Short Synthesis of New 23-Vinyl Steroid Derivatives from Sapogenins by the Action of 9-BBN on Vinylogous Esters

Jesús Sandoval-Ramírez,*[a] Socorro Meza-Reyes,[a] Rosa E. del Rio,[a] Fabiola Reyes- Vazques,[a] Rosa Luisa Santillán,[b] Said Achab,[c] and Luis Bohé*[c]

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Some new 16β-acetoxy-22,26-epoxy-23-vinylcholest-22-ene steroid derivatives have been synthesized from sapogenins via a two-step sequence involving the reduction of a vinylogous ester moiety by 9-BBN, a reaction with few precedents and for which a coherent mechanistic interpretation has not been given before now. Some mechanistic insight into this reaction was gained from NMR spectroscopic evidence. A plausible general mechanistic interpretation of the action of 9-BBN on vinylogous esters is proposed.

Introduction

Sapogenins, steroids with a spiroketal side-chain, occur naturally in plants as glycosides (saponins). Marker has carried out extensive work in this field, and established the spiroketal structure of the side-chain which consists of one five-membered ring (E) and one six-membered ring (F) fused at C22.[1] Isomerization of the spiroketal subunit into a furostene via selective opening of the F ring generates pseudosapogenins.[2] These compounds have been shown to be key intermediates in the synthesis of steroidal hormones from sapogenins, as oxidation of the C20−C22 double bond in pseudosapogenins leads to pregnane derivatives.[3] This methodology has conferred great economic importance to sapogenins, allowing, for example, industrial production of both progesterone, from diosgenin **1**,[4] and cortisone, from hecogenin **2**.[5] Most recently, pseudospirostane-type derivatives have proved to be useful intermediates in the synthesis of cephalostatins.[6]

Acetolysis of the side-chain of sapogenins promoted by boron trifluoride−diethyl ether leads to another family of steroidal derivatives arising from opening of the E ring, with retention of the natural configuration at C20 and C25, and containing a β-alkoxy-α,β-unsaturated ketone motif in the side-chain.[7] This vinylogous ester functionality offers an interesting, and as yet unexploited, entry to new steroidal derivatives through a variety of reactions. Herein, we report the synthesis of the new steroid derivatives **7**−**9** bearing vinyl substituents on C23. They were obtained in a two-step sequence from sapogenins **1**−**3** by the action of 9-BBN on the vinylogous ester moiety of compounds **4**−**6**, which were themselves formed via cleavage of the E ring of the spiroketal side-chains (Scheme 1).

Although the selective reduction of α,β-unsaturated aldehydes and ketones to give the corresponding allylic alcohols is a well documented application of 9-BBN in synthesis,[8] we have found only few examples of the use of this reagent for the reduction of vinylogous ester systems (Scheme 2).[9,10] On the one hand, the reduction by 9-BBN (1.05−1.8 equivalents) of furanones **10**, leading to furans **11**, has been applied to the synthesis of some natural products.[10] The furan derivatives **11** were isolated in high yields (71−97%) by chromatography, after a "neutral" work-up consisting of evaporation of the solvent from the reaction mixture and treatment of the residue with ethanolamine in pentane.[8] Alternatively, on one occasion, the residue obtained upon evaporation of the solvent was purified directly by chromatography.[10e] On the other hand, Meyers et al.[9] have reported the reduction of the naphthalene **12** by 9-BBN, leading, after mild hydrolytic work-up (quenching with saturated ammonium chloride solution at room temperature), either to the naphthalenone **13** or the enol ether **14**. When two equivalents of 9-BBN were used, an 80% yield of the enone **13** was obtained, along with a trace of the enol ether **14**. But when six equivalents of 9-BBN were added to the naphthalene **12**, the enol ether **14** (the so-called "over-reduced product") was the major product

[a] Facultad de Ciencias Químicas, Benemérita Universidad Autónoma de Puebla,
Puebla, Pue., 7200, México
E-mail: jsandova@siu.buap.mx
[b] Departamento de Química, Centro de Investigación y Estudios Avanzados del IPN,
México, D.F., 07000, México
[c] Institut de Chimie des Substances Naturelles, ICSN-CNRS,
Avenue de la Terrasse, 91198 Gif sur Yvette, France
E-mail: bohe@icsn.cnrs-gif.fr

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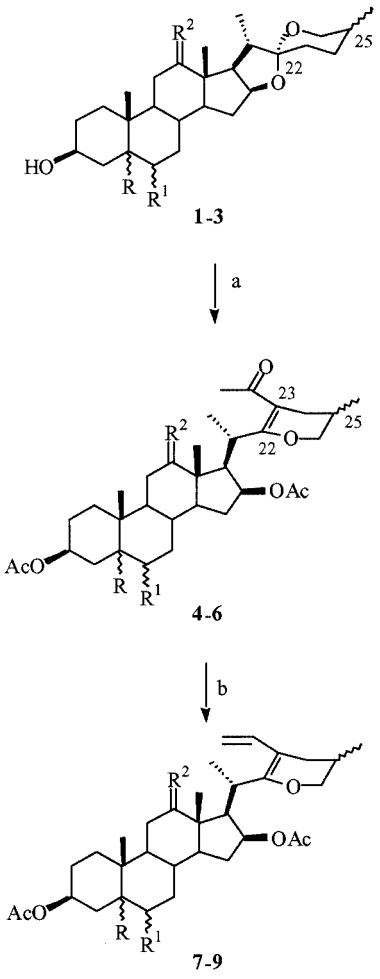
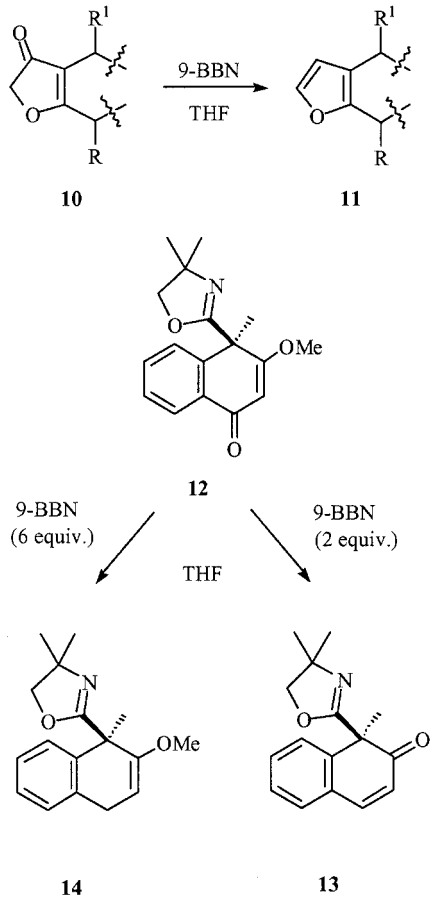


	C25	R	R^1	R^2
1, 4, 7	(25R)	>C=CH-		H_2
2, 5, 8	(25R)	αH	H	O
3, 6, 9	(25S)	βH	H	H_2

Scheme 1. a) Ac_2O, BF_3·OEt_2, room temp.; b) 9-BBN, THF, room temp.; 10h



Scheme 2

(74%). To the best of our knowledge, a coherent rationalization of these apparently dissimilar results is lacking. On the basis of NMR spectroscopic evidence from the second step in Scheme 1, which gives some mechanistic insight, a rationalization accounting for the whole set of results concerning this transformation is also proposed in this report (Schemes 4−6).

Results and Discussion

The boron trifluoride−diethyl ether (Et_2O·BF_3)-promoted acetolysis of diosgenin **1** and hecogenin **2** takes place readily at room temperature, with highly selective cleavage of the spiroketal E ring leading to the dihydropyran derivatives **4** and **5**, in 85% and 87% yields, respectively. Both compounds were fully characterized, and their structures were unambiguously established by X-ray analysis.[7b] The new structures **4** and **5** arise from opening of the E ring with retention of the natural configuration at C20 and C25 (20*R*,25*R*), which indicates that these stereogenic centers are not directly involved in this transformation.

The spiroketal side-chain of sarsasapogenin **3** is cleaved less selectively under similar conditions, but the dihydropyran derivative **6** is still the major product. While cleavage of the E ring leads exclusively to the dihydropyran derivative **6**, isolated by column chromatography in 49% yield, three furostene side-products are formed from opening of the F ring. The lower E to F selectivity in the acetolysis of the side-chain of sarsasapogenin (**3**) has been attributed to the fact that the β-elimination leading to the dihydropyran moiety is less favorable due to steric hindrance from the axial C25-methyl group.[7c] Compound **6** was fully characterized, and its structure was established by 2D NMR spectroscopy.[7c]

The reaction of compounds **4**−**6** with two equivalents of 9-BBN in THF at room temperature led to the reduction of the vinylogous ester moiety, giving the corresponding dienes **7**−**9**. They were isolated in 40−45% yields by chromatography (on silica gel) of the solid residue resulting from removal of the solvent under vacuum. The NMR spectra of compounds **7**−**9** strongly support the existence of a diene system containing a terminal monosubstituted double bond

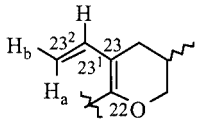
conjugated to a trisubstituted enol ether. In the ^{1}H spectrum, the terminal double bond is indicated by a downfield doublet of doublets (J_{trans} = 16−17 Hz, J_{cis} = 11 Hz) in the 6.7−6.8 ppm region, corresponding to H23^1, which is deshielded by the oxygen atom at C22, and two doublets at ca. 4.8 ppm (J_{trans} = 16−17 Hz) and ca. 4.7 ppm (J_{cis} = 11 Hz), corresponding to the gem-vinyl protons H_a23^2 and H_b23^2, respectively. In the ^{13}C spectrum, the electrophilic centers C22 and C23^1, α and γ to the oxygen, are deshielded, displaying signals at δ = 157−158 ppm and 134−135 ppm, respectively, while the nucleophilic centers C23 and C23^2, β and δ to the oxygen, are shielded, showing signals at δ = 104−105 ppm and 106−107 ppm, respectively. The individual ^{1}H and ^{13}C chemical shifts for these diene systems in compounds **7**−**9** are summarized in Table 1. They are in agreement with literature data for compounds containing similar diene patterns.[11] The NMR spectra of compounds **7**−**9** also display the characteristic signals for two acetates on C3 and C16, as shown in Table 2. The C5−C6 double bond of the diosgenin-derived compound **7** is indicated by ^{13}C signals at δ = 139.75 ppm (C5) and 122.39 ppm (C6) and a ^{1}H multiplet at δ = 5.30 ppm (H6). The C12 carbonyl of the hecogenin-derived compound **8** is indicated by a ^{13}C signal at δ = 213.50 ppm. Thus, we can see that the trisubstituted (C5−C6) double bond of **4** and the C12 carbonyl group of **5** are not affected under the reaction conditions leading to the reduction of the corresponding vinylogous ester moieties.

The reductive 1,3-carbonyl transposition of vinylogous esters is a well precedented reaction, initially introduced for the synthesis of cyclohexenones from the mono enol ethers of 1,3-cyclohexanediones via $LiAlH_4$ reduction of the free carbonyl, followed by acidic work-up.[12] Other reducing agents, such as Dibal,[10e][13a] or even $NaBH_4$,[14] proved to work equally well for the general transformation of β-diketones **15** into α,β-unsaturated ketones **16** by this method. In the event that reduction of **4**−**6** by 9-BBN follows a closely related pathway, one can assume that the initially formed borinic esters **17** were converted upon work-up into the allylic alcohols **18**, which then underwent dehydration on silica gel to form the terminal 1,3-diene moieties of compounds **7**−**9** (Scheme 3).

Besides some reports indicating that γ-alkoxy-allylic alcohols (vinylogous hemiacetals) similar to **18** may be preserved under mild hydrolytic conditions,[11b,15,16] and even in some cases purified by chromatography,[11b,15] evidence indicating that compounds **7**−**9** were probably not formed by the pathway shown in Scheme 3 came from examination of the proton NMR spectra of the crude products after evaporation of the reaction mixtures to dryness, which revealed that compounds **7**−**9** were already present. This was apparent from the signals of the terminal vinyl groups, and especially the doublet of doublets corresponding to H23^1, which resonates in a spectral region free from other signals, at δ = 6.7−6.8 ppm.

In order to get some insight into the reduction pathway leading to compounds **7**−**9**, the reduction of the hecogenin derivative **5** was monitored by ^{1}H NMR spectroscopy. In this way, we could observe the formation of diene **8** in the early stages of the reaction, and furthermore, we had evidence that **8** was produced from an intermediate (**17a**) arising from **5**, which itself was rapidly consumed. The concentration of intermediate **17a** rapidly increased until $t \approx$ 30 min and remained nearly constant in the interval t = 30−50 min. Then, after the disappearance of the starting material **5**, the intermediate faded out, disappearing completely at $t \approx$ 8 h. At the same time, the concentration of diene **8** gradually increased (Table 3).[17]

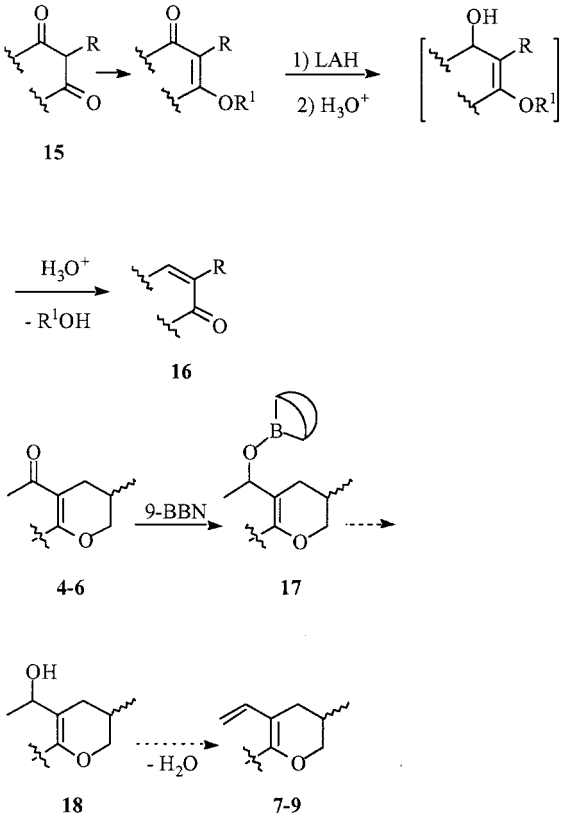
Table 1. ^{1}H and ^{13}C NMR chemical shifts for the diene systems of compounds **7**−**9**



	^{1}H NMR {δ (ppm), (multiplicity) [J (Hz)]}			^{13}C NMR [δ (ppm)]			
	H23^1	H_a23^2	H_b23^2	C22	C23	C23^1	C23^2
7	6.79 (dd) [16.1; 11]	4.84 (dd) [16.1; 1.2]	4.73 (dd) [11; 1.2]	157.95	104.69	134.64	106.52
8	6.73 (dd) [17.2; 11]	4.83 (dd) [17.2; 1.2]	4.70 (dd) [11; 1.2]	157.33	104.90	134.51	106.52
9	6.75 (dd) [17.2; 11]	4.81 (dd) [17.2; 1.5]	4.84 (dd) [11; 1.2]	157.62	104.45	134.63	106.78

Table 2. ^{1}H and ^{13}C NMR chemical shifts for the C3 and C16 acetates of compounds **7**−**9**

	^{1}H NMR {δ (ppm), (multiplicity)}				^{13}C NMR [δ (ppm)]	
Compd.	H3	MeC(O)O−C3	H16	MeC(O)O−C16	Me*C*(O)O−C3	Me*C*(O)O−C16
7	4.50 (m)	2.03 (s)	5.02 (m)	1.89 (s)	171.12	170.59
8	4.66 (m)	2.00 (s)	5.04 (m)	1.88 (s)	170.80	170.72
9	5.06 (m)	2.03 (m)	5.10 (m)	1.84 (s)	171.11	170.41



Scheme 3

Table 3. Reduction of compound **5** by 9-BBN in [D8]THF

Entry	Time	Molar ratio		
		5	**17a**	**8**
1	0	1	–	–
2	10 min	0.77	0.14	0.09
3	20 min	0.27	0.54	0.19
4	30 min	0.12	0.64	0.23
5	40 min	0.06	0.64	0.30
6	50 min	–	0.63	0.37
7	1 h	–	0.58	0.42
8	1.5 h	–	0.48	0.52
9	2 h	–	0.39	0.61
10	4 h	–	0.18	0.82
11	6 h	–	0.08	0.92
12	8 h	–	–	1

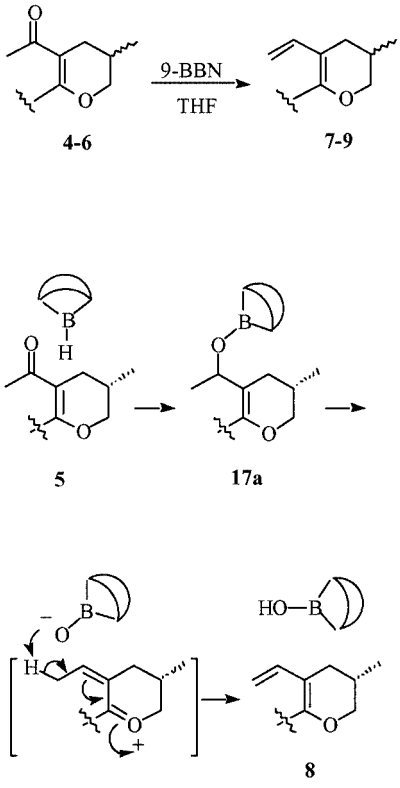
The presence of diene **8** from $t = 10$ min was shown by the appearance of the following signals: (1) a doublet of doublets at $\delta = 6.76$ ppm ($J = 16.91$, $J = 11.03$ Hz), (2) a doublet at $\delta = 4.81$ ppm ($J = 16.91$ Hz), (3) a multiplet appearing as a broad doublet of triplets at $\delta = 5.05$ ppm, just 0.08 ppm downfield from the signal at $\delta = 5.13$ ppm showing a similar multiplicity pattern and corresponding to H16 of the starting material (**5**), (4) a multiplet at $\delta = 3.11$ ppm. The two first signals are consistent with $H23^1$ and H_b23^2 of the terminal double bond. The multiplets at $\delta = 5.05$ ppm and 3.11 ppm correspond to H16 and H20, respectively. At this early stage, the doublet corresponding to H_a23^2 was hidden by the multiplet centered at $\delta = 4.63$ ppm (H3 of **5**), but it became easily visible as the concentration of **8** increased (after $t = 30$ min). The signals from the starting material (**5**) gradually diminished, finally disappearing at $t = 50$ min. The absence of the prominent singlet at $\delta = 2.13$ ppm, corresponding to the methyl group of the vinylogous ester moiety, proved the disappearance of **5** at $t = 50$ min.

A broad quadruplet at $\delta = 5.31$ ppm ($J \approx 6.6$ Hz) indicated the formation of the expected intermediate in the reduction of the carbonyl group by 9-BBN, the borinic ester **17a**, whose $H23^1$ proton is strongly shifted downfield, due to the >B−O substituent.[18] This quadruplet was apparent from $t = 10$ min, and rapidly gained in intensity to reach an almost stable level within the interval $t = 30-50$ min, after which, it slowly faded out, while at the same time, the signals corresponding to **8** increased proportionally. The vicinal methyl ($Me23^2$) was difficult to locate, due to signal overlapping. However, upon irradiation of the quadruplet $\delta = 5.31$ ppm, a singlet emerged from the methylene envelope at $\delta = 1.28$ ppm. The broad doublet of triplets at $\delta = 5.16$ ppm remaining after $t = 50$ min was consistent with H16 of **17a**. Before $t = 50$ min, this signal overlapped that of H16 of **5**. A singlet at $\delta = 8.13$ ppm, consistent with a B−OH proton[18] indicated the formation of the borinic acid >B−OH (>B− = 9-BBN).

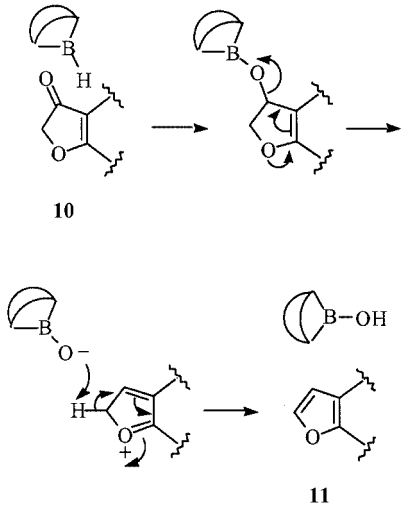
The fact that the terminal 1,3-diene moiety of compound **8** did not undergo hydroboration, despite the presence of an excess of 9-BBN, deserves some comment. At first glance, this seemed to be inconsistent with the known high reactivity of terminal alkenes towards hydroboration with 9-BBN (complete hydroboration in THF at room temperature in less than two hours).[19] But on the other hand, it has been shown that conjugation in dienes greatly decreases their reactivity towards hydroboration,[20] either by diborane,[20a] disiamylborane[20b] or 9-BBN,[20c] and moreover, that 1,3-dienes with more extensive conjugation proved to be remarkably resistant toward hydroboration with 9-BBN. Nevertheless, the hydroboration of the terminal double bond of two more-or-less related O-substituted dienic moieties by 9-BBN has been described.[21] Therefore, control experiments were run. They showed that not only diene **8**, but also dienes **7** and **9**, failed to react with two equivalents of 9-BBN in THF at room temperature to any significant extent, and confirmed that, probably for electronic and steric reasons, dienes **7**−**9** are not prone to hydroboration by 9-BBN under the conditions leading to the reduction of the vinylogous ester systems of **4**−**6**.

These data suggest the reduction pathway shown in Scheme 4, involving the O-assisted elimination of borinate (>B−O$^-$) from the intermediate borinic ester **17a**. Furthermore, such a pathway also provides a coherent rationalization for the apparently dissimilar results found in the literature.[9,10] On the one hand, the formation of the furan derivatives **11** in the reduction of corresponding furanones **10** (upper reaction in Scheme 2). Obviously, these results, which have been rationalized on the basis of the hypothetical "spontaneous elimination of borinic acid from the inter-

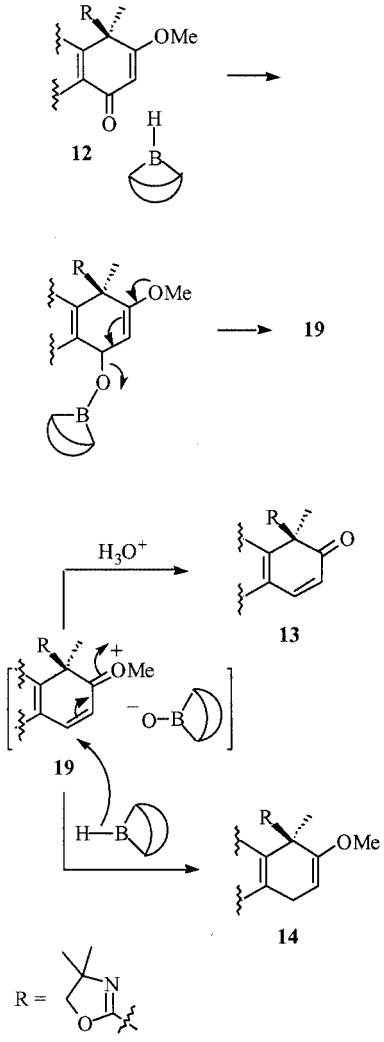
mediate borinic ester, presumably favored by the bulkiness of the group"[10a,10] are consistent with the reduction pathway involving O-assisted elimination of borinate as shown in Scheme 5. On the other hand, a similar pathway involving the ether-assisted elimination of borinate anion may also account for Meyer's results[9] as shown in Scheme 6. Thus, the reduction of the naphthalene **12** by 9-BBN, leading either to the naphthalenone **13** or the enol ether **14** (lower line in Scheme 2), may actually operate through a common intermediate **19**. In the reaction involving two equivalents of 9-BBN, this intermediate may give the enone **13** upon hydrolytic work-up, whereas in the reaction performed with six equivalents of 9-BBN, the enol ether **14** may be formed via regioselective reduction of **19** by the excess of 9-BBN. In this case, one can assume that the 1,4-reduction of **19** was favoured over a 1,2-reduction, owing to steric hindrance from the substituents (methyl and oxazoline) attached to the benzylic carbon atom.



Scheme 4



Scheme 5



Scheme 6

Conclusion

In summary, we have synthesized new steroid derivatives with a vinyl substituent on C23, starting from sapogenins, via a two-step sequence involving the reduction of a vinylogous ester moiety by 9-BBN, a reaction with few precedents and for which a coherent mechanistic interpretation had not been given before now. Some mechanistic insight into this reaction came from NMR spectroscopic evidence, which suggests a plausible general mechanistic interpretation of the action of 9-BBN on vinylogous esters, involving the O-assisted elimination of borinate anion from the initially formed borinic ester. The resonance-stabilized cationic intermediate thus liberated should evolve into prod-

ucts depending on the structure of the substrate and the reaction conditions. Further experimental work to confirm this mechanistic interpretation is underway.

Experimental Section

General Remarks: ^{1}H and ^{13}C NMR spectra were recorded with a JEOL ECLIPSE NMR spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C) and a Bruker DMX500 spectrometer (500 MHz for ^{1}H and 125 MHz for ^{13}C) Chemical shifts (δ) are reported in ppm, and are referenced to TMS or to the central ^{13}C triplet signal (δ = 77.0 ppm) of $CDCl_3$. IR spectra were recorded with a Nicolet Magna FT-IR 750 spectrophotometer using KBr pellets; wavenumbers ($\tilde{\nu}$) are given in cm^{-1}. Mass spectra were obtained with a HP 5989A spectrometer using Electron Impact Ionization. UV spectra were determined with a Beckman DU-7500 spectrophotometer in ethanol solutions; wavelengths (λ) are expressed in nm. Optical rotations were determined with a Perkin−Elmer 241 polarimeter. Melting points were obtained on a Gallenkamp MFB 595 apparatus and were not corrected. Elemental analyses were performed at the ICSN-CNRS, France. Analytical TLC was performed on silica gel ALUGRAM®SIL G/UV-252 plates. Column chromatography was carried out on silica gel Davisil™ grade 633 (200−425 mesh).

General Procedure for the Preparation of 4, 5, and 6: $BF_3{\cdot}OEt_2$ (1.5 mL, 11.8 mmol) was added to a suspension of the sapogenin (**1**−**3**, 1 mmol) in Ac_2O (5.0 mL, 52.9 mmol). The mixture was stirred at room temperature for 10 min. The reaction mixture, which became homogeneous, was then poured into ice and extracted with CH_2Cl_2. The organic layer was neutralized with aqueous $NaHCO_3$, washed with water, then with brine, dried with anhydrous $MgSO_4$ and concentrated under vacuum. The residue was purified by chromatography on silica gel (hexanes/EtOAc, 9:1).

(25*R*)-23-Acetyl-22,26-epoxycholest-5,22-diene-3β,16β-diyl Diacetate (4): Yield (460 mg, 85%); m.p. 95−96 °C. $[\alpha]_D^{25} = -24.0$ (*c* = 0.65, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.34 (d, 1 H, H-6), 5.12 (ddd, $J_1 = J_2 = 7.5$, $J_3 = 4.5$ Hz, 1 H, H-16), 4.57 (m, 1 H, H-3), 4.05 (m, 1 H, H-20) 2.18 (s, 3 H, H-23^2), 2.00 (s, 3 H, CH_3CO_2-3), 1.82 (s, 3 H, CH_3CO_2-16), 1.15 (d, $J_{20,21} = 7.0$ Hz, CH_3-21, 3 H), 1.01 (s, 3 H, CH_3-19), 0.94 (d, $J_{25,27} = 6.5$ Hz, 3 H, CH_3-27), 0.89 (s, 3 H, CH_3-18) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.23 (C23^1), 171.44 (C22), 170.72 (CH_3CO_2-3), 170.55 (CH_3CO_2-16), 139.89 (C5), 122.27 (C6), 106.99 (C23) ppm. UV: $\lambda_{max.}$ (ε) = 275 nm (10,300). IR: $\tilde{\nu}$ = 1732, 1660, 1566, 1366, 1248 cm^{-1}. MS: *m*/*z* = 540 [M^+]. $C_{33}H_{48}O_6$ (540.7): calcd. C 73.30, H 8.95, O 17.75; found C 73.29, H 9.28, O 17.43.

(25*R*)-23-Acetyl-22,26-epoxy-12-oxo-5α-cholest-22-ene-3β,16β-diyl Diacetate (5): Yield (483 mg, 87%); m.p. 194−195 °C. $[\alpha]_D^{25} = +37.6$ (*c* = 0.62, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.04 (m, 1 H, H-16), 4.63 (dddd, $J_1 = J_2 = 10.8$, $J_3 = J_1 = 5.7$ Hz, 1 H, H-3), 3.99 (m, 1 H, H-20) 2.13 (s, 3 H, CH_3CO-23), 1.97 (s, 3 H, CH_3CO_2-3), 1.80 (s, 3 H, CH_3CO_2-16) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 213.30 (C12), 197.86 (C23^1), 171.29 (C22), 170.35 (CH_3CO_2-3), 170.21 (CH_3CO_2-16), 106,.80 (C23) ppm. UV: $\lambda_{max.}$ (ε) = 274 nm (9,620). IR: $\tilde{\nu}$ = 1734, 1708, 1665, 1566, 1374, 1243 cm^{-1}. MS: *m*/*z* = 556 [M^+]. $C_{33}H_{48}O_7$ (556.7): calcd. C 71.19, H 8.69, O 20.12; found C 71.03, H 8.69, O 20.28.

(25*S*)-23-Acetyl-22,26-epoxy-5β-cholest-22-ene-3β,16β-diyl Diacetate (6): Yield (257 mg, 49%); m.p. 77−79 °C. $[\alpha]_D^{25} = +96.8$ (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.14 (m, 1 H, H-16), 5.06 (m, 1 H, H-3), 3.98 (dq, $J_1 = 9.0$ and $J_2 = 7.0$ Hz, 1 H, H-20), 2.20 (s, 3 H, H-23^2), 2.04 (s, 3 H, CH_3CO_2-3), 1.82 (s, 3 H, CH_3CO_2-16), 1.16 (d, $J_{20,21} = 7.0$ Hz, 3 H, CH_3-21), 0.98 (s, 3 H, CH_3-19), 0.96 (d, $J_{25,27} = 6.0$ Hz, 3 H, CH_3-27), 0.89 (s, 3 H, CH_3-18) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.21 (C23^1), 171.52 (C22), 170.70 (CH_3CO_2-3), 170.55 (CH_3CO_2-16), 107.54 (C23) ppm. UV: $\lambda_{max.}$ (ε) = 276 nm (11,400). IR: $\tilde{\nu}$ = 1734, 1667, 1569, 1375, 1254 cm^{-1}. MS: *m*/*z* = 542 [M^+]. $C_{33}H_{50}O_6$ (542.7): calcd. C 73.03, H 9.29, O 17.69; found C 72.77, H 9.63, O 17.54.

General Procedure for the Preparation of 7, 8 and 9: A solution of 9-BBN (244 mg, 2 mmol) in THF (4 mL) was added to a solution of the vinylogous ester derivative (**4**−**6**, 1 mmol) in THF (5 mL) and the reaction mixture was stirred 10 h at room temperature. The solvent was removed under vacuum and the solid residue was purified by chromatography on silica gel (hexanes/EtOAc, 8:2).

***s-cis*-(25*R*)-3β,16β-Diacetoxy-22,26-epoxy-23-vinylcholesta-5,22-diene (7):** Yield (210 mg, 40.1%); m.p. 159−161 °C. $[\alpha]_D^{25} = -0.8$ (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.79 (dd, J_1 = 16.12, J_2 = 11.00 Hz, 1 H, H-23^1), 5.30 (m, 1 H, H-6), 5.02 (m, 1 H, H-16), 4.84 (dd, J_1 = 16.12, J_2 = 1.12, 1 H, H_a-23^2), 4.73 (dd, J_1 = 11.0, J_2 = 1.12 Hz, 1 H, H_b-23^2), 4.50 (s, 1 H, H-3), 3.20 (m, 1 H, H-20), 2.03 (s, 3 H, CH_3CO_2-3), 1.89 (s, 3 H, CH_3CO_2-16), 1.15 (d, $J_{20,21} = 7.0$ Hz, 3 H, CH_3-21), 1.03 (s, 3 H, CH_3-19), 0.94 (d, $J_{27,25} = 8.4$ Hz, 3 H, CH_3-27), 0.93 (s, 3 H, CH_3-18) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.12 (CH_3CO_2-3), 170.59 (CH_3CO_2-16), 157.95 (C22), 139.75 (C5), 134.64 (C23^1), 122.39 (C6), 106.52 (C23^2), 104.69 (C23) ppm. UV: $\lambda_{max.}$ (ε) = 256 nm (11,600). IR: $\tilde{\nu}$ = 2937, 1735, 1630 cm^{-1}. MS: *m*/*z* = 524 [M^+]. $C_{33}H_{48}O_5$ (524.7): calcd. C 75.53, H 9.22, O 15.24; found C 75.45, H 9.52, O 15.15.

***s-cis*-(25*R*)-3β,16β-Diacetoxy-22,26-epoxy-12-oxo-23-vinyl-5α-cholest-22-ene (8):** Yield (228 mg, 42.2%); m.p. 132−134 °C. $[\alpha]_D^{25} = +26.6$ (*c* = 0.9, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.73 (dd, J_1 = 17.20, J_2 = 11.00 Hz, 1 H, H-23^1), 5.04 (m, 1 H, H-16), 4.83 (dd, *J* = 17.20 Hz, 1 H, H_a-23^2), 4.70 (dd, *J* = 11.0 Hz, 1 H, H_b-23^2), 4.66 (s, 1 H, H-3), 3.19 (m, 1 H, H-20), 2.00 (s, 3 H, CH_3CO_2-3), 1.88 (s, 3 H, CH_3CO_2-16), 1.05 (d, $J_{20-21} = 7.0$ Hz, 3 H, CH_3-21), 0.91 (s, 3 H, CH_3-19), 0.92 (d, $J_{27,25} = 8.4$ Hz, 3 H, CH_3-27), 1.24 (s, 3 H, CH_3-18) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 213.50 (C12), 170.80 (CH_3CO_2-3), 170.72 (CH_3CO_2-16), 157.33 (C22), 134.51 (C23^1), 106.52 (C23^2), 104.90 (C23) ppm. UV: $\lambda_{max.}$ (ε) = 264 nm (12,542). IR: $\tilde{\nu}$ = 2930, 1733, 1629 cm^{-1}. MS: *m*/*z* = 540 [M^+]. HRMS (FAB): *m*/*z* calcd. for $C_{33}H_{48}O_6$ 540.3451; found 540.3462

***s-cis*-(25*S*)-3β,16β-Diacetoxy-22,26-epoxy-23-vinyl-5β-cholest-22-ene (9):** (246 mg, 45.4%); m.p. 76−78 °C. $[\alpha]_D^{25} = +35.1$ (*c* = 0.50, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.75 (dd, J_1 = 11.0 and J_2 = 17.24 Hz, 1 H, H-23^1), 5.06 (s, 1 H, H-3), 5.10 (m, 1 H, H-16), 4.81 (dd, J_1 = 1.5 and J_2 = 17.24 Hz, 1 H, H_a-23^2), 4.71 (dd, J_1 = 1.5 and J_2 = 11.0 Hz, 1 H, H_b-23^2), 3.16 (dq, J_1 = 6.6 and J_2 = 11.0 Hz, 1 H, H-20), 2.03 (s, 3 H, CH_3CO_2-3), 1.84 (s, 3 H, CH_3CO_2-16), 0.96 (s, 3 H, CH_3-19), 1.00 (d, $J_{20,21} = 6.6$ Hz, 3 H, CH_3-21), 0.92 (d, $J_{27,25} = 6.6$ Hz, 3 H, CH_3-27), 0.89 (s, 3 H, CH_3-4.63 (C23^1), 106.78 (C23^2), 104.45 (C23) ppm. UV: $\lambda_{max.}$ (ε) = 259 nm (16,249). IR: $\tilde{\nu}$ = 2935, 1736, 1634 cm^{-1}. MS: 526 [M^+]. $C_{33}H_{50}O_5$ (526.7): calcd. C 75.25, H 9.57, O 15.19; found C 75.12, H 9.64, O 15.34.

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[17] Reaction conditions: **5** (0.1 mmol) and 9-BBN (ca. 2 equivalents) were dissolved in [D_8]THF (1 mL) at room temperature. The solution was transferred to an NMR tube and the proton spectra were recorded at the indicated times with a Bruker spectrometer at 300 MHz. The molar ratios (**5**:**17a**:**8**) were determined by the integration of the signals corresponding to $H23^1$ of **8** at $\delta = 6.76$ ppm (dd, $J = 16.91$ Hz, $J = 11.03$ Hz); to $H23^1$ of **17a** at $\delta = 5.31$ ppm (q, $J \approx 6.6$ Hz) and to the H16 protons of of the three compounds (**5, 17a** and **8**) that resonate in the region $\delta = 5.20-5.00$ ppm.
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