reaction being controlled by a $LUMO_{azide}$–$HOMO_{olefin}$ interaction.[4] In the case of both NVP and NVA this is evident from the effect of substituents on the aryl azide; electron-withdrawing groups on the phenyl ring facilitate reaction (compounds 1–4, 9, and 11) while electron-releasing groups have a retarding effect (compounds 6, 7, 14, and 15) (Table I).

In conclusion, this work has successfully demonstrated the dipolarophilic activity of the vinylic bond in enamides by the 1,3-dipolar cycloaddition of aryl azides to NVP and the related NVA, and the synthesis of a number of 1-aryl-5-amido-1,2,3-triazolines bearing 2-oxo-1-pyrrolidinyl or *N*-methyl-*N*-acetamido groups.

Experimental Section

Melting points are uncorrected. NMR spectra were run on a 300-MHz spectrometer in $CDCl_3$ solutions with TMS as internal standard. C, H, and N elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

1,3-Dipolar Cycloaddition of Aryl Azides to the Enamides *N*-Vinyl-2-pyrrolidinone and *N*-Methyl-*N*-vinylacetamide: Synthesis of 1-Aryl-5-(2-oxo-1-pyrrolidinyl)- (IIc) and 1-Aryl-5-(*N*-methyl-*N*-acetamido)-1,2,3-triazolines (IId). A mixture of the enamide (0.06 mol) and aryl azide (0.06 mol) was placed in a loosely capped dark brown bottle and allowed to stand, protected from light, with periodic shaking. The reaction course was followed by the appearance of the product as a crystalline mass from the oily reaction mixture and worked up when all or most of the oil had solidified. The chunky crystalline mass was triturated with small portions of ethanol, suction filtered, and washed several times with ether or an ether–petroleum ether mixture, as the case may be, until all of the unreacted residual enamide was removed, as indicated by the absence of the characteristic unpleasant odor of the enamide reagent.

Crystallization was effected from acetone or acetone–petroleum ether mixture. As the amidotriazolines are sensitive to heat and yield the 1-aryltriazoles by loss of an amide molecule, the crystallization had to be conducted with minimum heating. Hot acetone was added to the products until solution was achieved and then filtered. The filtrate was either treated with petroleum ether and cooled or concentrated under reduced pressure and then cooled; if crystals failed to appear, petroleum ether was added. The results are presented in Table I.

Reaction of Aryl Azides with Enamides in Refluxing Ethanol: Synthesis of 1-Aryl-1,2,3-triazoles. A mixture of enamide (0.02 mol) and aryl azide (0.02 mol) in ethanol (7 mL) was refluxed on a steam bath. At the end of the reaction, the mixture was poured into crushed ice and cooled. The solid products were filtered, washed with petroleum ether–ether mixture to remove the unreacted oily enamide, and crystallized from acetone–petroleum ether mixture or from methanol.

NVP and 4-$(NO_2)PhN_3$, after 24 h of reflux, gave 1-(4-nitrophenyl)-1,2,3-triazole, mp 202–204 °C (lit.[21] mp 203–204 °C), yield, 66%. When 25 mL of EtOH was used, the yield of triazole was reduced to 34%: ^1H NMR δ 7.93 (s, br, 4-CH), 8.14 (s, br, 5-CH).

NVP and 4-(Cl)PhN_3, after 38.5 h of reflux, gave 1-(4-chlorophenyl)-1,2,3-triazole, mp 114–115.5 °C (lit.[24] mp 115 °C), yield 50%: ^1H NMR δ 7.86 (s, br, 4-CH), 8.00 (s, br, 5-CH).

NVA and 4-(Cl)PhN_3 similarly yielded 53% of the triazole.

NVP and PhN_3 gave after 90 h of reflux 1-phenyl-1,2,3-triazole, mp 53–55.5 °C (lit.[25] mp 56 °C), yield 17%: ^1H NMR δ 7.83 (d, 4-CH), 8.04 (d, 5-CH); $J_{4H,5H} = J_{5H,4H} = 1.2$ Hz. A 20 h reflux gave no triazole.

Reaction of 1-Aryl-5-amidotriazolines with KOH. To a solution of 0.5 g of triazoline 11 in methanol (10 mL) was added a solution of KOH (2 N, 10 mL), and the mixture was refluxed with magnetic stirring for 30 min. The reaction mixture was diluted with ice-cold water and cooled to afford 1-(4-chlorophenyl)-1,2,3-triazole as a pure, crystalline material, mp 114–115.5 °C, yield 84%.

Similar treatment of triazoline 3 yielded the identical triazole, mp 114–115 °C, yield 70%.

Acknowledgment. The author thanks undergraduate laboratory assistants, Michelle Morgan, and Andrea Moore for their skillful assistance and the University of Kentucky Medical Center Research Advisory Committee for partial support.

Registry No. 1, 139871-49-1; 2, 139895-24-2; 3, 121318-96-5; 4, 139871-50-4; 5, 139871-51-5; 6, 139871-52-6; 7, 139871-53-7; 8, 121318-95-4; 9, 139871-54-8; 10, 139871-55-9; 11, 139871-56-0; 12, 139871-57-1; 13, 139871-59-3; 15, 139871-60-6; 16, 139871-61-7; 4-$NO_2C_6H_4N_3$, 1516-60-5; 3,4-$Cl_2C_6H_3N_3$, 66172-16-5; 4-$ClC_6H_4N_3$, 3296-05-7; 4-$CF_3C_6H_4N_3$, 5586-13-0; 3-$CF_3C_6H_4N_3$, 22001-17-8; 4-$CH_3C_6H_4N_3$, 2101-86-2; 4-$CH_3OC_6H_4N_3$, 2101-87-3; PhN_3, 622-37-7; 1-vinyl-2-pyrrolidinone, 88-12-0; *N*-vinylacetamide, 5202-78-8; 1-(4-nitrophenyl)-1,2,3-triazole, 1204-91-7; 1-(4-chlorophenyl)-1,2,3-triazole, 20320-16-5; 1-phenyl-1,2,3-triazole, 1453-81-2.

(24) El Khadem, H.; Mansour, H. A. R.; Meshreki, M. H. *J. Chem. Soc. C* **1968**, 1329.
(25) Begtrup, M. *Acta Chem. Scand.* **1973**, *27*, 3101.

Synthesis of 1-Deoxycastanospermine and Stereoisomers

Yves St-Denis and Tak-Hang Chan*

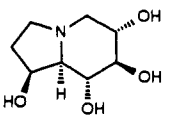
Department of Chemistry, McGill University, Montréal, Québec, Canada H3A 2K6

Received October 29, 1991

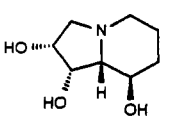
Four different isomers of 1-deoxycastanospermine (6,7,8-trihydroxyindolizidine) were synthesized. Their basic skeleton was constructed from a proline derivative and the anion of allyl phenyl sulfide, followed by an allylic sulfide rearrangement and a subsequent nucleophilic cyclization. The aminotriols were obtained in good yields with a concise overall sequence.

Introduction

Castanospermine 1[1] and swainsonine 2[2] have attracted much attention over the past decade. These two polyhydroxylated indolizidine alkaloids have displayed a wide variety of biological properties.[3] In a recent review,[3]



Castanospermine 1



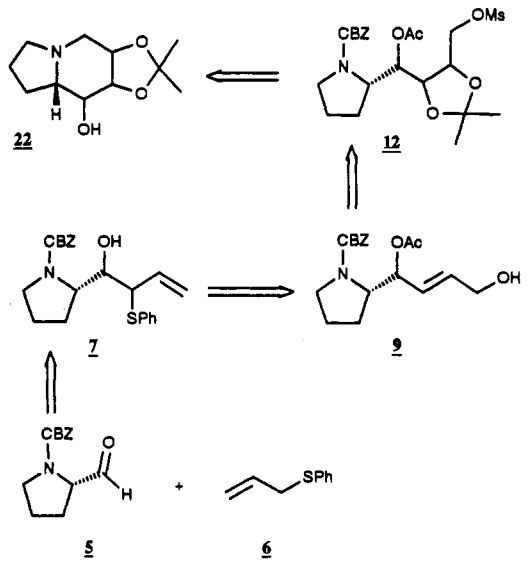
Swainsonine 2

castanospermine has been reported to function as a plant

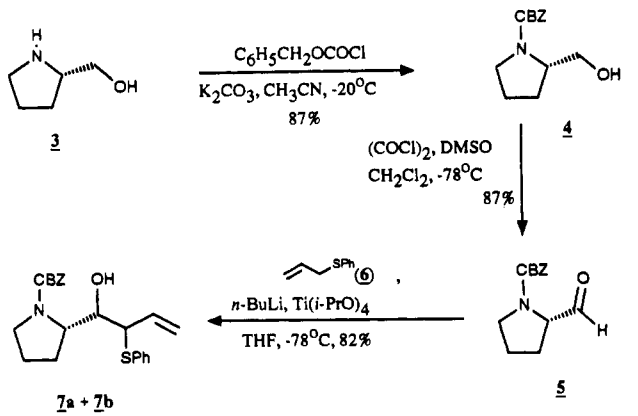
(1) Hohenschutz, L. D.; Bell, E. A.; Jewess, P. J.; Leworthy, D. P.; Pryce, R. J.; Arnold, E.; Clardy, J. *Phytochemistry* **1981**, *20*, 811.
(2) Nash, R. J.; Fellows, L. E.; Dring, J. V.; Stirton, C. H.; Hegarty, M. P.; Bell, E.A. *Phytochemistry* **1988**, *27*, 1403.

0022-3263/92/1957-3078$03.00/0

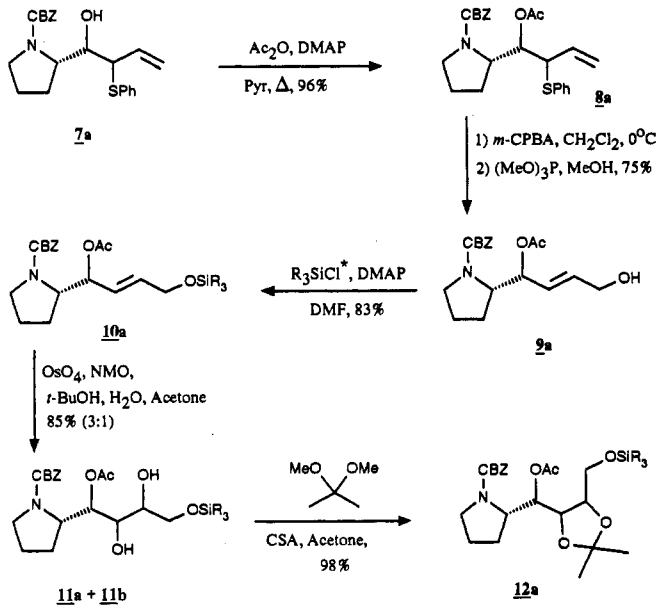
Scheme I



Scheme II



Scheme III



growth regulator; as an insect antifeedant; as an inhibitor of allergic encephalomyelitis; as a disaccharidase inhibitor, with implications for the treatment of diabetes mellitus; as an antiretroviral agent; and as a possible therapeutic agent against human cytomegalovirus, a virus not harmful to healthy adults but which frequently attacks patients suffering from AIDS. Moreover, of particular interest is the finding that 3′-azido-3′-deoxythymidine (AZT) and castanospermine can operate synergistically in the inhibition of HIV (human immunodeficiency virus) replication in vitro. Many syntheses of these two alkaloids, as well as their isomers, have been reported over the last 10 years.[4] Most of these syntheses have used sugars as starting materials. The first noncarbohydrate-based synthesis of castanospermine was reported in 1989 by Vogel and Reymond[5] and for swainsonine in 1985 by Sharpless and coworkers.[6] We wish to report here our own noncarbohydrate-based synthesis of castanospermine analogues.

Scheme I illustrates our retrosynthetic analysis. The formation of the bicyclic system **22** can be achieved by the intramolecular nucleophilic cyclization of **12**, which can be produced from **9** by a series of functional group manipulations. Compound **9** can be formed through the allylic rearrangement of sulfide **7**, which can be constructed by the coupling of proline derivative **5** and the anion of allyl phenyl sulfide **6**. This key reaction was studied by Yamamoto and co-workers[7,8] and reported to give an excellent erythro selectivity. This selectivity is of no real interest to us since the chirality of the carbon bearing the sulfide group will be lost during the allylic rearrangement. Unfortunately, the authors did not report any results on the relative stereochemistry of the newly introduced hydroxy group with respect to an already existing chiral center.

* R_3SiCl = *t*-BuPhe$_2$SiCl

Results and Discussion

(2*S*)-*N*-(Benzoxycarbonyl)pyrrolidine-2-carboxaldehyde (**5**) was prepared in two steps from the commercially available L-prolinol **3** (Scheme II). Reaction of **3** with benzyl chloroformate afforded the primary alcohol **4** in 87% yield,[9] which was oxidized to the aldehyde **5** using Swern's methodology[10] (87%). Addition of the titanium salt of allyl phenyl sulfide **6**[11] to aldehyde **5** was carried out according to the literature methodology[7,8] and gave a mixture of only two out of the four possible isomers in a ratio of 2:1 (82% yield). The two isomers could be separated readily by flash chromatography. At this point, NMR analysis did not help very much in the assignment of the relative stereochemistries of alcohols **7a** and **7b**. The stereochemistries of these alcohols were determined at the subsequent bicyclic stage.

The next few steps introduced both the reactive functionalities and the leaving group by an allylic sulfoxide rearrangement (Scheme III). It was carried out only with

(3) Michael, J. P. *Nat. Prod. Rep.* **1990**, *7*(6), 485 and references cited therein.

(4) Castanospermine: (a) Miller, S. A.; Chamberlain, A. R. *J. Am. Chem. Soc.* **1990**, *112*, 8100. (b) Bhide, R.; Mortezaei, R.; Scilimati, A.; Sih, C. J. *Tetrahedron Lett.* **1990**, *31*(34), 4827. (c) See also ref 5. Swainsonine: (d) See ref 4a. (e) Bennett, R. B., III; Choi, J. R.; Montgomery, W. D.; Chai, J. K. *J. Am. Chem. Soc.* **1989**, *111*, 2580. (f) Dener, J. M.; Hart, D. J.; Ramesh, S. *J. Org. Chem.* **1988**, *53*, 6022.

(5) Reymond, J.-L.; Vogel, P. *Tetrahedron Lett.* **1989**, *30*(6), 705.

(6) Adams, C. E.; Walker, F. J.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50* 420.

(7) Ikeda, Y.; Furuta, K.; Meguriya, N.; Ikeda, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1982**, *104*, 7663.

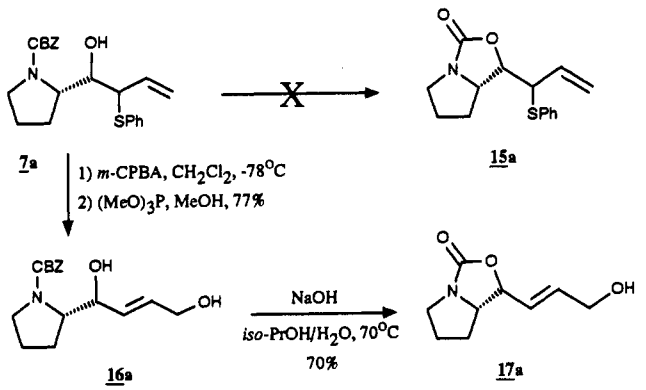
(8) Ikeda, Y.; Furuta, K.; Meguriya, N.; Ikeda, N.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2781.

(9) All compounds reported herein were fully characterized by their optical rotation (when relevant), IR, and ^{1}H and ^{13}C NMR. Satisfactory high-resolution mass spectra were obtained for all new compounds.

(10) Mancuso, A. J.; Huang, S. L.; Swern, D. *J. Org. Chem.* **1978**, *43* (12), 2480.

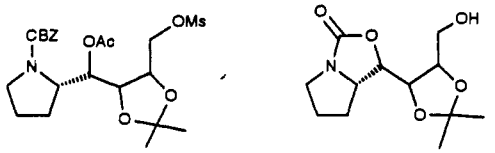
(11) (a) Hurd, C. D.; Greengard, H. *J. Am. Chem. Soc.* **1930**, *52*, 3356. (b) Kwart, H.; Evans, E. R. *J. Org. Chem.* **1966**, *31*, 413.

Scheme IV



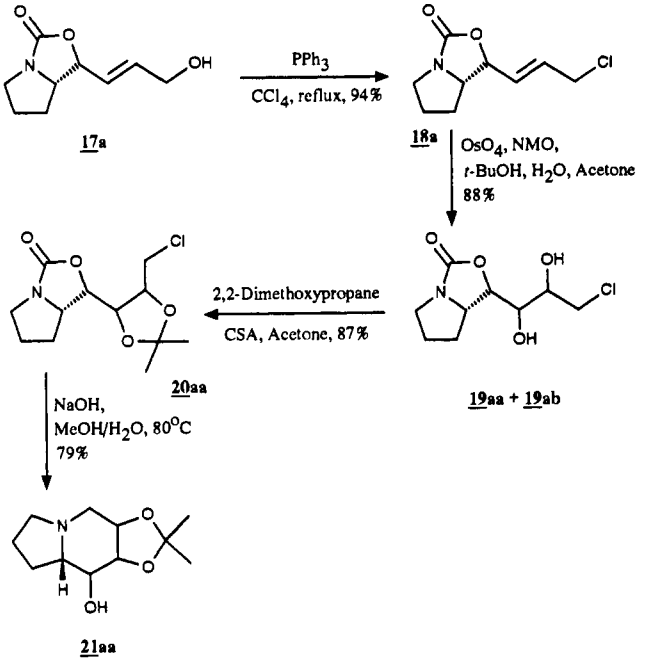
compound **7a** as a test. The alcohol **7a** was protected as **8a** in 96% yield. The sulfide **8a** was then oxidized with *m*-chloroperoxybenzoic acid to the sulfoxide, which was treated immediately with trimethyl phosphite[12] to give the allylic alcohol **9a** in 75% overall yield. Protection of the alcohol with *tert*-butylchlorodiphenylsilane[13] gave compound **10a** in 83% yield, which was dihydroxylated with osmium tetroxide using *N*-methylmorpholine *N*-oxide[14] as a cooxidant to give a mixture of two separable isomers **11aa** and **11ab** in a 3:1 ratio (85%). Here again, the stereochemistry was not determined and the sequence was continued with the major isomer. Protection of the diol with 2,2-dimethoxypropane in acetone afforded isopropylidene **12a** in 98% yield.

Attempts to form mesylate **13a** and then cyclize, as proposed in Scheme I, failed to produce the desired bicyclic compound due to the strong resistence of the carbamate protecting group to hydrogenolysis conditions. In the process, we found that **12a** rearranged into bicyclic carbamate **14a** very easily under basic hydrolytic conditions (K_2CO_3, $MeOH/H_2O$). It appeared then that this carbamate **14a** was a very good protecting group and that it could be introduced at the very beginning of the synthesis, avoiding the use of an acetate group and a CBZ group and all their subsequent problems.

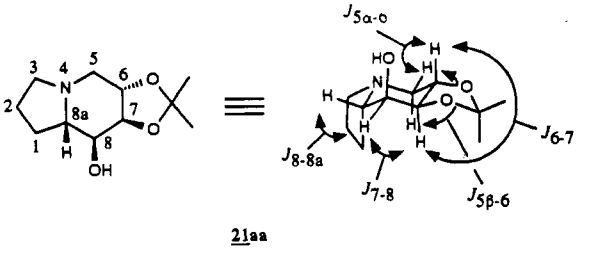


Attempts to cyclize **7a** using similar hydrolytic conditions[15] failed to give the desired carbamate **15a** (Scheme IV). On the other hand, when the sulfoxide rearrangement was carried out directly on **7a** (not protected as an acetate), the allylic diol obtained (**16a**: 77%) easily cyclized to form the cyclic carbamate **17a** (70%). At this point, the sequence shown previously could have been used in order to finish the synthesis via **14a**. But there were good chances that the mesylate of **14a** would not survive the strong basic conditions required to hydrolyze the cyclic carbamate. The primary allylic alcohol **17a** was thus transformed directly into the chloride **18a** using triphenylphosphine in carbon tetrachloride[16] (94%), which

Scheme V



Scheme VI



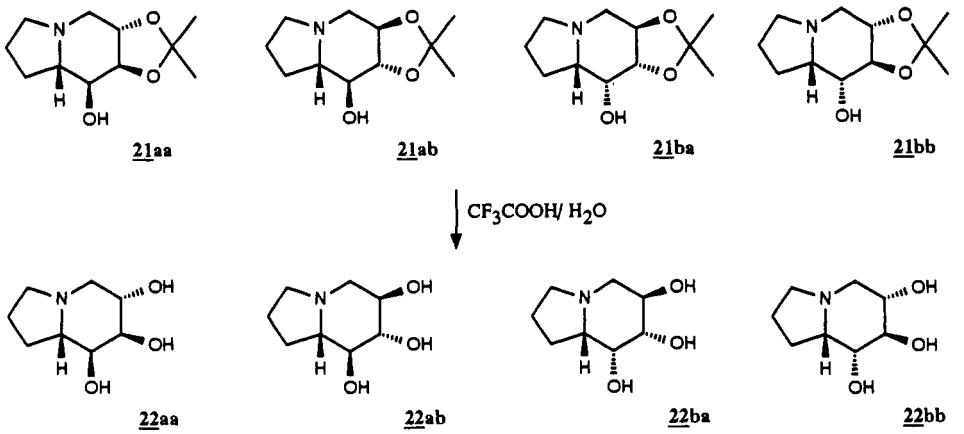
Coupling constants (Hz)	
$J_{5\alpha\text{-}5\beta}$	9.7
$J_{5\alpha\text{-}6}$	4.1
$J_{5\beta\text{-}6}$	9.7
$J_{6\text{-}7}$	9.7
$J_{7\text{-}8}$	2.2
$J_{8\text{-}8a}$	2.2

was then hydroxylated to the diols **19aa** and **19ab** (3:1 mixture, 88%). Here again, only the major isomer **19aa** was used to continue the sequence. Protection of the diol with 2,2-dimethoxypropane in acetone gave protected chloride **20aa** in 87% yield. The cyclic carbamate protecting group was then hydrolyzed with NaOH in a methanol/water mixture to give an amino alcohol intermediate which cyclized in situ to bicyclic amine **21aa** in 79% yield (Scheme V).

The next task was to determine the stereochemistry of **21aa**. With the help of COSY, HETCOR, and decoupling experiments, all the protons were assigned. Using the coupling constants of each peak, the stereochemistry was determined as shown in Scheme VI. The coupling constants $J_{7\text{-}8}$ and $J_{8\text{-}8a}$ are important in the determination of the stereochemistry of **21aa**. On the other hand, the coupling constant $J_{6\text{-}7}$ will always be a large constant, whatever the conformation of the product, since they will always have a trans diaxial relationship (because the hy-

(12) Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147.
(13) Hanessian, S.; Lavallée, P. *Can. J. Chem.* **1975**, *53*, 2974.
(14) For a review on osmium oxidations, see: Schröder, M. *Chem. Rev.* **1980**, *80*, 187.
(15) 2-Propanol was used instead of methanol to prevent the opening of the carbamate.
(16) Lee, J. B.; Nolan, T. J. *Can. J. Chem.* **1966**, *44*, 1331. For a review, see: Appel, R. *Angew. Chem., Int. Engl.* **1975**, *14*, 801.

Scheme VII



droxylation reaction always gives a cis diol and after rotation, the two hydrogens are always trans diaxial due to the presence of the acetonide). The relation between H6, H5α, and H5β will also be similar regardless of the conformation: there will always be one proton with a trans diaxial relationship (large constant) with H6 and one with a cis axial–equatorial relationship (small constant) with H6. Since the absolute stereochemistry at C8a is known, it is easy, with the help of the observed J_{7-8} and J_{8-8a}, to determine the stereochemistry at C8 and, thus, the conformation of the whole molecule. Since H8 displays two small coupling constants, the only possibility is the one shown in Scheme VI.

The stereochemistry of carbon 8 of **21aa** is generated by the very first step of the sequence, that is the addition of the titanium reagent to aldehyde **5**. The stereochemical outcome of this reaction should be governed by rules such as Cram's[17] or Felkin's[18] rules. Using one or the other set of rules, one discovers that the predicted major isomer is indeed the one that was obtained. The relative stereochemistry between carbons 8 and 8a in **21aa** is the same as in both castanospermine and swainsonine.

The stereochemistry of carbons 7 and 6 is generated by the hydroxylation reaction (**18a** → **19aa**). The stereochemical outcome of the hydroxylation of a double bond that has a chiral center (one of the substituents of that chiral center being a protected alcohol) at the allylic position has been studied extensively by Kishi et al.[19] The result for the hydroxylation of **18a** is in complete agreement with the rules proposed by Kishi. Unfortunately, the relative stereochemistry of carbons 8, 7, and 6 in **19aa** is wrong as far as catanospermine is concerned, the stereochemistry of both carbons 7 and 6 being the opposite one. Thus, the minor compound in the hydroxylation of **4.5a** (compound **19ab**) would have those three centers with the right relative stereochemistry.

Having thus completed the sequence for the major isomer of the bicyclic amino alcohol, the next task was to synthesize the three other possible isomers (Scheme VII): **21ab** (major alkylation, minor hydroxylation), **21ba** (minor alkylation, major hydroxylation), and **21bb** (minor alkylation, minor hydroxylation). Deprotection of the four acetonides was accomplished using trifluoroacetic acid[20] in water to give the four different amino triols **22aa–bb**. The ^1H and ^{13}C NMR chemical shifts of the four different isomers (as the acetonide, since the ^1H NMR patterns are clearer) are shown in Tables I and II, respectively. The coupling constants and the conformations of the four isomers are also reported (Table III).

Table I. ^1H NMR of the Acetonides of 1-Deoxycastanospermine and Stereoisomers (Chemical Shifts in ppm, in $CDCl_3$)

isomer	H1 + H2 (4H)	H3 (2 H)	H5α	H5β	H6	H7	H8	H8a
21aa	1.95–1.63	3.02 + 2.28	2.21	3.37	4.01	3.39	4.12	2.28
21ab	1.98–1.55	2.94 + 2.75	2.93	2.63	3.62	3.64	4.13	2.76
21ba	2.01–1.50	2.92 + 2.58	2.96	2.72	4.11	3.70	4.19	2.92
21bb	2.15–1.55	2.99 + 2.35	2.24	3.26	3.64	3.33	3.54	2.05

Conclusion

We have described here the preparation of four stereoisomers of 1-deoxycastanospermine by a short sequence and good overall yield. The synthetic route allows for the construction of many other analogues through simple synthetic modifications. Also, the introduction of oxygen functionalities in the five-membered ring could provide an eventual pathway to the natural castanospermine and swainsonine and their isomers.

Experimental[21] Section

(2*S*)-*N*-(Benzoxycarbonyl)-2-(hydroxymethyl)pyrrolidine (4). To a solution of L-prolinol (**3**) (2.05 g, 20.23 mmol) and finely powdered K_2CO_3 (6.71 g, 2.4 equiv) in 20 mL of dry acetonitrile, at −20 °C, under argon, was added slowly a solution of benzyl chloroformate (3.17 mL, 1.1 equiv) in 5 mL of acetonitrile. After the addition was completed, the solution was stirred at −20 °C for 2 h. Water was then added (50 mL), and the aqueous phase was extracted with $CHCl_3$ (4×). The combined organic extracts were washed successively with water (1×), 5% HCl (1×), water (1×), and brine. After the extracts were dried with $MgSO_4$, the solvent was removed under vacuum and the crude product was purified by flash chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 4.14 g (87%) of **4** as a colorless oil: $[\alpha]^{20}_D = -41.4°$ (*c* 2.2 in $CHCl_3$); IR (neat) 3413 (broad), 2958, 2880, and 1688 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.42–7.28 (m, 5 H), 5.13 (s, 2 H), 4.47–4.38 (m, 1 H), 4.09–3.91 (m, 1 H), 3.70–3.32 (m, 4 H), 2.10–1.51 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 157.6, 137.0, 129.0, 128.6, 128.4, 67.6, 66.9, 60.9, 47.6, 28.7, 24.2; exact mass calcd for $C_{13}H_{17}NO_3$ ($M^{\cdot+}$ + H^+) 236.1287, found 236.1287.

(17) (a) Cram, D. J.; Abd Elhafez, F. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828. (b) Cram, D. J.; Greene, F. D. *Ibid.* **1953**, *75*, 6005. (c) Cram, D. J.; Wilson, D. R. *Ibid.* **1963**, *85*, 1245.

(18) Chérest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199.

(19) (a) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron Lett.* **1983**, *24*(37), 3943. (b) Cha, J. K.; Christ, W. J.; Kishi, Y. *Ibid.* **1983**, *24*(37), 3947.

(20) Bashyal, B. P.; Fleet, G. W. J.; Gough, M. J.; Smith, P. W. *Tetrahedron* **1987**, *43*(13), 3083.

(21) For general experimental conditions, see: Horvath, R. F.; Chan, T. H. *J. Org. Chem.* **1989**, *54*, 317. The assignment of the peaks for some ^{13}C NMR was problematic due to the geometrical isomers produced by the CBZ protecting group. Those compounds are **7a** and **b**, **8a**, **9a**, **10a**, **12aa** and **16b**.

(2S)-N-(Benzoxycarbonyl)pyrrolidine-2-carboxaldehyde (5). A solution of DMSO (1.77 mL, 2.84 equiv) in 5 mL of dry CH_2Cl_2 was slowly added, via a double-tipped needle, to a stirring solution of oxalyl chloride (1.08 mL, 1.41 equiv) in 15 mL of CH_2Cl_2, under Ar, at −45 °C. The colorless solution was stirred for 15 min after which a solution of alcohol 4 (2.06 g, 8.76 mmol) in 5 mL of CH_2Cl_2 was added dropwise over a period of 15 min. A white precipitate formed, and the suspension was stirred for 1 h. Triethylamine (6.02 mL, 5 equiv) in CH_2Cl_2 (5 mL) was added, and the solution was allowed to slowly warmed to room temperature. The reaction mixture was diluted with 50 mL of CH_2Cl_2, washed successively with 5% HCl, water, and brine, and was dried over $MgSO_4$. Evaporation of the solvent under vacuum gave a pale brown oil which was purified by flash chromatography (silica gel, 1:1 hexanes/ethyl acetate, 1.77 g, 87%): $[\alpha]^{20}_D$ = −63.7° (c 1.3 in MeOH); IR (neat) 2978, 2881, 1736, and 1693 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.62 + 9.50 (2d, 1 H), 7.46–7.27 (m, 5 H), 5.18 + 5.14 (2s, 2 H), 4.39–4.18 (2m, 1 H), 3.67–3.40 (m, 2 H), 1.70–2.28 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 156.0 + 155.1 (1 C), 137.0, 136.8, 129.0, 128.6, 128.5, 67.6, 65.6 + 65.2 (1 C), 47.6 + 47.0 (1 C), 28.0 + 26.8 (1 C), 24.7 + 23.9 (1 C); exact mass calcd for $C_{13}H_{15}NO_3$ ($M^{\cdot+}$ + H^+) 234.1131, found 234.1130.

Allyl Phenyl Sulfide (6). To a freshly prepared solution of sodium ethoxide in ethanol (1.25 g of Na, 1 equiv, in 18.0 mL of absolute ethanol) at 0 °C, under Ar, were added successively thiophenol (5.59 mL, 54.4 mmol) and then slowly allyl bromide (5.18 mL, 1.1 equiv). The solution was stirred at rt for 15 h, and the ethanol and excess allyl bromide were evaporated. The residual slurry was dissolved in water, the aqueous phase was extracted with ether (2×), and the combined organic extracts were dried over $MgSO_4$. Filtration followed by evaporation of the solvent gave a yellow oil that was distilled (48 °C (0.025 mmHg)) to yield 7.30 g (90%) of the sulfide as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.38–7.15 (m, 5 H), 5.83 (ddt, 1 H, J = 6.5, 10, 18 Hz), 5.02 (dd, 1 H, J = 1, 18 Hz), 4.98 (dd, 1 H, J = 1, 10 Hz), 3.43 (d, 2 H, J = 6.5 Hz); exact mass calcd for $C_9H_{10}S$ ($M^{\cdot+}$ + H^+) 151.0582, found 151.0582.

(2S,1'S,2'S)- and (2S,1'R,2'R)-N-(Benzoxycarbonyl)-2-[1'-hydroxy-2'-(phenylthio)-3'-butenyl]pyrrolidine (7a and 7b). To a solution of allyl phenyl sulfide (6) (0.23 g, 1.5 equiv) in 3.46 mL of dry THF, at −78 °C, under argon, was added *n*-BuLi (2.0 M in pentane, 0.74 mL, 1.5 equiv), and the solution was stirred at 0 °C for 30 min. It was then cooled to −78 °C, and titanium(IV) isopropoxide (0.44 mL, 1.5 equiv) was added slowly. After 10 min, the aldehyde 5 (0.23 g, 0.99 mmol, in 0.5 mL of THF) was added over a period of 10 min. The solution was stirred for 10 min and warmed to 0 °C for 30 min. It was then poured into saturated aqueous NH_4Cl and extracted with ether (3×). The combined organic extracts were worked up and chromatographed (silica gel, 8:2 hexanes/ethyl acetate; for prevention of thioallylic rearrangements of the produced phenyl sulfides, small amounts of 2,6-di-*tert*-butyl-4-methylphenol were added to the solvents during the workup and chromatographic operations[22]) to give two different isomers **7a** and **b** in a total combined yield of 82% (**a**:**b** = 1.7:1.0). **7a** (2S,1'S,2'S): 0.20 g, 52%; $[\alpha]^{20}_D$ = −107.7° (c 1.54 in $CDCl_3$); IR (neat) 3328 (broad), 2976, 2883, and 1666 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.62–7.20 (m, 10 H), 6.12 (m, 1 H), 5.32 (bs, 1 H), 5.14 (s, 2 H), 5.08 (dd, 1 H, J = 0.7, 6.8 Hz), 4.88 (dd, 1 H, J = 0.7, 11.4 Hz), 3.99 (m, 1 H), 3.84 (m, 1 H), 3.66–3.54 (m, 2 H), 3.34 (dt, 1 H, J = 4.4, 7.2 Hz), 2.06–1.60 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 159.1, 136.8, 134.2, 133.7, 129.3, 129.1, 128.7, 128.6, 127.9, 118.5, 77.8, 68.0, 61.9, 57.7, 47.5, 28.6, 24.3; exact mass calcd for $C_{22}H_{25}NO_3S$ ($M^{\cdot+}$ + H^+) 384.1635, found 384.1633. **7b** (contamined with a small amount of **7a**) (2S,1'R,2'R): 0.12 g, 30%; $[\alpha]^{20}_D$ = −35.7° (c 1.86 in $CHCl_3$); IR (neat) 3380 (broad), 2976, 2880, and 1666 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.62–7.20 (m, 10 H), 5.82 (m, 1 H), 5.20–4.75 (m, 4 H), 4.31–3.90 (m, 2 H), 3.72–3.20 (m, 4 H), 2.15–1.60 (m, 4 H); ^{13}C NMR δ 156.6, 137.3, 135.3, 133.6, 129.4, 129.0, 128.6, 128.5, 128.0, 117.8, 77.8, 67.3, 61.6, 56.0, 47.8, 26.6, 24.6; exact mass calcd for $C_{22}H_{25}NO_3S$ ($M^{\cdot+}$ + H^+) 384.1635, found 384.1633.

(2S,1'S,2'S)-N-(Benzoxycarbonyl)-2-[1'-acetoxy-2'-(phenylthio)-3'-butenyl]pyrrolidine (8a). To a solution of alcohol 7a (0.14 g, 0.36 mmol) in 3.6 mL of dry pyridine, at rt, under Ar, were added successively 4-(dimethylamino)pyridine (4.4 mg, 0.1 equiv) and acetic anhydride (0.14 mL, 4 equiv) and the solution was warmed to 70 °C for 15 h. The pyridine was then evaporated and the residue taken up in ethyl acetate and washed with 5% HCl, saturated aqueous $NaHCO_3$, and brine. Workup followed by flash chromatography (silica gel, 8:2 hexanes/ethyl acetate) gave 0.15 g (96%) of acetate **8a** as a pale yellow oil: $[\alpha]^{20}_D$ = −32.9° (c 1.91 in $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.62–7.20 (m, 10 H), 5.89 (m, 1 H), 5.22–4.86 (m, 5 H), 4.27 (m, 1 H), 3.70 (m, 1 H), 3.48 (m, 1 H), 3.32 (m, 1 H), 1.90 (s, 3 H), 1.98–1.60 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 155.9, 134.3 134.0, 129.4, 129.0, 128.4, 119.1, 77.7, 75.2, 74.7, 67.1, 58.5, 58.4, 54.8, 46.6, 29.3, 28.4, 23.8, 23.0, 20.8; exact mass calcd for $C_{24}H_{27}NO_4S$ ($M^{\cdot+}$ + H^+) 426.1740, found 426.1737.

(2S,1'R)-N-(Benzoxycarbonyl)-2-(1'-acetoxy-4'-hydroxy-2'-butenyl)pyrrolidine (9a). To a solution of acetoxy sulfide **8a** (0.14 g, 0.32 mmol) in 3.2 mL of dry CH_2Cl_2, at 0 °C, under Ar, was added *m*-CPBA (69.4 mg, 1.3 equiv), and the solution was stirred for 2 h. It was then dissolved in ether, washed with saturated aqueous $NaHCO_3$ (2×), dried over $MgSO_4$, and filtered, and the solvent was evaporated. The residue was dissolved in 3.2 mL of dry MeOH, and trimethyl phosphite (0.38 mL, 10 equiv) was added slowly. After 3 h of stirring, the MeOH was evaporated and the thick oil was purified by flash chromatography (silica gel, 1:1 hexanes/ethyl acetate) to give 80.2 mg (75%) of the pure allylic alcohol **9a**: $[\alpha]^{20}_D$ = −55.2° (c 1.50 in $CHCl_3$); IR (neat) 3345 (broad), 2978, 1733, and 1693 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50–7.22 (m, 5 H), 5.93–5.50 (m, 2 H), 5.51 (dd, 1 H, J = 6.0), 5.15 (m, 2 H), 4.10 (m, 3 H), 3.51 (m, 1 H), 3.34 (m, 1 H), 1.90 (s, 3 H), 2.05–1.75 (m, 5 H); exact mass calcd for $C_{18}H_{23}NO_5$ ($M^{\cdot+}$ + H^+) 334.1655, found 334.1656.

(2S,1'R)-N-(Benzoxycarbonyl)-2-[1'-acetoxy-4'-[(*tert*-butyldiphenylsilyl)oxy]-2'-butenyl]pyrrolidine (10a). To a solution of allylic alcohol **9a** (0.32 g, 0.95 mmol) in 1.90 mL of dry DMF, at rt, under Ar, were added successively imidazole (0.26 g, 4 equiv) and *tert*-butylchlorodiphenylsilane (0.50 mL, 2 equiv). The solution was heated at 70 °C for 5 h, was then dissolved in ether and washed with water (2×) and brine, and was dried over $MgSO_4$. Evaporation of the solvent was followed by flash chromatography (silica gel, 7:3 hexanes/ethyl acetate) to give the protected allylic alcohol **10a** as a colorless oil (0.45 g, 83%): $[\alpha]^{20}_D$ = −26.5° (c 1.46 in $CHCl_3$); IR (neat) 3070, 2930, 1741, and 1711 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.65 (m, 4 H), 7.50–7.22 (m, 11 H), 5.77 (m, 2 H), 5.58 (m, 1 H), 5.18 (m, 2 H), 4.15 (m, 3 H), 3.52 (m, 1 H), 3.33 (m, 1 H), 1.99 (s, 3 H), 2.05–1.75 (m, 4 H), 1.07 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 170.5, 155.7, 136.0, 134.3, 134.0, 130.3, 129.0, 128.5, 128.2, 124.6, 124.1, 74.1, 67.1, 63.7, 59.9, 59.2, 47.3, 46.9, 27.0, 23.5, 23.4, 21.3, 19.5; exact mass calcd for $C_{34}H_{41}NO_5Si$ ($M^{\cdot+}$ + H^+ − CH_3COOH) 512.2623, found 512.2623.

(2S,1'S,2'R,3'S)- and (2S,1'S,2'R,3'R)-N-(Benzoxycarbonyl)-2-[1'-acetoxy-2',3'-dihydroxy-4'-[(*tert*-butyldiphenylsilyl)oxy]butyl]pyrrolidine (11aa and 11ab). To a solution of *N*-methylmorpholine *N*-oxide (0.10 g, 1.1 equiv) and OsO_4 (10.0 mg, 0.05 equiv) in a mixture of water/*t*-BuOH (6/1, 0.7 mL) at rt was added the protected allylic alcohol **10a** (0.45 g, 0.78 mmol) dissolved in 0.25 mL of acetone. The solution was stirred for 15 h, after which 2 mL of a solution–suspension of magnesium silicate and sodium hydrosulfite (1.2 g and 0.1 g, respectively, in 8 mL of water) was added. The slurry was filtered through Celite and the cake rinsed with acetone. The solvents were evaporated, and the residue was acidified to pH 2 with 10 M sulfuric acid, saturated with solid NaCl, and extracted with ethyl acetate. The combined organic extracts were worked up to give a dark brown oil, which was purified by flash chromatography (silica gel, 7:3 hexanes/ethyl acetate) affording two diols **11aa** and **11ab** (3:1 mixture) in a total yield of 85%. **11aa** (2S,1'S,2'R,3'S): 0.30 g, 64%; $[\alpha]^{20}_D$ = −42.1° (c 1.53 in $CHCl_3$); IR (neat) 3383 (broad), 2957, 1746, and 1674 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.65 (m, 4 H), 7.50–7.22 (m, 11 H), 5.37–5.00 (m, 4 H), 4.53 (m, 1 H), 3.90–3.39 (m, 6 H), 2.51 (m, 1 H), 2.12 (s, 3 H), 2.05–1.77 (m, 4 H), 1.07 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 171.3, 158.1, 136.8, 136.1, 134.1, 130.3, 129.1, 128.8, 128.5, 128.3, 77.8, 76.0, 70.3, 68.0, 67.8, 64.8, 57.4, 47.8, 28.7, 27.1, 24.3, 21.4, 19.5; exact mass calcd for $C_{34}H_{43}NO_7Si$ ($M^{\cdot+}$ + H^+) 606.2889, found 606.2887.

(2S,1'S,2'S,3'S)-N-(Benzoxycarbonyl)-2-[1'-acetoxy-2',3'-O-isopropylidene-2',3'-dihydroxy-4'-[(*tert*-butyldi-

(22) Kozikowski, A. P.; Huie, E. *J. Am. Chem. Soc.* **1982**, *104*, 2059.

phenylsilyl)oxy]butyl]pyrrolidine (12aa). To a solution of diol **11aa** (0.30 g, 0.50 mmol) in 1.99 mL of dry acetone, at rt, under Ar, were added 2,2-dimethoxypropane (0.27 mL, 4.4 equiv) and camphorsulfonic acid (6.0 mg, 0.05 equiv). The solution was stirred for 15 h after which a few drops of concd NH_4OH were added. The solvent was evaporated and the residue taken up in ether. It was washed with water and brine and dried over magnesium sulfate. Evaporation of the solvent followed by purification (flash chromatography: silica gel, 8:2 hexanes/ethyl acetate) yielded 0.32 g (98%) of **12aa** as a colorless oil: $[\alpha]^{20}_D = -2.9°$ (*c* 0.8 in $CHCl_3$); IR (neat) 3070, 2930, 1753, and 1704 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.65 (m, 4 H), 7.50–7.22 (m, 11 H), 5.18–4.90 (m, 3 H), 4.40–3.27 (m, 7 H), 2.11–1.78 (m, 4 H), 1.73 (s, 3 H), 1.40 (m, 6 H), 1.07 (s, 9 H); exact mass calcd for $C_{37}H_{47}NO_7Si$ ($M^{\bullet+} + H^+$) 646.3202, found 646.3202.

(2*S*,1′*R*)-*N*-(Benzoxycarbonyl)-2-(1′,4′-dihydroxy-2′-butenyl)pyrrolidine (16a). To a solution of hydroxy sulfide **7a** (2.79 g, 7.27 mmol) in 73 mL of dry CH_2Cl_2, at −78 °C, under Ar, was added *m*-CPBA (1.88 g, 1.4 equiv), and the solution was stirred for 2 h. It was then dissolved in ether, washed with saturated aqueous $NaHCO_3$ (2×), dried over $MgSO_4$, and filtered, and the solvent was evaporated. The residue was dissolved in 73 mL of dry MeOH, and trimethyl phosphite (9.0 mL, 10 equiv) was added slowly. After 3 h of stirring, the MeOH was evaporated and the thick oil was purified by flash chromatography (silica gel, 1:1 hexanes/ethyl acetate, under the fumehood) to give 1.63 g (77%) of pure allylic diol **16a**: $[\alpha]^{20}_D = -46.1°$ (*c* 1.36 in $CHCl_3$); IR (neat) 3383 (broad), 3085, 2865, and 1685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.31 (m, 5 H), 5.88 (m, 1 H), 5.63 (m, 1 H), 5.11 (s, 2 H), 4.09 (m, 2 H), 3.89 (m, 1 H), 3.50 (m, 1 H), 3.36 (m, 1 H), 1.95–1.63 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 157.7, 136.4, 132.5, 130.2, 128.5, 128.1, 127.9, 76.0, 67.4, 63.0, 54.4, 54.3, 47.3, 28.1, 24.0; exact mass calcd for $C_{16}H_{21}NO_4$ ($M^{\bullet+} + H^+$) 292.1550, found 292.1549.

(2*S*,1′*S*)-*N*-(Benzoxycarbonyl)-2-(1′,4′-dihydroxy-2′-butenyl)pyrrolidine (16b). See experimental for compound **16a**: 80%, $[\alpha]^{20}_D = -47.0°$ (*c* 1.06 in $CHCl_3$); IR (neat) 3363 (broad), 3080, 2990, and 1685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.32 (m, 5 H), 5.84 (dt, 1 H, *J* = 4.6, 15.5 Hz), 5.61 (dd, 1 H, *J* = 6.3, 15.6 Hz), 5.09 (s, 2 H), 4.30 (m, 1 H), 4.04 (d, 2 H, *J* = 4.6 Hz), 3.55 (m, 1 H), 3.31 (m, 1 H), 2.03–1.61 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 156.9, 134.3, 132.1, 129.2, 128.5, 128.1, 127.9, 74.3, 67.3, 63.1, 54.4, 54.4, 27.7, 24.1; exact mass calcd for $C_{16}H_{21}NO_4$ ($M^{\bullet+} + H^+$) 292.1550, found 292.15488.

(2*S*,1′*R*)-1,1′-*N*,*O*-Carbonyl-2-(1′,4′-dihydroxy-2′-butenyl)pyrrolidine (17a). To a solution of allylic diol **16a** (1.63 g, 5.60 mmol) in 56 mL of a 1:1 mixture of 2-propanol/water was added finely powdered K_2CO_3 (2.32 g, 3 equiv), and the solution was heated at 70 °C for 15 h. The solvent was evaporated and the residue purified by flash chromatography (silica gel, ethyl acetate) to give 1.14 g (70%) of allylic alcohol **17a** as a colorless oil: $[\alpha]^{20}_D = -78.6°$ (*c* 1.32 in $CHCl_3$); IR (neat) 3359 (broad), 2978, 2880, and 1736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.94 (dt, 1 H, *J* = 4.2, 15.5 Hz), 5.80 (dd, 1 H, *J* = 6.6, 15.5 Hz), 4.69 (dd, 1 H, *J* = 4.2, 6.6 Hz), 4.12 (d, 2 H, *J* = 4.2 Hz), 3.56 (m, 2 H), 3.08 (ddd, 1 H, *J* = 4.7, 8.8, 11.3 Hz), 2.96 (bs, 1 H), 2.15–2.77 (m, 3 H), 1.49 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 162.5, 135.7, 128.1, 82.0, 66.3, 63.2, 47.0, 31.6, 27.0; exact mass calcd for $C_9H_{13}NO_3$ ($M^{\bullet+} + H^+$) 184.0974, found 184.0974.

(2*S*,1′*S*)-1,1′-*N*,*O*-Carbonyl-2-(1′,4′-dihydroxybutenyl)pyrrolidine (17b). See experimental data for compound **17a**: 71%, $[\alpha]^{20}_D = -42.4°$ (*c* 0.77 in $CHCl_3$); IR (neat) 3423 (broad), 2967, 2904, 1741, and 1676 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.02 (dt, 1 H, *J* = 4.2, 15.5 Hz), 5.72 (dd, 1 H, *J* = 6.7, 15.5 Hz), 5.13 (dd, 1 H, *J* = 5.7, 6.7 Hz), 4.16 (d, 2 H, *J* = 4.2 Hz), 3.86 (ddd, 1 H, *J* = 5.7, 7.6, 10.5 Hz), 3.59 (m, 1 H), 3.14 (ddd, 1 H, *J* = 3.7, 9.25, 11.6 Hz), 2.11–1.62 (m, 3 H), 1.48 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 162.1, 135.5, 123.7, 76.4, 63.8, 62.5, 46.3, 26.1, 25.4; exact mass calcd for $C_9H_{13}NO_3$ ($M^{\bullet+} + H^+$) 184.0974, found 184.0974.

(2*S*,1′*R*)-1,1′-*N*,*O*-Carbonyl-2-(1′-hydroxy-4′-chloro-2′-butenyl)pyrrolidine (18a). To a solution of allylic alcohol **17a** (0.33 g, 1.80 mmol) in 18.0 mL of a 4:1 mixture of dry CCl_4/CH_2Cl_2 were added successively finely powdered K_2CO_3 (0.50 g, 2 equiv) and triphenylphosphine (1.18 g, 2.5 equiv), and the solution was stirred at 60 °C for 8 h. The solvent was evaporated, and the residue was purified by flash chromatography (silica gel, 3:7 hexanes/ethyl acetate) affording 0.34 g (94%) of allylic chloride **18a** as a white solid (mp 55–57 °C): $[\alpha]^{20}_D = -49.1°$ (*c* 1.37 in $CHCl_3$); IR (neat) 3004, 2975, and 1751 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.03–5.80 (m, 2 H), 4.69 (dd, 1 H, *J* = 4.0, 5.2 Hz), 4.03 (d, 2 H, *J* = 4.8 Hz), 3.56 (m, 2 H), 3.09 (ddd, 1 H, *J* = 4.6, 8.9, 11.3 Hz), 2.15–1.76 (m, 3 H), 1.48 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 161.3, 131.4, 130.2, 79.7, 65.1, 46.0, 43.7, 30.5, 25.8; exact mass calcd for $C_9H_{12}NO_2Cl$ ($M^{\bullet+} + H^+$) 202.0635, found 202.0635.

(2*S*,1′*S*)-1,1′-*N*,*O*-Carbonyl-2-(1′-hydroxy-4′-chlorobutenyl)pyrrolidine (18b). See experimental data for compound **18a**: 78%, $[\alpha]^{20}_D = -57.7°$ (*c* 1.30 in $CHCl_3$); IR (neat) 2978, 2952, and 1751 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.04 (dtd, 1 H, *J* = 1.1, 6.4, 15.2 Hz), 5.77 (ddt, 1 H, *J* = 1.1, 5.9, 15.2 Hz), 5.13 (dd, 1 H, *J* = 6.8 Hz), 4.05 (dt, 2 H, *J* = 1.1, 6.4 Hz), 3.88 (ddd, 1 H, *J* = 5.6, 7.7, 10.3 Hz), 3.60 (m, 1 H), 3.15 (ddd, 1 H, *J* = 3.8, 9.0, 11.3 Hz), 2.15–1.63 (m, 3 H), 1.45 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 162.3, 131.7, 128.7, 76.4, 64.5, 47.4, 44.8, 27.3, 26.6; exact mass calcd for $C_9H_{12}NO_2Cl$ ($M^{\bullet+} + H^+$) 202.0635, found 202.0635.

(2*S*,1′*S*,2′*R*,3′*R*)- and (2*S*,1′*S*,2′*S*,3′*S*)-1,1′-*N*,*O*-Carbonyl-2-(1′,2′,3′-trihydroxy-4′-chlorobutyl)pyrrolidine (19aa and 19ab). To a solution of allylic chloride **18a** (0.34 g, 1.70 mmol) in 3.4 mL of a 6:3:1 mixture of acetone/water/2-methyl-2-propanol were added successively *N*-methylmorpholine *N*-oxide (0.24 g, 1.2 equiv) and OsO_4 (21.6 mg, 0.05 equiv). The orange solution was stirred at room temperature for 3 h, after which 2 mL of a solution–suspension of magnesium silicate and sodium hydrosulfite (1.2 and 0.1 g, respectively, in 8 mL of water) was added. The slurry was filtered through Celite and the cake rinsed with acetone. The solvents were evaporated, and the dark oil was purified by flash chromatography (silica gel, 2:8 hexanes/ethyl acetate) providing 0.35 g (88%) of a 2:1 mixture (by NMR) of diols **19aa** and **19ab**, respectively. Only **19aa** was isolated as a pure compound at this stage: $[\alpha]^{20}_D = -56.7°$ (*c* 1.93 in MeOH); IR (neat) 3357 (broad), 2938, 1751, and 766 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.33 (dd, 1 H, *J* = 4.0, 7.8 Hz), 4.05–3.93 (m, 2 H), 3.80 (bt, 1 H, *J* = 7.0), 3.64–3.42 (m, 3 H), 3.16 (ddd, 1 H, *J* = 4.1, 8.9, 11.4 Hz), 2.19–1.80 (m, 3 H), 1.50 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 162.4, 81.1, 72.4, 71.3, 63.4, 46.7, 46.6, 32.3, 27.3; exact mass calcd for $C_9H_{14}NO_4Cl$ ($M^{\bullet+} + H^+$) 236.0690, found 236.0690.

(2*S*,1′*R*,2′*S*,3′*S*)- and (2*S*,1′*R*,2′*R*,3′*R*)-1,1′-*N*,*O*-Carbonyl-2-(1′,2′,3′-trihydroxy-4′-chlorobutyl)pyrrolidine (19ba and 19bb). See experimental compounds for **19aa** and **ab**. The mixture of isomers was unseparable by flash chromatography: IR (neat) 3333 (broad), 2967, 1736, and 771 cm^{-1}; ^1H NMR ($CDCl_3$) **19ba + bb** δ 4.70 (m, 1 H), 4.35–3.41 (m, 7 H), 3.28–3.07 (m, 2 H), 2.21–1.78 (m, 3 H), 1.70–1.45 (m, 1 H); ^{13}C NMR ($CDCl_3$) **19ba** δ 161.5, 73.9, 69.9, 69.2, 62.6, 45.4, 45.2, 25.5, 25.2; **19bb** 161.1, 71.6, 69.0, 61.7, 45.3, 44.4, 31.0, 25.8, 25.3; exact mass calcd for $C_9H_{14}NO_4Cl$ ($M^{\bullet+} + H^+$) 236.0690, found 236.0690.

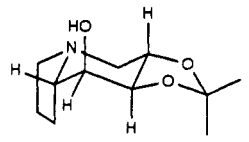
(2*S*,1′*S*,2′*S*,3′*R*)-1,1′-*N*,*O*-Carbonyl-2-(1′,2′,3′-trihydroxy-2′,3′-*O*-isopropylidene-4′-chlorobutyl)pyrrolidine (20aa). To a solution of diol **19aa** (0.19 g, 0.82 mmol) in 4.1 mL of dry acetone, at rt, under Ar, were added 2,2-dimethoxypropane (0.4 mL, 4 equiv) and camphorsulfonic acid (9.5 mg, 0.05 equiv). The solution was stirred for 15 h after which a few drops of concd NH_4OH were added. The solvent was evaporated and the residue taken up in ethyl acetate. Workup and evaporation of the solvent followed by flash chromatography purification (silica gel, 1:1 hexanes/ethyl acetate) yielded **20aa** as a colorless oil: $[\alpha]^{20}_D = -23.1°$ (*c* 0.93 in $CHCl_3$); IR (neat) 2986, 1751, and 751 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.26 (dd, 1 H, *J* = 3.5, 8.1 Hz), 4.18 (ddd, 1 H, *J* = 3.8, 5.2, 6.9 Hz), 4.02 (dd, 1 H, *J* = 6.9, 8.1 Hz), 3.85 (ddd, 1 H, *J* = 3.5, 5.6, 9.4 Hz), 3.79 (dd, 1 H, *J* = 3.8, 11.9 Hz), 3.64 (dd, 1 H, *J* = 5.2, 11.9 Hz), 3.59 (m, 1 H), 3.16 (ddd, 1 H, *J* = 4.3, 9.0, 11.4 Hz), 2.18–1.80 (m, 3 H), 1.45 (m, 1 H), 1.41 (s, 3 H), 1.37 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 161.4, 112.1, 81.4, 80.6, 79.6, 63.7, 46.9, 45.7, 32.0, 28.5, 28.4, 27.0; exact mass calcd for $C_{12}H_{18}NO_4$ ($M^{\bullet+} + H^+$) 276.1003, found 276.1003.

(2*S*,1′*S*,2′*R*,3′*S*)-1,1′-*N*,*O*-Carbonyl-2-(1′,2′,3′-trihydroxy-2′,3′-*O*-isopropylidene-4′-chlorobutyl)pyrrolidine (20ab). See experimental data for compound **20aa**. The reaction was performed on a mixture of **19aa** and **19ab** from the hydroxylation reaction. Compounds **20aa** and **20ab** were separated by flash chromatography (silica gel, 7:3 hexanes/ethyl acetate) to give a total yield of 87% (0.23 g of **20aa** and 0.12 g of **20ab**). **20ab**: white solid; mp 92–94 °C; $[\alpha]^{20}_D = -54.9°$ (*c* 1.23 in $CHCl_3$); IR (solution in $CHCl_3$) 2988 and 1751 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.40 (dd, 1

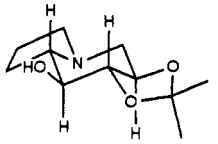
Table II. ^{13}C NMR of the Acetonides of 1-Deoxycastanospermine and Stereoisomers (Chemical Shifts in ppm, in $CDCl_3$)

isomer	C1 + C2	C3	C5	C6	C7	C8	C8a
21aa	23.8 + 22.4	52.6	52.8	65.5	71.2	83.1	65.2
21ab	22.5 + 21.4	51.1	54.4	69.1	74.5	81.4	65.0
21ba	26.7 + 21.9	52.2	54.2	67.2	71.0	78.5	67.2
21bb	26.7 + 22.3	52.0	52.4	72.8	75.0	85.0	67.7

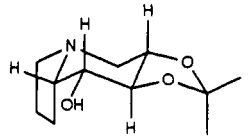
Table III: Coupling Constants of the Acetonides of 1-Deoxycastanospermine and Stereoisomers (Coupling Constants in Hz)



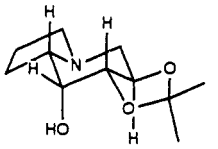
21aa



21ab



21bb



21ba

isomer	$J_{5\alpha-5\beta}$	$J_{5\alpha-6}$	$J_{5\beta-6}$	J_{6-7}	J_{7-8}	J_{8-8a}
21aa	9.7	9.7	4.1	9.7	2.2	2.2
21ab	9.7	4.6	9.7	9.4	8.6	6.2
21ba	9.6	5.6	9.6	9.6	3.6	3.6
21bb	9.7	9.7	3.8	9.3	9.3	8.6

H, J = 2.0, 3.7 Hz), 4.34 (ddd, 1 H, J = 4.6, 6.4, 7.5 Hz), 4.06 (dd, 1 H, J = 2.0, 7.5 Hz), 3.84 (ddd, 1 H, J = 3.7, 5.5, 9.4 Hz), 3.69 (dd, 1 H, J = 4.6, 11.4 Hz), 3.60 (dd, 1 H, J = 6.4, 11.4 Hz), 3.57 (m, 1 H), 3.19 (ddd, 1 H, J = 4.0, 8.6, 10.8 Hz), 2.20–1.75 (m, 3 H), 1.45 (m, 1 H), 1.41 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 162.1, 112.1, 81.4, 79.1, 76.9, 62.9, 47.1, 45.3, 32.4, 28.6, 27.9, 26.9; exact mass calcd for $C_{12}H_{18}NO_4Cl$ ($M^{\cdot+}$ + H^+) 276.1003, found 276.1003.

(2*S*,1′*R*,2′*R*,3′*S*)- and (2*S*,1′*R*,2′*S*,3′*R*)-1,1′-*N*,*O*-Carbonyl-2-(1′,2′,3′-hydroxy-2′,3′-*O*-isopropylidene-4′-chlorobutyl)pyrrolidine (20ba and 20bb). See experimental data for compound **20aa**. The two isomers were separated by flash chromatography (silica gel, 1:1 hexanes/ethyl acetate). **20ba**: $[\alpha]^{20}_D$ = −37.5° (c 0.81 in CH_3OH); IR (solution in $CHCl_3$) 2978 and 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.54 (dd, 1 H, J = 7.3, 9.5 Hz), 4.24 (ddd, 1 H, J = 3.1, 5.3, 7.1 Hz), 3.93 (dd, 1 H, J = 7.1, 9.5 Hz), 3.91 (m, 1 H), 3.83 (dd, 1 H, J = 3.1, 12.0 Hz), 3.63 (dd, 1 H, J = 5.3, 12.0 Hz), 3.57 (ddd, 1 H, J = 7.7, 7.7, 11.3 Hz), 3.17 (ddd, 1 H, J = 3.1, 8.9, 11.3 Hz), 2.18–1.79 (m, 3 H), 1.55 (m, 1 H), 1.42 (s, 3 H), 1.39 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 161.0, 111.3, 80.8, 76.3, 75.7, 62.7, 45.9, 44.4, 27.5, 27.3, 25.8, 25.5; exact mass calcd for $C_{12}H_{18}NO_4Cl$ ($M^{\cdot+}$ + H^+) 276.1003, found 276.1003. **20bb**: $[\alpha]^{20}_D$ = +23.3° (c 0.84 in CH_3OH); IR (solution in $CHCl_3$) 2969 and 1747 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.68 (dd, 1 H, J = 1.1, 8.4 Hz), 4.34 (ddd, 1 H, J = 4.2, 6.5, 7.7 Hz), 4.15 (m, 1 H), 4.02 (dd, 1 H, J = 1.1, 7.7 Hz), 3.72 (dd, 1 H, J = 4.2, 11.5 Hz), 3.62 (dd, 1 H, J = 6.5, 11.5 Hz), 3.53 (m, 1 H), 3.13 (ddd, 1 H, J = 4.6, 8.2, 10.9 Hz), 2.21–1.73 (m, 4 H), 1.42 (s, 3 H), 1.41 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 160.2, 111.6, 78.45, 8.44, 75.0, 61.8, 45.5, 43.9, 27.6, 27.1, 26.8, 26.6; exact mass calcd for $C_{12}H_{18}NO_4Cl$ ($M^{\cdot+}$ + H^+) 276.1003, found 276.1003.

(6*S*,7*S*,8*S*,8a*S*)-6,7-*O*-Isopropylidene-6,7,8-trihydroxyindolizidine (21aa). To a solution of chloride **20aa** (0.56 g, 0.2.03 mmol) in 20 mL of a 2:1 mixture of $MeOH/H_2O$ was added NaOH (0.24 g, 3.0 equiv), and the solution was heated at 80 °C for 15 h. The solvents were evaporated, and the residue was dissolved in CH_2Cl_2 and filtered. Flash chromatography purification (silica gel, 7% $MeOH/CH_2Cl_2$; spray reagent: cobalt(II) isocyanate) gave 0.34 g (79%) of the bicyclic amino alcohol **21aa**: $[\alpha]^{20}_D$ = −23.3° (c 1.64 in MeOH); IR (neat) 3341 and 2957 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.12 (t, 1 H, J = 2.2 Hz), 4.01 (ddd, 1 H, J = 4.1, 9.7, 9.7 Hz), 3.39 (dd, 1 H, J = 2.2, 9.7 Hz), 3.37 (dd, 1 H, J = 4.1, 9.7 Hz), 3.02 (t, 1 H, J = 8.1 Hz), 2.36–2.20 (m, 2 H), 2.21 (dd, 1 H, J = 9.7, 9.7 Hz), 1.95–1.63 (m, 4 H), 1.44 (s, 3 H), 1.42 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 110.8, 83.1, 71.2, 65.5, 65.2, 52.8, 52.6, 26.8, 26.5, 23.7, 22.4; exact mass calcd for $C_{11}H_{19}NO_3$ ($M^{\cdot+}$ + H^+) 214.1444, found 214.1443.

(6*R*,7*R*,8*S*,8a*S*)-6,7-*O*-Isopropylidene-6,7,8-trihydroxyindolizidine (21ab). See experimental data for compound **21aa**: 78% (silica gel, 10% $MeOH/CH_2Cl_2$); $[\alpha]^{20}_D$ = −9.9° (c 0.81 in MeOH); IR (solution in $CHCl_3$) 3360 (broad) and 2965 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.13 (dd, 1 H, J = 6.2, 8.6 Hz), 3.64 (dd, 1 H, J = 8.6, 9.4 Hz), 3.60 (ddd, 1 H, J = 4.6, 9.4, 9.7 Hz), 3.19 (ddd, 1 H, J = 6.2, 6.2, 9.0 Hz), 2.95 (m, 1 H), 2.93 (dd, 1 H, J = 4.6, 9.7 Hz), 2.76 (ddd, 1 H, J = 8.5, 8.5, 11.5 Hz), 2.63 (t, 1 H, J = 9.7 Hz), 1.98–1.55 (m, 4 H), 1.40 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 111.4, 81.4, 74.5, 69.1, 65.0, 54.4, 51.1, 26.9, 26.8, 22.5, 21.4; exact mass calcd for $C_{11}H_{19}NO_3$ ($M^{\cdot+}$ + H^+) 214.1444, found 214.1443.

(6*R*,7*R*,8*R*,8a*S*)-6,7-*O*-Isopropylidene-6,7,8-trihydroxyindolizidine (21ba). See experimental data for compound **21aa**: 68% (silica gel, 10% $MeOH/CH_2Cl_2$); $[\alpha]^{20}_D$ = +65.0° (c 1.05 in $CHCl_3$); IR (neat) 3350 (broad) and 2954 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.19 (t, 1 H, J = 3.6 Hz), 4.11 (ddd, 1 H, J = 5.6, 9.6, 9.6 Hz), 3.70 (dd, 1 H, J = 3.6, 9.6 Hz), 2.96 (dd, 1 H, J = 5.6, 9.6 Hz), 2.95–2.88 (m, 2 H), 2.72 (dd, 1 H, J = 9.6, 9.6 Hz), 2.58 (ddd, 1 H, J = 9.0, 11.0 Hz), 2.01–1.79 (m, 2 H), 1.68 (m, 1 H), 1.50 (m, 1 H), 1.41 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 111.3, 78.5, 71.0, 67.3, 67.2, 54.2, 52.2, 27.1, 26.7, 21.9; exact mass calcd for $C_{11}H_{19}NO_3$ ($M^{\cdot+}$ + H^+) 214.1444, found 214.1443.

(6*S*,7*S*,8*R*,8a*S*)-6,7-*O*-Isopropylidene-6,7,8-trihydroxyindolizidine (21bb). See experimental data for compound **21aa**: 77% (silica gel, 7% $MeOH/CH_2Cl_2$); $[\alpha]^{20}_D$ = −59.4° (c 1.58 in $CHCl_3$); IR (neat) 3399 (broad) and 2985 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.64 (ddd, 1 H, J = 3.8, 9.3, 9.7 Hz), 3.54 (dd, 1 H, J = 8.6, 9.3 Hz), 3.44 (bs, 1 H), 3.33 (dd, 1 H, J = 9.3, 9.3 Hz), 3.26 (dd, 1 H, J = 3.8, 9.7 Hz), 2.99 (ddd, 1 H, J = 2.8, 8.6, 8.6 Hz), 2.35 (dd, 1 H, J = 8.6 Hz), 2.24 (dd, 1 H, J = 9.7, 9.7 Hz), 2.15–1.95 (m, 2 H), 1.91–1.71 (m, 2 H), 1.55 (m, 1 H), 1.40 (s, 6 H); ^{13}C ($CDCl_3$) δ 111.52, 85.01, 75.03, 72.75, 67.72, 52.40, 51.69, 27.24, 26.80, 26.72, 22.32; exact mass calcd for $C_{11}H_{19}NO_3$ ($M^{\cdot+}$ + H^+) 214.1444, found 214.1443.

(6*S*,7*R*,8*S*,8a*S*)-6,7,8-Trihydroxyindolizidine (22aa). Amino alcohol **21aa** (0.34 g, 1.60 mmol) was dissolved in 8.0 mL of a 4:1 mixture of trifluoroacetic acid/water. The solution was stirred at room temperature for 50 h after which the solvents were evaporated. The thick dark oil was dissolved in methanol and stirred with amberlyst A-26 (OH^- form) resin for 2 h. The solution was filtered, and the solvent was evaporated. Flash chromatography purification (silica gel, 1:1 chloroform/ethanol, then ethanol; spray reagent: $KMnO_4$/NaOH in water) gave **22aa** (0.28 g, quantitative) as a waxy solid: $[\alpha]^{20}_D$ = −36.5° (c 1.11 in MeOH); IR (KBr) 3450 cm^{-1}; ^1H NMR (CD_3OD) δ 4.59 (dd, 1 H, J = 1.1, 3.0 Hz), 4.50 (ddd, 1 H, J = 5.3, 9.2, 11.1 Hz), 4.10–3.96 (m, 3 H), 3.87 (bt, 1 H, J = 8.5 Hz), 3.54 (m, 1 H), 3.28 (dd, 1 H, J = 11.1, 11.1 Hz), 2.72–2.43 (m, 4 H); ^{13}C NMR (CD_3OD) δ 77.3, 70.8, 69.5, 68.6, 55.9, 55.6, 25.8, 23.6; exact mass calcd for $C_8H_{15}NO_3$ ($M^{\cdot+}$ + H^+) 174.1131, found 174.1130.

(6*R*,7*S*,8*S*,8a*S*)-6,7,8-Trihydroxyindolizidine (22ab). See experimental data for compound **22aa**: $[\alpha]^{20}_D$ = +22.5° (c 1.13 in MeOH); IR (KBr) 3487 cm^{-1}; ^1H NMR (CD_3OD) δ 4.49–4.32 (m, 3 H), 4.85 (m, 1 H), 3.78 (dd, 1 H, J = 2.6, 12.4 Hz), 3.62 (t, 1 H, J = 6.2 Hz), 3.49 (dd, 1 H, J = 2.0, 12.4 Hz), 3.24 (q, 1 H, J = 9.4 Hz), 2.50–2.33 (m, 4 H); ^{13}C NMR (CD_3OD) δ 71.9, 71.8, 71.6, 66.6, 56.8, 56.4, 25.9, 22.4; exact mass calcd for $C_8H_{15}NO_3$ ($M^{\cdot+}$ + H^+) 174.1131, found 174.1130.

(6*R*,7*S*,8*R*,8a*S*)-6,7,8-Trihydroxyindolizidine (22ba). See experimental data for compound **22aa**: $[\alpha]^{20}_D$ = −17.3 (c 0.85 in MeOH); IR (KBr) 3500 cm^{-1}; ^1H NMR (CD_3OD) δ 4.52–4.20 (m, 3 H), 3.90–3.55 (m, 2 H), 3.48–3.10 (m, 3 H), 2.65 (m, 1 H), 2.55–2.10 (m, 3 H); ^{13}C NMR (CD_3OD) δ 73.4, 72.7, 71.9, 66.0, 56.3, 55.1, 29.6, 22.7; exact mass calcd for $C_8H_{15}NO_3$ ($M^{\cdot+}$ + H^+) 174.1131, found 174.1130.

(6*S*,7*R*,8*R*,8a*S*)-6,7,8-Trihydroxyindolizidine (22bb). See experimental data for compound **22aa**: $[\alpha]^{20}_D$ = −40.8° (C 1.28 in MeOH); IR (KBr) 3470 cm^{-1}; ^1H NMR (CD_3OD) δ 4.15 (m, 2 H), 3.90–3.58 (m, 4 H), 2.85–2.52 (m, 4 H), 2.40 (m, 2 H), 2.15 (m, 1 H); ^{13}C NMR (CD_3OD) δ 81.9, 77.1, 73.0, 70.7, 58.1, 55.9,

30.3, 24.1; exact mass calcd for $C_8H_{15}NO_3$ ($M^{\bullet+}$ + H^+) 174.1131, found 174.1130.

Acknowledgment. Financial support from NSERC and FCAR is gratefully acknowledged.

Supplementary Material Available: ^1H and ^{13}C NMR for all compounds (51 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfiche version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Radical Cyclization of (Bromomethyl)dimethylsilyl Propargyl Ethers. Regio-, Chemo-, and Stereoselectivity

Michel Journet and Max Malacria*

Université Pierre et Marie Curie, Paris VI-Laboratoire de Chimie Organique de Synthèse, URA 408, tour 44, B. 229, 4, Place Jussieu, 75252-Paris Cedex 05, France

Received December 4, 1991

Radical cyclization of (bromomethyl)dimethylsilyl propargyl ether derivatives 1 is a powerful reaction with a high degree of regio-, chemo-, and stereoselectivity. Trisubstituted olefins 3, cyclopentene derivatives 5, and diquinane system 7j are obtained in good yields by a judicious choice of unsaturated substituents. Triquinane frameworks could be obtained stereoselectively from a suitable acyclic substrate of type 1 in a one-pot reaction. First attempts have not yet allowed us to aim at this goal due to interesting (1,5) hydrogen transfers. Moreover, we have intercepted, for the first time, the α-cyclopropyl radical which is involved in the Stork–Beckwith mechanism of the 5-versus 6-membered ring formation in the vinyl radical cyclization.

Introduction

Over the last ten years, tin hydride based methods have greatly expanded the repertoire of bond-forming reactions at the disposal of the synthetic organic chemist.[1] Recently, radical cyclizations of (bromomethyl)dimethylsilyl allyl ethers have been used[2] to provide 1,3-diols after a Tamao oxidation.[3] We subsequently applied this reaction to propargyl ethers 1, which leads to a new type of heterocycle easily converted regio- and stereoselectivity into di- and trisubstituted functionalized double bonds of type 3.[4] The intermediate exocyclic vinyl radical 2 involved in this reaction can be trapped intramolecularly to afford regioselectively functionalized unsaturated five-membered carbocycles 5 in high yields.[5] Moreover, a remarkable 3,5-cis stereoselectivity is observed.[6] Very recently, a new strategy for [3 + 2] annulation involving a homoallyl radical and an electron-deficient alkene receptor has been developed.[7] Therefore, 4 appears to be a convenient intermediate in such a process and, indeed, radical cyclization of 4-[(bromomethyl)dimethylsiloxy]-2-methyl-1-undecen-5-yne (1j) in the presence of acrylonitrile leads stereoselectively via a sequence of intra-, intra-, inter-, and intramolecular processes to diquinane system 7j (Scheme I). This one-pot reaction allows the consecutive formation of four carbon–carbon bonds with two contiguous quaternary centers and controls the stereoselective construction of four stereogenic centers.[6] Work in our laboratory is aimed at developing a one-pot stereoselective synthesis of angular and linear triquinane frameworks from acyclic substrates (Scheme II). We have examined the behavior of β-silyl radical intermediate 6, which could be trapped by unsaturation present either on substituent R^3 to give an angular triquinane or on substituent R^1 to give a linear triquinane. Radical cyclizations have been used successfully in syntheses of triquinanes from cyclic substrates,[8] but stereoselectivity was not observed with acyclic ones.[9]

Table I. Stereoselective H-Abstraction of Trisubstituted Vinyl Radicals 2

entry	R^1	R^2	R^3	X	olefin[a] *E*-3:*Z*-3	yield (%)
1a	CH_3	CH_3	$CH_2CH{=}CH_2$	OH	70:30	67
1b	CH_3	CH_3	$(CH_2)_2CH{=}CH_2$	OH	75:25	75
1b	CH_3	CH_3	$(CH_2)_4CH{=}CH_2$	OH	95:5[b]	70
1d	CH_3	CH_3	$(CH_2)_3OTHP$	$SiMe_3$	0:100	60
1e	H	n-C_4H_9	n-C_4H_9	OH	100:0[b]	65
1f	CH_3	CH_3	C_6H_5	OH	25:75[c]	84
1g	CH_3	CH_3	$SiMe_3$	OH	35:65	85

[a] The stereoselectivity of olefins 3 was assigned by γ-gauche effects in the ^{13}C-NMR spectra and confirmed by ^1H-NMR NOE measurements. The chemical shift of CH_2OH is 58 ppm for the *E* olefin versus 68 ppm for the *Z* olefin. [b] Radical-induced intramolecular (1,5) hydrogen atom transfers are well known. The inter- vs intramolecular mode for hydrogen abstraction of the very reactive vinyl radicals 2c and 2e have not yet been established. However, a (1,5) hydrogen shift can be ruled out because the resulting 5-hexenyl radical should give a 5-*exo-trig* cyclization.[12] Studies using Bu_3SnD are in progress in our laboratory in order to confirm that the tin hydride is the hydrogen donor. [c] The formation of a 25:75 ratio of *E*:*Z* olefins 3 is kinetically controlled. The thermodynamic ratio of 99:1 for *Z*:*E* heterocycles 2′ was obtained by AM1 calculations.

Stereoselective Hydrogen Abstraction by Trisubstituted Vinyl Radicals. Stereoselectivity in free-radical

(1) (a) Curran, D. P. *Synthesis* **1988**, 417 and 489. (b) Giese, B. *Radicals in Organic Synthesis; Formation of Carbon-Carbon Bonds*; Pergamon Press: Oxford, 1986. (c) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (d) Hart, D. J. *Science* **1984**, *223*, 883.

(2) (a) Nishiyama, N.; Kitajama, T.; Matsumoto, M.; Itoh, K. *J. Org. Chem.* **1985**, *49*, 2298. (b) Stork, G.; Kahn, M. *J. Am. Chem. Soc.* **1985**, *107*, 500.

(3) Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M. *Organometallics* **1983**, *2*, 1694.

(4) (a) Magnol, E.; Malacria, M. *Tetrahedron Lett.* **1986**, *27*, 2255. (b) Agnel, G.; Malacria, M. *Synthesis* **1989**, 687. (c) Journet, M.; Magnol, E.; Smadja, W.; Malacria, M. *Synlett* **1991**, 58.

(5) Journet, M.; Magnol, E.; Agnel, G.; Malacria, M. *Tetrahedron Lett.* **1990**, *31*, 4445.

(6) Journet, M.; Smadja, W.; Malacria, M. *Synlett* **1990**, 320.

(7) (a) Cekovic, Z.; Saicic, R. *Tetrahedron Lett.* **1986**, *27*, 5893. (b) Curran, D. P.; Chen, M. H. *J. Am. Chem. Soc.* **1987**, *109*, 6558. (c) Curran, D. P.; Van Elburg, P. A. *Tetrahedron Lett.* **1989**, *30*, 2501.

(8) Curran, D. P.; Rakiewicz, D. M. *J. Am. Chem. Soc.* **1985**, *107*, 1448. (b) Curran, D. P.; Kuo, S. C. *Ibid.* **1986**, *108*, 1106. (c) Winkler, J. D.; Sridar, V. *Ibid.* **1986**, *108*, 1708.

(9) Beckwith, A. L. J.; Roberts, D. H.; Schiesser, C. H.; Wallner, A. *Tetrahedron Lett.* **1985**, *26*, 3349.

0022-3263/92/1957-3085$03.00/0