Celastrofurans A–G: Dihydro- β -agarofurans from the Australian Rainforest Vine *Celastrus subspicata* and Their Inhibitory Effect on Leucine Transport in Prostate Cancer Cells

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ABSTRACT: Seven new dihydro- β -agarofurans, celastrofurans A–G (**1–7**), along with two known secondary metabolites, 9 β -benzoyloxy-1 α -furoyloxydihydro- β -agarofuran (**8**) and (1*R*,2*R*,4*R*,5*S*,7*R*,9*S*,10*R*)-2-acetoxy-9-benzoyloxy-1-furoyloxydihydro- β -agarofuran (**9**) were obtained from the leaves of the Australian rainforest vine, *Celastrus subspicata*. The structures of the new compounds were determined by detailed spectroscopic (1D/2D NMR) and MS data analysis. The absolute configurations of compounds **1–4** were defined by ECD and single-crystal X-ray diffraction studies. All compounds were found to exhibit inhibitory activity on leucine transport in the human prostate cancer cell line LNCaP with IC₅₀ values ranging from 7.0–98.9 μ M. Dihydro- β -agarofurans **1–9** showed better potency than the L-type amino acid transporter (LAT) family inhibitor, 2-aminobicyclo[2.2.1]-heptane-2-carboxylic acid (BCH).

L-type amino acid transporters (LATs) uptake neutral amino acids including leucine into cells. LATs are vital for protein synthesis as well as stimulating the mammalian target of rapamycin complex 1 (mTORC1) signaling pathway. The mTORC1 pathway acts as a master regulator of cell growth, proliferation, and metabolism.¹ The LAT family is expressed in both normal and cancer cells, and the expression levels of LAT family members are upregulated in various human cancers, including prostate cancer.²⁻⁵ Leucine plays an important role as a rate-limiting signaling molecule in the mTORC1 pathway;^{6,7} therefore, targeting LATs by inhibiting leucine uptake affects cancer growth through the inhibition of mTORC1.³ Accordingly, the inhibition of leucine transporters may be a novel therapeutic approach for treating a variety of cancers.⁸ Currently, the leucine analogue 2-aminobicyclo[2.2.1]heptane-2-carboxylic acid (BCH) is used commonly to inhibit L-type amino acid transport in vitro with millimolar activity.⁹ In our previous studies on the chemistry of Australian Celastraceae plants, several dihydro- β -agarofurans were found to inhibit leucine transport in a prostate cancer cell line.^{10,11} As part of our ongoing investigations into the discovery and identification of bioactive dihydro- β -agarofurans from Australian plants,¹⁰⁻¹³ we conducted a phytochemical study on the leaves of *Celastrus subspicata* Hook. (Celastraceae), which had never been analyzed before.

Celastrus subspicata is a vine that is found in the rainforests of Queensland and New South Wales.¹³ Historically, the genus *Celastrus* has been broadly used in Chinese indigenous medicine.¹⁴ While plants of the genus *Celastrus* have been reported to produce sesquiterpenoids, diterpenoids, triterpenoids, and flavonoids,¹⁴ the chemistry of *C. subspicata* has been superficially explored with only one phytochemical study reported to date.¹³ A previous study on the seeds of this plant reported the isolation of two new dihydro- β -agarofurans (**10** and **11**).¹³ Herein, we report the isolation and structure elucidation of seven

new (**1–7**) and two known (**8** and **9**) dihydro- β -agarofurans as well as their leucine transport inhibitory effects on the human prostate cancer cell line, LNCaP.

RESULTS AND DISCUSSION

The CH₂Cl₂ extract of air-dried and ground leaves of *C. subspicata* was subjected to extensive chromatography to yield seven new dihydro- β -agarofurans, celastrofurans A–G (**1–7**) and two known analogues, 9 β -benzoyloxy-1 α -furoyloxydihydro- β -agarofuran (**8**) and (1*R*,2*R*,4*R*,5*S*,7*R*,9*S*,10*R*)-2-acetoxy-9-benzoyloxy-1-furoyloxydihydro- β -agarofuran (**9**) (Figure 1).

Celastrofuran A (**1**) was isolated as a white amorphous powder with a molecular formula of C₂₉H₃₄O₅ as suggested by the (+)-HRESIMS data (m/z 485.2294 [M+Na]⁺, calcd 485.2298). The ¹H NMR spectrum (Table 1) of **1** showed signals of four methyl protons (δ_H 1.12, 1.23, 1.38, and 1.39), four sets of methylene protons (δ_H 1.48/2.32, 1.72/1.99, 2.09/2.21, and 2.04/2.09), four methine protons (δ_H 1.91, 2.01, 5.04 and 5.70), and two benzoate groups (10H, δ_H 7.24, 7.31, 7.41, 7.46, 7.58, and 7.84). The ¹³C NMR (Table 2) and edited HSQC spectra revealed the presence of 29 carbons corresponding to four methyl, four methylene, 14 methine, and seven nonprotonated carbons. The ¹³C NMR resonances at δ_C 165.75 and 165.81 suggested the presence of two ester functionalities in **1**, which was further supported by the IR data that showed an absorption at 1711 cm⁻¹. These data indicated that compound **1** belonged to the dihydro- β -agarofuran class of compounds.^{10,11} The COSY spectrum (Figure 2) of **1** established the fragments of H-1/H₂-2/H₂-3/H-4/H₃-14 and H₂-6/H-7/H₂-8/H-9. The core structure of dihydro- β -agarofuran in **1** was determined by HMBC correlations (Figure 2). The two benzoate groups were located on C-1 and C-9 based on HMBC correlations from H-1 (δ_H 5.70) and H-9 (δ_H 5.04) to the ester carbonyl carbons at δ_C 165.75 and 165.81, respectively.

The relative configuration of **1** was determined based on the analysis of ROESY data (Figure 2) and ^1H - ^1H coupling constants. The β -orientation of H-1 was suggested by the large coupling constants between H-1 and H-2 ($J_{1,2} = 12.0$ Hz), while the ROESY correlations between H₃-14 and H₃-15 as well as between H-9 and H₃-15 indicated that CH₃-14, CH₃-15 and H-9 were all α -oriented. The absolute configuration of **1** was resolved by the dibenzoate chirality method,^{15,16} which has been used routinely to determine the absolute configuration of dihydro- β -agarofurans bearing two benzoate chromophores.¹⁷⁻¹⁹ The ECD spectrum of **1** (Figure 4) exhibited a Davydov-type splitting with a positive first Cotton effect at 240 nm ($\Delta\epsilon = +4.08$) and a negative second Cotton effect at 223 nm ($\Delta\epsilon = -2.67$) due to the coupling of the two benzoates at C-1 α and C-9 β . Thus, the absolute configuration of **1** was assigned as (1*S*,4*R*,5*S*,7*R*,9*S*,10*S*)-1,9-dibenzoyloxydihydro- β -agarofuran.

Celastrofuran B (**2**) was purified as stable colorless crystals and was assigned the molecular formula C₃₁H₃₆O₇ following analysis of the (+)-HRESIMS data. The ^1H and ^{13}C NMR spectra of **2** were similar with those of **1**, except for the presence of an acetate group (δ_{H} 1.79 and δ_{C} 21.2, 170.9) and an additional oxygenated methine (δ_{H} 5.33 and δ_{C} 69.5) in **2**. Detailed analysis of the HMBC spectrum revealed that the acetate group was located at C-2 in **2** since correlations from both H-2 (δ_{H} 5.33) and the methyl protons at δ_{H} 1.79 to an ester carbonyl carbon at δ_{C} 170.9 were observed. The relative configuration of **2** was assigned following analysis of ^1H - ^1H coupling constants and the ROESY spectrum. A large coupling constant ($J_{1,2} = 10.6$ Hz) between H-1 and H-2 indicated the β -orientation of H-1 and the α -orientation of H-2. The ROESY correlations between H₃-14 and H₃-15; and between H-9 and H₃-15 indicated that CH₃-14, CH₃-15 and H-9 were cofacial. The structure of **2** was confirmed by a single-crystal X-ray diffraction study (Figure 3), which also established its absolute configuration as (1*R*,2*R*,4*R*,5*S*,7*R*,9*S*,10*R*)-2-acetoxy-1,9-dibenzoyloxydihydro- β -agarofuran.

The molecular formula of compound **3** was determined as C₃₁H₃₆O₈ based on the (+)-HRESIMS data. The ¹H and ¹³C NMR spectra of **3** were very similar with those of **2**. Comparison of the NMR and MS data between **2** and **3** revealed that both compounds had the same ester substitution, but the MS data indicated that the latter natural product contained a –CHOH– moiety. The hydroxy group was positioned at C-8 based on the deshielded resonances of CH-8 (δ_{H} 4.12 and δ_{C} 72.8), and was further supported following detailed HMBC analysis (see Supporting Information). The α -orientation of OH-8 was assigned by the ROESY correlation between H-8 and H₃-12. The ECD spectrum of **3** (Figure 4) exhibited a positive Cotton effect at 241 nm ($\Delta\epsilon = +10.58$) and a negative Cotton effect at 221 nm ($\Delta\epsilon = -4.37$) due to the coupling of the two benzoate chromophores at C-1 α and C-9 β . Therefore, the structure of **3** (celastrofuran C) was assigned as (1*R*,2*R*,4*R*,5*S*,7*S*,8*R*,9*R*,10*R*)-2-acetoxy-1,9-dibenzoyloxy-8-hydroxydihydro- β -agarofuran.

Celastrofuran D (**4**), isolated as stable colorless crystals, was assigned the molecular formula, C₂₉H₃₂O₉, following analysis of the (+)-HRESIMS and NMR data. The ¹H and ¹³C NMR data of **4** were similar to those of compound **3**, indicating that compound **4** was based on the same dihydro- β -agarofuran skeleton. Analysis of the NMR data of **4** and comparison with **3** revealed that the benzoate moiety at C-1 in **3** was replaced by a furoate group in **4**. This was established by HMBC correlations (Figure 5) from H-1 (δ_{H} 5.86) to the carbonyl carbon of the furoate group at δ_{C} 161.3. In addition, the secondary hydroxy group in **3** was oxidized to a carbonyl (C-8) in **4**. HMBC correlations from H-6, H-7, and H-9 to a carbonyl carbon at δ_{C} 205.6 further confirmed the presence of a ketone functionality at C-8 in **4**. The relative configuration of **4** was ascertained to be the same as that of **3** following ROESY data (Figure 5) analysis. The structure of celastrofuran D (**4**) was confirmed unequivocally by X-ray crystallography studies (Figure 3), which also permitted the assignment of its absolute

configuration. Accordingly, compound **4** was assigned as (1*R*,2*R*,4*R*,5*S*,7*R*,9*R*,10*S*)-2-acetoxy-1,9-difuroyloxy-8-oxodihydro- β -agarofuran.

Celastrofuran E (**5**), a stable colorless gum, was found to possess a molecular formula of C₂₉H₃₄O₉ following interpretation of its (+)-HRESIMS and NMR data. The ¹H and ¹³C NMR data of **5** closely resembled those of **4**. However, NMR data comparison showed that the C-8 ketone functionality in **4** was reduced to a secondary hydroxy in **5**. The presence of an additional oxymethine signal (CH-8, δ_{H} 4.45 and δ_{C} 68.2) and HMBC correlations (Figure 6) from H-6, H-7, and H-9 to C-8 (δ_{C} 68.2) further supported the presence of the secondary hydroxy group at C-8 in **5**. Analysis of the ROESY spectrum (Figure 6) and ¹H-¹H coupling constants allowed the determination of the relative configuration of **5**. A large coupling constant ($J_{1,2} = 10.3$ Hz) between H-1 and H-2 indicated that both protons were axially oriented. The β -orientation of H-8 and H-9 was suggested by a small coupling ($J_{8,9} = 4.6$ Hz) between H-8 and H-9. This was further confirmed by ROESY correlations from both H-8 and H-9 to H₃-12. A ROESY correlation between H₃-14 and H₃-15 revealed that CH₃-14 and CH₃-15 were α -oriented. Consequently, the structure of **5** was established as 2 β -acetoxy-9 α -benzoyloxy-1 α -furoyloxy-8 α -hydroxydihydro- β -agarofuran.

The molecular formula of compound **6** was assigned as C₂₇H₃₂O₁₀ by (+)-HRESIMS and ¹³C NMR data analysis. The NMR spectra of **6** showed it to have similar features to those of **5**, with the only difference being the replacement of the benzoate group at C-9 in **5** by a furoate group in **6**. This was supported by HMBC correlations from H-1 (δ_{H} 5.56) and the protons of the furoate group (δ_{H} 6.39, 7.26) to the ester carbonyl carbon at δ_{C} 162.2. The relative configuration of **6** was deemed to be identical as **5** following ROESY data interpretation. Hence, the structure of **6** was established as 2 β -acetoxy-1 α ,9 α -difuroyloxy-8 α -hydroxydihydro- β -agarofuran and was assigned the trivial name celastrofuran F (**6**).

Celastrofuran G (**7**) was obtained as a white amorphous powder. The (+)-HRESIMS data indicated that **7** had a molecular formula of C₃₁H₃₆O₁₀. Analysis of the NMR spectra indicated that **7** was related structurally to **5**, with the difference being the presence of an additional acetate group (δ_{H} 1.96 and δ_{C} 21.2, 169.7) in **7**. HMBC correlations from H-8 (δ_{H} 5.64) and the acetate methyl (δ_{H} 1.96) to the ester carbonyl carbon at δ_{C} 169.7 positioned the acetate group at C-8. The same relative configuration previously determined for **5** was also assigned for **7** following analysis of ¹H-¹H coupling constants and the ROESY spectrum. Therefore, the structure of compound **7** was elucidated as 2 β ,8 α -diacetoxo-9 α -benzoyloxy-1 α -furoyloxy-dihydro- β -agarofuran.

The known compounds 9 β -benzoyloxy-1 α -furoyloxydihydro- β -agarofuran (**8**) and (1*R*,2*R*,4*R*,5*S*,7*R*,9*S*,10*R*)-2-acetoxo-9-benzoyloxy-1-furoyloxydihydro- β -agarofuran (**9**) were identified by comparison of their spectroscopic data with those reported in the literature.^{20,21} Compound **8** was previously isolated from the root bark of *Osyris lanceolata* (Santalaceae), while compound **9** was obtained originally from the fruits of *Maytenus jelskii* (Celastraceae). It is worth mentioning that compound **9** has been reported to block P-glycoprotein in human MDR1 cells.²¹ Herein, the ECD data are included for the known compounds **8** and **9**, which were not reported in the original papers. Comparison of ECD spectra (Figure 4) and the specific rotations of compounds **1** and **8** showed that both compounds had identical absolute configurations. Thus, the structure and absolute configuration of compound **8** was defined as (1*S*,4*R*,5*S*,7*R*,9*S*,10*S*)-9-benzoyloxy-1-furoyloxydihydro- β -agarofuran. Previous studies on the seeds of *C. subspicata* have led to the isolation of **10** and **11**,¹³ but neither of these compounds was identified during our studies on the leaves of this vine.

Due to our previous discovery of dihydro- β -agarofurans that inhibited leucine transport,^{10,11} compounds **1–9** were evaluated for their effects on leucine transport in the LNCaP human

prostate cancer cell line. All compounds inhibited leucine uptake in LNCaP cells with IC_{50} values ranging from 7.0 to 98.9 μ M (Table 3 and Figure 7), which was lower than the currently utilized LAT family inhibitor BCH (IC_{50} = 4060 μ M).²²

Comparison of the leucine uptake inhibition of compounds **1–3**, **8**, and **9** showed that compounds without a hydroxy moiety at C-8 (**1**, **2**, **8**, and **9**) were more active than the natural product **3**, which has C-8 hydroxylation. This indicated that the presence of OH-8 decreased the leucine uptake inhibition. Furthermore, substituting the C-8 methylene unit in **9** with a ketone functionality in **4** resulted in 2.6-fold decrease in the activity. Compounds **5–7** also exhibited leucine uptake inhibition with **7** being the most active in this series with an IC_{50} value of 15.2 μ M. These data suggested that for this particular agarofuran series acetylation rather than hydroxylation at C-8 conferred better activity. For example, replacing the hydroxy group (OH-8) of **5** with an acetoxy group in **7** resulted in a 6.5-fold increase in leucine uptake activity. Moreover, the minimal difference between the activity of **5** and **6** indicated that the type of ester substitution for this series had no profound effect on bioactivity. In conclusion, these studies identified celastrofuran B (**2**) as the most active compound that inhibited leucine uptake with an IC_{50} value of 7.0 μ M (Figure 7). This activity is comparable or better than the recently reported natural products from the plants *Pittosporum venulosum*, *Maytenus bilocularis*, and *Denhamia pittosporoides*.^{10,11,22,23} These findings warrant future investigation on how these compounds inhibit leucine uptake in cancer cells.

EXPERIMENTAL SECTION

General Experimental Procedures. Melting points were measured using a Cole-Parmer melting point apparatus and are uncorrected. Specific rotations were determined on a JASCO P-1020 polarimeter. UV spectra were recorded using a JASCO V-650 UV/vis

spectrophotometer. ECD spectra were obtained on a JASCO J-715 spectropolarimeter and processed using the software SDAR.²⁴ IR data were acquired using an attached Universal Attenuated Total Reflectance (UATR) Two module on a PerkinElmer spectrophotometer. NMR spectra were recorded on a Bruker AVANCE HDX 800 MHz NMR spectrometer equipped with a TCI cryoprobe at 25 °C. The ¹H and ¹³C NMR chemical shifts were referenced to the solvent peaks for CDCl₃ at δ_{H} 7.26 and δ_{C} 77.16, respectively. LRESIMS data were recorded on a Waters ZQ ESI mass spectrometer. HRESIMS data were acquired on a 12 T SolariX XR FT-ICR-MS. Alltech Davisil 30–40 μm 60 Å Si gel packed into an open glass column (25 × 130 mm) was used for flash column chromatography. Thin-layer chromatography (TLC) and preparative TLC was carried out on Merck Si gel 60 F₂₅₄ pre-coated aluminum plates and was observed using UV light. Activon phenyl-bonded or Alltech C₁₈-bonded Si (35–75 μm , 150 Å) was used for pre-adsorption work, and the resulting material was packed into an Alltech stainless steel guard cartridge (10 × 30 mm) prior to HPLC separations. A Waters 600 pump fitted with a Waters 996 photodiode array detector and Gilson 717-plus autosampler was used for semi-preparative HPLC separations. Phenomenex Luna 5 μm 90–110 Å phenyl-hexyl (250 × 10 mm), Phenomenex Luna 5 μm 90–110 Å C₁₈ (250 × 10 mm), and Betasil 5 μm 100 Å C₁₈ (150 × 21.2 mm) columns were used for semi-preparative HPLC separations. A Fritsch Universal Cutting Mill Pulverisette 19 was used to grind the air-dried plant material. An Edwards Instrument Company Bio-line orbital shaker was used for plant extraction. All solvents used for chromatography, specific rotation, ECD, UV and MS were Honeywell Burdick & Jackson (B&J) HPLC grade. H₂O was Millipore Milli-Q PF filtered. All compounds were analyzed for purity by ¹H NMR spectroscopy and shown to be >95%, unless otherwise stated. NMR spectra were processed using MestReNova version 11.0.

Plant Material. Leaves of *Celastrus subspicata* were purchased from Burringbar Rainforest Nursery (Burringbar, New South Wales, Australia) in March 2016. A voucher specimen (RAD079) has been deposited at the Griffith Institute for Drug Discovery, Griffith University, Brisbane, Australia.

Extraction and Isolation. The air-dried and ground leaves of *C. subspicata* (20 g) were extracted with CH₂Cl₂ (2 × 250 mL) at room temperature. The organic solvent was removed under reduced pressure to afford 1.9 g of CH₂Cl₂ extract. The extract was chromatographed on a Si gel flash column using a stepwise gradient solvent system of *n*-hexane/EtOAc (100% *n*-hexane to 100% EtOAc) to give 89 fractions (~20 mL each). Similar fractions were combined following (+)-LRESIMS analysis to give 22 fractions (F1–F22). Fraction F3 (82.1 mg) was pre-adsorbed to phenyl-bonded Si gel (~1 g), packed into a guard cartridge, and attached to a semi-preparative phenyl-hexyl HPLC column. A linear gradient solvent system of 70% MeOH/H₂O to 95% MeOH/H₂O at a flow rate of 4 mL/min over 60 min was then employed to afford celastrofuran A (**1**, 3.6 mg, *t_R* 40–41 min, 0.018% dry wt). Fraction F4 (64.9 mg) was pre-adsorbed to phenyl-bonded Si gel (~1 g), packed into a guard cartridge, and attached to a semi-preparative phenyl-hexyl HPLC column. A linear gradient solvent system of 60% MeOH/H₂O to 95% MeOH/H₂O at a flowrate of 4 mL/min over 60 min was employed to furnish compound **8** (10.8 mg, *t_R* 43–44 min, 0.054% dry wt). Fraction F7 (63.7 mg) was pre-adsorbed to phenyl-bonded Si gel (~1 g), packed into a guard cartridge, and attached to a semi-preparative phenyl-hexyl HPLC column. A linear gradient solvent system of 55% MeOH/H₂O to 100% MeOH at a flow rate of 4 mL/min over 60 min was then employed to afford celastrofuran B (**2**, 19.9 mg, *t_R* 45–46 min, 0.0995% dry wt). Fraction F9 (63.7 mg) was pre-adsorbed to C₁₈-bonded Si gel (~1 g), packed into a guard cartridge, and attached to a semi-preparative C₁₈ HPLC column (250 × 10 mm). A linear gradient solvent system of 60% MeOH/H₂O to 95% MeOH/H₂O at a flow rate of 4 mL/min over 60 min was

then employed to afford compound **9** (6.1 mg, t_R 33 min, 0.0305% dry wt). Fraction F12 (60.0 mg) was further purified using the same protocol detailed for the separation of fraction F7 to afford celastrofuran G (**7**, 5.9 mg, t_R 39 min, 0.0295% dry wt). Fraction F13 (188.6 mg) was pre-adsorbed to C₁₈-bonded Si gel (~1 g), packed into a guard cartridge, and attached to a semi-preparative C₁₈ HPLC column (150 × 21.2 mm). A linear gradient solvent system of 50% MeOH/H₂O to 95% MeOH/H₂O at a flow rate of 9 mL/min over 60 min was then employed to yield celastrofuran C (**3**, 2.6 mg, t_R 33 min, 0.013% dry wt) and celastrofuran E (**5**, 91.6 mg, t_R 28–29 min, 0.458% dry wt). Fraction F14 (62.7 mg) was pre-adsorbed to phenyl-bonded Si gel (~1 g), packed into a guard cartridge, and attached to a semi-preparative phenyl-hexyl HPLC column. A linear gradient solvent system of 45% MeOH/H₂O to 90% MeOH/H₂O at a flow rate of 4 mL/min over 60 min was then run. Sixty fractions were collected from the start of HPLC run. Fractions eluting at 47–48 min were pooled and further purified using a semi-preparative C₁₈ HPLC column (250 × 10 mm). A linear gradient solvent system of 50% MeOH/H₂O to 95% MeOH/H₂O at a flow rate of 4 mL/min over 60 min was run to afford celastrofuran D (**4**, 5.9 mg, t_R 34–35 min, 0.0295% dry wt). Fraction F16 (61.3 mg) was pre-adsorbed to C₁₈-bonded Si gel (~1 g), packed into a guard cartridge, and attached to a semi-preparative C₁₈ HPLC column. A linear gradient solvent system of 50% MeOH/H₂O to 88% MeOH/H₂O at a flow rate of 4 mL/min over 60 min was then employed. Sixty fractions were collected from the start of HPLC run. Fraction eluting at 32 min (13.9 mg) was further purified using preparative TLC (1% MeOH/CH₂Cl₂) to give celastrofuran F (**6**, 7.7 mg, 0.0385% dry wt).

Celastrofuran A (1): white amorphous powder; $[\alpha]_D^{24} +33.3$ (c 0.03, MeOH); ECD λ_{ext} ($\Delta\epsilon$) (MeOH) 223 (–2.67), 240 (+4.08), 280 (–0.30) nm; UV (MeOH) λ_{max} (log ϵ) 229 (4.08), 270 (3.12) nm; IR (UATR) ν_{max} 2932, 1711, 1651, 1282, 1112, 1015, 706 cm^{–1}; ¹H NMR (CDCl₃, 800 MHz) see Table 1 and δ_H 7.84 (2H, m, OBz-9), 7.58 (2H, m, OBz-1), 7.46 (1H, m, OBz-

9), 7.41 (1H, m, OBz-1), 7.31 (2H, m, OBz-9), 7.24 (2H, m, OBz-1); ^{13}C NMR (CDCl_3 , 200 MHz) see Table 2 and δ_{C} 165.81 (C, OBz-9), 165.75 (C, OBz-1), 132.8 (CH, OBz-9), 132.4 (CH, OBz-1), 130.8 (C, OBz-1), 130.0^a (C, OBz-9), 130.0^a (2CH, OBz-9), 129.2 (2CH, OBz-1), 128.03^b (2CH, OBz-9), 128.02^b (2CH, OBz-1) ^aOverlapping signals, ^bInterchangeable signals; (+)-LRESIMS m/z 485 (100) $[\text{M}+\text{Na}]^+$; (+)-HRESIMS m/z 485.2294 $[\text{M}+\text{Na}]^+$ (calcd for $\text{C}_{29}\text{H}_{34}\text{O}_5\text{Na}$, 485.2298).

Celastrofuran B (2): stable colorless rod crystals; mp 194–195 °C; $[\alpha]_{\text{D}}^{24} +51.3$ (c 0.12, MeOH); ECD λ_{ext} ($\Delta\epsilon$) (MeOH) 222 (−3.31), 239 (+9.19), 280 (−0.63) nm; UV (MeOH) λ_{max} ($\log \epsilon$) 230 (4.33), 273 (3.32) nm; IR (UATR) 2981, 1733, 1707, 1281, 1116, 1016, 713 cm^{-1} ; ^1H NMR (CDCl_3 , 800 MHz) see Table 1 and δ_{H} 8.01 (2H, m, OBz-9), 7.56 (2H, m, OBz-1), 7.54 (1H, m, OBz-9), 7.43 (1H, m, OBz-1), 7.42 (2H, m, OBz-9), 7.26 (2H, m, OBz-1), 1.79 (3H, s, OAc-2); ^{13}C NMR (CDCl_3 , 200 MHz) see Table 2 and δ_{C} 170.9 (C, OAc-2), 165.8 (C, OBz-9), 165.1 (C, OBz-1), 132.8 (CH, OBz-9), 132.6 (CH, OBz-1), 130.43 (2CH, OBz-9), 130.38 (C, OBz-1), 130.2 (C, OBz-9), 129.3 (2CH, OBz-1), 128.2 (2CH, OBz-1), 128.0 (2CH, OBz-9), 21.2 (CH_3 , OAc-2); (+)-LRESIMS m/z 543 (100) $[\text{M}+\text{Na}]^+$; (+)-HRESIMS m/z 543.2346 $[\text{M}+\text{Na}]^+$ (calcd for $\text{C}_{31}\text{H}_{36}\text{O}_7\text{Na}$, 543.2353).

Celastrofuran C (3): white amorphous powder; $[\alpha]_{\text{D}}^{24} +67.7$ (c 0.07, MeOH); ECD λ_{ext} ($\Delta\epsilon$) (MeOH) 221 (−4.37), 241 (+10.58), 279 (−0.94) nm; UV (MeOH) λ_{max} ($\log \epsilon$) 232 (4.46), 274 (2.84) nm; IR (UATR) ν_{max} 3471, 2979, 1729, 1274, 1269, 1110, 1027, 993, 708 cm^{-1} ; ^1H NMR (CDCl_3 , 800 MHz) see Table 1 and δ_{H} 7.95 (2H, m, OBz-9), 7.56 (1H, m, OBz-9), 7.52 (2H, m, OBz-1), 7.42 (3H, m, OBz-1, OBz-9), 7.24 (2H, m, OBz-1), 1.81 (3H, s, OAc-2); ^{13}C NMR (CDCl_3 , 200 MHz) see Table 2 and δ_{C} 170.9 (C, OAc-2), 166.2 (C, OBz-9), 165.2 (C, OBz-1), 133.2 (CH, OBz-1), 132.7 (CH, OBz-9), 130.5 (2CH, OBz-1), 130.3 (C, OBz-9), 129.30 (C, OBz-1), 129.26 (2CH, OBz-9), 128.2 (2CH, OBz-1), 128.1 (2CH, OBz-9), 21.2

(CH₃, OAc-2); (+)-LRESIMS m/z 559 (100) [M+Na]⁺; (+)-HRESIMS m/z 559.2293 [M+Na]⁺ (calcd for C₃₁H₃₆O₈Na, 559.2302).

Celastrofuran D (4): stable colorless block crystals; mp 189–191 °C; $[\alpha]_D^{24}$ +141.4 (*c* 0.30, MeOH); ECD λ_{ext} ($\Delta\epsilon$) (MeOH) 244, (+3.15), 310 (+4.50) nm; UV (MeOH) λ_{max} (log ϵ) 235 (4.37), 276 (3.31) nm; IR (UATR) ν_{max} 2979, 1736, 1244, 1014, 1135, 710 cm⁻¹; ¹H NMR (CDCl₃, 800 MHz) see Table 1 and δ_{H} 7.88 (2H, m, OBz-9), 7.61 (1H, dd, *J* = 1.8, 0.6 Hz, OFu-1), 7.51 (1H, m, OBz-9), 7.36 (2H, m, OBz-9), 7.26 (1H, dd, *J* = 1.8, 1.8 Hz, OFu-1), 6.28 (1H, dd, *J* = 1.8, 0.6 Hz, OFu-1), 1.83 (3H, s, OAc-2); ¹³C NMR (CDCl₃, 200 MHz) see Table 2 and δ_{C} 170.8 (C, OAc-2), 165.0 (C, OBz-9), 161.3 (C, OFu-1), 147.6 (CH, OFu-1), 143.4 (CH, OFu-1), 133.2 (CH, OBz-9), 130.4 (2CH, OBz-9), 129.3 (C, OBz-9), 128.1 (2CH, OBz-9), 119.0 (C, OFu-1), 109.6 (CH, OFu-1), 21.1 (CH₃, OAc-2); (+)-LRESIMS m/z 547 (100) [M+Na]⁺; (+)-HRESIMS m/z 547.1934 [M+Na]⁺ (calcd for C₂₉H₃₂O₉Na, 547.1939).

Celastrofuran E (5): colorless gum; $[\alpha]_D^{24}$ −80.3 (*c* 0.30, MeOH); ECD λ_{ext} ($\Delta\epsilon$) (MeOH) 233 (−1.59), 252 (+0.21), 272 (−0.47) nm; UV (MeOH) λ_{max} (log ϵ) 230 (4.46), 273 (3.42) nm; IR (UATR) ν_{max} 3356, 2981, 1728, 1161, 1008 cm⁻¹; ¹H NMR (CDCl₃, 800 MHz) see Table 1 and δ_{H} 7.79 (2H, m, OBz-9), 7.48 (1H, dd, *J* = 1.9, 0.7 Hz, OFu-1), 7.40 (1H, m, OBz-9), 7.19 (2H, m, OBz-9), 6.98 (1H, dd, *J* = 1.9, 1.9 Hz, OFu-1), 6.21 (1H, dd, *J* = 1.9, 0.7 Hz, OFu-1), 1.82 (3H, s, OAc-2); ¹³C NMR (CDCl₃, 200 MHz) see Table 2 and δ_{C} 170.9 (C, OAc-2), 165.3 (C, OBz-9), 162.2 (C, OFu-1), 147.5 (CH, OFu-1), 143.1 (CH, OFu-1), 133.1 (CH, OBz-9), 129.51 (2CH, OBz-9), 129.45 (C, OBz-9), 128.0 (2CH, OBz-9), 119.2 (C, OFu-1), 109.4 (CH, OFu-1), 21.2 (CH₃, OAc-2); (+)-LRESIMS m/z 549 (100) [M+Na]⁺; (+)-HRESIMS m/z 549.2091 [M+Na]⁺ (calcd for C₂₉H₃₄O₉Na, 549.2095).

Celastrofuran F (6): colorless gum; $[\alpha]_D^{24}$ −62.1 (*c* 0.39, MeOH); ECD λ_{ext} ($\Delta\epsilon$) (MeOH) 250 (−1.44) nm; UV (MeOH) λ_{max} (log ϵ) 235 (3.95) nm; IR (UATR) ν_{max} 3409, 2965, 1725, 1643, 1305, 1239, 1161, 1004, 755 cm⁻¹; ¹H NMR (CDCl₃, 800 MHz) see Table 1 and δ_{H}

7.69 (1H, dd, $J = 1.9, 0.7$ Hz, OFu-9), 7.68 (1H, dd, $J = 1.9, 0.7$ Hz, OFu-1), 7.20 (1H, dd, $J = 1.9, 1.9$ Hz, OFu-9), 7.19 (1H, dd, $J = 1.9, 1.9$ Hz, OFu-1), 6.48 (1H, dd, $J = 1.9, 0.7$ Hz, OFu-9), 6.39 (1H, dd, $J = 1.9, 0.7$ Hz, OFu-1), 1.84 (3H, s, OAc-2); ^{13}C NMR (CDCl_3 , 200 MHz) see Table 2 and δ_{C} 170.9 (C, OAc-2), 162.2 (C, OFu-1), 161.9 (C, OFu-9), 147.8^a (CH, OFu-1), 147.6^a (CH, OFu-9), 143.6^b (CH, OFu-1), 143.5^b (CH, OFu-9), 119.4 (C, OFu-1), 118.9 (C, OFu-9), 109.4 (2C, OFu-1 and OFu-9) ^{a,b}Interchangeable signals; (+)-LRESIMS m/z 539 (100) $[\text{M}+\text{Na}]^+$; (+)-HRESIMS m/z 539.1885 $[\text{M}+\text{Na}]^+$ (calcd for $\text{C}_{27}\text{H}_{32}\text{O}_{10}\text{Na}$, 539.1888).

Celastrofuran G (7): white amorphous powder; $[\alpha]_{\text{D}}^{24} -65.4$ (c 0.30, MeOH); ECD λ_{ext} ($\Delta\epsilon$) (MeOH) 222 (+0.46), 234 (−0.69), 250 (+0.17) nm; UV (MeOH) λ_{max} ($\log \epsilon$) 230 (4.16), 275 (3.12) nm; IR (UATR) ν_{max} 3352, 2979, 1730, 1273, 1232, 1013, 711 cm^{-1} ; ^1H NMR (CDCl_3 , 800 MHz) see Table 1 and δ_{H} 7.74 (1H, dd, $J = 1.8, 0.6$ Hz, OFu-1), 7.71 (2H, m, OBz-9), 7.36 (1H, m, OBz-9), 7.16 (2H, m, OBz-9), 6.97 (1H, dd, $J = 1.8, 1.8$ Hz, OFu-1), 6.20 (1H, dd, $J = 1.8, 0.6$ Hz, OFu-1), 1.96 (3H, s, OAc-8), 1.84 (3H, s, OAc-2); ^{13}C NMR (CDCl_3 , 200 MHz) see Table 2 and δ_{C} 170.9 (C, OAc-2), 169.7 (C, OAc-8), 165.0 (C, OBz-9), 162.1 (C, OFu-1), 147.5 (CH, OFu-1), 143.1 (CH, OFu-1), 132.7 (CH, OBz-9), 129.3 (2CH, OBz-9), 129.0 (C, OBz-9), 127.9 (2CH, OBz-9), 119.1 (C, OFu-1), 109.3 (CH, OFu-1), 21.2 (CH_3 , OAc-2), 21.1 (CH_3 , OAc-8); (+)-LRESIMS m/z 591 (100) $[\text{M}+\text{Na}]^+$; (+)-HRESIMS m/z 591.2196 $[\text{M}+\text{Na}]^+$ (calcd for $\text{C}_{31}\text{H}_{36}\text{O}_{10}\text{Na}$, 591.2201).

(1S,4R,5S,7R,9S,10S)-9-Benzoyloxy-1-furoyloxydihydro- β -agarofuran (8): white amorphous powder; $[\alpha]_{\text{D}}^{24} +79.8$ (c 0.54, CHCl_3); lit. $[\alpha]_{\text{D}}^{20} +14.2$ (c 0.016, CHCl_3);²⁰ ECD λ_{ext} ($\Delta\epsilon$) (MeOH) 237 (+3.32), 277 (−0.47) nm; (+)-LRESIMS m/z 475 (100) $[\text{M}+\text{Na}]^+$.

(1R,2R,4R,5S,7R,9S,10R)-2-Acetoxy-9-benzoyloxy-1-furoyloxydihydro- β -agarofuran (9): colorless gum; $[\alpha]_{\text{D}}^{24} +51.1$ (c 0.30, CHCl_3); lit. $[\alpha]_{\text{D}}^{25} +81.5$ (c 0.20, CHCl_3);²¹ ECD λ_{ext} ($\Delta\epsilon$) (MeOH) 234 (+1.96), 277 (−0.32) nm; (+)-LRESIMS m/z 533 (100) $[\text{M}+\text{Na}]^+$.

X-ray Crystallography Analysis. Intensity data for celastrofurane B (**2**) and celastrofurane D (**4**) were collected with an Oxford Diffraction SuperNova CCD diffractometer using Cu-K α radiation, the temperature during data collection was maintained at 130.0(1) K using an Oxford Cryosystems cooling device. The structure was solved by direct methods and difference Fourier Synthesis.²⁵ Hydrogen atoms bound to the carbon atom were placed at their idealized positions using appropriate HFIX instructions in SHELXL, and included in subsequent refinement cycles. The hydrogen atom attached to oxygen was located from difference Fourier maps and refined freely with isotropic displacement parameters. Thermal ellipsoid plots were generated using the program ORTEP-3²⁶ integrated within the WINGX suite of programs.²⁷ Crystallographic data for compounds **2** and **4** (CCDC Nos 1530798 and 1530799) have been deposited with the Cambridge Crystallographic Data Centre. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

Crystal Data for Celastrofurane B (2). C₃₁H₃₆O₇, $M = 520.60$, $T = 130.0(2)$ K, $\lambda = 1.54184$ Å, Orthorhombic, space group $P 2_1 2_1 2_1$ $a = 12.6896(2)$, $b = 13.4856(1)$, $c = 16.1709(2)$ Å, $V = 2767.28(6)$ Å³, $Z = 4$, $D_c = 1.250$ Mg M⁻³ $\mu = 0.714$ mm⁻¹, $F(000) = 1112$, crystal size $0.65 \times 0.19 \times 0.16$ mm. $\theta_{\max} = 77.23^\circ$, 27249 reflections measured, 5680 independent reflections ($R_{\text{int}} = 0.0386$) the final $R = 0.0293$ [$I > 2\sigma(I)$, 5518 data] and $wR(F^2) = 0.0737$ (all data) $\text{GOOF} = 1.050$, absolute structure parameter = 0.01(5) from 2340 quotients.

Crystal Data for Celastrofurane D (4). C₂₉H₃₂O₉, $M = 524.54$, $T = 130.0(2)$ K, $\lambda = 1.54184$ Å, Monoclinic, space group $P 2_1$ $a = 9.8482(2)$, $b = 14.0081(3)$, $c = 10.8615(2)$ Å, $\beta = 115.636(3)^\circ$ $V = 1350.89(6)$ Å³, $Z = 2$, $D_c = 1.290$ Mg M⁻³ $\mu = 0.794$ mm⁻¹, $F(000) = 556$, crystal size $0.68 \times 0.49 \times 0.34$ mm. $\theta_{\max} = 77.08^\circ$, 28110 reflections measured, 5612 independent reflections ($R_{\text{int}} = 0.0269$) the final $R = 0.0302$ [$I > 2\sigma(I)$, 5586 data] and $wR(F^2)$

= 0.0794 (all data) GOOF = 1.059, absolute structure parameter = 0.04 (3) from 2606 quotients.

Leucine Transport Inhibition Assay. The LNCaP human prostate cancer cell line was purchased from the American Type Culture Collection (Manassas, VA, USA). The LNCaP cell identity was confirmed by STR profiling in 2014 (Cellbank, Australia). Cells were cultured in RPMI 1640 medium (Life Technologies, Australia) containing 10% (v/v) fetal bovine serum (FBS), penicillin-streptomycin solution (Sigma-Aldrich, Australia) and 1 mM sodium pyruvate (Life Technologies, Australia). Cells were maintained at 37 °C in a fully humidified atmosphere containing 5% CO₂. The [³H]-L-leucine uptake assay was performed as detailed previously.⁵ Briefly, cells were cultured in 6-well plates in RPMI medium. After collecting and counting, cells (3×10⁴/well) were incubated with 0.3 μCi [³H]-L-leucine (200 nM; PerkinElmer) in leucine-free RPMI media (Invitrogen) with 10% (v/v) dialyzed FBS in the presence of different concentrations of compounds for 15 min at 37°C. Cells were collected, transferred to filter paper using a scintillation mat harvester (PerkinElmer), dried, exposed to scintillation fluid and counts measured using a MicroBeta2 scintillation counter (PerkinElmer). GraphPad Prism 6 was used to determine the IC₅₀ of each compound. Each data point was determined in triplicate, and repeated in three independent experiments.

ASSOCIATED CONTENT

Supporting Information

1D and 2D NMR spectra of celastrofurans A–G (**1–7**).

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Notes

The authors declare no competing financial interest.

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Figure 1. Structures of celastrofurans A–G (**1–7**), (1*S*,4*R*,5*S*,7*R*,9*S*,10*S*)-9-benzoyloxy-1-furoyloxydihydro- β -agarofuran (**8**), (1*R*,2*R*,4*R*,5*S*,7*R*,9*S*,10*R*)-2-acetoxy-9-benzoyloxy-1-furoyloxydihydro- β -agarofuran (**9**), 1 α -acetoxy-6 β ,9 α -dibenzoyloxy-4 β ,8 α -dihydroxy-dihydro- β -agarofuran (**10**), and 1 α ,8 α -diacetoxy-6 β ,9 α -dibenzoyloxy-4 β -hydroxy-dihydro- β -agarofuran (**11**) from *C. subspicata*.

Figure 2. COSY and selected HMBC/ROESY correlations for celastrofuran A (**1**).

Figure 3. ORTEP drawings of celastrofuran B (**2**, left) and celastrofuran D (**4**, right). Hydrogen atoms are omitted for clarity.

Figure 4. ECD spectra of celastrofurans A–C (**1–3**) and compound **8**.

Figure 5. COSY and selected HMBC/ROESY correlations for celastrol (4).

Figure 6. COSY and selected HMBC/ROESY correlations for celastrol (5).

Figure 7. Compound effects on leucine transport in LNCaP cells. $[^3\text{H}]\text{-L-Leucine}$ uptake assays were performed in the presence of different doses of compounds **1-9** in LNCaP cells ($n = 3$, means $\pm$ S.E.M). These data were used to generate the IC_{50} values in Table 3.

Table 1. ¹H NMR (800 MHz) Spectroscopic Data of Celastrofurans A–G (**1–7**) in CDCl₃.^a

	1	2	3	4	5	6	7
position	δ_{H} , mult. (<i>J</i> in Hz)	δ_{H} , mult. (<i>J</i> in Hz)	δ_{H} , mult. (<i>J</i> in Hz)	δ_{H} , mult. (<i>J</i> in Hz)	δ_{H} , mult. (<i>J</i> in Hz)	δ_{H} , mult. (<i>J</i> in Hz)	δ_{H} , mult. (<i>J</i> in Hz)
1	5.70, dd (12.0, 4.2)	6.00, d (10.6)	5.94, d (10.5)	5.86, d (10.2)	5.57, d (10.3)	5.56, d (10.3)	5.58, d (10.3)
2 α	1.72, m	5.33, ddd (12.6, 10.6, 4.3)	5.35, ddd (12.6, 10.5, 4.4)	5.29, ddd (12.7, 10.2, 4.7)	5.30, ddd (12.7, 10.3, 4.7)	5.29, ddd (12.8, 10.3, 4.8)	5.30, ddd (12.8, 10.3, 4.7)
2 β	1.99, m	-	-	-	-	-	-
3 α	1.48, ddd (10.1, 3.2, 1.4)	1.83, ddd (12.6, 4.3, 1.7)	1.83, ddd (12.6, 4.4, 1.6)	1.85, ddd (12.7, 4.7, 1.5)	1.77, ddd (12.7, 4.7, 1.7)	1.77, ddd (12.8, 4.8, 1.7)	1.79, ddd (12.8, 4.7, 1.7)
3 β	2.32, m	2.38, ddd (12.6, 12.6, 6.1)	2.37, ddd (12.6, 12.6, 6.2)	2.39, ddd (12.7, 12.7, 6.2)	2.22, ddd (12.7, 12.7, 6.0)	2.21, ddd (12.8, 12.8, 6.0)	2.23, ddd (12.8, 12.8, 6.0)
4	1.91, m	2.09, m	2.10, m	2.20, m	2.01, m	2.00, m	2.03, m
6 α	2.09, ^b m	2.16, m	2.56, d (12.9)	2.47, d (13.7)	2.72, d (12.8)	2.69, d (12.8)	2.57, d (12.3)
6 β	2.03, m	2.03, ^b m	2.00, ddd (12.9, 4.2, 1.2)	2.43, dd (13.7, 3.7)	1.88, ddd (12.8, 4.0, 0.8)	1.86, ddd (12.8, 4.0, 0.7)	1.94, ddd (12.3, 4.0, 1.2)
7	2.01, m	2.03, ^b m	2.20, br dd (4.2, 3.4)	2.77, d (3.7)	2.28, dd (4.0, 4.0)	2.27, dd (4.0, 4.0)	2.29, dd (4.0, 4.0)
8 α	2.09, ^b m	2.06, m	-	-	-	-	-
8 β	2.21, ddd (16.2, 6.7, 3.5)	2.14, m	4.12, br s	-	4.45, dd (4.6, 4.0)	4.40, dd (4.5, 4.0)	5.64, m
9	5.04, d (6.7)	4.95, d (6.6)	4.77, s	5.34, s	5.46, d (4.6)	5.40, d (4.5)	5.56, d (5.0)
12	1.38, s	1.38, s	1.33, s	1.45, s	1.52, s	1.49, s	1.61, s
13	1.23, s	1.24, s	1.26, s	1.32, s	1.25, s	1.24, s	1.25, s
14	1.12, d (7.8)	1.24, d (7.8)	1.26, d (8.3)	1.26, d (7.9)	1.26, d (8.0)	1.24, d (7.8)	1.27, d (7.9)
15	1.39, s	1.45, s	1.60, s	1.53, s	1.54, s	1.46, s	1.52, s

^aNMR data of the ester groups are provided in the Experimental Section. ^bOverlapping signals.

Table 2. ^{13}C NMR (200 MHz) Spectroscopic Data of Celastrofurans A–G (**1**–**7**) in CDCl_3 .^a

position	1	2	3	4	5	6	7
	δ_{C} , type	δ_{C} , type	δ_{C} , type	δ_{C} , type	δ_{C} , type	δ_{C} , type	δ_{C} , type
1	74.8, CH	73.9, CH	74.1, CH	72.6, CH	78.8, CH	78.9, CH	78.4, CH
2	22.1, CH_2	69.5, CH	69.4, CH	69.5, CH	68.1, CH	68.1, CH	68.0, CH
3	27.2, CH_2	33.3, CH_2	33.3, CH_2	32.9, CH_2	33.0, CH_2	33.0, CH_2	32.9, CH_2
4	40.2, CH	40.8, CH	40.6, CH	40.3, CH	40.8, CH	40.8, CH	40.8, CH
5	87.9, C	87.1, C	87.4, C	87.8, C	88.6, C	88.6, C	88.4, C
6	36.8, CH_2	36.4, CH_2	30.54, CH_2	33.6, CH_2	30.5, CH_2	30.4, CH_2	31.4, CH_2
7	44.0, CH	43.9, CH	50.3, CH	60.6, CH	49.6, CH	49.6, CH	47.9, CH
8	31.8, CH_2	31.4, CH_2	72.8, CH	205.6, C	68.2, CH	68.3, CH	70.1, CH
9	74.7, CH	74.2, CH	81.39, CH	77.5, CH	78.5, CH	78.0, CH	75.8, CH
10	48.5, C	49.9, C	48.8, C	49.4, C	49.2, C	49.1, C	49.2, C
11	82.3, C	82.7, C	81.40, C	82.4, C	81.3, C	81.3, C	81.5, C
12	24.5, CH_3	24.6, CH_3	24.4, CH_3	25.9, CH_3	22.9, CH_3	22.8, CH_3	22.9, CH_3
13	30.4, CH_3	30.3, CH_3	30.52, CH_3	28.9, CH_3	30.3, CH_3	30.3, CH_3	30.1, CH_3
14	18.1, CH_3	18.7, CH_3	18.6, CH_3	18.2, CH_3	18.2, CH_3	18.1, CH_3	18.1, CH_3
15	18.9, CH_3	19.5, CH_3	19.8, CH_3	20.6, CH_3	13.5, CH_3	13.4, CH_3	13.1, CH_3

^aNMR data of the ester groups are provided in the Experimental Section.

Table 3. Leucine uptake inhibition of compounds **1–9** in the LNCaP cell line

compound	IC ₅₀ (μM)
1	27.6
2	7.0
3	82.3
4	13.4
5	98.9
6	75.3
7	15.2
8	19.7
9	34.5

Table of Contents

Celastrofuran B
Leucine uptake inhibitor
($IC_{50} = 7.0 \mu M$)