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Enzyme-Catalyzed Regioselective Acylation of Castanospermine

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Abstract: Several biologically active esters of castanospermine [(1*S*,6*S*,7*R*,8*R*,8a*R*)-1,6,7,8-tetrahydroxyoctahydroindolizine] have been synthesized on a preparative scale in pyridine by using the proteolytic enzyme subtilisin as a catalyst. Under these conditions, subtilisin possesses a high regioselectivity and at the same time a broad substrate specificity and enantioselectivity. This fact makes possible the synthesis of a wide variety of 1-*O*-acyl derivatives via castanospermine esterification. It is possible to regulate the hydrophobicity of the acylating group (acetyl, butyryl, octanoyl) or to incorporate an aromatic moiety (phenylacetyl) or L and D amino acids (phenylalanyl, L- and D-alanyl). Since 1-esters of castanospermine are soluble in several organic solvents, they have been employed as intermediates in the preparation of diesters. Porcine pancreatic lipase, lipase from *Chromobacterium viscosum*, and subtilisin have been used as catalysts for further enzymatic acylation of 1-*O*-acyl derivatives of castanospermine in tetrahydrofuran. The regioselectivity of subtilisin is different from that of the lipases tested. Subtilisin shows a strong preference for acylation of the OH group at the C6 position, while lipases prefer the OH group at C7. Among lipases tested, the lipase from *C. viscosum* is especially active. The reactions catalyzed by this enzyme usually result in isolated yields of ~80%. In order to prepare mono-*O*-acyl compounds other than 1-*O*-acylcastanospermine, 1,7-di-*O*-butyrylcastanospermine has been enzymatically hydrolyzed. Two enzymes—porcine liver esterase and subtilisin—catalyzed this reaction with opposite regioselectivities: while esterase preferentially cleaves off the butyryl group from the C7 position with regioselectivity (C1:C7) better than 1:25, subtilisin hydrolyzes the ester bond at the C1 position with regioselectivity more than 25:1. For synthetic purposes this property of subtilisin is especially important, because it makes possible a three-step enzyme-catalyzed synthesis of 7-*O*-butyrylcastanospermine.

The plant alkaloid castanospermine is a potent inhibitor of the endoplasmic reticulum enzyme α-glucosidase I. It prevents removal of glucose residues during the normal processing of glycoproteins and therefore is highly biologically active.[1] The recent wave of interest in this compound is due to the fact that castanospermine may be of clinical value as an antineoplastic agent[2] and especially as a drug in the treatment of acquired immune deficiency syndrome (AIDS).[3] It has been reported that several *O*-acyl derivatives of castanospermine are as much as 20 times more active than castanospermine itself in inhibiting human im-

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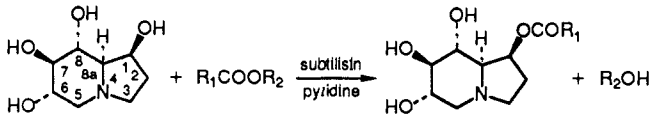
Scheme I[a]



[a] R_1 = alkyl, aryl, or α-aminoalkyl; R_2 = chloroethyl, 2,2,2-trichloroethyl, 2,2,2-trifluoroethyl, or vinyl.

munodeficiency virus (HIV) replication.[4] These findings make the synthesis of castanospermine analogues an extremely important and urgent goal.

Castanospermine [(1*S*,6*S*,7*R*,8*R*,8a*R*)-1,6,7,8-tetrahydroxyoctahydroindolizine] contains four secondary hydroxyl groups of similar reactivity and therefore represents a challenging target for regioselective modification. The synthesis of individual esters of castanospermine, as well as other amino sugars and carbohydrates, requires five to six steps involving protection and deprotection of neighboring hydroxyl groups.[5]

Enzymatic methods, with their unparalleled specificity, are an attractive alternative to the classical techniques of organic chemistry.[6] The use of organic solvents instead of water as a reaction medium for enzymatic reactions gave this methodology a powerful boost and allowed for several syntheses impossible in water.[7] The recent discovery that substrate specificity and enantioselectivity of enzymes may be dramatically altered, and sometimes predictably controlled, by changing the reaction medium creates new opportunities for organic chemistry.[8]

Recently, lipases and subtilisin have successfully been used for the regioselective acylation and deacylation of a number of carbohydrates and their derivatives, such as mono- and disaccharides and conjugates of sugars with aglycons.[9-12] In all reported examples, enzymes exhibit a predominant preference toward a primary hydroxyl group in both acylation and deacylation reactions. When the primary hydroxyl group is protected, several lipases regioselectively catalyze the acylation of secondary hydroxyl groups in monosaccharides.[13] It should be noted, however, that despite the obvious progress in selective modification of monosaccharides, this methodology has so far only been applied to the synthesis of model compounds. In the present work, we report the use of an enzymatic approach to regioselective esterification of castanospermine. We synthesized 17 analogues of castanospermine; evaluation of their antiretroviral activity is now underway.

Table I. Preparative Regioselective Synthesis of 1-*O*-Acylcastanospermine Catalyzed by Subtilisin in Anhydrous Pyridine[a,b,c]

acylating agent (mmol)	reaction time, h	isolated yield,[d] %
$H_3C(CH_2)_2CO_2CH_2CCl_3$ (1.8)	92	82
$H_3C(CH_2)_6CO_2CH_2CF_3$ (1.8)	96	23
$H_3CCO_2CH{=}CH_2$ (2.2)	84	91
$C_6H_5CH_2CO_2CH{=}CH_2$ (1.5)	96	30
N-Ac-L-Phe-OCH_2CH_2Cl (2.7)	96	49
N-Ac-L-Ala-OCH_2CH_2Cl (1.20)	96	44
N-Ac-D-Ala-OCH_2CH_2Cl (1.8)	120	31

[a] Reaction conditions: castanospermine (0.90 mmol) was dissolved in 15 mL of warm anhydrous pyridine, followed by addition of the amount of substrate given in the first column. Then 5 mg/mL subtilisin was added, and the suspension (the enzyme is not soluble in pyridine) was shaken at 45 °C for the periods of time indicated in the table. Next, the enzyme was removed by filtration, the solvent evaporated under vacuum, and the residue chromatographed on silica gel plates in an $EtOH/CH_2Cl_2$ eluent system. This procedure resulted in the isolated yields given in the last column. [b] The position of acylation has been established by ^1H NMR. [c] In no case were castanospermine analogues other than 1-*O*-acyl compounds found. No formation of di- or triacyl derivatives was detected by TLC. [d] Yields were not optimized.

We hope that this work will provide organic chemists with a general routine methodology that leads to selective modification of other biologically active polyhydroxylated octahydroindolizines and piperidine and pyrrolidine alkaloids.

Results and Discussion

Subtilisin Carlsberg (EC 3.4.21.4) has been used as a catalyst for enzymatic transesterification of castanospermine (Scheme I).

A typical experimental procedure using 1-*O*-butyrylcastanospermine as an example is illustrated below. We dissolved 170 mg (0.90 mmol) of castanospermine in 15 mL of warm anhydrous pyridine and added 396 mg (1.80 mmol) of (2,2,2-trichloroethyl)butyrate. Then 75 mg of subtilisin was added. (Preparation of the enzyme is described in the Experimental Section.) The suspension was shaken at 45 °C and 260 rpm for 4 days; periodically, aliquots were withdrawn and analyzed by TLC. Then the enzyme was removed by filtration, the pyridine was evaporated under vacuum, and the product was isolated and purified by radial silica gel chromatography. This procedure resulted in 192 mg (0.74 mmol, 82% isolated yield) of a white crystalline compound. The data of ^1H NMR, ^{13}C NMR, low- and high-resolution MS, and elemental analysis were consistent with the structure of 1-*O*-butyrylcastanospermine. Thus, the microbial protease subtilisin is able to regioselectively acylate castanospermine in anhydrous pyridine. Encouraged by this result, we decided to test the scope of this approach with other acylating agents (Table I).

Subtilisin catalyzes the synthesis of a wide variety of castanospermine analogues. It is possible to regulate the hydrophobicity of the acylating group (acetyl, butyryl, octanoyl) or to incorporate an aromatic moiety (phenylacetyl) or L or even D amino acids (phenylalanyl, L- and D-alanyl). These results clearly indicate that, in organic solvent, subtilisin possesses a high regioselectivity and at the same time a broad substrate specificity and enantioselectivity. (In all cases, no formation of di-, tri-, or mono-*O*-acyl derivatives other than 1-*O*-acylcastanospermine was observed.) This combination of broad substrate specificity and high regioselectivity in organic solvents makes subtilisin a powerful tool for organic synthesis. Monochloroethyl, trichloroethyl, trifluoroethyl, or vinyl esters of corresponding acids were used. The effectiveness of trichloroethyl, trifluoroethyl, and vinyl butyrate were compared in a direct experiment. The rate of 1-*O*-butyrylcastanospermine formation and its yield were similar for all acylating agents employed.

It is important to note that the reactions presented in Table I are very clean and proceed without formation of byproducts. This property allows two features that make these reactions even more attractive. First, unreacted castanospermine (by far the most

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Table II. Enzyme-Catalyzed Regioselective Modification of 1-*O*-Acylcastanospermine in Anhydrous THF[a]

substrate	acylating agent	enzyme[b]	product,[c] %		regioselectivity[d]
			1,6-isomer	1,7-isomer	
1-*O*-(phenylacetyl)castanospermine	2,2,2-trichloroethyl butyrate	subtilisin	23		>20
		lipase CV	30	58	0.52
		PPL	12	52	0.23
1-*O*-butyrylcastanospermine	2,2,2-trichloroethyl butyrate	subtilisin	20	8	2.30
		lipase CV	7	72	0.10
		PPL	10	57	0.18
1-*O*-acetylcastanospermine	2,2,2-trichloroethyl butyrate	subtilisin	10	3	2.63
		lipase CV	26	54	0.48
		PPL	15	47	0.32
1-*O*-butyrylcastanospermine	vinyl phenylacetate	lipase CV	39	36	1.10

[a] Each substrate, 1.5 mmol (entries 1–3) or 0.5 mmol (entry 4), was dissolved in 15 mL (entries 1–3) or 5 mL (entry 4) of anhydrous THF. Then 4 molar equiv of trichloroethyl butyrate (entries 1–3) or vinyl phenylacetate (entry 4) was added. In the first three cases the reaction mixture was divided into three portions, 5 mL each; then subtilisin (5 mg/mL), lipase CV (10 mg/mL), and PPL (100 mg/mL) were added to each sample, respectively, and the suspensions were shaken at 45 °C. (Subtilisin and lipase CV were lyophilized from 0.1 M phosphate buffer, pH 7.8 and 7.0, respectively, before use.) The reaction time was 4 days in all reactions catalyzed by subtilisin and PPL and 3 days in reactions catalyzed by lipase CV. Then the enzyme was filtered out, the THF was evaporated, and the residue was chromatographed by using radial chromatography in an $EtOH/CH_2Cl_2$ system. (See Experimental Section for details.) [b] No appreciable reaction was detected without enzyme. [c] The isolated yield after chromatography is presented. [d] Regioselectivity was calculated as a ratio of synthesized amounts of 1,6- to 1,7-isomers. In no case was information of any triester or 1,8-diester detected by TLC.

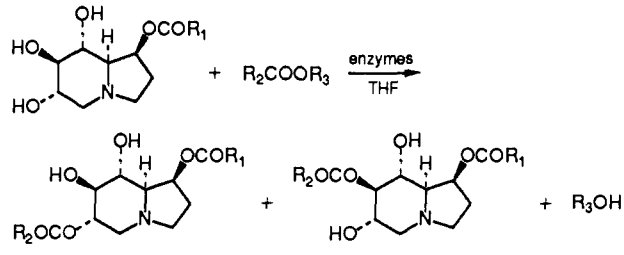
expensive reactant in this system) can be isolated and reused; in all cases, we isolated unreacted castanospermine in 90–97% yield. Second, chromatography can readily be omitted. The synthesis of 1-*O*-butyrylcastanospermine was repeated under standard conditions (see text). The residue obtained after filtration of subtilisin[14] and evaporation of pyridine was simply recrystallized from ethyl acetate, giving a white crystalline solid pure by TLC and ^1H NMR, in 69% isolated yield. It should also be noted that subtilisin is remarkably stable under these conditions. After 5 days' reaction in pyridine at 45 °C, the enzyme does not lose its catalytic activity and can be reused. This fact may significantly decrease the cost of the process on a large scale.

The high regioselectivity of subtilisin allows for preparation of a variety of 1-*O*-acyl derivatives without the formation of by-products; on the other hand, the same high regioselectivity precludes the synthesis of other castanospermine analogues. Unfortunately, few other enzymes are active in pyridine or dimethylformamide (the only organic solvents where castanospermine has reasonable solubility). Out of many enzymes tested, only porcine pancreatic lipase was catalytically active in pyridine, but to a much smaller extent than subtilisin. When the same experimental procedure was employed for the reaction of castanospermine with (2,2,2-trichloroethyl)butyrate catalyzed by porcine pancreatic lipase, it resulted in the synthesis of 6-*O*-butyryl- and 7-*O*-butyrylcastanospermine with isolated yields of 11% and 6%, respectively. These data indicate that although lipase has different regioselectivity, it cannot be used as an efficient catalyst in the preparative acylation of castanospermine. Here we describe another approach that may solve the aforementioned problem.

1-*O*-acyl derivatives of castanospermine are readily soluble in a variety of organic solvents. The use of tetrahydrofuran (THF) as a reaction medium, for example, allows us to exploit the regioselectivity of several lipases as well as subtilisin. Porcine pancreatic lipase (PPL), lipase from *Chromobacterium viscosum* (CV), and subtilisin Carlsberg have been used as catalysts for further enzymatic acylation of 1-*O*-acylcastanospermine (Scheme II). A typical reaction procedure is described in footnote *a* to Table II. Several 1-*O*-acyl derivatives of castanospermine have been used as substrates for enzymatic modification. It is clear that the regioselectivity of subtilisin is different from that of the lipases tested. Subtilisin shows a preference for acylation of the OH group at the C6 position, while in most cases lipases prefer the OH group at C7. This effect is especially striking when a bulky phenylacetyl group is attached to the hydroxyl group at the C1 position (entry 1). In this case, the regioselectivity of subtilisin for the C6 position is at least 80 times more than that of PPL.

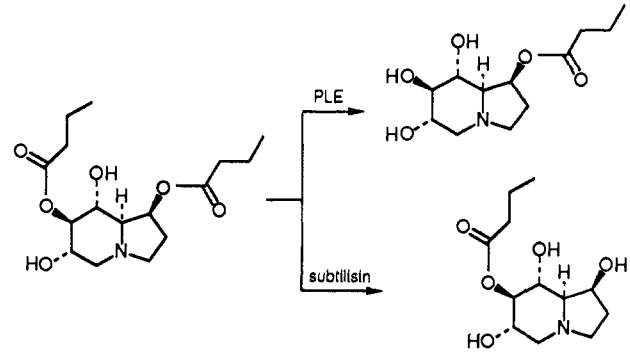
(14) Subtilisin is insoluble in anhydrous pyridine.

Scheme II[a]



[a] R_1 and R_2 = alkyl or aryl; R_3 = 2,2,2-trichloroethyl or vinyl.

Scheme III



It is important to mention that in no cases have triesters or 1,8-diesters of castanospermine been found. The yield of 1,6-isomer formation catalyzed by subtilisin is low and does not exceed 20%. On the other hand, the reactions catalyzed by lipases are more efficient. Among the lipases tested, lipase CV is especially active. The reactions catalyzed by this enzyme usually result in combined isolated yields of 80%.

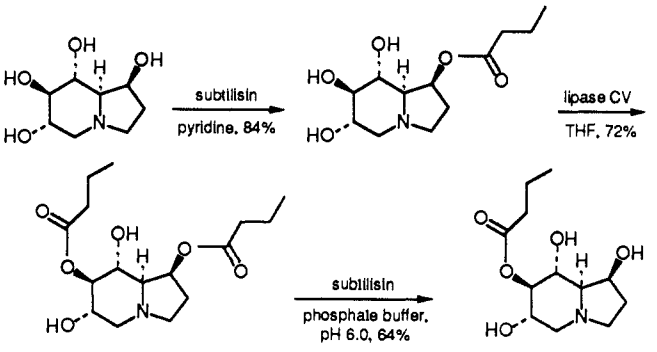
In order to overcome the high regioselectivity of subtilisin in pyridine, we tried to enzymatically hydrolyze these di-*O*-acyl derivatives of castanospermine to form mono-*O*-acyl compounds other than 1-*O*-acylcastanospermine (Scheme III). Several lipases, proteases, and esterases were tested for their ability to hydrolyze 1,7-di-*O*-butyrylcastanospermine in aqueous solution. Two enzymes—porcine liver esterase (PLE) and subtilisin—turn out to be active. The most interesting fact, however, is the reverse regioselectivity of these two enzymes. While PLE preferentially cleaves off the butyryl group from the C7 position with regioselectivity (C1:C7) better than 1:25, subtilisin hydrolyzes the ester bond at the C1 position with regioselectivity more than 25:1 (Table III, Scheme III). For synthetic purposes this property of subtilisin is very important, because it makes possible a three-step en-

Table III. Enzyme-Catalyzed Hydrolysis of 1,7-Di-*O*-butyrylcastanospermine[a]

enzyme[b]	reaction time, h	yield,[c] %	regioselectivity[d]
subtilisin	7	64	>25
PLE	19	75	<0.04

[a] Reaction conditions: 1,7-di-*O*-butyrylcastanospermine (189 mg, 0.57 mmol) was dissolved in 57 mL of 10 mM phosphate buffer (pH 6.0) containing 10% ethanol, followed by addition of subtilisin Carlsberg (5 mg/mL). The reaction took place at 20 °C for 7 h. The reaction was followed by TLC using 10% $EtOH/CH_2Cl_2$ to assay the formation of the 1-O-isomer (R_f 0.20) and 7-O-isomer (R_f 0.15) and hydrolysis of the substrate (R_f = 0.55). The formation of castanospermine (R_f = 0.13) was detected by TLC using $CH_2Cl_2/EtOH/NH_4OH$ (50:50:1). After castanospermine started to appear, the reaction was stopped by freezing and the reaction mixture was lyophilized. The lyophilized powder was subjected to radial chromatography with a mixture of 8% $EtOH/CH_2Cl_2$. Hydrolysis catalyzed by PLE was carried out as above with small modifications: no ethanol was added to the buffer and the PLE concentration was 200 μL/mL. [b] No appreciable reaction was detected without enzyme. [c] Measured as a combined isolated yield for both isomers before their separation. [d] Estimated by ^1H NMR and expressed as a ratio of synthesized amounts of 7-*O*-butyrylcastanospermine to 1-*O*-butyrylcastanospermine. In both cases, only one isomer has been detected.

Scheme IV



zyme-catalyzed synthesis of 7-*O*-butyrylcastanospermine (Scheme IV).

In summary, subtilisin catalyzes highly regioselective acylation of castanospermine in pyridine. Under these conditions, subtilisin possesses a broad substrate specificity that allows for preparative synthesis of several 1-*O*-acylcastanospermine derivatives. Further esterification catalyzed by lipases in anhydrous tetrahydrofuran leads to the preparation of diesters of castanospermine. Finally, the regioselective hydrolysis catalyzed by subtilisin in water makes possible the preparation of C7 esters. We believe that the developed methodology which combines enzyme-catalyzed synthesis in organic solvents and hydrolysis in water may be used for selective modification of other amino sugars with potential anti-HIV activities.

Experimental Section

Lipase from *C. viscosum* was purchased from Finnsugar Biochemicals (Schaumburg, IL). Porcine pancreatic lipase (EC 3.1.1.3), subtilisin (EC 3.4.21.4, protease from *Bacillus subtilis*), and esterase from porcine liver (EC 3.1.1.1) were obtained from Sigma (St. Louis, MO). Porcine pancreatic lipase was kept under vacuum for 2 days prior to use, which lowered its water content from 4.2% to 0.9%. Subtilisin and lipase from *C. viscosum* were dissolved in 0.1 M phosphate buffer, pH 7.8 and 7.0, respectively, and were freeze-dried prior to use. This "pH adjustment", first discovered by Zaks and Klibanov,[15] significantly increases the catalytic activity of enzymes in organic solvents.

Trichloroethyl butyrate, trifluoroethyl butyrate, and trifluoroethyl octanoate were synthesized from the corresponding acyl chlorides following a general methodology.[16] The characteristics of trichlorethyl butyrate[9] and trifluoroethyl butyrate[10a] were described previously. Trifluoroethyl octanoate was purified by bulb-to-bulb distillation at 120 °C and 15 mmHg and had the following characteristics: ^1H NMR ($CDCl_3$, 300 MHz) δ 0.88 (3 H, t, $-CH_3$), 1.30 [8 H, m, $(CH_2)_4$], 1.66 (2 H, quintet, $-CH_2-$), 2.41 (2 H, t, $-CH_2CO$), 4.46 (2 H, quartet, J_{HF} = 8.5 Hz, $-OCH_2CF_3$); MS *m/e* 227 (MH^+). Monochloroethyl esters of *N*-acetyl amino acids were prepared from the corresponding *N*-acetyl amino acids (obtained from Sigma) and 2-chloroethanol (Aldrich, Milwaukee, WI). The properties of these compounds were described previously.[10b] Vinyl acetate (bp 72–73 °C) was from Aldrich. Vinyl butyrate (bp 115–117 °C) and vinyl phenylacetate (bp 88–90 °C, 50 mm) were from Polysciences, Inc. (Warrington, PA) and were distilled prior to use. Castanospermine [(1*S*,6*S*,7*R*,8*R*,8a*R*)-1,6,7,8-tetrahydroxyoctahydroindolizine] was isolated from seeds of the Australian chestnut tree *Castanospermum australe* by Dow Chemical Co.

All melting points were determined on a Thomas-Hoover Unimelt apparatus and are uncorrected. Elemental analyses were carried out by the Analytical Department, Merrell Dow Research Institute. Low-resolution mass spectra were obtained on a Finnigan 4023 GC/MS/DS instrument operated in the chemical ionization (CI) mode. High-resolution mass spectra (HRMS) were recorded on a ZEB2-SE system using PFK as a mass reference. Analytical TLC was performed on Merck silica gel 60-F254 precoated (0.25 mm thick) glass plates. All acylating agents as well as 2,2,2-trichloroethanol, 2,2,2-trifluoroethanol, and 2-chloroethanol were detected by gas chromatography (GC) with a 5-m HP-1 capillary column coated with methylsilicone gum (Hewlett-Packard), with helium as a carrier gas. HPLC analyses were performed on a Waters system consisting of two pumps (Model 510), a controller, and a photodiode array detector (Model 990) and equipped with a μBondapak C-18 column. All silica gel chromatography separations were performed on a Chromatotron (Model 7924T, Harrison Research, CA) using 1- or 2-mm plates.

NMR Spectroscopy. ^1H NMR spectra were recorded on a Varian XL-300 NMR system. Spectra were acquired in the Fourier transform mode over a 4000-Hz spectral width with a digital resolution of 0.25 Hz/point. Samples were prepared by dissolving 2–5 mg of material in about 0.7 mL of DMSO-d_6. Chemical shifts (δ) are in parts per million (ppm) relative to Me_4Si. Spectra were first recorded in DMSO-d_6, and then a few drops of D_2O were added to each sample to exchange the hydroxyl protons and to simplify the spectrum. Coupling patterns, and therefore basic line shapes, for the various signals did not change appreciably on substitution. Therefore, spectral assignments for most signals were readily made by simple inspection. Notable exceptions were the signals for H7 and H8. Both of these signals possess two large couplings and appear as pseudotriplets (dd) in the spectra. These signals are readily distinguished by homonuclear decoupling. The regiochemistry of ester derivatives of castanospermine was verified by the well-established downfield shift (ca. 1 ppm) of methine protons due to the anisotropy of the adjacent ester carbonyl bond.[17] ^{13}C NMR spectra (75.4 MHz) were also recorded. While the ^{13}C spectra were indeed indicative of the indolizidine ring structure for castanospermine, they did not reflect adequate sensitivity to the various substitution patterns to be a reliable stereochemical probe.

Preparative Enzymatic Syntheses. The conditions for the syntheses of 1-*O*-acylcastanospermine derivatives are described in footnote *a* to Table I. Following filtration of the enzyme, the pyridine was evaporated under vacuum. The remaining residue was subjected to radial silica gel chromatography using $EtOH/CH_2Cl_2$ as a solvent, or the product was recrystallized from EtOAc.

Enzymatic Synthesis of 1-*O*-Acetylcastanospermine. Chromatography was performed with 8% $EtOH/CH_2Cl_2$ as the eluent. Recrystallization from EtOAc resulted in a white crystalline solid, mp 151–153 °C, R_f 0.22 (15% $EtOH/CH_2Cl_2$). ^1H NMR (DMSO-d_6, 300 MHz): δ 1.54 (1 H, m, H2α), 1.75 (1 H, dd, H5α), 1.82 (1 H, dd, H8a), 1.97 [3 H, s, $-C(O)CH_3$], 1.99 (1 H, ddd, H3α), 2.21 (1 H, m, H2β), 2.93–2.97 (3 H, m, H3β, H5β, H7), 3.34 (1 H, dd, H8), 3.35 (1 H, ddd, H6), 5.08 (1 H, m, H1). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 21.3 (CO_2Me), 32.0 (C2), 52.0 (C3), 56.9 (C5), 68.9 (C8), 70.4 (C1), 70.7 (C6), 72.9 (C8a), 79.5 (C7). MS: *m/e* 232 (MH^+), 214 ($MH^+ - H_2O$), 172 ($MH^+ - CH_3CO_2H$). Anal. Calcd for $C_{10}H_{17}O_5N$: C, 51.92; H, 7.41; N, 6.05. Found: C, 52.01; H, 7.58; N, 6.05.

Enzymatic Synthesis of 1-*O*-Butyrylcastanospermine. After the evaporation of pyridine, the remaining residue was crystallized from EtOAc. 1-*O*-Butyrylcastanospermine was a white crystalline solid, mp 150–151 °C, R_f 0.29 [$CH_2Cl_2/EtOH/NH_4OH$ (50:50:1)]. ^1H NMR (DMSO-d_6, 300 MHz): δ 0.97 [3 H, t, $-OC(O)CH_2CH_2CH_3$], 1.67 [2 H, sextet, $-OC(O)CH_2CH_2CH_3$], 2.38 [2 H, t, $-OC(O)CH_2CH_2CH_3$], 2.00 (1 H, m, H2α), 2.05 (1 H, dd, H5α), 2.06 (1 H, dd, H8a), 2.24 (1 H, ddd, H3α), 2.27 (1 H, m, H2β), 3.20–3.30 (3 H, H3β, H5β, H7), 3.39

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(1 H, dd, H8), 3.76 (1 H, ddd, H6), 5.28 (1 H, m, H1). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 30.5 (C2), 51.7 (C3), 55.6 (C5), 69.4 (C8), 70.2 (C1), 71.1 (C6), 74.1 (C8a), 79.1 (C7), 36.2 ($CH_2\alpha$), 18.4 ($CH_2\beta$), 13.6 ($CH_3\gamma$), 175.7 (CO). MS: *m/e* 260 (MH^+), 242 ($MH^+ - H_2O$), 172 [$MH^+ - HOC(O)CH_2CH_2CH_3$]. HRMS (CI, CH_4 as ionizing gas) for $C_{12}H_{22}O_5N$ ($M^+ + 1$): calcd 260.1498, found 260.1492. Anal. Calcd for $C_{12}H_{21}O_5N$: C, 55.58; H, 8.16; N, 5.40. Found: C, 55.79; H, 8.43; N, 5.28.

Enzymatic Synthesis of 1-*O*-Octanoylcastanospermine. Chromatography with 10% EtOH/CH_2Cl_2 resulted in a waxy yellow semisolid, F_f 0.23 (8% EtOH/CH_2Cl_2). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 0.86 [3 H, t, $-OC(O)CH_2(CH_2)_5CH_3$], 1.25 (8 H, s) and 1.50 (2 H, m) ($-OC(O)CH_2(CH_2)_5CH_3$), 2.24 [1 H, t, $-OC(O)CH_2(CH_2)_5CH_3$], 1.50 (1 H, m, H2α), 1.75 (1 H, dd, H5α), 1.82 (1 H, dd, H8a), 1.97 (1 H, ddd, H3α), 2.23 (1 H, m, H2β), 3.00 (3 H, H3β, H5β, H7), 3.35 (1 H, dd, H8), 3.37 (1 H, ddd, H6), 5.09 (1 H, m, H1). ^{13}C NMR (DMSO-d_6, 75.4 MHz): δ 32.2 (C2), 52.1 (C3), 56.9 (C5), 69.2 (C8), 70.4 (C1), 70.8 (C6), 73.0 (C8a), 79.7 (C7), 34.2, 31.5, 28.8, 24.8, 24.8, 22.5, and 14.4 (aliphatic chain), 173.6 (CO). MS: *m/e* 316 (MH^+), 298 ($MH^+ - H_2O$), 172 [$MH^+ - HOC(O)CH_2(CH_2)_5CH_3$]. Anal. Calcd for $C_{16}H_{29}O_5N$: C, 60.91; H, 9.27; N, 4.44. Found: C, 60.40; H, 9.44; N, 4.32.

Enzymatic Synthesis of 1-*O*-(Phenylacetyl)castanospermine. Silica gel chromatography using 8% EtOH/CH_2Cl_2 as the eluent resulted in a pale yellow crystalline solid, mp 110–112 °C, R_f 0.31 (8% EtOH/CH_2Cl_2). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.52 (1 H, m, H2α), 1.76 (1 H, dd, H5α), 1.85 (1 H, dd, H8a), 1.97 (1 H, ddd, H3α), 2.23 (1 H, m, H2β), 2.97–3.01 (3 H, H3β, H5β, H7), 3.38 (2 H, H6, H8), 3.65 (2 H, s, $-CH_2C_6H_5$), 5.13 (1 H, m, H1), 7.25–7.34 (5 H, aromatic). ^{13}C NMR (DMSO-d_6, 75.4 MHz): δ 32.1 (C2), 52.1 (C3), 56.9 (C5), 69.1 (C8), 70.4 (C1), 70.7 (C6), 73.5 (C8a), 79.6 (C7), 40.7 ($-CH_2C_6H_5$), 171.5 (CO), 134.8, 129.8, 128.8, and 127.2 (aromatic). MS: *m/e* 308 (MH^+), 290 ($MH^+ - H_2O$), 172 [$MH^+ - HOC(O)CH_2C_6H_5$]. HRMS (CI, CH_4 as ionizing gas) for $C_{16}H_{22}O_5N$ ($M^+ + 1$): calcd 308.1498, found 308.1514.

Enzymatic Synthesis of 1-*O*-(*N*-Acetyl-L-phenylalanyl)castanospermine. Silica gel chromatography using 15% EtOH/CH_2Cl_2 as the eluent resulted in a white crystalline solid, mp 165 °C dec, R_f 0.34 (15% EtOH/CH_2Cl_2). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.57 (1 H, m, H2α), 1.79 [3 H, d, $-C(O)CH_3$], 1.90 (1 H, dd, H8a), 2.00 (1 H, ddd, H5α), 2.26 (1 H, m, H2β), 2.82 (δ_A), 3.17 (δ_B), and 4.42 (δ_X) (3 H, "ABX", $-CHCH_2C_6H_5$), 2.96–3.00 (3 H, H3β, H5β, H7), 3.37 (1 H, ddd, H6), 3.38 (1 H, dd, H8), 5.12 (1 H, m, H1), 7.27 (5 H, aromatic), 8.29 (NH), 4.61, 4.76, and 4.84 (exchangeable OH). ^{13}C NMR (DMSO-d_6, 75.4 MHz): δ 31.9 (C2), 52.0 (C3), 56.9 (C5), 69.0 (C8), 70.2 (C1), 70.6 (C6)8, 73.8 (C8a), 79.6 (C7), 36.6 ($CH_2C_6H_5$), 171.4 and 171.2 (CO), 53.9 (CHa), 22.3 (CH_3), 137.7, 129.2, 128.5, and 126.7 (aromatic). MS: *m/e* 379 (MH^+), 361 ($MH^+ - H_2O$), 190, 172 [base; $MH^+ - HOC(O)CH(CH_2C_6H_5)NHC(O)CH_3$]. HRMS (CI, CH_4 as ionizing gas) for $C_{19}H_{27}O_6N_2$ ($M^+ + 1$): calcd 379.1869, found 379.1868.

Enzymatic Synthesis of 1-*O*-(*N*-Acetyl-L-alanyl)castanospermine. Silica gel chromatography using 50% EtOH/CH_2Cl_2 as the eluent resulted in a white crystalline solid, mp 196–198 °C, R_f 0.29(50% EtOH/CH_2Cl_2). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.26 (3 H, d, $-CHCH_3$), 1.55 (1 H, m, H2α), 1.77 (1 H, dd, H5α), 1.84 [3 H, s, $-C(O)CH_3$], 1.87 (1 H, dd, H8a), 1.98 (1 H, ddd, H3α), 2.23 (1 H, m, H2β), 2.94–3.00 (3 H, H3β, H5β, H7), 4.17 (1 H, m, CHα), 3.33 (1 H, dd, H8), 3.38 (1 H, ddd, H6), 5.10 (1 H, m, H1), 4.52, 4.75, and 4.80 (1 H each, exchangeable OH), 8.27 (NH). MS: *m/e* 303 (MH^+), 285 ($MH^+ - H_2O$), 190, 172 [$MH^+ - HOC(O)CH(CH_3)NHC(O)CH_3$]. HRMS (CI, CH_4 as ionizing gas) for $C_{13}H_{22}N_2O_6$ ($M^+ + 1$): calcd 303.1556, found 303.1534.

Enzymatic Synthesis of 1-*O*-(*N*-Acetyl-D-alanyl)castanospermine. Silica gel chromatography using 50% EtOH/CH_2Cl_2 as the eluent resulted in an oil, R_f 0.29 (50% EtOH/CH_2Cl_2). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.25 (3 H, d, $-CHCH_3$), 1.52 (1 H, m, H2α), 1.75 (1 H, dd, H5α), 1.84 [3 H, s, $-C(O)CH_3$], 1.86 (1 H, dd, H8a), 1.98 (1 H, ddd, H3α), 2.23 (1 H, m, H2β), 2.94–3.00 (3 H, H3β, H5β, H7), 3.34 (1 H, dd, H8), 3.35 (1 H, ddd, H6), 4.22 (1 H, m, CHα), 5.10 (1 H, m, H1), 4.53, 4.73, and 4.79 (1 H each, exchangeable OH), 8.25 (NH). MS: *m/e* 303 (MH^+), 285 ($MH^+ - H_2O$), 190, 172 [$MH^+ - HOC(O)CH(CH_3)NHC(O)CH_3$]. HRMS (CI, CH_4 as ionizing gas) for $C_{13}H_{22}N_2O_6$ ($M^+ + 1$): calcd 303.1556, found 303.1556.

Enzymatic Synthesis of 6-*O*-Butyrylcastanospermine and 7-*O*-Butyrylcastanospermine. Castanospermine, 68 mg (0.36 mmol), was dissolved in 6 mL of warm anhydrous pyridine, followed by addition of 158 mg (0.72 mmol) of (2,2,2-trichloroethyl)butyrate. Then 600 mg of crude porcine pancreatic lipase was added. (Preparation of the enzyme is described in the Experimental Section). The suspension was shaken for 4 days at 45 °C and 250 rpm. Then the lipase was removed by filtration, the pyridine evaporated under vacuum, and the product isolated and purified by radial silica gel chromatography using 20% EtOH/CH_2Cl_2 as the eluent. As a result pure 6-*O*-butyrylcastanospermine (9.9 mg, 0.038 mmol) and 7-*O*-butyrylcastanospermine (5.4 mg, 0.021 mmol) were isolated in a combined isolated yield of 16.4%.

6-*O*-Butyrylcastanospermine: white crystalline solid, mp 114–115 °C, R_f 0.39 (20% EtOH/CH_2Cl_2). ^{1}H NMR (DMSO-d_6, TMS reference): δ 0.88 [3 H, t, $-OC(O)CH_2CH_2CH_3$], 1.54 [2 H, sextet, $-OC(O)CH_2CH_2CH_3$], 2.27 [2 H, t, $-OC(O)CH_2CH_2CH_3$], ca. 1.57 (1 H, m, H2α), 1.65 (1 H, dd, H8a), 1.81 (1 H, dd, H5α), 1.94 (1 H, ddd, H3α), 2.09 (1 H, m, H2β), 2.95 (1 H, ddd, H3β), 3.03 (1 H, dd, H5β), 3.23 (1 H, dd, H7), 3.45 (1 H, dd, H8), 4.12 (1 H, m, H1), 4.62 (1 H, ddd, H6). MS: *m/e* 260 (MH^+), 242 ($MH^+ - H_2O$), 172 [$MH^+ - HOC(O)CH_2CH_2CH_3$].

7-*O*-Butyrylcastanospermine: oil, R_f 0.28 (20% EtOH/CH_2Cl_2). ^{1}H NMR (DMSO-d_6, TMS reference): δ 0.91 [3 H, t, $-OC(O)CH_2CH_2CH_3$], 1.57 [2 H, sextet, $-OC(O)CH_2CH_2CH_3$], 2.30 [2 H, t, $-OC(O)CH_2CH_2CH_3$], ca. 1.57 (1 H, m, H2α), 1.72 (1 H, dd, H8a), 1.86 (1 H, dd, H5α), 1.98 (1 H, ddd, H3α), 2.11 (1 H, m, H2β), 2.96 (1 H, ddd, H3β), 3.02 (1 H, dd, H5β), 3.49 (1 H, dd, H6), 3.52 (1 H, dd, H8), 4.13 (1 H, m, H1), 4.61 (1 H, dd, H7). MS: *m/e* 260 (MH^+), 242 ($MH^+ - H_2O$), 172 [$MH^+ - HOC(O)CH_2CH_2CH_3$]. Anal. Calcd for $C_{12}H_{21}O_5N$: C, 55.57; H, 8.17; N, 5.40. Found: C, 55.39; H, 8.17; N, 5.38.

The conditions of the syntheses of di-*O*-acyl derivatives of castanospermine are described in footnote *a* to Table II. Following filtration of the enzyme, the THF was evaporated under vacuum. The remaining residue was subjected to radial silica gel chromatography on a Chromatotron using EtOH/CH_2Cl_2 as the eluent.

Enzymatic Synthesis of 1,6-Di-*O*-butyrylcastanospermine. Chromatography was performed with 2% EtOH/CH_2Cl_2 as the eluent. Chromatography resulted in a waxy semisolid, R_f 0.47 (8% EtOH/CH_2Cl_2). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 0.87 [6 H, t, $-OC(O)CH_2CH_2CH_3$], 1.57 [4 H, sextet, $-OC(O)CH_2CH_2CH_3$], 2.30 [4 H, 2t, $-OC(O)CH_2CH_2CH_3$], 1.55 (1 H, m, H2α), 1.85 (1 H, dd, H5α), 1.92 (1 H, dd, H8a), 2.02 (1 H, m, H3α), 2.25 (1 H, m, H2β), 2.95 (1 H, dt, H3β), 3.06 (1 H, dd, H5β), 3.25 (1 H, dd, H7), 3.42 (1 H, dd, H8), 4.62 (1 H, ddd, H6), 5.12 (1 H, m, H1). MS: *m/e* 330 (MH^+), 312 ($MH^+ - H_2O$), 242 [$MH^+ - HOC(O)CH_2CH_2CH_3$]. Anal. Calcd for $C_{16}H_{27}O_6N$: C, 58.33; H, 8.27; N, 4.25. Found: C, 57.85; H, 8.02; N, 3.99.

Enzymatic Synthesis of 1,7-Di-*O*-butyrylcastanospermine. Chromatography was performed with 2% EtOH/CH_2Cl_2 as the eluent and resulted in an oil, R_f 0.41 (8% EtOH/CH_2Cl_2). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 0.87 [3 H, t, $-OC(O)CH_2CH_2CH_3$], 0.91 [3 H, t, $-OC(O)CH_2CH_2CH_3$], 1.54 [2 H, sextet, $-OC(O)CH_2CH_2CH_3$], 1.56 [2 H, sextet, $OC(O)CH_2CH_2CH_3$], 2.24 [2 H, t, $-OC(O)CH_2CH_2CH_3$], 2.28 [2 H, t, $-OC(O)CH_2CH_2CH_3$], 1.55 (1 H, m, H2a), 1.87 (1 H, dd, H5α), 1.98 (1 H, dd, H8a), 2.05 (1 H, quartet, H3α), 2.25 (1 H, m, H2β), 2.95 (1 H, dt, H3β), 3.03 (1 H, dd, H5β), 3.45 (1 H, t, H8), 3.49 (1 H, dt, H6), 4.58 (1 H, t, H7), 5.01 (1 H, m, H1). MS: *m/e* 330 (MH^+), 312 ($MH^+ - H_2O$), 242 [$MH^+ - HOC(O)CH_2CH_2CH_3$]. Anal. Calcd for $C_{16}H_{27}O_6N$: C, 58.33; H, 8.27; N, 4.25. Found: C, 58.43; H, 8.31; N, 3.93.

Enzymatic Synthesis of 1-*O*-Acetyl-7-*O*-butyrylcastanospermine. Chromatography was performed with 5% EtOH/CH_2Cl_2 (R_f 0.17) and resulted in a waxy semisolid. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 0.90 [6 H, t, $-OC(O)CH_2CH_2CH_3$ and $-OC(O)CH_3$], 1.57 [2 H, sextet, $-OC(O)CH_2CH_2CH_3$], 2.3 [2 H, t, $-OC(O)CH_2CH_2CH_3$], 1.55 (1 H, m, H2α), 1.87 (1 H, dd, H5α), 1.98 (1 H, dd, H8a), 2.05 (1 H, quartet, H3α), 2.30 (1 H, m, H2β), 3.02 (1 H, dt, H3β), 3.06 (1 H, dd, H5β), 3.30 (1 H, t, H8), 3.47 (1 H, dt, H6), 4.54 (1 H, t, H7), 5.08 (1 H, m, H1). MS: *m/e* 302 (MH^+), 284 ($MH^+ - H_2O$), 242 [$MH^+ - HOC(O)CH_3$], 214. Anal. Calcd for $C_{14}H_{23}O_6N$: C, 55.79; H, 7.70; N, 4.65. Found: C, 55.74; H, 7.98; N, 4.54.

Enzymatic Synthesis of 1-*O*-Acetyl-6-*O*-butyrylcastanospermine. Chromatography was performed with 5% EtOH/CH_2Cl_2 (R_f 0.21) and resulted in an oil: ^{1}H NMR (DMSO-d_6, 300 MHz): δ 0.87 [6 H, t, $-OC(O)CH_2CH_2CH_3$], 1.52 [2 H, sextet, $-OC(O)CH_2CH_2CH_3$], 2.25 [2 H, t, $-OC(O)CH_2CH_2CH_3$], 1.55 (1 H, m, H2α), 1.82 (1 H, dd, H5α), 1.92 (1 H, dd, H8a), 2.01 (1 H, ddd, H3α), 2.20 (1 H, m, H2β), 2.98 (1 H, dt, H3β), 3.05 (1 H, dd, H5β), 3.15 (1 H, dd, H7), 3.35 (1 H, dd, H8), 4.60 (1 H, ddd, H6), 5.10 (1 H, m, H1), 1.97 [3 H, s, $-OC(O)CH_3$]. MS: *m/e* 302 (MH^+), 284 ($MH^+ - H_2O$), 242 [$MH^+ - HOC(O)CH_2CH_2CH_3$], 214. Anal. Calcd for $C_{14}H_{23}O_6N$: C, 55.79; H, 7.70; N, 4.65. Found: C, 55.46; H, 7.68; N, 4.52.

Enzymatic Synthesis of 1-*O*-(Phenylacetyl)-6-*O*-butyrylcastanospermine. Chromatography with 2% EtOH/CH_2Cl_2 (R_f 0.29) resulted in white crystals, mp 107–109 °C. ^{1}H NMR (DMSO-d_6, 300

MHz): δ 0.90 [3 H, t, -OC(O)$CH_2CH_2CH_3$], 1.55 [2 H, sextet, -OC(O)$CH_2CH_2CH_3$], 2.28 [2 H, t, -OC(O)$CH_2CH_2CH_3$], 1.55 (1 H, m, H2α), 1.85 (1 H, dd, H5α), 1.95 (1 H, dd, H8a), 2.02 (1 H, ddd, H3α), 2.23 (1 H, m, H2β), 2.98 (1 H, dt, H3β), 3.05 (1 H, dd, H5β), 3.28 (1 H, dd, H7), 3.47 (1 H, dd, H8), 3.65 (2 H, s, -OC(O)$CH_2C_6H_5$), 4.62 (1 H, ddd, H6), 5.15 (1 H, m, H1), 7.25-7.35 (5 H, aromatic). MS: *m/e* 378 (MH^+), 360 ($MH^+ - H_2O$), 290 [MH^+ - HOC(O)$CH_2CH_2CH_3$], 242 [MH^+ - H(O)$COCH_2C_6H_5$]. Anal. Calcd for $C_{20}H_{27}O_6N$: C, 63.63; H, 7.21; N, 3.71. Found: C, 63.27; H, 7.28; N, 3.71.

Enzymatic Synthesis of 1-*O*-(Phenylacetyl)-7-*O*-butyryl-castanospermine. Chromatography with 5% EtOH/CH_2Cl_2 (R_f 0.15) resulted in an oil. ^1H NMR (DMSO-d_6, 300 MHz): δ 0.92 [3 H, t, -OC(O)$CH_2CH_2CH_3$], 1.60 [2 H, sextet, -OC(O)$CH_2CH_2CH_3$], 2.32 [2 H, t, -OC(O)$CH_2CH_2CH_3$], 1.55 (1 H, m, H2α), 1.88 (1 H, dd, H5α), 2.02 (1 H, dd, H8a), 2.05 (1 H, ddd, H3α), 2.25 (1 H, m, H2β), 2.98 (1 H, dt, H3β), 3.05 (1 H, dd, H5β), 3.50 (1 H, t, H8), 3.52 (1 H, dt, H6), 3.65 (2 H, s, -OC(O)$CH_2C_6H_5$), 4.57 (1 H, t, H7), 5.12 (1 H, m, H1), 7.25-7.35 (5 H, aromatic). MS: *m/e* 378 (MH^+), 360 ($MH^+ - H_2O$), 290 [MH^+ - HOC(O)$CH_2CH_2CH_3$], 242 [MH^+ - HOC(O)$CH_2C_6H_5$]. Anal. Calcd for $C_{20}H_{27}O_6N$: C, 63.63; H, 7.21; N, 3.71. Found: C, 63.30; H, 7.37; N, 3.39

Enzymatic Synthesis of 1-*O*-Butyryl-7-*O*-(phenylacetyl)castanospermine. Chromatography with 3.5% EtOH/CH_2Cl_2 (R_f 0.30) resulted in a waxy semisolid. ^1H NMR (DMSO-d_6, 300 MHz): δ 0.92 [3 H, t, -OC(O)$CH_2CH_2CH_3$], 1.58 [2 H, sextet, -OC(O)$CH_2CH_2CH_3$], 2.31 [2 H, t, -OC(O)$CH_2CH_2CH_3$], 1.55 (1 H, m, H2α), 1.88 (1 H, dd, H5α), 2.00 (1 H, dd, H8a), 2.02 (1 H, quartet, H3α), 2.25 (1 H, m, H2β), 2.98 (1 H, dt, H3β), 3.04 (1 H, dd, H5β), 3.51 (1 H, t, H8), 3.52 (1 H, dt, H6), 3.65 [2 H, s, -OC(O)$CH_2C_6H_5$], 4.62 (1 H, t, H7), 5.14 (1 H, m, H1), 7.25-7.35 (5 H, aromatic). MS: *m/e* 378 (MH^+), 360 ($MH^+ - H_2O$), 290 [MH^+ - HOC(O)$CH_2CH_2CH_3$], 242 [MH^+ - HOC(O)$CH_2C_6H_5$]. HRMS (CI, CH_4 as ionizing gas) for $C_{20}H_{28}O_6N$ ($M^+ + 1$): calcd 378.1838, found 378.1917.

Enzymatic Synthesis of 1-*O*-Butyryl-6-*O*-(phenylacetyl)castanospermine. Chromatography with 3.5% EtOH/CH_2Cl_2 (R_f 0.37) resulted in a waxy semiglass. ^1H NMR (DMSO-d_6, 300 MHz): δ 0.88 [3 H, t, -OC(O)$CH_2CH_2CH_3$], 1.52 [2 H, sextet, -OC(O)$CH_2CH_2CH_3$], 2.22 [2 H, t, -OC(O)$CH_2CH_2CH_3$], 1.52 (1 H, m, H2α), 1.85 (1 H, dd, H5α), 1.95 (1 H, dd, H8a), 2.02 (1 H, ddd, H3α), 2.22 (1 H, m, H2β), 2.95 (1 H, dt, H3β), 3.05 (1 H, dd, H5β), 3.28 (1 H, m, H7), 3.4 (1 H, dd, H8), 3.65 [1 H, s, -OC(O)$CH_2C_6H_5$], 4.62 (1 H, ddd, H6), 5.08 (1 H, m, H1), 7.25-7.35 (5 H, aromatic). MS: *m/e* 378 (MH^+), 360 ($MH^+ - H_2O$), 242 [MH^+ - HOC(O)$CH_2C_6H_5$], 137. HRMS (CI, CH_4 as ionizing gas) for $C_{20}H_{28}O_6N$ ($M^+ + 1$): calcd 378.1838; found 378.1917.

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MSXα Study of Absorption Spectra of Free Radicals. Characterization of Rydberg and Valence Transitions in Alkyl Derivatives of Group 14 Centered Radicals

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Abstract: Ionization potentials, electronic transition energies, and oscillator strengths were computed by the MSXα method for methyl, ethyl, isopropyl, *tert*-butyl, and $X_3M^•$ radicals (M = Si, Ge, Sn; X = H, CH_3). The best procedure, within the MSXα framework, for assigning optical absorption spectra in radicals was established. In alkyl and $H_3M^•$ radicals, the transition energies are in very good agreement with experiment and available ab initio CI calculations. The optical spectra of alkyl derivatives of heteroatom-centered radicals are assigned for the first time. The low-lying transitions are predominantly Rydberg in character and are red shifted as the degree of alkyl substitution increases or the electronegativity of the central atom M decreases in accordance with the trend of the vertical ionization potentials. In heteroatom-centered radicals, the first valence transition from the M-C bond to SOMO is strongly red shifted and occurs in the range of the lowest Rydberg transitions.

Short-lived radicals and their chemical behavior are usually investigated by optical detection techniques. In spite of the large number of electronic absorption spectra of free radicals reported in the literature, information on the nature of optical transitions is scarce.[1] For example, although the ultraviolet absorption of the methyl radical was assigned over 30 years ago, due to the work of Herzberg,[2] only recently have the electronic spectra of other simple alkyl radicals been characterized[3] and understood by means of ab initio calculations.[4] However, the most accurate theoretical methods, which involve some form of configuration interaction (CI), are prohibitive for the interpretation of electronic properties of large radicals or radicals containing heavy atoms.

The multiple scattering Xα (MSXα) method could be a powerful tool for assigning optical transitions in radicals.[5] As opposed to traditional LCAO methods, it requires little computational effort, so that large polyatomic systems can be investigated, and it treats, at the same level of accuracy, both valence excited and Rydberg states owing to the radial flexibility of the wave functions. It is well established that the MSXα method satisfactorily describes the electronic properties of molecules in ground and valence excited states. Indeed, ionization potentials,[6] electron affinities,[7] and electronic transitions[8] are reproducible with an accuracy comparable with LCAO-CI calculations with extended basis sets.

In this work, we have studied a number of group 14 centered radicals to see if the MSXα method can correctly predict electronic

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