm the carbon skeleton of **3**. The ^{1}H–^{15}N *g*HMBC (50.7 MHz, J = 10 Hz) experiment showed correlations between N (δ_N 51.2) and 2H-4 (δ_H 2.83), 6H-9,10 (δ_H 1.52), which corroborated the structure proposed for**3**, and requires a revision of the previously published structure **9** for 6,7-dihydroxy-1,1-dimethylisochromane (Hsu and Chen, 1993). Thus, alkaloid **3** is 6,7-dihydroxy-1,1-dimethyl-1,2,3,4-tetrahydroisoquinoline. This alkaloid has been synthesized (Roger et al., 1979) and also isolated from natural sources (Tono, 1971) as hydrobromide and hydrochloride derivatives, respectively.

The molecular formula of **4** was established as $C_{14}H_{21}NO_4$ based on a combination of ESI-MS and ^{13}C NMR spectra. In addition to the molecular ion at *m*/*z* 267 $[M]^{+\cdot}$, the LSI-MS spectrum (nitrobenzyl alcohol matrix) displayed peaks at *m*/*z* 563 $[(CH_2NCH(CH_2OH)_2+3NBA+H]^+$ and 284 $[(CH_3)_2CNCH$-



R
2 H
6 CH_3

Fig. 1. Selected nOe interactions for compounds **2** and **6**.

Table 4
^{13}C spectral data for alkaloids **3**–**5** (126 MHz, D_2O, δ)[a]

C	**3**	**4**		**5**
	^{13}C (δ)[b,c]	^{13}C (δ)[b]	*g*HMBC	^{13}C (δ)[b,c]
1	57.3 (*s*)	57.0 (*s*)	H-3, H-8, H-9,10	57.7 (*s*)
3	36.5 (*t*)	37.5 (*t*)	H-4	36.5 (*t*)
4	24.3 (*t*)	24.5 (*t*)	H-3, H-5	24.0 (*t*)
4a	122.5 (*s*)	122.6 (*s*)	H-3, H-8	121.8 (*s*)
5	116.0 (*d*)	116.0 (*d*)	H-4	115.0 (*d*)
6	144.0 (*s*)	144.0 (*s*)	H-8	145.5 (*s*)
7	143.9 (*s*)	143.8 (*s*)	H-5	144.0 (*s*)
8	112.5 (*d*)	112.5 (*d*)		112.5 (*d*)
8a	129.5 (*s*)	130.0 (*s*)	H-5, H-4, H-9,10	128.5 (*s*)
9, 10	27.1 (*q*)	27.5 (*q*)	H-9,10	27.5 (*q*)
1′, 3′	–	64.4, 64.4 (*t*)	H-1′, H-3′	49.8 (*t*)
2′	–	73.8 (*d*)		15.0 (*q*)

[a] Multiplicity was established by DEPT pulse sequence.
[b] Assignments were made with the assistance of *g*HMQC.
[c] *g*HMBC for compounds **3** and **5** gave the same correlations between ^{13}Cs (C-1–C-10) and ^{1}Hs as showed for **4**.

$(CH_2OH)_2 + NBA]^{+\cdot}$ arising from fragmentation at the B ring. The ^1H and ^{13}C NMR spectra of **4** in D_2O were very similar to those of **3**, except for the presence of additional signals related to the three carbons and five carbinolic hydrogens (Tables 3 and 4). The multiplicities of these carbons (determined by DEPT pulse sequences) and these hydrogens suggested the presence of a $CH(CH_2OH)_2$ group in the molecule. The positions of the aromatic ring substituents were established by ^1H–^{13}C *g*HMBC, and the groups linked to the N atom were readily confirmed by ^1H–^{15}N *g*HMBC based on correlations between N (δ_N 52.6) and 2H-4 [δ_H 2.85 (2H)], H-1′,3′ [δ_H 3.44 (2H), 3.52 (2H)], and 6H-9,10 [δ_H 1.55 (6H)]. Moreover, the ESI-MS of the dimethoxy derivative **4a** obtained by methylation of **4** was consistent with the proposed structure. Therefore, alkaloid **4** was characterized as 6,7-dihydroxy-1,1-dimethyl-*N*-(2′-glyceryl)-1,2,3,4-tetrahydroisoquinoline.

Alkaloids **5** and **6** differed from **3** only by additional ethyl and fructopyranosyl substituents, respectively, at the N atoms. These differences were supported by ^1H and ^{13}C NMR spectroscopy (Tables 1–4), in that the data obtained for the *N*-fructopyranosyl substituent were comparable to those for the same substituent in **2**. ESI-MS spectra of **5** displayed a molecular ion at *m*/*z* 221 $[M]^{+\cdot}$ and a fragment ion at *m*/*z* 57 $[CH_2NCH_2CH_3]^{+\cdot}$, whereas the corresponding ions from **6** obtained by LSI-MS were at *m*/*z* 508 $[M + NBA]^{+\cdot}$ and *m*/*z* 191. For both alkaloids, 2D NMR such as *g*NOESY, *g*HMBC, and ^1H–^{13}C *g*COSY experiments did not provide connectivity information between additional *N*-substituents and the atoms at A or B rings, but selective irradiation of the methylenic hydrogens at δ 3.52 for **5** resulted in nOe effects on 6H-9,10, 3H-2′, and 2H-3 (Table 3), whereas irradiation at δ 1.50 and δ 3.32 for **6** showed enhancement of the signals for H-6′a,b (δ 3.38 and δ 3.54, respectively, Fig. 1), which helped to establish the structures of these alkaloids as 6,7-dihydroxy-1,1-dimethyl-*N*-ethyl-1,2,3,4-tetrahydroisoquinoline (**5**) and 6,7-dihydroxy-1,1-dimethyl-*N*-(6′-fructopyranosyl)-1,2,3,4-tetrahydroisoquinoline (**6**).

The IR, ESI-MS, ^1H and ^{13}C NMR spectroscopic data obtained from compound **7**, together with an $[\alpha]_D$ of +8.6° (*c* 1.0, H_2O), allowed this compound to be identified as 2-deoxy-D-ribono-1,4-lactone (Nakaminami et al., 1972; Kitajima et al., 1999).

The ^{13}C and ^1H NMR spectra of compound **8** were very similar to those of compound **7**, although they were measured using different solvents due to their different solubilities (DMSO-d_6 for **7** and D_2O for **8**). Compound **8** showed the presence of a γ-lactone carbonyl (δ_C 180.6), a methylene [δ_C 38.8, δ_H 2.93 (1H), 2.46 (1H)], and three carbinolic groups (δ_C 90.0, 69.3, 62.0, δ_H 3.75 (1H), 3.65 (1H), 4.40–4.42 (1H), 4.42–4.44 (1H)]. The main difference between these spectra was that the ^1H NMR spectra of compound **7** showed additional signals related to two hydroxyl groups at δ 5.53 (*br d*, *J* = 3.5 Hz) and δ 5.12 (*t*, *J* = 6.0 Hz), which disappeared on the addition of D_2O. Furthermore, ^1H–^1H COSY and TOCSY experiments led to the establishment of the γ-lactone structure for compound **8**, which was confirmed by an absorption band at 1767 cm^{-1} in its IR spectra. The positive ESI-MS spectra of compound **8** displayed a molecular ion $[M]^{+\cdot}$ at *m*/*z* 612 ($C_5H_{14}O_{22}P_6$), a base peak at *m*/*z* 284 $[CH_2CHO(HPO_3)_3H]^{+\cdot}$ and ions at *m*/*z* 256 $[H_3PO_{10}]^{+\cdot}$, whereas the negative ESI-MS displayed a base peak at *m*/*z* 63 $[PO_2]^-$ and peaks at *m*/*z* 80 $[HPO_3]^-$, 98 $[H_3PO_4]^-$ 160 $[H_2P_2O_6]^-$, and 224 $[H_3P_3O_8]^-$, which suggested the presence of two tripolyphosphate groups in the molecule. The ^{31}P NMR spectrum corroborated this suggestion, since it showed a broad signal at δ_P −7.93 (Bovey, 1988; Harris et al., 2001). Therefore, **8** was characterized as 2-deoxy-D-ribono-3,5-bis(tripolyphosphate)-1,4-lactone.

It has been reported that salsolinol (**1**) and *N*- and *O*-methylated salsolinols were isolated from several Papaveraceae and Asclepiadaceae plants, and from tissue-cultured cells derived from these plants (Iwasa et al., 1993). Salsolinol (**1**) is formed by the condensation of dopamine with acetaldehyde, and it has been suggested that the *O*-methylating enzymes of salsolinol may be different from those of dopamine (Iwasa et al., 1993). These proposed biosynthetic pathways led us to suggest that the alkaloids **3**–**6** come from acetoacetate condensation with a dopamine derivative followed by decarboxylation.

3. Experimental

3.1. General experimental procedures

The NMR spectra were measured on a Varian spectrometer (11.7 T) at 500 MHz (^1H), 126 MHz (^{13}C), 51 MHz (^{15}N), and 202 MHz (^{31}P), using the solvents as an internal standards unless otherwise noted. ^{15}N *g*HMBC spectra (optimized for *J* = 10 Hz) were calibrated using nitromethane as an external standard and by setting the chemical shift to 381.9 so that the ^{15}N chemical shifts were reported relative to liquid ammonia; ^{31}P and ^{13}C NMR spectra were calibrated using H_3PO_4 and 1,4-dioxane, respectively, as external standards (Harris et al., 2001). Mass spectra were obtained on an ITD 800 Finnigan MAT (ion trap detector) spectrometer (EI-MS) and on a Fisons Platform II by flow injection into the electrospray source (ESI-MS). The instrument was operated in the positive and negative ion mode. LSI-MS was recorded on a VG Quattro spectrometer by bombardment of samples (dissolved in a nitrobenzyl alcohol matrix) with Cesium, 20 kV. The IR spectra

were obtained on a Nicolet-730 FT-IR spectrometer using KBr discs. UV absorption was measured in a Hewlett Packard 8452 A diode array spectrophotometer. Optical rotations were measured on a Polamat A Carl Zeiss Jena. Melting points were recorded on a Fisher–John melting point apparatus and were uncorrected.

3.2. Standard chemicals

Salsolinol, fructose, sucrose and glycerol were purchased from either Aldrich Chemical Co. or Sigma Chemical Co.

3.3. Plant material

The plant material was collected in Araraquara, SP, Brazil, and identified as *A. arcuata* Mast. (cv. *silvestris* Hoehne) by Dr. Condorcet Aranha. A voucher specimen was deposited at the herbarium of the Instituto Agronômico de Campinas, Campinas SP, Brazil (Watanabe and Lopes, 1995). The fresh leaves (2.55 kg) of *A. arcuata* were dried, ground and extracted exhaustively at room temp. with hexane, Me_2CO, and EtOH successively, and then conc. as previously described (Watanabe and Lopes, 1995).

3.4. Isolation

The acetone extract (6.0 g) was fractionated by CC (silica gel, 100.0 g, $CHCl_3$–MeOH–0.5% NH_4OH, gradient) to give 13 fractions. Fr. 2 gave eupomatenoid-7 (150 mg); fr. 4 gave **4** (94 mg), fr. 3 by repetitive precipitation from acetone gave **7** (precipitate, 17 mg) and the combined acetone solutions after concentration gave **8** (5 mg). Frs. 9–13 were individually subjected to crystallization from acetone + H_2O to give sequoyitol (523 mg), fructose (317 mg), sucrose (687 mg), and glycerol (>44 mg), respectively. The yield of this last compound (liquid) could not be determined since fr. 13 and subsequent solutions were subjected to concentration under reduced pressure, and the glycerol was partially evaporated together with the solvents. By CC (PVPP 10 g, MeOH), fr. 5 gave **3** (20 mg), **4** (12 mg), and **5** (3 mg); fr. 6 gave **6** (18 mg), and pinitol (17 mg); fr. 7 gave **1** (17 mg) and **3** (3mg); and fr. 8 gave **2** (8 mg), **6** (10 mg), and pinitol (7 mg).

3.5. 6,7-Dihydroxy-1-methyl-N-(6′-fructopyranosyl)-1,2,3,4-tetrahydroisoquinoline (2)

Amorphous brownish solid, 105° decomp. (MeOH). $[\alpha]_D^{25}$ −45° (MeOH;*c* 1.90). (Found: C, 57.0; H, 7.0. $C_{16}H_{23}O_7N$ requires: C, 56.3; H, 6.8%). UV λ_{max}^{MeOH} nm (ε): 290 (2.9). Positive ESI-MS (probe) 70 eV, *m/z* (rel. int.): 342 $[M+H]^+$ (2), 279 (28), 205 (11), 203 (37), 194 (100), 178 (26), 163 (28), 150 (13), 61 (43). IR ν_{max}^{KBr} cm^{-1}: 3404, 2942, 1634, 1385, 1071. For ^1H NMR and ^{13}C NMR, see Tables 1 and 2.

3.6. 6,7-Dihydroxy-1,1-dimethyl-1,2,3,4-tetrahydroisoquinoline (3)

Amorphous brownish solid, 250° decomp. (MeOH). $[\alpha]_D^{25}$ +13° (Me_2CO;*c* 0.61). (Found: C, 68.3; H, 7.9. $C_{11}H_{15}O_2N$ requires: C, 68.4; H, 7.8%). UV λ_{max}^{MeOH} nm (ε): 289 (3.0). Positive ESI-MS (probe) 70 eV, *m/z* (rel. int.): 194 $[M+H]^+$ (100%). IR ν_{max}^{KBr} cm^{-1}: 3399, 2962, 1617, 1528, 1438, 1380, 1235. For ^1H NMR and ^{13}C NMR see Tables 3 and 4; ^{15}N NMR (51 MHz, D_2O) δ 51.2 see Results and discussion section.

3.7. 6,7-Dihydroxy-1,1-dimethyl-N-(2′-glyceryl)-1,2,3,4-tetrahydroisoquinoline (4)

Amorphous brownish solid, 174° decomp. (MeOH). $[\alpha]_D^{25}$ −11° (MeOH;*c* 0.72). (Found: C, 63.0; H, 8.0. $C_{14}H_{21}O_4N$ requires: C, 62.9; H, 7.9%). UV λ_{max}^{MeOH} nm (ε): 286 (3.1). LSI-MS (nitrobenzyl alcohol matrix) 20 kV*m/z* (rel. int.): 267 $[M]^{+\cdot}$ (100%), 563 $[CH_2NCH(CH_2OH)_2+3NBA+H]^+$ (73), 251 $[M\text{-}16]^{+\cdot}$ (72), 284 $[(CH_3)_2CNCH(CH_2OH)_2+NBA]^{+\cdot}$ (65). Positive ESI-MS (probe) 70 eV, *m/z* (rel. int.): 268 $[M+H]^+$ (100%), 267 $[M]^{+\cdot}$ (8). IR ν_{max}^{KBr} cm^{-1}: 3406, 3036, 2980, 2934, 2830, 1627, 1532, 1385, 1229, 1045. For ^1H NMR and ^{13}C NMR see Tables 3 and 4; ^{15}N NMR (51 MHz, D_2O) δ 51.6 see Results and discussion section.

A sample of **4** (2 mg) was subjected to methylation (CH_2N_2, standard conditions) and yielded **4a** (2 mg). Positive ESI-MS (probe) 70 eV, *m/z* (rel. int.): 318 $[M+Na]^+$ (5%), 159 (39), 144 (28), 131 (43), 116 (71), 115 (100).

3.8. 6,7-Dihydroxy-1,1-dimethyl-N-ethyl-1,2,3,4-tetrahydroisoquinoline (5)

Amorphous brownish solid, 184° decomp. (MeOH). $[\alpha]_D^{25}$ +13° (MeOH;*c* 0.70). (Found: C, 70.5; H, 8.6. $C_{13}H_{19}O_2N$ requires: C, 70.6; H, 8.7%). UV λ_{max}^{MeOH} nm (ε): 285 (3.5). Positive ESI-MS (probe) 70 eV, *m/z* (rel. int.): 222 $[M+H]^+$ (22%), 221 $[M]^{+\cdot}$ (23), 194 (100), 57 (28). IR ν_{max}^{KBr} cm^{-1}: 3445, 2924, 2858, 1635, 1466, 1384, 1046. For ^1H and ^{13}C NMR, see Tables 3 and 4.

3.9. 6,7-Dihydroxy-1,1-dimethyl-N-(6′-fructopyranosyl)-1,2,3,4-tetrahydroisoquinoline (6)

Amorphous brownish solid, 105° decomp. (MeOH). $[\alpha]_D^{25}$ −44° (MeOH;*c* 0.26). (Found: C, 57.8; H, 7.2. $C_{17}H_{25}O_7N$ requires: C, 57.5; H, 7.1%). UV λ_{max}^{MeOH} nm (ε): 287 (3.4). IR ν_{max}^{KBr} cm^{-1}: 3441, 2969, 1631, 1529,

1454, 1383. LSI-MS (nitrobenzyl alcohol matrix) 20 kV, *m/z* (rel. int.): 508 $[M+NBA]^{+\cdot}$ (1%), 359 $[206+NBA]^{+}$ (4), 329 $[176+NBA]^{+}$ (7), 289 $[136+NBA]^{+\cdot}$ (7), 195 (15), 194 (100), 191(8). For ^{1}H and ^{13}C NMR, see Tables 1 and 2.

*3.10. 3,4-Trans(erythro)-3,5-Bis(tripolyphosphate)-4-pentanolide or 2-deoxy-D-ribono-3,5-bis(tripolyphosphate)-1,4-lactone (**8**)*

Colorless solid, mp. 189–190 °C (MeOH). $[\alpha]_D^{25}$ −1.9−(H_2O;*c* 1.65). (Found: C, 9.7; H, 2.3. $C_5H_{14}O_{22}P_6$ requires: C, 9.8; H, 2.3%). Positive ESI-MS (probe) 70 eV, *m/z* (rel. int.): 612 $[M]^{+\cdot}$ (38%), 386 (57), 364 (47), 338 (54), 284 (100), 256 (48), 225 (23), 100 (28), 84 (38). Negative ESI-MS (probe) 40 eV, *m/z* (rel. int.): 611 $[M-H]^{-}$ (<1%), 315 (4), 293 (7), 224 (3), 195 (8), 160 (5), 98 (8), 80 (7), 63 (100). IR ν_{max}^{KBr} cm^{-1}: 3406, 2941, 1767, 1639, 1382, 1192, 1082. ^{1}H NMR (500 MHz, D_2O): δ 4.44–4.42 (1H, *m*, H-4), 4.42–4.40 (1H, *m*, H-3), 3.75 (1H, *dd*, *J* = 12.5, 3.0, H-5), 3.65 (1H, *dd*, *J* = 12.5, 4.5, H-5), 2.93 (1H, *dd*, *J* = 18.5, 7.0, H-2), 2.46 (1H, *dd*, *J* = 18.5, 3.0, H-2). ^{31}P NMR (202 MHz, D_2O): δ −7.93 (*br s*). ^{13}C NMR (126 MHz, D_2O): δ (C-1–C-5): 180.6, 38.8, 69.3, 90.0, 62.0.

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