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NEW SYNTHESIS OF CASTASTERONE

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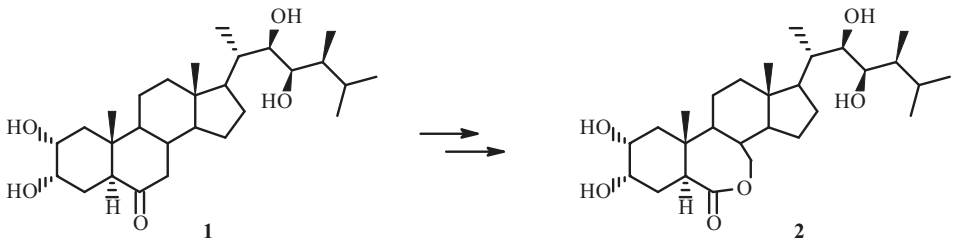
An improved synthesis that could produce gram quantities of castasterone was proposed. The starting material was stigmasterol, the cyclic part of which was transformed in the first synthetic step into the 3α,5-cyclo-6-ketone. The side-chain carbon skeleton in the target compound was constructed with the required stereochemistry of the C-24 methyl via addition of methylacetylene, hydrogenation of the propargyl alcohol over Lindlar catalyst, and Claisen rearrangement. Diols were introduced using Sharpless asymmetric dihydroxylation of the intermediate $\Delta^{2,22}$-dienone in the presence of $(DHQD)_2AQN$. A unique feature of the synthesis was the avoidance of chromatographic separations of propargyl alcohols with similar chromatographic mobilities because the C-22 diastereomers were enriched in subsequent redox reactions.

Keywords: brassinosteroids, castasterone, Claisen rearrangement, diastereomeric enrichment.

The discovery in 1979 of brassinolide (**2**) in rape pollen became an event [1] that had a great conceptual influence on hormonal regulation of plant growth and development. About 70 related brassinolides were identified in subsequent years and were called brassinosteroids (BS). Nanomolar concentrations of them were capable of affecting all of the most important aspects of plant vital functions [2–5]. The two most active BS, **2** and its biosynthetic precursor castasterone (**1**), stimulated the most interest among researchers studying phytohormone activity on the molecular level. Natural raw material cannot be considered a source for ensuring their availability because they occur at exceptionally low concentrations in plants. Chemical synthesis remains the only solution to the problem. An unresolved issue is the production of **1** because the transition from **1** to **2** is thoroughly understood [3].



The C_{23}–C_{28} side chain must also be constructed to synthesize **1**, in contrast with related BS that can be prepared comparatively readily from sterols with the appropriate carbon skeleton (epicastasterone from ergosterol and homocastasterone from stigmasterol), because a suitable starting material with the castasterone carbon skeleton is not available. Although many synthetic methods for **1** have been reported [6–19], it is still poorly accessible even for scientific research because of their deficiencies (multiple steps, low yields, costly reagents, required separation of pure intermediates).

Therefore, the goal of the present work was to develop a synthetic approach that could produce gram quantities of **1**. It would be based on known methods (including those attempted by us previously), the efficiency of which would be improved by using selective reagents, setting the optimum reaction conditions, and using special techniques to separate isomeric mixtures and to isolate the target products.

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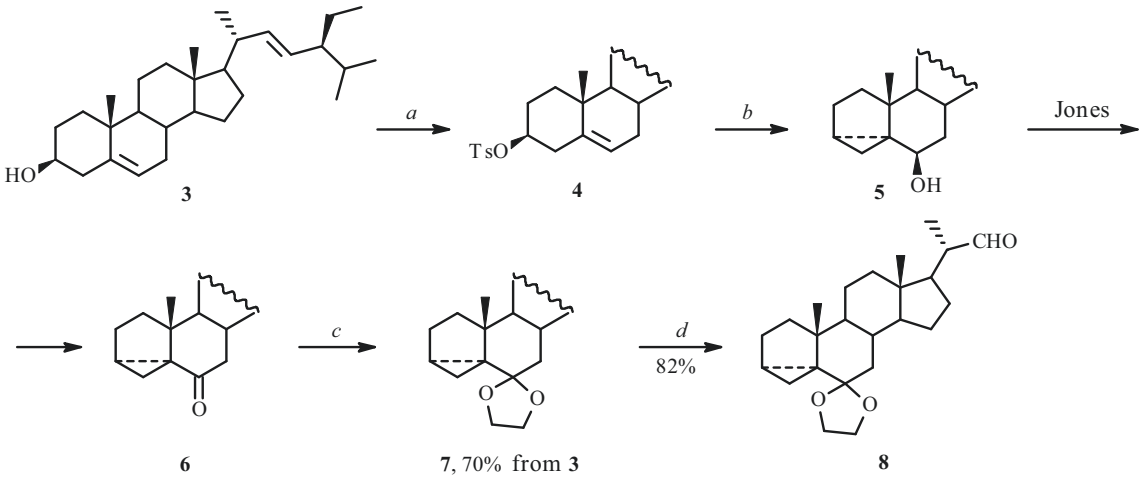
Stigmasterol (**3**), which is manufactured on industrial scales from soy oil, was chosen as the starting material. Use of **3** to synthesize BS necessitated oxidative cleavage of the Δ^{22}-bond to produce the corresponding 22-aldehyde and subsequent replacement of the carbon side chain and construction of an AB-cyclic portion that was stable to the reaction conditions. Aldehyde **8**, which was accessible in five steps and was used earlier to synthesize 27C- [20, 21], 28C- [11], and 29C-BS [22], was a convenient intermediate for preparing **1**.



3 **4** **5** **6** **7**, 70% from **3** **8**

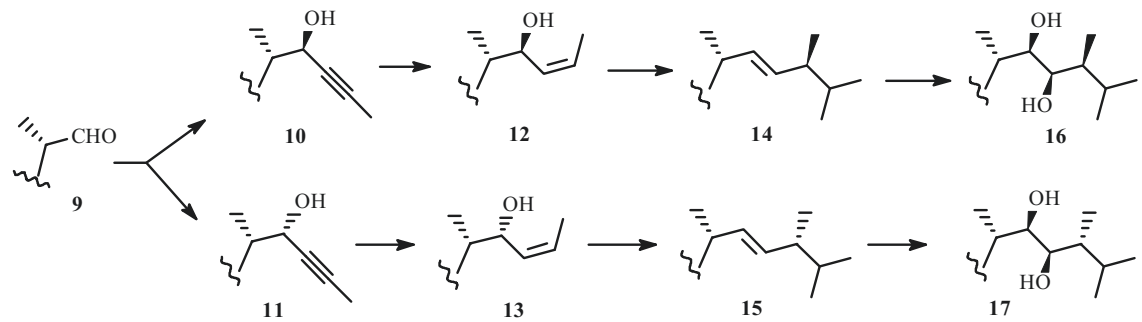
a. TsCl/Py; *b*. $Me_2CO–H_2O$, KOAc; *c*. $(CH_2OH)_2$, $CH(OEt)_3$, TsOH; *d*. O_3

The procedure for preparing **8** was slightly updated by us. The usual conditions for the *i*-steroid rearrangement are refluxing a solution of tosylate **4** in an $Me_2CO–H_2O$ mixture in the presence of KOAc. A drawback of this method is the need to use dilute solutions (0.3–0.5%) of the reagents because of the poor solubility of **4**. We found that it did not necessarily have to be completely dissolved. The yield of alcohol **5** was essentially unaffected if the volume of the solvents was decreased by 6–8 times. In this instance, a suspension of **4** was stirred and refluxed until it was completely dissolved.

Another improvement to the procedure for producing **8** was the use of triethyl orthoformate to add the dioxalane protection. A solution of **6** in CH_2Cl_2 was held at room temperature for 20 min in the presence of ethylene glycol and triethyl orthoformate to produce **7**. However, a previous method [11] suggested refluxing for several hours a solution of **6** in C_6H_6 with a Dean–Stark trap for azeotropic removal of H_2O.

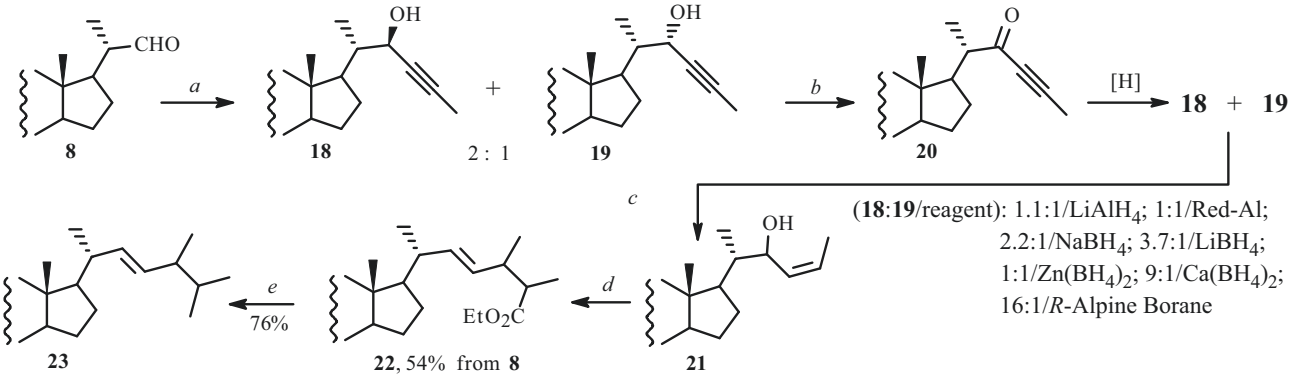
Ozonolysis of **7** used a MeOH–$CHCl_3$ mixture in the presence of small amounts of Sudan III dye, $NaHCO_3$, and Py. The dye was used to determine the ozonolysis end point. The other reagents were added to avoid acidification of the reaction mixture, which is especially critical when ozone is generated from atmospheric oxygen.

Construction of the side-chain carbon skeleton was the most difficult part of the castasterone synthesis. Claisen rearrangement of allyl alcohol **12** [23–26] was especially attractive among the variety of proposed strategies for solving this problem [6–19]. This reaction typically has high stereoselectivity and yields, does not require inert conditions, and is easily scaled up. Syntheses of BS based on it usually include addition of methylacetylene to 22-aldehyde **9** to give a mixture of propargyl alcohols **10** and **11**. They had to be separated by chromatography for the present approach because the C-24 stereochemistry of Claisen rearrangement product **14** was determined by the configuration of the C-22 hydroxyl of **10** [27]. A choke point in the method as a whole was the need for preliminary separation of C-22 isomers **10** and **11**, which have very similar chromatographic mobilities. This prevented it from being scaled up. Based on previous research [11], we supposed that the isomers could also be separated in the later step for **16** and **17** with fully constructed side chains.



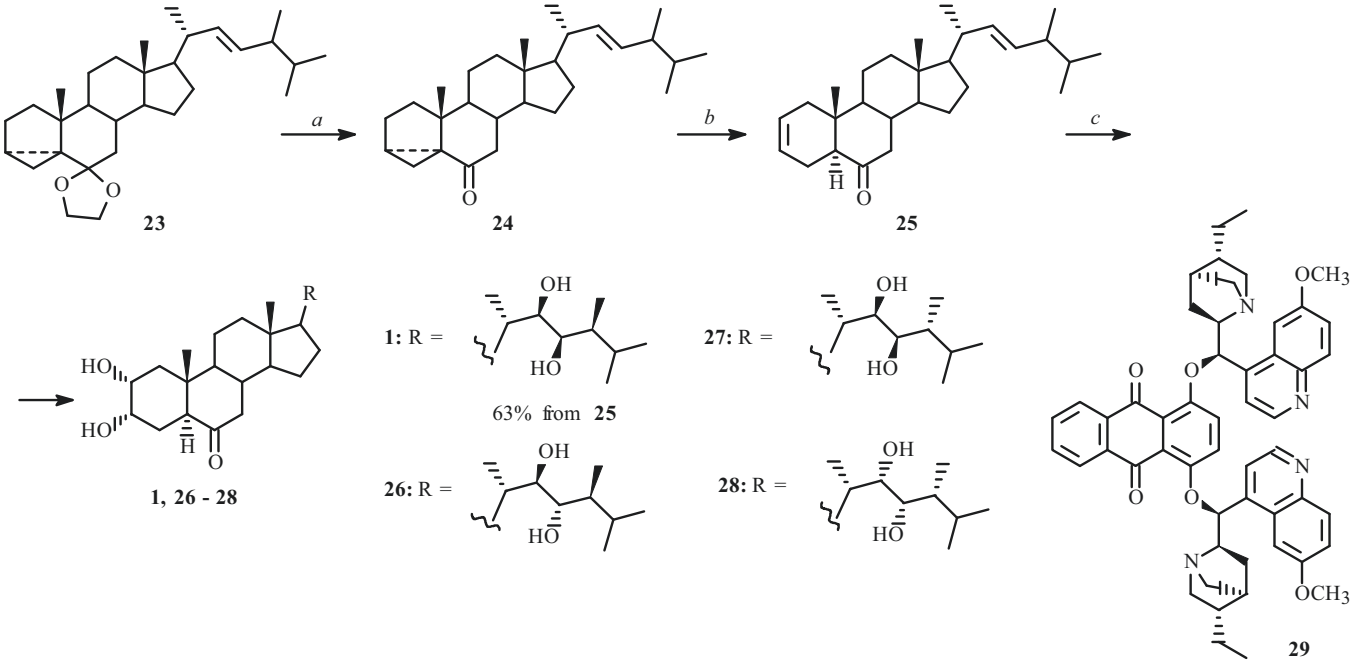
9 **10** **12** **14** **16** **11** **13** **15** **17**

In our instance, such an approach would allow the mixture of propargyl alcohols **18** and **19** to be used to synthesize **1** without separating them into the pure components. Also, increasing the fraction of isomer **18** in the mixture would be desirable because the sequence of conversions for **19** gave a product with the side chain of 24-epicastasterone. Thus, the mixture of **18** and **19** was oxidized to ketone **20**, reduction of which gave mixtures of these same compounds but in different ratios.



a. Li-C≡C-CH_3; *b.* PDC; *c.* H_2/Pd, quinoline; *d.* $MeC(OEt)_3$, $EtCO_2H$; *e.* 1. $LiAlH_4$, 2. TsCl, 3. $LiAlH_4$

The best results (**18**:**19** ratio of 16:1) were obtained using *R*-Alpine-Borane as the reductant, like for 25C- and 27C-type Δ^5-22-ketones [28]. The main drawback of this reagent is the relatively high cost. Therefore, derivatives of borohydrides and aluminum hydrides were also studied for the reduction of **20**. Acceptable results (**18**:**19** ratio of 9:1) were obtained for $Ca(BH_4)_2$, which was generated *in situ* from $NaBH_4$ and $CaCl_2$. The mixture of diastereomerically enriched acetylenic alcohols **18** and **19** was converted into olefin **23** by sequential hydrogenation over Lindlar catalyst, Claisen rearrangement of allylic alcohol **21**, and transformation of the ester of **22** into a methyl.



a. PPTS; *b.* PyH^+Br^-; *c.* K_2OsO_4

The dioxolane protection was removed to regenerate the C-6 carbonyl by treating **23** with pyridinium *p*-toluenesulfonate (PPTS). Dienone **25** was obtained in one step by refluxing cycloketone **24** in dimethylacetamide (DMA) in the presence of pyridinium bromide as before [29]. Compound **25** contained two double bonds, *cis*-hydroxylation of which by OsO_4 was the most obvious method for introducing the diol. The reaction of the Δ^2-derivatives with OsO_4 occurred with preferential formation of the required 2α,3α-diols [30]. Therefore, the problem with *cis*-dihydroxylation of **25** consisted of providing the required stereochemistry for the diol in the side chain. This reaction without a catalyst gave mainly the non-natural 22*S*,23*S*-diols [31]. The problem was solved by using quinidine-type catalysts [32, 33]. However, the *cis*-dihydroxylation yields are often <50% for 24*S*-alkyl-Δ^{22}-steroids because the oxidation goes too far. We used $(DHQD)_2AQN$

[**29**, hydroquinidine(anthraquinon-1,4-diyl)diether] as the catalyst in order to minimize the side formation of the 22,23-diketones [34]. The *cis*-dihydroxylation of **25** gave a mixture of **1** and its isomers **26**–**28**. The target product was readily isolated from the reaction mixture despite its complexity. Analytically pure **1** was obtained via double crystallization from MeOH in 63% yield.

Thus, the developed synthetic scheme produced **1** in 16 chemical steps in 11% overall yield from **3**. Its advantage was the facile scale up because chromatographic separation of intermediates with similar chromatographic mobilities could be avoided. This allowed gram quantities of the target product to be produced.

EXPERIMENTAL

NMR spectra were recorded on a Bruker Avance DRX-500 instrument (Germany). Chemical shifts were measured relative to residual solvent resonances ($CHCl_3$, δ 7.26 ppm for ^1H and δ 77.00 ppm for ^{13}C; C_5H_5N, δ 135.91 for ^{13}C). High-resolution mass spectra were taken on a 6550 iFunnel Q-TOF LC/MS (APCI and ESI, Agilent Technologies). All reactions involving organometallic reagents were performed under Ar as customary with dried reagents, solvents, and glassware. TLC used Kieselgel 60 F_{254} chromatographic plates; column chromatography, Kieselgel 60 (VWR, Art. 7734). Melting points were measured on a Kofler block.

(22*E*,24*S*)-6-(1,3-Dioxolan-2-yl)-3α,5-cyclo-24-ethyl-5α-cholest-22-ene (7). A solution of **3** (100 g, 0.24 mol) in Py (560 mL) in a 6-L flask was stirred, cooled in an ice bath, treated with TsCl (92.6 g, 0.49 mol), left for 1 d at room temperature, treated slowly with H_2O (50 mL), stirred for 30 min to destroy the excess of TsCl, and treated slowly with H_2O (5.6 L) to precipitate the product. The supernatant liquid was separated by back filtration. The resulting crystals were rinsed with H_2O (3 × 5 L). The obtained tosylate **4** was used in the next step without further purification.

Crude tosylate **4** in a flask was treated with Me_2CO (2.5 L), KOAc (138 g, 1.41 mol), and H_2O (630 mL); refluxed for 2 d; and evaporated *in vacuo*. The solid was extracted with EtOAc (2 × 500 mL). The organic layer was dried over Na_2SO_4 and evaporated at reduced pressure.

The solid was dissolved in Me_2CO (1.5 L), cooled to 0°C, treated slowly with Jones reagent (92 mL), stirred at 0°C for 20 min, treated with *i*-PrOH (40 mL) over 40 min, and treated with a mixture of $CHCl_3$ (1.5 L) and H_2O (1.5 L). The aqueous phase was separated and extracted with $CHCl_3$ (500 mL). The combined organic phases were washed with H_2O and $NaHCO_3$ solution until gas evolution stopped, dried over Na_2SO_4, and evaporated. The solid was dissolved in EtOAc (300 mL), filtered through a layer of Kieselgel, and evaporated. Yield of **6**, 93.5 g.

Compound **6** was dissolved in CH_2Cl_2 (1.3 L); stirred; treated with ethylene glycol (36 mL, 0.64 mol), triethyl orthoformate (72 mL, 0.43 mol), and *p*-TsOH (1.9 g, 11 mmol); stirred at room temperature for 20 min; and washed with saturated $NaHCO_3$ solution until gas evolution stopped. The organic layer was dried over Na_2SO_4 and evaporated. The solid was placed onto a column of SiO_2 and eluted by petroleum ether–EtOAc (9:1) to afford **7** (77 g, 70%) as an oil. ^1H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 5.14 (1H, dd, J = 15.1, 8.7), 5.01 (1H, dd, J = 15.1, 8.7), 4.02 (1H, dt, J = 7.8, 6.3), 3.93–3.87 (1H, m), 3.84 (1H, dd, J = 12.4, 6.6), 3.74 (1H, q, J = 6.5), 2.08–1.99 (1H, m), 1.96 (1H, dt, J = 12.5, 3.2), 1.01 (6H, d, J = 6.6), 1.00 (4H, s), 0.84 (4H, d, J = 6.4), 0.80 (6H, t, J = 7.1), 0.73 (3H, s), 0.61 (1H, dd, J = 8.1, 4.6), 0.32 (1H, t, J = 4.2). ^{13}C NMR spectrum (125 MHz, $CDCl_3$, δ, ppm): 138.3, 129.2, 109.9, 64.9, 64.6, 56.4, 56.0, 51.2, 47.4, 45.6, 42.7, 40.5, 40.2, 40.0, 39.2, 34.1, 33.2, 31.9, 28.9, 25.4, 24.9, 24.2, 23.0, 22.6, 21.2, 21.1, 19.0, 12.3, 12.2, 7.3. ESI-HR-MS *m/z* 455.3880 $[M + H]^+$. Calcd for $C_{31}H_{51}O_2$, 455.3884.

(20*S*)-6-(1,3-Dioxolan-2-yl)-20-formyl-3α,5-cyclo-5α-pregnane (8). A solution of **7** (34.0 g, 75 mmol) in $CHCl_3$ (300 mL) and MeOH (600 mL) was stirred; treated with $NaHCO_3$ (6.2 g, 74 mmol), Sudan III (20 mg), and Py (3 mL); cooled to –60°C, purged with ozone until the red color started to fade, purged with O_2, treated with Me_2S (18 mL, 0.25 mol), left overnight to warm to room temperature, and filtered. The filtrate was evaporated. The solid was separated over a column of SiO_2 with elution by petroleum ether–EtOAc (95:5) to afford aldehyde **8** (22.9 g, 82%) as an oil. ^1H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 9.56 (1H, d, J = 3.3), 4.04–3.98 (1H, m), 3.92–3.86 (1H, m), 3.86–3.80 (1H, m), 3.77–3.71 (1H, m), 2.36 (1H, ddd, J = 10.2, 6.8, 3.3), 1.11 (3H, d, J = 6.8), 1.00 (3H, s), 0.76 (3H, s), 0.61 (1H, dd, J = 8.2, 4.4), 0.32 (1H, t, J = 4.4). ^{13}C NMR spectrum (125 MHz, $CDCl_3$, δ, ppm): 205.3, 109.9, 65.0, 64.8, 55.7, 51.3, 49.6, 47.6, 45.7, 43.6, 40.3, 39.9, 39.4, 34.2, 33.4, 27.2, 25.0, 24.7, 23.1, 22.7, 19.1, 13.6, 12.7, 7.4.

(22*R*)-6-(1,3-Dioxolan-2-yl)-3α,5-cyclo-26,27-bis-nor-5α-cholest-23-yn-22-ol (18) and (22*S*)-6-(1,3-Dioxolan-2-yl)-3α,5-cyclo-26,27-*bis*-nor-5α-cholest-23-yn-22-ol (19). A solution of methylacetylene (40 mL, 0.53 mol) in THF (150 mL) was cooled to –60°C, treated slowly with a solution of BuLi (2.1 M) in hexanes (88.3 mL, 0.186 mol), stirred

at –60°C for 15 min, treated with a solution of **8** (22.9 g, 61 mmol) in THF (50 mL), left overnight to warm to room temperature, treated with NH_4Cl (33 g, 0.62 mol), diluted with H_2O (0.5 L), and extracted with $CHCl_3$ (3 × 200 mL). The combined organic layers were dried over Na_2SO_4 and evaporated. The solid was chromatographed over a column of SiO_2 (petroleum ether–EtOAc, 85:15→75:25) to afford a mixture of **18** and **19** (23.4 g, 92%) as an oil (**18**:**19** ratio 2:1 based on integrated intensities of PMR resonances [35]).

Synthesis of 6-(1,3-Dioxolan-2-yl)-3α,5-cyclo-26,27-bis-nor-5α-cholest-23-yn-22-one (20) and its Reduction by $Ca(BH_4)_2$. A mixture of **18** and **19** (9.4 g, 23 mmol), PDC (17.2, 49 mmol), and CH_2Cl_2 (250 mL) was stirred at room temperature for 24 h. The precipitate was filtered off. The filtrate was evaporated. The resulting ketone **20** was dissolved in EtOH (200 mL), treated with $CaCl_2$ (9.8 g, 88 mmol), cooled to –78°C, treated in portions with $NaBH_4$ (5.7 g, 151 mmol), stirred at –78°C for 10 min, allowed to warm slowly to room temperature, treated with H_2O (200 mL), and extracted with EtOAc (3 × 150 mL). The organic layers were dried over Na_2SO_4 and evaporated. The solid was placed onto a column of SiO_2 and eluted by petroleum ether–EtOAc (85:15→80:20) to afford a mixture of propargyl alcohols **18** and **19** as an oil (**18**:**19** ratio 9:1 based on integrated intensities of PMR resonances [35]).

(22*E*)-6-(1,3-Dioxolan-2-yl)-3α,5-cyclo-24-methyl-5α-cholest-22-en-26-oic Acid Ethyl Ester (22). A solution of a mixture of **18** and **19** (9:1, 4.32 g, 10.5 mmol) in EtOH (50 mL) and THF (7 mL) was treated with Pd on $BaSO_4$ (0.65 g, 5%) and quinoline (0.71 mL, 6 mmol), and hydrogenated until H_2 absorption stopped. The catalyst was separated. The filtrate was evaporated. The resulting allylic alcohol **21** was used in the next step without further purification.

A mixture of **21** from the previous step, triethyl orthopropionate (40.3 mL, 0.24 mol), and propionic acid (1.03 mL, 13.8 mmol) in C_6H_6 (130 mL) was refluxed under Ar for 2 h, cooled to room temperature, diluted with H_2O, and extracted with EtOAc. The organic phase was dried over Na_2SO_4 and evaporated. The solid was placed onto a column of SiO_2 and eluted by petroleum ether–EtOAc (90:10→85:15) to afford **22** (4.91 g, 94% for the two steps) as an oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 5.25 (1H, dd, J = 15.2, 8.6), 5.09 (1H, dd, J = 15.2, 8.5), 4.16–4.06 (2H, m), 4.04–3.98 (1H, m), 3.92–3.86 (1H, m), 3.86–3.80 (1H, m), 3.76–3.70 (1H, m), 2.39–2.26 (1H, m), 2.25–2.17 (1H, m), 2.05–1.91 (2H, m) 1.78–0.67 (18H, m), 1.25 (3H, t, J = 7.2), 1.06 (3H, d, J = 7.0), 1.00 (3H, s), 1.02–0.93 (6H, m), 0.71 (3H, s), 0.60 (1H, dd, J = 8.2, 4.4), 0.32 (1H, t, J = 4.4). ^{13}C NMR spectrum (125 MHz, $CDCl_3$, δ, ppm): 176.5, 137.9, 130.1, 110.0, 65.0, 64.8, 60.2, 56.5, 56.0, 47.6, 45.8, 45.7, 42.9, 40.4, 40.3, 40.3, 40.2, 39.4, 34.3, 33.4, 28.9, 25.1, 24.4, 23.2, 22.7, 20.9, 19.5, 19.1, 15.2, 14.4, 12.5, 7.4. ESI-HR-MS *m/z* 499.3780 $[M + H]^+$. Calcd for $C_{32}H_{51}O_4$, 499.3782.

(22*E*)-6-(1,3-Dioxolan-2-yl)-3α,5-cyclo-24α-methyl-5α-cholest-22-ene (23). A solution of **22** (12.4 g, 25 mmol) in THF (300 mL) was treated in portions with $LiAlH_4$ (2.8 g, 75 mmol) and stirred at room temperature for 20 min. The excess of $LiAlH_4$ was decomposed by successive addition of H_2O (2.8 mL), NaOH solution (15%, 2.8 mL), and H_2O (8.4 mL). The precipitate was filtered off. The filtrate was evaporated. The solid was dissolved in Py (150 mL), treated with TsCl (14.2 g, 75 mmol), held at room temperature for 20 h, diluted with saturated NaCl solution, and extracted with $CHCl_3$ (3 × 150 mL). The extract was dried over Na_2SO_4 and evaporated. The solid was dissolved in Et_2O (300 mL), stirred, treated in portions with $LiAlH_4$ (2.8 g, 75 mmol), stirred at room temperature for 45 min, and treated with H_2O (2.8 mL), NaOH solution (15%, 2.8 mL), and H_2O (8.4 mL) to decompose the excess of $LiAlH_4$. The resulting precipitate was filtered off. The filtrate was evaporated. The solid was chromatographed over a column of SiO_2 with elution by cyclohexane–EtOAc (30:1→5:1) to isolate **23** (8.3 g, 76%) as an oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 5.16 (2H, m, H-22, 23), 3.73–4.05 (4H, m, dioxolane), 1.01 (3H, s, 19-Me), 0.73 (3H, s, 18-Me). ^{13}C NMR spectrum (125 MHz, $CDCl_3$, δ, ppm): 135.9, 131.7, 109.8, 64.7, 64.5, 55.9, 56.3, 42.9, 45.5, 47.3, 39.9, 42.6, 40.2, 40.1, 39.1, 28.7, 33.1, 34.0, 24.8, 22.9, 20.9, 18.9, 22.5, 17.9, 24.1, 19.5, 20.0, 12.2, 7.1.

(22*E*)-3α,5-Cyclo-24α-methyl-5α-cholest-22-en-6-one (24). A solution of **23** (7.76 g, 17.6 mmol) in Me_2CO (370 mL) was treated with H_2O (8 mL) and PPTS (0.93 g, 3.70 mmol), held at room temperature for 8 h, and evaporated at reduced pressure. The solid was chromatographed over a column of SiO_2 with elution by petroleum ether–toluene to afford **24** (6.65 g, 95%) as an oil. ^{1}H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 5.21–5.10 (2H, m), 2.47–2.37 (1H, m), 2.06–0.68 (23H, m), 1.02–0.99 (6H, m), 0.91 (3H, d, J = 6.9), 0.83 (3H, d, J = 6.8), 0.81 (3H, d, J = 6.8), 0.72 (3H, s). ^{13}C NMR spectrum (125 MHz, $CDCl_3$, δ, ppm): 209.8, 135.9, 132.2, 57.2, 56.0, 46.9, 46.5, 46.3, 44.9, 43.2, 42.7, 40.4, 39.8, 35.4, 34.9, 33.6, 33.3, 28.9, 26.0, 24.2, 23.0, 21.1, 20.3, 19.8, 19.8, 18.2, 12.4, 11.8. ESI-HR-MS *m/z* 397.3467 $[M + H]^+$. Calcd for $C_{28}H_{45}O$, 397.3465.

(22*E*)-24α-Methyl-5α-cholesta-2,22-dien-6-one (25). A mixture of **24** (5.13 g, 12.9 mmol), pyridinium bromide (4.15 g, 26 mmol), and DMA (50 mL) was stirred, heated at 160°C under Ar for 1 h, cooled, and evaporated at reduced pressure. The solid was partitioned between petroleum ether (40 mL) and H_2O (20 mL). The aqueous layer was extracted with

petroleum ether (3 × 20 mL). The combined organic phases were dried over Na_2SO_4 and evaporated at reduced pressure. The solid was chromatographed over a column of SiO_2 with elution by petroleum ether–EtOAc (90:10) to afford **25** (4.03 g, 79%), mp 108–109°C (petroleum ether). ^{1}H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 5.70–5.65 (1H, m), 5.58–5.53 (1H, m), 5.21–5.10 (2H, m), 2.37–0.60 (22H, m), 1.00 (3H, d, J = 6.6), 0.90 (3H, d, J = 6.9), 0.83 (3H, d, J = 6.8), 0.81 (3H, d, J = 6.8), 0.70 (3H, s), 0.68 (3H, s). ^{13}C NMR spectrum (125 MHz, $CDCl_3$, δ, ppm): 212.1, 135.9, 132.2, 125.1, 124.7, 57.0, 56.1, 54.0, 53.6, 47.2, 43.2, 42.9, 40.3, 40.2, 39.5, 39.5, 37.9, 33.3, 28.8, 24.1, 21.9, 21.3, 21.1, 20.3, 19.8, 18.2, 13.6, 12.3.

(22*R*,23*R*,24*S*)-2α,3α,22,23-Tetrahydroxy-24-methyl-5α-cholest-6-one (1) (castasterone, 1). A solution of **25** (4.79 g, 12.1 mmol) in *t*-BuOH (275 mL) was stirred, treated with H_2O (275 mL), $K_3[Fe(CN)_6]$ (23.7 g, 72 mmol), K_2CO_3 (9.95 g, 72 mmol), $K_2OsO_4 \cdot 2H_2O$ (178 mg, 0.48 mmol), $(DHQD)_2AQN$ (1.04 g, 1.2 mmol), and $CH_3SO_2NH_2$ (3.42 g, 36 mmol); stirred at room temperature for 2 d; treated with Na_2SO_3 (18.3 g, 0.145 mol); stirred for 1 h; and diluted with H_2O (1.5 L) and $CHCl_3$ (500 mL). The aqueous phase was extracted with $CHCl_3$–MeOH (4:1, 3 × 150 mL). The combined organic phases were washed with H_2SO_4 (0.1 N, 3 × 250 mL) and dried over Na_2SO_4. The solid was filtered off. The solvent was evaporated at reduced pressure. Double recrystallization from MeOH (300 mL, 70 mL) afforded white crystals of **1** (3.56 g, 63%), mp 250–256°C (MeOH). The spectral data of **1** agreed with those reported for castasterone [36]. ESI-HR-MS *m*/*z* 469.3284 $[M - H_2O + Na]^+$. Calcd for $C_{28}H_{46}O_4Na$, 469.3288.

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