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Polyoxygenated cyclohexene derivatives from *Monanthotaxis congoensis*

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Abstract

A phytochemical investigation of *Monanthotaxis congoensis* afforded eight new polyoxygenated cyclohexenes as well as the known compound crotepoxide. The structures were determined using NMR, MS, and optical rotation. One of the new compounds (**7**) displayed moderate antiproliferative activity against NCI-H460 and M14 cancer cells.

Keywords

Monanthotaxis congoensis; Annonaceae; polyoxygenated cyclohexene; cytotoxicity

1. Introduction

Natural product libraries screened against biological targets continue to be valuable sources of structurally diverse compounds that provide leads and inspiration for drug discovery and development. In our continuing effort to explore minor components of plants, we have applied our miniaturized high-throughput natural product discovery process (Eldridge et al., 2002; Hu et al., 2005) to a taxonomically diverse set of plants. This process, which involves prefractionation of plant extracts into 96-well format library, enables the compounds at low concentrations in plants to be screened at normalized, detectable concentrations in biological assays. A screen of the resulting natural product library for cytotoxicity against a small panel of human cancer cells revealed an active well from the African shrub *Monanthotaxis congoensis* Baill. (Annonaceae). From this well we isolated eight new polyoxygenated cyclohexenes (**1-8**) along with the known polyoxygenated cyclohexane crotepoxide (**9**). One of the new compounds (**7**) displayed moderate antiproliferative activity against human cancer cells.

2. Results and discussion

An organic extract of *M. congoensis* was subjected to normal phase flash chromatography and reversed phase HPLC to yield eight new cyclohexenes (**1-8**) and one known cyclohexane (**9**). For each new compound, ¹H chemical shifts are listed in Table 1, and ¹³C chemical shifts are listed in Table 2. Crotepoxide was identified by examination of the 1D

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and 2D NMR data, and by comparison with published chemical shifts and optical rotation data (Kupchan et al., 1969; Nighat et al., 2009).

The HRESIMS of **1** indicated a molecular formula of $C_{18}H_{20}O_8$. The 1H and HSQC NMR spectra indicated the presence of two acetates, a benzoate, three oxygenated methines (δ_H 5.71, 5.30, 4.48), and two olefinic methines (δ_H 5.77, 5.59). These data and the HMBC and COSY spectra were consistent with an oxygenated cyclohexene. The locations of the benzoate and acetate groups were assigned based on HMBC correlations and chemical shifts of the adjacent protons, and the relative stereochemistry was assigned based on ROESY correlations and proton coupling constants. In particular, a ROESY correlation between H-3 and H-7 indicated that H-3 and the C-7 methylene group are on the same face of the cyclohexene ring in a 1,3 diaxial orientation. Similarly, a ROESY correlation between H-2 and H-6 placed these two protons in a 1,3 diaxial orientation on the opposite face of the cyclohexene ring.

Due to the small size of **1** and the possibility of allylic coupling across the double bond, placement of the double bond was not straightforward; two different isomeric structures (**1** and **1a**) initially appeared consistent with the available NMR data. Upon searching the literature, we found that the chemical shifts closely matched those reported for (–)-senediol (Lange et al., 1992), which has the same planar structure and relative configuration as **1**. In contrast, the chemical shifts reported for a compound with the same planar structure as **1a** [compound 9 in reference (Kupchan et al., 1969)] did not match those of our compound. We thus hypothesized that the double bond should be placed as in **1**. Structure **1** was further supported by the appearance of H-6 as a broad singlet; for structure **1a**, one would expect a larger coupling constant between this proton signal (which would be assigned to H-4) and H-3. To better quantitate these expected coupling constants, structures of **1** and **1a** were drawn and their energies minimized using Chem3D (CambridgeSoft). Structure **1** had a dihedral angle of 87.4° between H-5 and H-6, corresponding to a coupling constant of 1.4 Hz using the Karplus equation, whereas structure **1a** had a dihedral angle of 159.3° , corresponding to a coupling constant of 9.2 Hz. Thus, we concluded that this compound has the structure **1** (relative configuration).

Compound **1** has the same planar structure and relative configuration as (–)-senediol, but its specific rotation of **1** is opposite in sign (Hollands et al., 1968). We have thus assigned the name (+)-senediol **1**, with the absolute configuration as drawn. (–)-Senediol was originally prepared as an unnamed synthetic derivative of senepoxide (Hollands et al., 1968), the absolute configuration of which was determined using Horeau's method (Horeau, 1961) and circular dichroism. It was later isolated as a natural product from *Piper ribesioides*, at which point it was given the name (–)-senediol (Ruangrunsi et al., 1992).

A compound named artabotrene has been described in the literature and assigned the structure **1a** (Murphy et al., 2008). Its NMR data closely matched those of compound **1**, and it has a positive optical rotation. Thus, we concluded that these two samples are the same compound, and that the structure of artabotrene should be revised to be **1**.

HRESIMS indicated that **2** is isomeric with **1**. The 1H NMR spectra of the two compounds were similar, except that the sharp H-2 doublet of **1** (δ_H 5.30) had shifted upfield in **2** (δ_H 4.03), and likewise, the broad H-6 singlet of **1** (δ_H 4.48) had shifted downfield in **2** (δ_H 5.52). This suggested that the two acetates in **2** should be placed at the 3- and 6-positions. Coupling constants and ROESY correlations indicated that the relative stereochemistry is the same as for **1**.

Compound **3** has a molecular formula of $C_{20}H_{22}O_9$, consistent with a structure containing one more acetate than compound **1**. Its 1H NMR spectrum resembled that of **1**, but had

signals for three acetate methyl groups (δ_{H} 1.96, 2.02, 2.03), and the signals for H-2, H-3, and H-6 were all shifted downfield consistent with the attachment of acetate groups. Thus, **3** is the 6-acetyl analogue of **1**.

Compounds **4** and **5** each have a molecular formula of $\text{C}_{16}\text{H}_{18}\text{O}_7$, consistent of one fewer acetate group than **1**. In compound **4**, the remaining acetate was determined to be at the 2-position based on the downfield chemical shift of the sharp H-2 doublet (δ_{H} 5.05). The location of H-2 was further supported by its coupling to H-3 ($J = 6$ Hz) and an HMBC correlation to C-7. The relative configuration of **4** was determined to be the same as in compounds **1-3** based on coupling constants and ROESY correlations; in particular, ROESY correlations were observed between H-2 and H-6 (δ_{H} 4.37), and between H-3 (δ_{H} 4.39) and H-7 (δ_{H} 4.64, 4.69).

In compound **5**, the remaining acetate was placed at the 3-position based on the downfield chemical shift of the broad H-3 singlet (δ_{H} 5.59). The assignment of H-3 was confirmed by HMBC correlations to the acetate carbonyl carbon (δ_{C} 170.7) and to C-4 (δ_{C} 124.7) and C-5 (δ_{C} 131.9), as well as a COSY correlation to H-2 (δ_{H} 3.95). The ROESY spectrum also supported the relative stereochemistry as drawn, via correlations analogous to those described for **4**.

HRESIMS indicated that compound **6** has a molecular formula of $\text{C}_{16}\text{H}_{22}\text{O}_7$. Its ^1H spectrum contained signals for one acetate group, plus a triplet methyl group and an oxygenated methine. These data suggested that **6** is substituted with one acetate group and one ethoxyl group. Based on chemical shifts, the acetate and ethoxyl groups were placed at H-2 and H-6, respectively. These placements were further supported by an HMBC correlation from H-2 (δ_{H} 5.06) to the acetate carbonyl carbon (δ_{C} 171.8), and a ROESY correlation between H-6 (δ_{H} 4.12) and the ethoxyl methylene protons (δ_{H} 3.74, 3.83). Compound **6** is thus the 6-ethoxy derivative of **4**.

HRESIMS of **7** indicated that it is isomeric with **1**. Examination of chemical shifts and 2D NMR data indicated that compounds **1** and **7** share a planar structure as well. As in **1**, a ROESY correlation between H-2 and H-6 in **7** placed the substituents at positions 2 and 6 on the same face of the cyclohexene ring. Likewise, the coupling constant between H-2 and H-3 ($J = 8$ Hz) indicated *trans* placement of the substituents at the 2 and 3 positions. Thus, compounds **1** and **7** must differ in the configuration at C-1. This arrangement is consistent with the lack of ROESY correlation between H-3 and H-7, a correlation that was observed for the other compounds in the series but not for **7**. A compound (**7a**) with the same relative configuration but an optical rotation of opposite sign has been reported (Liu et al., 2009). Based on the differing signs for optical rotation, we assigned the absolute configuration of **7** as shown. In the original report of **7a**, however, the absolute configuration was assigned based on a weak Cotton effect, and so this assignment should be considered tentative.

The molecular formula and NMR data for **8** were consistent with the presence of two acetate groups and one ethoxyl group. Based the chemical shifts of H-2, H-3, and H-6, the acetates were placed at positions 2 and 3, and the ethoxyl group at position 6. This assignment was further supported by an HMBC correlation from H-6 (δ_{H} 4.19) to the methylene carbon of the ethoxyl group (δ_{C} 68.5). The configurations at positions 2, 3, and 6 were assigned based on ROESY correlations and coupling constants; thus, compound **8** represented the 6-ethoxy derivative of compound **1** or **7**. The configuration at position 1 was assigned to be the same as in **7** based on the lack of ROESY correlation between H-3 and H-7.

All of the compounds isolated were initially screened for inhibition of cell proliferation against NCI-H460 lung cancer cells in vitro. Only **7** showed > 50% inhibition at 5 $\mu\text{g}/\text{ml}$. Its

IC₅₀ was then determined to be 7 μ M against NCI-H460 cells, and 14 μ M against M14 melanoma cells.

3.1. Concluding remarks

In this study, a phytochemical investigation of *Monanthotaxis congoensis* afforded eight new polyoxygenated cyclohexenes as well as the known compound crotopoxide. Their antiproliferative activity has been evaluated. Polyoxygenated cyclohexene natural products have previously been isolated from plants families including the Annonaceae, Euphorbiaceae, Piperaceae, and Zingiberaceae (Stevenson et al., 2007; Taneja et al., 1991; Zhang et al.) (Kupchan et al., 1969). Several have been reported to have biological activity, including antitumor (Kupchan et al., 1969) and antimicrobial (Wirasathien et al., 2006) activities. The polyoxygenated cyclohexenes are synthetically accessible targets for drug development, as evidenced by the reported stereoselective syntheses of **9** and other related compounds (Shing and Tam, 1998).

3. Experimental

3.1. General experimental procedures

NMR spectra were acquired at 600 MHz on a Bruker Avance 600 MHz spectrometer equipped with a 5 μ l CapNMR capillary microcoil probe with a 1.5 μ l active volume (Magnetic Resonance Microsystems, Savoy, IL). Spectra for compound **5**, which was available in a very limited amount, were also obtained in the Bruker BioSpin TCI 1.7 mm MicroCryoProbe. For each compound, ¹H, gCOSY, ROESY, HSQC, and HMBC spectra were acquired; ¹³C chemical shifts were obtained from the HSQC and HMBC spectra. Spectra were recorded in CDCl₃, and chemical shifts are reported with respect to the residual non-deuterated solvent signal. HRESIMS was done on a Waters LCT time-of-flight mass spectrometer with an electrospray interface and polyethylene glycol as the internal standard. The amount of each compound isolated was determined using HPLC/ELSD as previously described (Hu et al., 2005). Semipreparative HPLC was performed on a Beckman HPLC system including a Beckman 168 diode array UV detector, a Sedere Sedex 75 ELSD detector, and an ISCO Foxy Jr. fraction collector. A splitter was used to divert 10% of the eluent to the ELSD detector, while the rest passed through the diode array UV detector and was then collected. UV_{max} values were taken from the diode array detector during semipreparative HPLC purification in 15-50% CH₃CN with 0.05% TFA. Optical rotation was measured on Jasco P-1010 polarimeter using a 100 μ L cell with a 0.1 dm path length. Coupling constants were calculated from the Karplus equation using MestReJ (v1.1).

3.2. Plant material

Leaves and green fruits of *M. congoensis* were collected from the Lope-Okanda game preserve in Gabon in November of 2000 in by J. Stone, G. Walters, J.M. Moussavou, and B. Nziengui of the Missouri Botanical Garden. The plant was identified by Y. Issembe. A voucher specimen (#Stone-3151) is kept at the Missouri Botanical Garden (USA).

3.3 Extraction and isolation

Compounds **1-9** were isolated using published methods (Eldridge et al., 2002). Approximately 150 g of dry leaves and fruit were extracted over a 24 h period with EtOH/EtOAc (1:1 v/v, 2 $\times$ 750 ml) to yield 9.59 g dry extract. This extract was separated by silica gel flash chromatography in 1 g portions as previously described (Eldridge et al., 2002) to generate flash fractions 1-5. Fraction 2 material (which eluted in hexanes-EtOAc, 3:1 v/v) from four runs (328 mg) was pooled and applied to a 5 g C18 solid phase extraction (SPE) column (Phenomenex Strata C18-E) that had been equilibrated in 50% MeOH. The column was then eluted with MeOH (30 ml) to yield 250 mg SPE product. A portion (50 mg) of the

SPE product was then separated by reversed phase preparative HPLC to generate the *M. congoensis* fraction 2 library. The chromatography employed a Thermo Electron Betasil C18 column (5 μ m particle size, 250 $\times$ 21.2 mm) with a flow rate of 20 ml/min. The column was eluted with CH₃CN-H₂O (60:40) for 2 min, followed by a 30 minute gradient to CH₃CN. The solvents contained 0.05% (v/v) TFA. Forty one-minute fractions were collected from 0-40 min.

The active compounds of interest were isolated from preparative HPLC fractions 3-5 on a semi-preparative HPLC system. Multiple injections were performed using a Phenomenex Synergi Fusion-RP 80 (4 μ m particle size, 250 $\times$ 10 mm) at 3.0 ml/min. The gradient ran from 15%-50% CH₃CN in H₂O over 55 mins. The solvents contained 0.05% TFA. The amount of each compound was estimated by ELSD using the process detailed by Hu et al (2005). A typical run yielded: Compound **1** (110 μ g), **2** (5 μ g), **3** (65 μ g), **4** (65 μ g), **5** (35 μ g), **6** (10 μ g), **7** (60 μ g), **8** (60 μ g), and **9** (7 μ g). Twenty-six runs were carried out to provide material for structure determination, activity assessment, and measurement of optical rotation.

3.4 Cytotoxicity assay

NCI-H460 (lung carcinoma) cells were obtained from ATCC, and M14 (melanoma) cells were obtained from the National Cancer Institute. Cells were grown in RPMI-1640 with 10% FBS supplemented with L-glutamine and HEPES. Cells were seeded into 96-well plates at 6×10^2 cells/well and 5×10^3 cells/well, respectively, and allowed to adhere overnight; the medium was then removed. A stock solution of test compound in DMSO was diluted in medium to generate a series of working solutions. Aliquots (100 μ l) of the working solutions were added to the appropriate test wells to expose cells to the final concentrations of compound in a total volume of 100 μ l. Eight different concentrations were tested, with 2-5 wells per concentration. Camptothecin was used as a positive control; wells containing vehicle without compound were used as negative controls. Plates were kept for 48-72 h in a 37° C, 5% CO₂ incubator. After incubation, viable cells were detected with the CellTiter 96 AQueous Non-Radioactive Cell Proliferation Assay (Promega). Dose-response curves were generated and IC₅₀ values were determined using GraphPad Prism 5 software.

3.6 (+)-Senediol (**1**)

$[\alpha]_D^{25} +198^\circ$ (c 2.33, MeOH); UV $\lambda_{\max}$ 202, 232, 275 nm; ¹H: see Table 1; ¹³C NMR: see Table 2; HR-ESIMS m/z 356.1256 [M+H]⁺ (calcd for C₁₈H₂₁O₈: 356.1236).

3.7 1S,2R,3R,4S-2-[(benzoyloxy)methyl]cyclohex-5-ene-1,2,3,4-tetrol, 1,4-diacetate (**2**)

$[\alpha]_D^{25} +164^\circ$ (c 0.037, MeOH); UV $\lambda_{\max}$ 200, 232, 277 nm; ¹H: see Table 1; ¹³C NMR: see Table 2; HR-ESIMS m/z 365.1213 [M+H]⁺ (calcd for C₁₈H₂₁O₈: 365.1236).

3.8 1S,2R,3R,4S-2-[(benzoyloxy)methyl]cyclohex-5-ene-1,2,3,4-tetrol, 1,3,4-triacetate (**3**)

$[\alpha]_D^{25} +355^\circ$ (c 0.355, MeOH); UV $\lambda_{\max}$ 204, 232, 274 nm; ¹H: see Table 1; ¹³C NMR: see Table 2; HR-ESIMS m/z 407.1329 [M+H]⁺ (calcd for C₂₀H₂₃O₉: 407.1342).

3.9 1S,2R,3R,4S-2-[(benzoyloxy)methyl]cyclohex-5-ene-1,2,3,4-tetrol, 3-acetate (**4**)

$[\alpha]_D^{25} +368^\circ$ (c 0.283, MeOH); UV $\lambda_{\max}$ 204, 236, 276 nm; ¹H: see Table 1; ¹³C NMR: see Table 2; HR-ESIMS m/z 323.1126 [M+H]⁺ (calcd for C₁₆H₁₉O₇: 323.1131).

3.10 1S,2R,3R,4S-2-[(benzoyloxy)methyl]cyclohex-5-ene-1,2,3,4-tetrol, 4-acetate (**5**)

$[\alpha]_D^{25} +452^\circ$ (c 0.089, MeOH); UV $\lambda_{\max}$ 205, 233, 275 nm; ¹H: see Table 1; ¹³C NMR: see Table 2; HR-ESIMS m/z 323.1115 [M+H]⁺ (calcd for C₁₆H₁₉O₇: 323.1131).

3.11 1S,2R,3R,4S-1-ethoxy-2-[(benzoyloxy)methyl]cyclohex-5-ene-2,3,4-triol, 3-acetate (6)

$[\alpha]_D^{25} +237^\circ$ (c 0.042, MeOH); UV $\lambda_{\max}$ 200, 232, 275 nm; ^1H : see Table 1; ^{13}C NMR: see Table 2; HR-ESIMS m/z 351.1464 $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{16}\text{H}_{23}\text{O}_7$: 351.1444).

3.12 1S,2S,3R,4S-2-[(benzoyloxy)methyl]cyclohex-5-ene-1,2,3,4-tetrol, 3,4-diacetate (7)

$[\alpha]_D^{25} +420^\circ$ (c 0.055, MeOH); UV $\lambda_{\max}$ 205, 232, 274 nm; ^1H : see Table 1; ^{13}C NMR: see Table 2; HR-ESIMS m/z 365.1265 $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{18}\text{H}_{21}\text{O}_8$: 356.1236).

3.13 1S,2S,3R,4S-1-ethoxy-2-[(benzoyloxy)methyl]cyclohex-5-ene-2,3,4-triol, 3,4-diacetate (8)

$[\alpha]_D^{25} +283^\circ$ (c 0.33, MeOH); UV $\lambda_{\max}$ 204, 232, 274 nm; ^1H : see Table 1; ^{13}C NMR: see Table 2; HR-ESIMS m/z 410.1849 $[\text{M}+\text{NH}_4]^+$ (calcd for $\text{C}_{20}\text{H}_{28}\text{NO}_8$: 410.1815).

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References

- Eldridge GR, Vervoort HC, Lee CM, Cremin PA, Williams CT, Hart SM, Goering MG, O'Neil-Johnson M, Zeng L. High-Throughput Method for the Production and Analysis of Large Natural Product Libraries for Drug Discovery. *Anal. Chem.* 2002; 74:3963–3971. [PubMed: 12199561]
- Hollands R, Becher D, Gaudemer A, Polonsky J, Ricroch N. Constituents of *Uvaria catocarpa* fruits. Structure of senepoxide and seneol. *Tetrahedron.* 1968; 24:1633–1650.
- Horeau A. Principle and applications of a new method of determination of configurations termed “by partial resolution.”. *Tetrahedron Lett.* 1961:506–512.
- Hu J-F, Garo E, Yoo H-D, Cremin PA, Zeng L, Goering MG, O'Neil-Johnson M, Eldridge GR. Application of capillary-scale NMR for the structure determination of phytochemicals. *Phytochem. Anal.* 2005; 16:127–133. [PubMed: 15881121]
- Kupchan SM, Hemingway RJ, Smith RM. Tumor inhibitors. XLV. Crotepoxide, a novel cyclohexane diepoxide tumor inhibitor from *Croton macrostachys*. *The Journal of Organic Chemistry.* 1969; 34:3898–3902. [PubMed: 5390655]
- Lange GL, Organ MG, Ruangrunsi N, Prathanturug S. An N-methyl aristolactam and an oxygenated cyclohexane derivative from *Piper ribesioides*. *Phytochemistry.* 1992; 31:2397–2400.
- Liu A, Xu L, Zou Z. Studies on chemical constituents of *Uvaria tonkinensis* var. subglabra. *Zhongguo Zhongyao Zazhi.* 2009; 34:567–570. [PubMed: 19526784]
- Murphy BT, Cao S, Brodie PJ, Miller JS, Ratovoson F, Birkinshaw C, Rakotobe E, Rasamison VE, Tendyke K, Suh EM, Kingston DGI. Antiproliferative compounds of *Artabotrys madagascariensis* from the Madagascar rainforest. *Nat. Prod. Res.* 2008; 22:1169–1175. [PubMed: 18855218]
- Nighat N, Koul S, Qurishi MA, Taneja SC, Qazi GN. Lipase catalyzed regioselective hydrolysis of Crotepoxide isolated from *Piper cubeb* Cass DC. *Journal of Molecular Catalysis B: Enzymatic.* 2009; 59:121–125.
- Ruangrunsi N, Prathanturug S, Lange GL, Organ MG. Studies on Thai Medicinal Plants. Part 13. An N-methyl aristolactam and an oxygenated cyclohexane derivative from *Piper ribesioides*. *Phytochemistry.* 1992; 31:2397–2400.

- Shing TKM, Tam EKW. Enantiospecific Syntheses of (+)-Crotepoxide, (+)-Boesenoxide, (+)- $\dot{I}^2$ -Senepoxide, (+)-Pipoxide Acetate, (-)-iso-Crotepoxide, (-)-Senepoxide, and (-)-Tingtanoxide from (-)-Quinic Acid. *J. Org. Chem.* 1998; 63:1547–1554.
- Stevenson PC, Veitch NC, Simmonds MSJ. Polyoxygenated cyclohexane derivatives and other constituents from *Kaempferia rotunda* L. *Phytochemistry* (Elsevier). 2007; 68:1579–1586.
- Taneja SC, Koul SK, Pushpangadan P, Dhar KL, Daniewski WM, Schilf W. Oxygenated cyclohexanes from *Piper species*. *Phytochemistry*. 1991; 30:871–874.
- Wirasathien L, Pengsuparp T, Moriyasu M, Kawanishi K, Suttisri R. Cytotoxic C-benzylated chalcone and other constituents of *Ellipeiopsis cherreensis*. *Arch. Pharmacol Res.* 2006; 29:497–502.
- Zhang C-R, Wu Y, Yue J-M. Polyoxygenated seco-cyclohexene derivatives from *Uvaria tonkinensis* var. *subglabra*. *Zhongguo Tianran Yaowu*. 8:84–87.

Highlights

- Eight new polyoxygenated cyclohexenes were isolated from *Monanthotaxis congoensis*.
- The compounds were isolated using a high-throughput natural products discovery approach.
- The structures were determined using NMR, MS, and optical rotation.
- One of the new compounds displayed moderate antiproliferative activity against NCI-H460 and M14 cancer cells.

Table 1

¹H NMR Spectroscopic Data for **1-9**^a

Proton	1	2	3	4	5 ^b	6	7	8
2	5.30 <i>d</i> (8.6)	4.03 <i>d</i> (8.5)	5.39 <i>d</i> (8.3)	5.05 <i>d</i> (6.0)	3.95 <i>d</i> (6.9)	5.06 <i>d</i> (7.7)	5.36 <i>d</i> (7.9)	5.31 <i>d</i> (8.8)
3	5.71 <i>br d</i> (8.2)	5.54 <i>br d</i> (8.8)	5.67 ^d	4.39 <i>d</i> ^d	5.59 <i>br d</i> (6.4)	4.43 <i>br d</i> (7.5)	5.75 <i>br d</i> (8.0)	5.72 ^d
4	5.59 <i>br d</i> (9.8)	5.81 <i>br d</i> (10.1)	5.69 <i>br d</i> (11.5)	5.85 ^d	5.62 <i>br d</i> (10.5)	5.83 <i>br d</i> (10.9)	5.81 <i>br d</i> (10.7)	5.71 ^d
5	5.77 <i>br d</i> (10.4)	5.67 <i>br d</i> (10.5)	5.79 <i>br d</i> (10.7)	5.85 ^d	5.87 <i>br d</i> (10.5)	5.79 <i>br d</i> (11.0)	5.93 <i>br d</i> (10.3)	5.84 <i>br d</i> (10.0)
6	4.48 <i>br s</i>	5.52 <i>br s</i>	5.62 <i>br s</i>	4.37 ^d	4.35 <i>br s</i>	4.12 <i>br s</i>	4.82 ^d	4.19 <i>br s</i>
7	4.58 <i>d</i> (12.3)	4.59 <i>d</i> (11.9)	4.55 <i>s</i> , 2H	4.64 <i>d</i> (12.6)	4.64 <i>d</i> (12.0)	4.58 <i>d</i> (12.9)	4.60 <i>d</i> (12.3)	4.56 <i>d</i> (13.0)
	4.63 <i>d</i> (12.6)	4.65 <i>d</i> (12.1)		4.69 <i>d</i> (12.6)	4.82 <i>d</i> (12.4)	4.68 <i>d</i> (12.9)	4.84 <i>d</i> ^d	4.79 <i>d</i> (13.2)
2', 6'	8.03 <i>d</i> (7.8)	8.02 <i>d</i> (7.6)	8.02 <i>d</i> (7.8)	8.06 <i>d</i> (7.8)	8.05 <i>d</i> (7.6)	8.08 <i>d</i> (7.8)	8.10 <i>d</i> (7.3)	8.10 <i>d</i> (7.8)
3', 5'	7.42 <i>t</i> (7.7)	7.46 <i>t</i> (7.4)	7.43 <i>t</i> (7.7)	7.47 <i>t</i> (7.7)	7.47 <i>t</i> (7.7)	7.47 <i>t</i> (7.7)	7.47 <i>t</i> (7.4)	7.48 <i>t</i> (7.7)
4'	7.55 <i>t</i> (7.4)	7.58 <i>t</i> (7.3)	7.56 <i>t</i> (7.3)	7.60 <i>t</i> (7.4)	7.60 <i>t</i> (7.4)	7.60 <i>t</i> (7.4)	7.60 <i>t</i> (7.7)	7.60 <i>t</i> (7.3)
2-OAc	1.87 <i>s</i>		1.96 <i>s</i>	1.98 <i>s</i>		1.88 <i>s</i>	1.84 <i>s</i>	1.77 <i>s</i>
3-OAc	1.99 <i>s</i>	2.14 <i>s</i> ^c	2.03 <i>s</i> ^c		2.12 <i>s</i>		2.06 <i>s</i>	2.04 <i>s</i>
6-OAc		2.02 <i>s</i> ^c	2.02 <i>s</i> ^c					
6-OEt						3.74 <i>m</i>		3.75 <i>quint</i> (7.6)
						3.83 <i>m</i>		3.88 <i>quint</i> (7.6)
						1.21 <i>t</i> (7.5)		1.22 <i>t</i> (7.0)

^aThe coupling constants (*J*) are in parentheses and reported in Hz; chemical shifts are given in ppm.^bNMR data obtained using Bruker BioSpin TCI 1.7 mm MicroCryoProbe^cSignals within column may be interchanged.^dCoupling constant not determined due to overlapping signals.

Table 2

¹³C NMR Spectroscopic Data for **1-9**^a

Carbon	1	2	3	4	5 ^b	6	7	8
1	76.6	nd ^c	nd ^c	75.6	75.3	76.1	76.1	77.2
2	75.3	75.7	74.8	76.7	74.1	78.1	74.8	75.3
3	71.9	72.9	71.2	68.9	72.9	69.3	70.7	71.7
4	125.4	128.3	128.8	129.2	124.7	129.0	126.8	125.4
5	132.8	128.4	127.6	129.2	131.9	128.7	130.9	131.2
6	73.9	76.8	75.6	72.5	72.2	80.9	62.0	81.3
7	64.7	63.3	63.9	65.8	63.7	65.7	66.6	66.3
7-CO	168.2	168.2	167.0	168.6	167.8	168.2	168.4	168.7
1'	126.0	130.7	130.0	129.9	127.4	129.2	129.8	130.5
2', 6'	130.2	130.2	130.2	130.1	129.7	129.8	130.3	130.3
3', 5'	128.8	129.1	129.0	128.9	128.5	128.6	129.0	128.7
4'	133.9	133.9	133.8	133.8	133.6	133.6	134.0	133.6
2-OAc	171.0, 20.9		170.8, 21.1	171.3, 21.1		171.8, 20.8	170.6, 20.7	171.2, 20.6
3-OAc	171.0, 21.2	172.8, 21.5	171.4, 21.2		170.7, 20.9		170.6, 21.3	171.2, 22.4
6-OAc		173.3, 21.3	170.8, 21.2					
6-OEt						67.8, 15.6		68.5, 15.6

^aChemical shifts are given in ppm.^bNMR data obtained using Bruker BioSpin TCI 1.7 mm MicroCryoProbe^cNot determined; no HMBC correlations were observed to allow unambiguous chemical shift assignment.