Synthesis F. Noack et al. Paper

Access to 5(6→7)*abeo*-Steroids through Benzilic Acid Rearrangement of *i*-Steroids

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Dedicated to Barbara, Kurt, and Konrad Krieger

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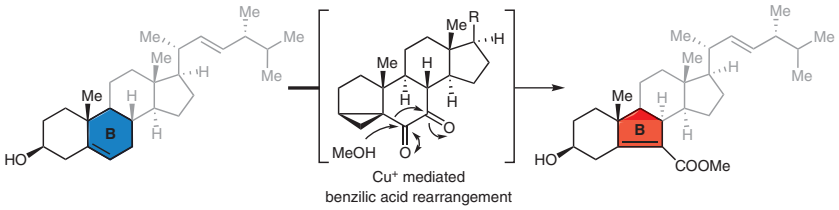

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Abstract Benzilic acid rearrangement of *i*-steroid ketones and their subsequent opening gives access to 5(6→7)*abeo*-steroids. The functional group tolerance is demonstrated by several examples, including substrates with additional olefinic groups. The method opens a potential route to the synthesis of complex natural products such as solanioic acid from abundant steroid starting materials like ergosterol.

Key words *abeo*-steroids, benzilic acid rearrangement, *i*-steroids, natural products, total synthesis

Among the class of steroids, 5(6→7)*abeo*-steroids constitute a rather small subgroup with only few examples reported as isolated natural products[1] or semisynthetic analogs.[2] In recent years, especially the isolation of solanioic acid (**1**, Figure 1), a potent antibacterial natural product isolated from the tubers of *Cyperus rotundus*, drew some attention because of its intriguing structural complexity.[3] Despite the mentioned 5(6→7)*abeo*-motif, an additional 11,12-*seco*-motif is present in its molecular framework, and a biosynthetic rationale may trace back these structural elements to ergosterol as a potential precursor. Another recently isolated example is 3β,5β,6-trihydroxy-B-norsitostane (**2**, Figure 1), although no biological activity could be identified so far.[4] 5(6→7)*abeo*-Steroids have also been known to affect myelin degradation in the central nervous system, a process serving as a clinical hallmark of multiple sclerosis.[5] Atheronal B (**3**, Figure 1), thus, modulates misfolding of apolipoprotein B_{100}, β-amyloid protein, α-synuclein, and κ- and λ-antibody light chains. Specifically, **3** forms imines with lysine side chains, a process that effectively reduces the cationic nature of, e.g., the myelin basic protein, which leads to structural changes and a decrease in myelin stability and may contribute to the onset and progression of multiple sclerosis. The biosynthetic origin of atheronal B (**3**) was subject to some controversy with speculations regarding the possible formation of ozone (O_3) in brain tissue and its reaction with, e.g., cholesterol (**4**, Scheme 1, lower part).[6] Although tempting, neither O_3 nor the corresponding ozonides could be detected so far, and it thus appears much more likely that a sequence consisting of the Schenck ene reaction, Hock rearrangement, and aldol addition is operative and leads to the formation of **3** (Scheme 1, **4**→**5**→**A**→**B**→**3**).[7]

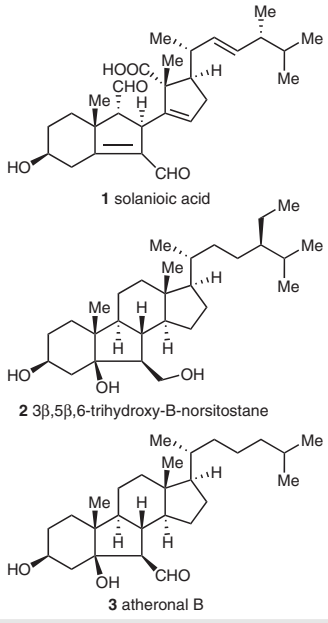
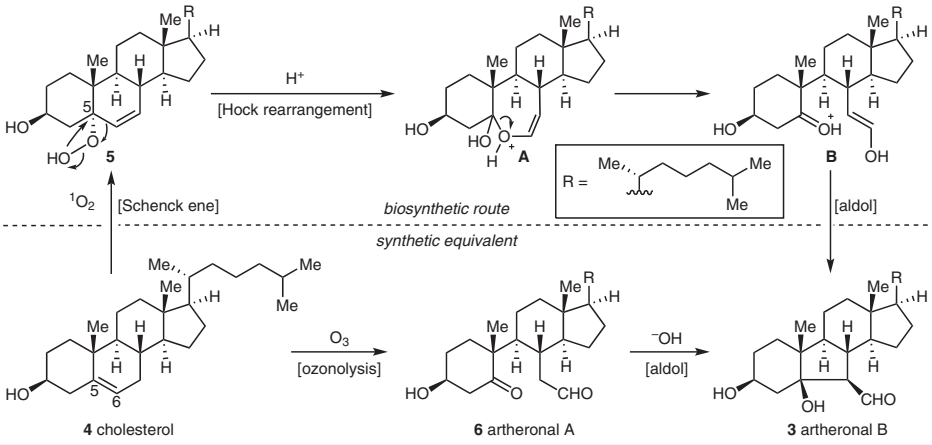


Figure 1 Molecular structures of 5(6→7)*abeo*-steroids solanioic acid (**1**), 3β,5β,6-trihydroxy-B-norsitostane (**2**), and atheronal B (**3**)



Scheme 1 Biosynthetic route (top) and synthetic equivalent (bottom) to the metabolites atheronal A (**6**) and atheronal B (**3**)

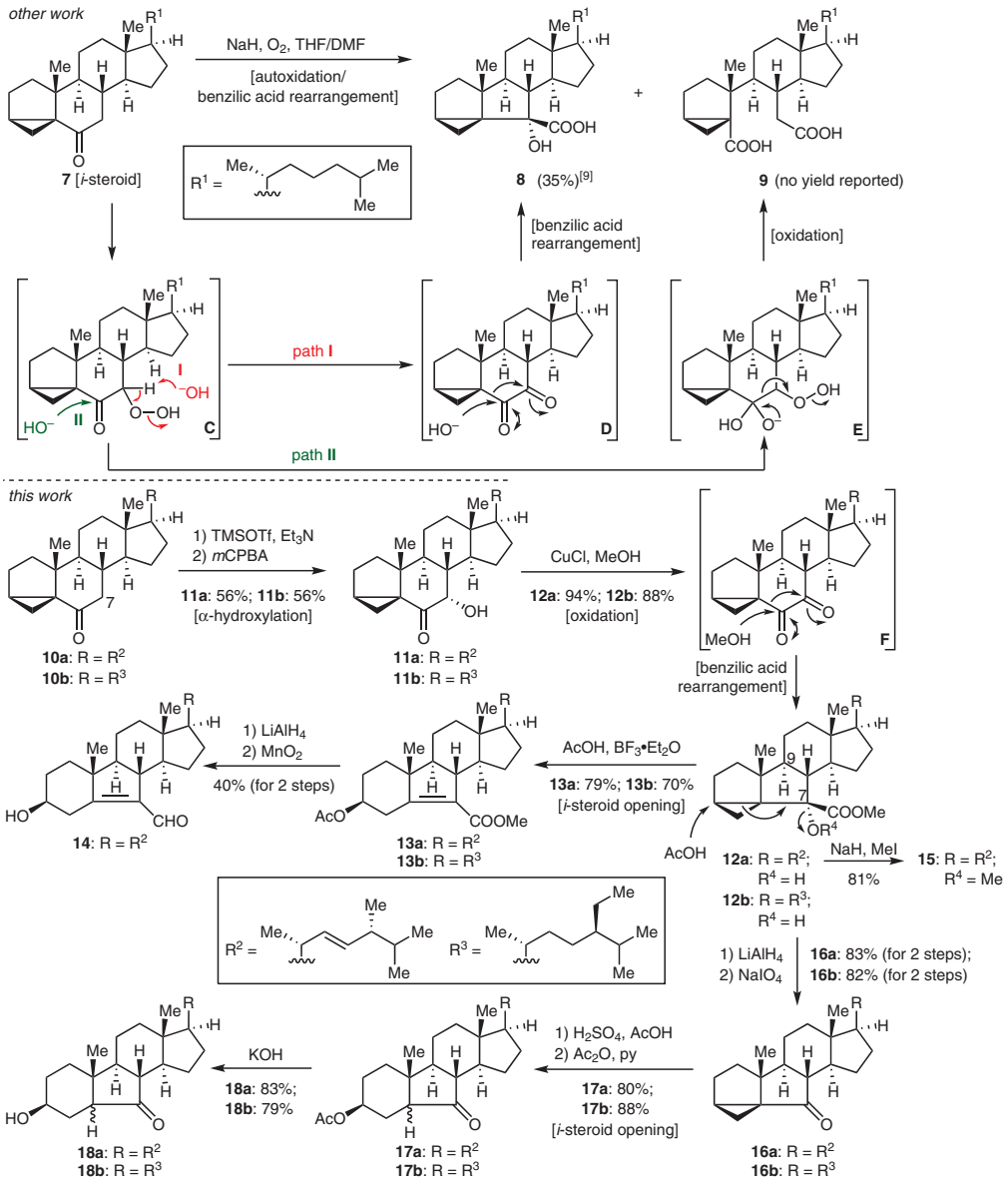
From a synthetic point of view, ozonolysis is a viable means to convert Δ^5-steroids like cholesterol (**4**) into keto aldehydes (such as atheronal A, **6**, Scheme 1).[8] A limitation to this strategy is the presence of additional double bonds in the starting material. The aldol condensation to forge the B-*nor*-ring (as in atheronal B, **3**, or solanioic acid, **1**) was also reported, but suffered equally from low yields, harsh conditions and extended reaction times.[8]

We were facing these problems in our work on analogs of solanioic acid (**1**), when considering dienes derived from ergosterol (with an additional reactive Δ^{22} olefin) as intermediates towards the formation of the 5(6→7)*abeo*-motif. An alternative access to this substructure that does not employ ozonolysis and an aldol reaction (or a related process) could be the benzilic acid rearrangement of diones of type **D** and **F** (see Scheme 2) to first yield α-hydroxy esters (or acids) such as **8** and **12**, which would then be transformed to the desired unsaturated products, such as **14**. The general viability of the benzilic acid rearrangement of cholesterol-derived **7** was reported by Liang, but suffered from several drawbacks.[9] Since the starting 6,7-diones are typically fleeting species that could not be accessed or isolated in pure form, only autoxidation of **7** under strongly basic conditions (NaH, O_2, DMF) for extended periods of time could provide them *in situ* (Scheme 2, path I, **7**→**C**→**D**). Trace amounts of water in the reaction mixture may then form hydroxide ions to initiate the benzilic acid rearrangement (**D**→**8**), although in rather low efficiency (35% yield reported for **7**→**8**). A byproduct in this reaction was diacid **9**, the formation of which can be explained through the competing rearrangement of hydroperoxide **C** (path II, **C**→**E**→**9**).[9c]

We were, thus, reinvestigating our options to access the required diones as well as their controlled rearrangement. Starting from ergosterol-derived *i*-steroid **10a**,[10] Rubottom oxidation gave access to α-hydroxy ketone **11a** (Scheme 2).[11] Its treatment with excess CuCl then resulted in the formation of the desired dione **F**, which was not isolated, but immediately underwent benzilic acid rearrangement through nucleophilic attack of MeOH. A similar sequence was previously applied in the synthesis of K252a from staurosporine.[12] α-Hydroxy ester **12a** was thus formed as a single product in almost quantitative yield. Methylation of the tertiary alcohol in **12a** to yield methyl ether **15** was performed and NOE experiments (cross peak between methoxy group at C7 and H14) resulted in its assignment as 7*S*. With a high-yielding access to B-*nor* derivative **12a** in hand, we then investigated the crucial *i*-steroid opening.[13] Gratifyingly, under treatment with $BF_3{\cdot}Et_2O$ in AcOH,[14] the cyclopropyl moiety underwent C–C cleavage through the nucleophilic attack of acetate and loss of the hydroxyl moiety at C7 (**12a**→**13a**). All that remained was reduction of the methyl ester in **13a** and concomitant removal of the acetate ($LiAlH_4$, THF, 66 °C), followed by selective oxidation of the thus-obtained allylic alcohol (MnO_2, CH_2Cl_2) to deliver **14**, an A,B-ring mimic of solanioic acid (**1**).

Since several B-*nor*-7-oxo-derived positive modulators of the $GABA_A$ receptor were reported recently,[2] we also applied our method to the expedient synthesis of this structural motif. Thus, reduction and oxidative cleavage of **12a** using 1. $LiAlH_4$ and 2. $NaIO_4$ gave B-*nor*-*i*-steroid ketone **16a** (Scheme 2), the cyclopropyl opening of which was realized with H_2SO_4 in AcOH, followed by acetylation (Ac_2O, py) of the partly deacetylated 3-hydroxy moiety to deliver **17a** in good yield as a mixture of epimers at C5 (approximately 4:1 ratio, respective stereoconfigurations at C5 were not assigned). Removal of the acetate using KOH in MeOH then gave the desired B-*nor*-7-oxo steroid **18a**. The exact same sequence was repeated for *i*-steroid ketone **10b**[15] derived from commercial sitosterol and gave **13b** and **18b**, respectively, as the final products in comparably good yields (Scheme 2).

To further elucidate the generality and functional group tolerance of our method, we synthesized several more *i*-steroid ketones, some of them previously reported in the liter-

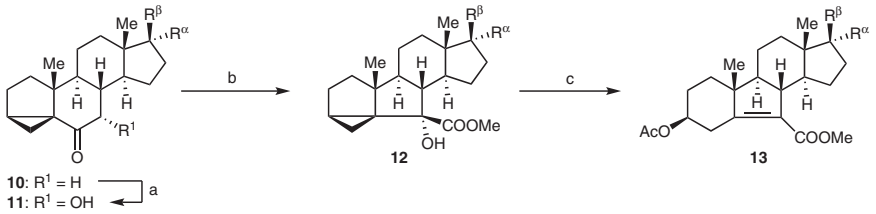


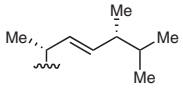
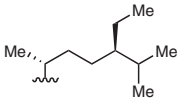
Scheme 2 Liang's autoxidation–rearrangement procedure for the benzilic acid rearrangement of cholesterol-derived **7** (top) and this work's approach (bottom)

ature (**10c**[16] and **10e**,[17] Table 1) and another one, substrate **10g**, prepared as shown in Scheme 3 by a simple sequence starting from dehydroepiandrosterone-derived **19**[18] (sequence **19**→**20**→**21**→**10g**), and subjected these starting materials **10** to our three-step sequence (Table 1). Compounds **11d** and **11f** were byproducts of the Rubottom oxidation and were formed by treatment with excess TMSOTf and Et_3N (during generation of the required silyl enol ethers). Their intentionally incomplete removal during treatment with TBAF allowed for both, the isolation of **11c** and **11d**, as well as **11e** and **11f**, and their use in the benzilic acid rearrangement.

As shown in Table 1, most of these substrates successfully underwent the rearrangement. Especially **10a** (entry 1, with an additional double bond in the side chain) and **10b** (entry 2) were smoothly converted into the desired B-*nor*-derivatives **12a** and **12b**, respectively. While a secondary TMS ether could not be retained in the rearrangement step (entry 4) and gave the same product as in the unprotected case (entry 3), a tertiary TMS ether (entry 6) and the corresponding unprotected case (entry 5) led to extensive decomposition with no desired product isolated. This might, however, be attributed to the presence of an alkyne and Meyer–Schuster or Rupe rearrangements occur-

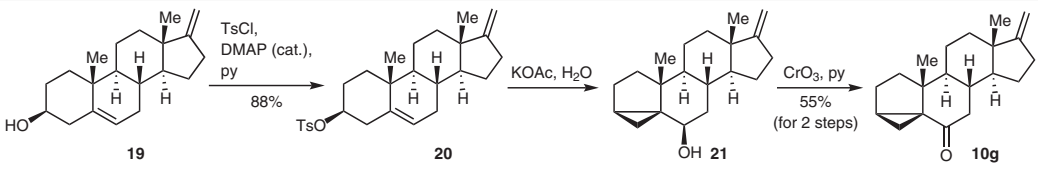
Table 1 Substrate Scope of the Three-Step Procedure for the Synthesis of B-*nor*-Steroids[a]



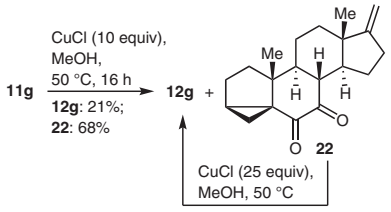
Entry	R^β	R^α	Yield [%] of oxidation product **11** (R^1 = OH)	Yield [%] of rearrangement product **12**	Yield [%] of *i*-steroid opening product **13**
1		H	**11a**: 56 (82[11])	**12a**: 94	**13a**: 79
2		H	**11b**: 56	**12b**: 88	**13b**: 70
3	OH	H	**11c**: 37	**12c**: 61	**13c**: 42
4	OTMS	H	**11d**: 23	**12c**: 83[b]	–[c]
5	OH		**11e**: 30	**12e**: –[d]	–[c]
6	OTMS		**11f**: 13	**12f**: –[d]	–[c]
7			**11g**: 38 (recovered **10g**: 44%)	**12g**: 85	**13g**: –[d]

[a] Reaction conditions: (a) 1. TMSOTf (3.0 equiv), Et_3N (4.0 equiv), CH_2Cl_2, 0 °C, 20 min; 2. *m*CPBA (1.1 equiv), CH_2Cl_2, –40 °C, 2 h; (b) CuCl (20 equiv), MeOH, 50 °C, 3–16 h; (c) $BF_3{\cdot}Et_2O$ (80 equiv), AcOH (200 equiv), Et_2O, 25 °C, 15 h.
[b] The TMS ether was cleaved during the rearrangement step and the same product as in the unprotected case was obtained.
[c] Reaction was not performed since the required rearrangement product could not be obtained in the previous step.
[d] No desired product could be isolated.

ring under the reaction conditions. Substrate **10g** underwent the oxidation and rearrangement steps without incident, but failed to undergo the final *i*-steroid opening, likely due to Lewis acid-promoted double bond isomerization of the *exo* double bond into the D ring or Wagner–Meerwein-type rearrangements occurring. In an additional experiment, we lowered the number of equivalents of CuCl in the oxidation/rearrangement step for substrate **10g** and observed a much more sluggish reaction and only 21% of rearrangement product **11g** being isolated. Interestingly, the major product under these conditions (68% yield) was assigned by 2D NMR spectroscopic analysis to be the assumed intermediate dione **22** (Scheme 4). This species proved isolable by column chromatography and was stable in pure form for an extended period of time. Replacing MeOH as the solvent in the reaction for non-nucleophilic CH_2Cl_2 resulted in the recovery of starting material and no formation of either **12g** or **22**. Dione **22** was found to be capable of reentering the reaction when resubjected to the original conditions (using 25 equiv CuCl) and gave **12g**. This result also served as confirmation of the intermediacy of a dione in the mechanistic rationale.



Scheme 3 Synthesis of substrate **10g**



Scheme 4 Synthesis of dione intermediate **22** and its conversion into **12g**

In summary, we herein reported a novel method for the preparation of B-*nor*-steroids that makes use of a Cu-mediated one-pot oxidation/benzilic acid rearrangement. The substrate scope was explored and the tolerance of our conditions towards additional functionalities was examined. These results will be useful in our ongoing work on solaniolic acid analogs and, thus, present an opportunity for biological studies and a deepened understanding of the underlying biology of this class of natural products.

All reactions sensitive to moisture and/or air were carried out using heat-gun dried glassware, an argon atmosphere, and anhyd solvents. Anhyd dichloromethane and diethyl ether were prepared by an M. Braun GmbH MB SPS-800 solvent purification system. Anhyd toluene and methanol were purchased from Acros (extra anhyd quality). Ethyl acetate and *n*-hexane were purified by distillation on a rotary evaporator. All other solvents and commercially available reagents were used without further purification unless otherwise stated. Reactions were monitored by TLC carried out on Merck Silica Gel 50 F_{245} plates and visualized by fluorescence quenching under UV light, or an aqueous solution of cerium sulfate and phosphomolybdic acid, or ceric ammonium molybdate (CAM), or an acidic methanolic solution of vanillin and heat as developing agent. Column chromatographic purifications were performed on Macherey-Nagel Silica Gel 60 M (40–60 µm) and preparative TLC was performed on Merck Silica Gel 50 F_{245}-plates. Concentration under reduced pressure was performed by rotary evaporation at 40 °C and the appropriate pressure and subsequent exposure to vacuum (1×10^{-3} mbar) at 25 °C. NMR spectra were recorded on a Jeol ECP500 (500 MHz), Bruker AVANCE III 500 (500 MHz), or Bruker AVANCE III 700 (700 MHz, with CryoProbe) spectrometer. Chemical shifts were calibrated by using the residual undeuterated solvent signals ($CDCl_3$: ^{1}H, δ = 7.26; ^{13}C, δ = 77.16; CD_3OD: ^{1}H, δ = 3.31; ^{13}C, δ = 49.00) as internal reference at 298 K and are repoted in ppm. The given multiplicities are phenomenological, thus the actual appearance of the signals is stated and not the theoretically expected one. In case no multiplicity could be identified, the chemical shift range of the signal is given. IR spectra were measured on a Jasco FT/IR-4100 Type A spectrometer with a TGS detector. HRMS was carried out by using an Agilent 6210 ESI-TOF spectrometer. Optical rotations were measured on a JASCO P-2000 polarimeter at 589 nm by using 100 mm cells; the solvent and concentration (g/100 mL) are indicated. Melting points were measured on a Stuart SMP30 melting point apparatus and are uncorrected.

α-Hydroxy Ketones 11 by Rubottom Oxidation of 6-Oxo-*i*-steroids 10; General Procedure A

The appropriate ketone **10** (1.0 equiv) was dissolved in CH_2Cl_2 (0.1 M) and the solution was cooled to 0 °C. Then Et_3N (4.0 equiv) was added followed by dropwise addition of TMSOTf (3.0 equiv) over 20 min. The organic phase was then washed with sat. aq $NaHCO_3$, separated, dried over $MgSO_4$, and filtered. All volatiles were removed under reduced pressure to yield the silyl enol ether as a colorless solid that was used in the next step without further purification.

The silyl enol ether thus obtained was dissolved in CH_2Cl_2 (0.1 M), and a solution of freshly purified 0.1 M *m*CPBA in CH_2Cl_2 (1.1 equiv) was added dropwise at –40 °C. After 2 h, sat. aq Na_2SO_3 was added and the mixture was stirred for 15 min at 25 °C. The organic phase was washed sequentially with sat. aq $NaHCO_3$, 1 M aq HCl, and sat. brine, dried over $MgSO_4$, and filtered. All volatiles were removed under reduced pressure and the thus-obtained residue was purified by column chromatography (silica gel, *n*-hexane–EtOAc) to yield the corresponding α-hydroxy ketone **11** as a colorless solid.

α-Hydroxy Ketone 11a

Ketone **10a** (221 mg, 0.56 mmol, 1.0 equiv) was processed as described in general procedure A and the thus-obtained crude product was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 10:1) to yield α-hydroxy ketone **11a** as a colorless solid. All analytical data were in agreement with those reported previously.[11]

Yield: 129 mg (0.31 mmol, 56%).

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 5.25–5.13 (m, 2 H), 3.78 (t, *J* = 3.5 Hz, 1 H), 2.05–2.01 (m, 4 H), 1.90–1.61 (m, 8 H), 1.62–1.56 (m, 3 H), 1.53–1.42 (m, 2 H), 1.34–1.19 (m, 3 H), 1.11–1.06 (m, 1 H), 1.03 (d, *J* = 6.6 Hz, 3 H), 0.98 (s, 3 H), 0.91 (d, *J* = 6.9 Hz, 3 H), 0.84–0.80 (m, 6 H), 0.72 (s, 3 H), 0.70 (t, *J* = 5.0 Hz, 1 H).

α-Hydroxy Ketone 11b

Ketone **10b** (480 mg, 1.16. mmol, 1.0 equiv) was processed as described in general procedure A and the thus-obtained crude product was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to yield α-hydroxy ketone **11b** as a colorless solid.

Yield: 288 mg (0.67 mmol, 56%); mp 152–154 °C ($CHCl_3$); $[\alpha]_D^{20}$ +23.7 (*c* 1.00, $CHCl_3$); R_f = 0.30 (*n*-hexane–EtOAc, 9:1, CAM [blue]).

IR (neat): 3398 (b), 2957 (m), 2869 (w), 2360 (s), 2341 (s), 1675 (w), 1376 (w), 1302 (w) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.78 (s, 1 H), 2.24 (s, 1 H), 2.10–1.98 (m, 2 H), 1.96–1.83 (m, 1 H), 1.82–1.75 (m, 2 H), 1.75–1.62 (m, 3 H), 1.62–1.54 (m, 1 H), 1.52–1.08 (m, 18 H), 0.98 (s, 3 H), 0.93 (d, *J* = 6.7 Hz, 3 H), 0.86–0.83 (m, 3 H), 0.83 (d, *J* = 6.8 Hz, 3 H), 0.81 (d, *J* = 6.8 Hz, 3 H), 0.70 (s, 3 H), 0.69 (m, 1 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 210.6, 73.2, 55.9, 49.5, 47.4, 46.0, 44.3, 39.5, 39.2, 37.7, 37.7, 36.3, 34.0, 33.8, 29.3, 28.4, 26.3, 26.1, 23.6, 23.2, 22.9, 20.0, 19.4, 19.2, 18.9, 12.1, 11.9, 10.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{48}NaO_2$: 451.3547; found: 451.3556.

α-Hydroxy Ketones 11c and 11d

Ketones **11c** and **11d** were prepared according to general procedure A. Ketone **10c** (154 mg, 0.53 mmol, 1.0 equiv) was processed as described in general procedure A and the thus-obtained crude product was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 7:1→1:1) to yield α-hydroxy ketone **11d** (23%) and α-hydroxy ketone **11c** (37%), both as colorless solids.

11c

Yield: 59 mg (0.2 mmol, 37%); mp 163–164 °C ($CHCl_3$); $[\alpha]_D^{20}$ +6.4 (*c* 1.00, $CHCl_3$); R_f = 0.55 (*n*-hexane–EtOAc, 1:3, CAM [blue]).

IR (neat): 3393 (b), 2995 (m), 2870 (w), 2360 (s), 2341 (s), 1682 (s), 1455 (m), 1375 (m), 1046 (m), 1019 (m), 736 (s) cm^{-1}.

^1H NMR (CD_3OD, 500 MHz): δ = 3.67 (d, *J* = 2.2 Hz, 1 H), 3.64 (d, *J* = 8.7 Hz, 1 H), 2.13–1.99 (m, 3 H), 1.90–1.79 (m, 4 H), 1.77–1.61 (m, 5 H), 1.56–1.44 (m, 2 H), 1.32 (td, *J* = 11.9, 5.9 Hz, 1 H), 1.13 (td, *J* = 12.9, 4.1 Hz, 1 H), 1.08–1.02 (m, 1 H), 1.00 (s, 3 H), 0.79 (s, 3 H), 0.69 (t, *J* = 4.9 Hz, 1 H).

^{13}C NMR (CD_3OD, 126 MHz): δ = 211.9, 82.3, 73.5, 45.4, 45.2, 44.3, 44.0, 41.1, 39.2, 37.6, 37.3, 34.6, 30.6, 27.1, 23.5, 23.5, 19.5, 11.4, 10.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{28}NaO_3$: 327.1931; found: 327.1944.

11d

Yield: 46 mg (0.12 mmol, 23%); mp 93–94 °C ($CHCl_3$); $[\alpha]_D^{20}$ +5.4 (*c* 1.00, $CHCl_3$); R_f = 0.47 (*n*-hexane–EtOAc, 1:1, CAM [blue]).

IR (neat): 2969 (w), 2954 (w), 2359 (s), 2341 (m), 1737 (s), 1682 (w), 1372 (s), 1228 (m), 1216 (s), 840 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 3.79–3.76 (m, 1 H), 3.63 (t, *J* = 8.4 Hz, 1 H), 2.34 (s, 1 H), 2.03 (dtd, *J* = 17.0, 8.2, 4.1 Hz, 1 H), 1.98–1.87 (m, 2 H), 1.84–1.57 (m, 7 H), 1.54–1.43 (m, 2 H), 1.35–1.23 (m, 2 H), 1.12–0.99 (m, 2 H), 0.99 (s, 3 H), 0.90–0.82 (m, 1 H), 0.75 (s, 3 H), 0.71 (t, *J* = 4.9 Hz, 1 H), 0.08 (s, 9 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 210.6, 81.6, 72.6, 47.3, 44.4, 43.9, 43.1, 39.3, 38.1, 37.9, 36.6, 33.8, 30.8, 26.3, 22.9, 22.5, 19.5, 11.2, 11.0, 0.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{28}NaO_3$: 399.2326; found: 399.2344.

α-Hydroxy Ketones 11e and 11f

Ketones **11e** and **11f** were prepared according to general procedure A. Ketone **10e** (116 mg, 0.37 mmol, 1.0 equiv) was processed as described in general procedure A and the thus-obtained crude product was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 7:1→4:1) to yield α-hydroxy ketone **11f** (13%) as a colorless foam and α-hydroxy ketone **11e** (30%) as a colorless solid.

11e

Yield: 36 mg (0.11 mmol, 30%); mp 163–164 °C ($CHCl_3$); $[\alpha]_D^{20}$ –18.6 (*c* 1.00, $CHCl_3$); R_f = 0.15 (*n*-hexane–EtOAc, 7:1, CAM [blue]).

IR (neat): 3420 (b), 3305 (m), 2956 (s), 2931 (s), 2871 (m), 2360 (s), 2341 (m), 1675 (s), 1376 (s), 1301 (m), 1252 (m), 1148 (m), 1046 (s), 754 (s) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 3.77 (d, *J* = 3.3 Hz, 1 H), 3.47 (s, 1 H), 2.60 (s, 1 H), 2.34 (ddd, *J* = 13.8, 9.8, 5.6 Hz, 1 H), 2.17 (td, *J* = 11.8, 7.5 Hz, 1 H), 1.91 (td, *J* = 11.3, 3.4 Hz, 1 H), 1.86–1.77 (m, 5 H), 1.74–1.72 (m, 4 H), 1.65–1.58 (m, 1 H), 1.46 (qd, *J* = 13.4, 4.1 Hz, 1 H), 1.35 (qd, *J* = 12.1, 5.6 Hz, 1 H), 1.06–1.01 (m, 1 H), 0.99 (s, 3 H), 0.89 (s, 3 H), 0.71 (t, *J* = 5.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 210.7, 87.4, 79.8, 74.5, 72.4, 47.2, 46.9, 44.4, 43.7, 39.8, 39.0, 38.0, 37.7, 33.8, 32.4, 26.2, 22.6, 22.5, 19.5, 12.7, 11.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{28}NaO_3$: 351.1931; found: 351.1935.

11f

Yield: 21 mg (0.05 mmol, 13%); mp 81–81.5 °C ($CHCl_3$); $[\alpha]_D^{20}$ –24.3 (*c* 1.00, $CHCl_3$); R_f = 0.48 (*n*-hexane–EtOAc, 7:1, CAM [blue]).

IR (neat): 3386 (b), 3307 (w), 2956 (s), 2872 (m), 2360 (w), 2340 (w), 1677 (s), 1378 (m), 1303 (w), 1248 (s), 1148 (m), 1137 (m), 1087 (s), 917 (m), 890 (m), 842 (s) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 3.77 (t, *J* = 3.2 Hz, 1 H), 2.56 (s, 1 H), 2.41 (d, *J* = 3.8 Hz, 1 H), 2.27 (ddd, *J* = 13.5, 9.8, 5.4 Hz, 1 H), 2.13 (td, *J* = 11.6, 7.6 Hz, 1 H), 2.10–2.02 (m, 1 H), 1.99–1.86 (m, 2 H), 1.84–1.54 (m, 9 H), 1.50–1.39 (m, 1 H), 1.32 (qd, *J* = 12.1, 5.4 Hz, 1 H), 1.05–1.00 (m, 1 H), 0.99 (s, 3 H), 0.81 (s, 3 H), 0.70 (t, *J* = 5.0 Hz, 1 H), 0.17 (s, 9 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 210.6, 87.8, 80.6, 75.1, 72.6, 47.7, 47.3, 44.4, 42.6, 40.4, 40.0, 37.8, 37.8, 33.8, 32.3, 26.6, 22.8, 22.6, 19.5, 12.7, 11.0, 2.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{36}NaO_3Si$: 423.2326; found: 423.2331.

α-Hydroxy Ketone 11g

Ketone **10g** (408 mg, 1.43 mmol, 1.0 equiv) was processed as described in general procedure A and the thus-obtained crude product was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 15:1→7:1) to yield α-hydroxy ketone **11g** (38%) as a colorless foam and recovered ketone **10g** (180 mg, 0.63 mmol, 44%).

Yield: 165 mg (0.55 mmol, 38%); mp 63–64.5 °C ($CHCl_3$); $[\alpha]_D^{20}$ –8.1 (*c* 1.00, $CHCl_3$); R_f = 0.38 (*n*-hexane–EtOAc, 9:1, CAM [red]).

IR (neat): 3304 (b), 2959 (s), 2872 (m), 1737 (m), 1693 (s), 1678 (s), 1655 (m), 1452 (w), 1373 (s), 1302 (w), 1216 (w), 1160 (w), 875 (m), 850 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 4.69–4.64 (m, 2 H), 3.84 (t, *J* = 2.9 Hz, 1 H), 2.59–2.50 (m, 1 H), 2.49–2.44 (m, 1 H), 2.36–2.26 (m, 1 H), 2.04 (dtd, *J* = 17.1, 8.1, 4.0 Hz, 1 H), 1.93 (td, *J* = 11.3, 3.3 Hz, 1 H), 1.88–1.79 (m, 4 H), 1.76–1.64 (m, 4 H), 1.60 (dd, *J* = 8.3, 5.0 Hz, 1 H), 1.52 (tdd, *J* = 13.6, 12.1, 4.1 Hz, 1 H), 1.38–1.27 (m, 2 H), 1.08–1.01 (m, 1 H), 1.00 (s, 3 H), 0.83 (s, 3 H), 0.71 (t, *J* = 5.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 210.6, 161.0, 101.3, 73.0, 47.7, 47.3, 44.4, 44.1, 39.2, 38.0, 37.8, 35.3, 33.8, 29.5, 26.3, 23.7, 22.8, 19.5, 18.2, 11.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{28}NaO_2$: 323.1982; found: 323.1997.

Methyl Esters 12 by Oxidation and Benzilic Acid Rearrangement of 7-Hydroxy-6-oxo-*i*-steroids 11; General Procedure B

The appropriate α-hydroxy ketone **11** (1.0 equiv) was suspended in MeOH (0.04 M) and CuCl (20 equiv) was added. The resulting suspension was stirred at 50 °C for 3–16 h. After cooling to ambient temperature, the suspension was filtered through a plug of Celite, all volatiles were removed under reduced pressure, and the thus-obtained residue was purified by column chromatography (silica gel, *n*-hexane–EtOAc) to give the corresponding B-*nor*-α-hydroxy methyl ester **12** as a colorless oil or colorless solid.

B-*nor*-α-Hydroxy Methyl Ester 12a

α-Hydroxy ketone **11a** (139 mg, 0.33 mmol, 1.0 equiv) was processed as described in general procedure B and the thus-obtained crude product was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to give **12a** as a colorless oil.

Yield: 139 mg (0.31 mmol, 94%); $[\alpha]_D^{20}$ –19.2 (*c* 1.00, $CHCl_3$); R_f = 0.68 (*n*-hexane–EtOAc, 7:1, CAM [blue]).

IR (neat): 3524 (w), 2951 (s), 2929 (m), 2866 (s), 1723 (s), 1455 (m), 1379 (m), 1270 (w), 1247 (s), 1215 (m), 1159 (s), 1107 (m), 1097 (m), 1072 (w), 1015 (w), 971 (m), 754 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 700 MHz): δ = 5.21–5.14 (m, 2 H), 3.76 (s, 3 H), 2.87 (s, 1 H), 2.29 (t, *J* = 11.5 Hz, 1 H), 2.07–1.99 (m, 1 H), 1.97 (dt, *J* = 12.5, 3.0 Hz, 1 H), 1.84 (td, *J* = 6.9, 5.8 Hz, 1 H), 1.74–1.56 (m, 5 H), 1.52–1.43 (m, 4 H), 1.40–1.33 (m, 2 H), 1.27–1.12 (m, 4 H), 1.02 (d, *J* = 6.6 Hz, 3 H), 0.93 (s, 3 H), 0.90 (d, *J* = 6.8 Hz, 3 H), 0.83 (d, *J* = 6.8 Hz, 3 H), 0.81 (d, *J* = 6.8 Hz, 3 H), 0.68 (s, 3 H), 0.54 (t, *J* = 5.4 Hz, 1 H), 0.50 (dd, *J* = 8.8, 5.5 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 176 MHz): δ = 178.5, 136.0, 132.0, 80.5, 55.3, 53.0, 52.0, 50.7, 50.4, 50.3, 50.0, 44.7, 43.0, 40.1, 39.1, 34.2, 33.3, 28.9, 25.9, 24.0, 23.6, 21.8, 21.3, 20.1, 19.8, 18.5, 17.8, 12.9, 11.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{46}NaO_3$: 465.3339; found: 465.3345.

B-*nor*-α-Hydroxy Methyl Ester 12b

α-Hydroxy ketone **11b** (202 mg, 0.47 mmol, 1.0 equiv) was processed as described in general procedure B and the thus-obtained crude product was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to give **12b** as a colorless oil.

Yield: 190 mg (0.41 mmol, 88%); $[\alpha]_D^{20}$ +13.1 (*c* 1.00, $CHCl_3$); R_f = 0.57 (*n*-hexane–EtOAc, 9:1, CAM [blue]).

IR (neat): 2950 (s), 2934 (s), 2865 (s), 1724 (s), 1462 (m), 1378 (m), 1271 (w), 1247 (s), 1215 (w), 1159 (m), 1108 (w), 1049 (w), 954 (m), 754 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 3.77 (s, 3 H), 2.88 (s, 1 H), 2.28 (t, *J* = 11.4 Hz, 1 H), 2.01 (dt, *J* = 12.6, 3.0 Hz, 1 H), 1.87 (dddd, *J* = 15.3, 13.3, 9.1, 5.7 Hz, 2 H), 1.72 (dd, *J* = 14.0, 9.4 Hz, 1 H), 1.69–1.61 (m, 3 H), 1.56 (s, 1 H), 1.52–1.44 (m, 3 H), 1.39–1.30 (m, 3 H), 1.30–1.20 (m, 3 H), 1.19–1.10 (m, 3 H), 1.07–0.95 (m, 2 H), 0.94–0.92 (m, 8 H), 0.84–0.80 (m, 6 H), 0.81 (d, *J* = 6.8 Hz, 3 H), 0.67 (s, 3 H), 0.54 (t, *J* = 5.4 Hz, 1 H), 0.50 (dd, *J* = 8.8, 5.5 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 178.6, 80.5, 55.2, 53.0, 52.0, 50.7, 50.4, 50.2, 50.0, 46.0, 44.7, 39.2, 36.2, 34.2, 34.2, 29.3, 28.8, 26.2, 25.9, 24.0, 23.6, 23.2, 21.9, 19.9, 19.2, 19.0, 18.5, 12.6, 12.1, 11.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{50}NaO_3$: 481.3652; found: 481.3659.

B-*nor*-α-Hydroxy Methyl Ester 12c

α-Hydroxy ketone **11d** (20 mg, 0.05 mmol, 1.0 equiv) was processed as described in general procedure B and the thus-obtained crude product was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 1:1) to give **12c** as a colorless oil.

Yield: 14 mg (0.04 mmol, 83%; from **11c**: 61%); $[\alpha]_D^{20}$ –4.4 (*c* 1.00, $CHCl_3$); R_f = 0.46 (*n*-hexane–EtOAc, 1:1, CAM [blue]).

IR (neat): 3481 (b), 2947 (w), 2865 (w), 2360 (s), 2341 (m), 1719 (s), 1455 (w), 1978 (w), 1274 (w), 1252 (s), 1160 (m), 1106 (m), 1096 (m), 1051 (m) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 3.78 (s, 3 H), 3.71 (t, *J* = 8.5 Hz, 1 H), 2.36 (t, *J* = 11.5 Hz, 1 H), 2.07 (dtd, *J* = 13.6, 9.3, 6.0 Hz, 1 H), 1.91–1.85 (m, 1 H), 1.82 (dt, *J* = 12.6, 3.1 Hz, 1 H), 1.75–1.70 (m, 1 H), 1.70–1.63 (m, 2 H), 1.58–1.35 (m, 7 H), 1.17 (qd, *J* = 12.2, 6.0 Hz, 1 H), 1.07 (td, *J* = 12.5, 4.1 Hz, 1 H), 0.98 (ddd, *J* = 13.8, 10.8, 8.8 Hz, 1 H), 0.94 (s, 3 H), 0.77 (s, 3 H), 0.55 (t, *J* = 5.5 Hz, 1 H), 0.52–0.49 (m, 1 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 178.4, 81.3, 80.1, 53.1, 51.9, 50.4, 50.3, 50.2, 45.6, 45.1, 36.2, 34.2, 30.8, 25.8, 24.0, 23.1, 21.5, 18.5, 11.7, 11.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{30}NaO_4$: 357.2036; found: 357.2043.

B-*nor*-α-Hydroxy Methyl Ester 12g

α-Hydroxy ketone **11g** (80 mg, 0.26 mmol, 1.0 equiv) was processed as described in general procedure B by using CuCl (20 equiv) and a shorter reaction time of 3 h. The thus-obtained crude product was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to give **12g** as a colorless solid.

Yield: 73 mg (0.22 mmol, 85%); mp 78–80 °C ($CHCl_3$); $[\alpha]_D^{20}$ +13.8 (*c* 1.00, $CHCl_3$); R_f = 0.64 (*n*-hexane–EtOAc, 9:1, CAM [blue]).

IR (neat): 2929 (m), 2864 (w), 2360 (s), 2341 (s), 1722 (m), 1653 (w), 1455 (w), 1375 (w), 1274 (m), 1260 (m), 1157 (w), 1091 (w), 875 (w), 764 (s), 750 (s) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 4.64 (ddt, *J* = 4.2, 2.1, 1.3 Hz, 2 H), 3.78 (s, 3 H), 2.89 (s, 1 H), 2.46 (ddq, *J* = 17.1, 10.0, 2.2 Hz, 1 H), 2.39–2.32 (m, 1 H), 2.26 (dtt, *J* = 17.3, 8.8, 2.0 Hz, 1 H), 1.94–1.80 (m, 2 H), 1.79–1.70 (m, 2 H), 1.67–1.58 (m, 2 H), 1.55–1.44 (m, 2 H), 1.42–1.37 (m, 1 H), 1.28–1.13 (m, 2 H), 1.03–0.97 (m, 1 H), 0.95 (s, 3 H), 0.80 (s, 3 H), 0.56 (t, *J* = 5.5 Hz, 1 H), 0.51 (dd, *J* = 8.9, 5.6 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 178.4, 160.5, 100.9, 80.2, 53.0, 51.9, 50.5, 50.4, 50.3, 48.6, 46.1, 35.1, 34.2, 29.7, 25.9, 24.0, 23.7, 21.6, 19.1, 18.5, 11.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{30}NaO_3$: 353.2087; found: 353.2101.

B-*nor*-Acrylic Esters 13 by *i*-Steroid Opening of B-*nor*-α-Hydroxy Methyl Esters 12; General Procedure C

The appropriate B-*nor*-α-hydroxy methyl ester **12** (1.0 equiv) was dissolved in Et_2O (0.04 M). Glacial AcOH (200 equiv) and $BF_3{\cdot}Et_2O$ (80 equiv) were added and the resulting mixture was stirred for 15 h at 25 °C. The solution was diluted with EtOAc and carefully poured onto sat. aq $NaHCO_3$. The organic phase was separated and the aqueous phase was extracted with EtOAc (2×); the combined organic extracts were washed with sat. brine, dried over $MgSO_4$, and filtered. All volatiles were removed under reduced pressure and the thus-obtained residue was purified by column chromatography (silica gel, *n*-hexane–EtOAc) to give the corresponding B-*nor*-acrylic ester **13** as a colorless oil.

B-*nor*-Acrylic Ester 13a

Ester **12a** (94 mg, 0.21 mmol, 1.0 equiv) was processed as described in general procedure C and the thus-obtained crude product was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to give **13a** as a colorless oil.

Yield: 80 mg (0.17 mmol, 79%); $[\alpha]_D^{23}$ –68.9 (*c* 1.00, $CHCl_3$); R_f = 0.32 (*n*-hexane–EtOAc, 9:1, CAM [blue, UV]).

IR (neat): 2953 (m), 2869 (w), 2360 (m), 1735 (m), 1716 (s), 1456 (m), 1370 (m), 1235 (s), 1035 (m), 971 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 700 MHz): δ = 5.23–5.14 (m, 2 H), 4.72 (tt, *J* = 11.5, 4.6 Hz, 1 H), 3.68 (s, 3 H), 3.26 (ddd, *J* = 13.9, 4.9, 2.1 Hz, 1 H), 2.63 (td, *J* = 10.7, 4.4 Hz, 1 H), 2.04 (s, 3 H), 2.02–1.97 (m, 3 H), 1.87–1.80 (m, 2 H), 1.68–1.60 (m, 2 H), 1.50–1.42 (m, 4 H), 1.41–1.31 (m, 2 H), 1.29–1.24 (m, 3 H), 1.16–1.13 (m 3 H), 1.01 (d, *J* = 6.6 Hz, 3 H), 0.92 (s, 3 H), 0.91 (d, *J* = 6.9 Hz, 3 H), 0.83 (d, *J* = 6.8 Hz, 3 H), 0.81 (d, *J* = 6.8 Hz, 3 H), 0.73 (s, 3 H).

^{13}C NMR ($CDCl_3$, 176 MHz): δ = 170.4, 168.2, 156.4, 135.9, 132.0, 131.4, 72.9, 60.4, 55.3, 54.6, 51.0, 47.7, 45.9, 45.2, 43.0, 40.0, 39.9, 36.3, 33.3, 30.6, 28.9, 27.7, 25.3, 21.5, 21.4, 20.9, 20.1, 19.8, 17.7, 15.4, 12.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{48}NaO_4$: 507.3445; found: 507.3451.

B-*nor*-Acrylic Ester 13b

Ester **12b** (78 mg, 0.17 mmol, 1.0 equiv) was processed as described in general procedure C and the thus-obtained crude product was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to give **13b** as a colorless oil.

Yield: 58 mg (0.12 mmol, 70%); $[\alpha]_D^{20}$ –40.0 (*c* 1.00, CH_2Cl_2); R_f = 0.40 (*n*-hexane–EtOAc, 9:1, CAM [blue, UV]).

IR (neat): 2955 (m), 2870 (w), 2360 (w), 2341 (w), 1730 (m), 1717 (s), 1456 (w), 1434 (w), 1376 (w), 1362 (w), 1238 (s), 1139 (w), 1078 (w), 1035 (m), 754 (s) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 4.71 (tt, *J* = 11.5, 4.5 Hz, 1 H), 3.68 (s, 3 H), 3.25 (ddd, *J* = 13.9, 4.9, 2.0 Hz, 1 H), 2.63 (td, *J* = 10.7, 4.3 Hz, 1 H), 2.03 (s, 3 H), 1.97 (dd, *J* = 32.6, 12.2 Hz, 1 H), 1.81 (d, *J* = 13.4 Hz, 2 H), 1.70–1.58 (m, 1 H), 1.56–1.05 (m, 20 H), 0.92 (d, *J* = 6.6 Hz, 3 H), 0.91 (s, 3 H), 0.85 (s, 1 H), 0.82 (d, *J* = 7.5 Hz, 3 H), 0.81 (s, 3 H), 0.80 (d, *J* = 6.8 Hz, 3 H), 0.72 (s, 3 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 170.4, 168.2, 156.3, 131.4, 72.9, 60.3, 55.3, 54.5, 51.0, 47.7, 46.0, 45.9, 45.3, 40.0, 36.3, 36.1, 34.1, 30.6, 29.3, 28.8, 27.7, 26.3, 25.3, 23.2, 21.5, 20.9, 20.0, 19.2, 19.1, 15.3, 12.6, 12.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{32}H_{52}NaO_4$: 523.3758; found: 523.3764.

B-*nor*-Acrylic Ester 13c

Ester **12c** (19 mg, 0. 06 mmol, 1.0 equiv) was processed as described in general procedure C and the thus-obtained crude product was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 4:1) to give **13c** as a colorless oil.

Yield: 9 mg (0.02 mmol, 42%); $[\alpha]_D^{24}$ –18.9 (*c* 0.48, $CHCl_3$); R_f = 0.81 (*n*-hexane–EtOAc, 1:1, CAM [blue, UV]).

IR (neat): 3734 (b), 2952 (m), 2860 (w), 2360 (s), 2341 (s), 1733 (m), 1716 (w), 1540 (m), 1507 (w), 1260 (m), 750 (m) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 4.72 (tt, *J* = 11.5, 4.6 Hz, 1 H), 4.62 (dd, *J* = 9.3, 7.8 Hz, 1 H), 3.70 (s, 3 H), 3.35 (ddd, *J* = 13.9, 4.8, 2.1 Hz, 1 H), 2.70 (td, *J* = 10.9, 4.3 Hz, 1 H), 2.18–2.09 (m, 1 H), 2.04 (s, 3 H), 2.02–1.92 (m, 1 H), 1.83 (dt, *J* = 13.4, 3.5 Hz, 1 H), 1.80–1.76 (m, 1 H), 1.74–1.68 (m, 1 H), 1.68–1.54 (m, 1 H), 1.52–1.36 (m, 2 H), 1.31–1.23 (m, 1 H), 1.22–1.10 (m, 2 H), 0.93 (s, 3 H), 0.87 (d, *J* = 0.7 Hz, 3 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 171.3, 170.4, 167.7, 157.9, 82.3, 72.8, 60.3, 51.0, 49.2, 47.3, 45.9, 45.2, 37.1, 36.2, 30.7, 27.9, 27.6, 25.2, 21.3, 20.3, 15.5, 12.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{32}NaO5$: 399.2141; found: 399.2137.

B-*nor*-Aldehyde 14

Step 1 giving the corresponding B-nor-allylic alcohol: A solution of B-*nor*-acrylic ester **13a** (58 mg, 0.12 mmol, 1.0 equiv) in THF (0.6 mL) was added dropwise to a suspension of $LiAlH_4$ (22 mg, 0.59 mmol, 4.0 equiv) in THF (0.6 mL) at 25 °C. The resulting mixture was stirred at the same temperature for 3 h. A sat. aq potassium/sodium tartrate solution (2 mL) was added and the mixture was stirred for 15 min. The phases were separated and the aqueous phase was extracted with EtOAc (2 × 3 mL). The combined organic extracts were washed with sat. brine, dried over $MgSO_4$, and filtered. All volatiles were removed under reduced pressure and the thus-obtained residue was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 1:1→1:3) to give the corresponding B-*nor*-allylic alcohol as a colorless solid.

Yield: 25 mg (0.06 mmol, 50%); mp 183.5–184.5 °C ($CHCl_3$); $[\alpha]_D^{20}$ –102.7 (*c* 1.00, $CHCl_3$); R_f = 0.26 (*n*-hexane–EtOAc, 1:1, CAM [blue]).

IR (neat): 3275 (b), 2954 (m), 2926 (w), 2866 (w), 2360 (s), 2338 (s), 1457 (w), 1368 (m), 1273 (w), 1016 (w), 975 (m), 751 (m) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 5.24–5.14 (m, 2 H), 4.14 (d, *J* = 11.6 Hz, 1 H), 4.06 (d, *J* = 11.6 Hz, 1 H), 3.53 (tt, *J* = 11.2, 4.4 Hz, 1 H), 2.80 (ddd, *J* = 13.7, 4.6, 2.0 Hz, 1 H), 2.37 (td, *J* = 10.8, 4.0 Hz, 1 H), 2.08–1.98 (m, 2 H), 1.93–1.82 (m, 4 H), 1.78 (dt, *J* = 13.2, 3.4 Hz, 2 H), 1.75–1.04 (m, 13 H), 1.02 (d, *J* = 6.6 Hz, 3 H), 0.91 (d, *J* = 6.8 Hz, 3 H), 0.87 (s, 3 H), 0.83 (d, *J* = 6.8 Hz, 3 H), 0.82 (d, *J* = 6.8 Hz, 3 H), 0.71 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 145.9, 136.9, 136.0, 132.0, 71.7, 61.3, 57.5, 55.2, 54.1, 47.5, 45.3, 44.8, 43.0, 40.0, 39.9, 37.2, 33.5, 33.3, 32.0, 29.1, 24.9, 21.4, 21.0, 20.1, 19.8, 17.7, 15.3, 12.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{44}NaO_2$: 437.3390; found: 437.3398.

Step 2 giving B-nor-aldehyde ***14***: The B-*nor*-allylic alcohol thus-obtained (25 mg, 0.06 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (1 mL) and MnO_2 (50 mg, 0.6 mmol, 10.0 equiv) was added. The resulting dark suspension was allowed to stir for 48 h at 25 °C. The suspension was diluted with CH_2Cl_2 (2 mL) and filtered through a plug of Celite. All volatiles were removed under reduced pressure and the thus-obtained residue was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 1:1) to give **14** as a colorless solid.

Yield: 20 mg (0.05 mmol, 80%; 40% over 2 steps); mp 124–124.5 °C ($CHCl_3$); $[\alpha]_D^{20}$ –58.4 (*c* 0.47, $CHCl_3$); R_f = 0.51 (*n*-hexane–EtOAc, 1:1, CAM [blue]).

IR (neat): 3321 (b), 2955 (s), 2928 (s), 2867 (s), 2359 (w), 1675 (s), 1596 (m), 1370 (w), 1239 (w), 1071 (m), 970 (m), 817 (w) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.96 (s, 1 H), 5.26–5.12 (m, 2 H), 3.70 (tt, *J* = 11.2, 4.5 Hz, 1 H), 3.47 (ddd, *J* = 14.3, 4.6, 2.0 Hz, 1 H), 2.56 (td, *J* = 10.8, 4.0 Hz, 1 H), 2.14–1.99 (m, 3 H), 1.97–1.10 (m, 17 H), 1.02 (d, *J* = 6.7 Hz, 3 H), 0.94 (s, 3 H), 0.91 (d, *J* = 6.8 Hz, 3 H), 0.82 (t, *J* = 6.6 Hz, 6 H), 0.74 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 189.8, 169.0, 139.4, 135.8, 132.0, 71.0, 60.3, 55.4, 54.7, 46.4, 45.3, 43.0, 40.0, 36.3, 34.0, 33.3, 33.2, 31.4, 28.8, 26.7, 26.7, 21.4, 20.8, 20.1, 19.8, 17.7, 15.8, 12.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{44}NaO_2$: 435.3234; found: 435.3240.

Substrate 10g

Tosylate 20

17-Methylenedehydroepiandrosterone[18] (**19**; 580 mg, 2.02 mmol, 1.0 equiv) was dissolved in pyridine (20 mL) and DMAP (24 mg, 0.2 mmol, 0.1 equiv) was added. Then TsCl (1.93 g, 10.1 mmol, 5.0 equiv) was added and the resulting mixture was stirred for 16 h at 25 °C. The solution was poured onto ice water (70 mL) and extracted with Et_2O (3 × 25 mL). The organic phase was separated and washed sequentially with H_2O (2 × 50 mL) and sat. brine (100 mL). The organic phase was then dried over $MgSO_4$ and filtered, and all volatiles were removed under reduced pressure. The thus-obtained residue was dis-

solved in toluene (2 × 15 mL) and concentrated under reduced pressure to give tosylate **20** as a colorless solid which was used in the next step without further purification.

Yield: 781 mg (1.77 mmol, 88%); mp 127–128.5 °C ($CHCl_3$); $[\alpha]_D^{20}$ –59.3 (*c* 1.00, CH_2Cl_2); R_f = 0.47 (*n*-hexane–EtOAc, 9:1, CAM [orange, UV]).

IR (neat): 2944 (m), 2907 (w), 2360 (s), 2341 (m), 1716 (w), 1652 (w), 1455 (w), 1362 (s; 1187 (s), 1175 (s), 1098 (w), 939 (s), 888 (m), 864 (s), 813 (m), 667 (s) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 7.80 (d, *J* = 8.3 Hz, 2 H), 7.33 (d, *J* = 7.7 Hz, 2 H), 5.34–5.30 (m, 1 H), 4.70–4.60 (m, 2 H), 4.33 (tt, *J* = 11.5, 4.8 Hz, 1 H), 2.57–2.45 (m, 1 H), 2.45 (s, 3 H), 2.34–2.17 (m, 3 H), 2.06–1.99 (m, 1 H), 1.86–1.79 (m, 3 H), 1.76–1.65 (m, 2 H), 1.62–1.42 (m, 4 H), 1.34–1.17 (m, 2 H), 1.07–1.00 (m, 1 H), 0.99 (s, 3 H), 0.98–0.87 (m, 2 H), 0.78 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 161.7, 144.5, 139.1, 134.9, 129.9, 127.8, 123.5, 101.1, 82.4, 54.8, 50.3, 44.0, 39.0, 37.1, 36.6, 35.6, 31.8, 31.8, 29.5, 28.8, 24.4, 21.8, 21.1, 19.4, 18.4.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{36}NaO_3S$: 463.2277; found: 463.2280.

6-Hydroxy-*i*-steroid 21

Tosylate **20** (780 mg, 1.77 mmol, 1.0 equiv) was suspended in a mixture of acetone and H_2O (4:1, 22.5 mL) in a pressure vessel and KOAc (694 mg, 7.08 mmol, 4.0 equiv) was added. The resulting mixture was stirred for 16 h at 85 °C. After cooling of the mixture to ambient temperature, H_2O (15 mL) was added and the mixture was extracted with Et_2O (3 × 10 mL). The combined organic phases were washed with sat. brine, dried over $MgSO_4$, and filtered, and all volatiles were removed under reduced pressure to give **21** (500 mg, 1.77 mmol, quant.) as a pale yellow oil which was used in the next step without further purification. A small sample of this material was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to yield pure **21** as a colorless oil.

$[\alpha]_D^{20}$ +40.7 (*c* 1.00, $CHCl_3$); R_f = 0.35 (*n*-hexane–EtOAc, 9:1, CAM [green]).

IR (neat): 2927 (s), 2865 (m), 2360 (s), 2341 (m), 1737 (s), 1653 (w), 1455 (m), 1373 (s), 1228 (m), 1216 (s), 1025 (m), 875 (m), 668 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 4.66–4.59 (m, 2 H), 3.27 (t, *J* = 2.9 Hz, 1 H), 2.51 (ddq, *J* = 17.1, 10.1, 2.3 Hz, 1 H), 2.24 (dtt, *J* = 17.4, 8.7, 2.0 Hz, 1 H), 1.95–1.86 (m, 2 H), 1.83 (ddd, *J* = 12.4, 3.9, 2.9 Hz, 1 H), 1.80–1.69 (m, 2 H), 1.61–1.52 (m, 4 H), 1.52–1.31 (m, 3 H), 1.22 (dtd, *J* = 14.1, 12.6, 3.5 Hz, 2 H), 1.08 (s, 3 H), 1.08–1.01 (m, 1 H), 0.92–0.85 (m, 2 H), 0.84 (s, 3 H), 0.53 (dd, *J* = 4.8, 3.7 Hz, 1 H), 0.32–0.28 (m, 1 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 162.1, 100.8, 73.9, 54.7, 48.1, 44.4, 43.2, 39.1, 37.1, 36.1, 33.4, 30.0, 29.6, 25.2, 24.4, 24.3, 22.7, 20.4, 18.8, 11.8.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{30}NaO$: 309.2189; found: 309.2201.

i-Steroid Ketone 10g

CrO_3 (1.42 g, 14.4 mmol, 4.0 equiv) was added portionwise to pyridine (15 mL) under stirring at 0 °C. Then, 6-hydroxy-*i*-steroid **21** (1.02 g, 3.56 mmol, 1.0 equiv), dissolved in pyridine (15 mL), was added via cannula to the brown suspension. The resulting, dark solution was stirred for 15 h at 25 °C. Et_2O (60 mL) was added and the solution was filtered over Celite and rinsed with Et_2O (2 × 30 mL). The filtrate was washed sequentially with H_2O (2 × 50 mL) and sat. brine (50 mL), dried over $MgSO_4$, and filtered. All volatiles were removed under reduced pressure and the thus-obtained residue was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to yield *i*-steroid ketone **10g** as a colorless solid.

Yield: 555 mg (1.95 mmol, 55% over 2 steps); mp 176–177 °C ($CHCl_3$); $[\alpha]_D^{20}$ +41.0 (*c* 1.00, $CHCl_3$); R_f = 0.45 (*n*-hexane–EtOAc, 9:1, CAM [green]).

IR (neat): 2946 (m), 2906 (m), 1680 (s), 1454 (w), 1372 (w), 1295 (w), 1161 (w), 875 (m), 809 (w), 737 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 4.69–4.65 (m, 2 H), 2.58–2.46 (m, 2 H), 2.32–2.23 (m, 1 H), 2.06–1.92 (m, 2 H), 1.89 (ddd, *J* = 12.6, 4.2, 3.1 Hz, 2 H), 1.83 (dd, *J* = 13.7, 8.1 Hz, 1 H), 1.74–1.68 (m, 4 H), 1.59–1.49 (m, 2 H), 1.37–1.27 (m, 3 H), 1.19 (ddd, *J* = 12.8, 10.2, 6.4 Hz, 1 H), 1.03 (s, 3 H), 1.02–0.98 (m, 1 H), 0.84 (s, 3 H), 0.73 (t, *J* = 4.9 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 209.5, 161.1, 101.4, 55.1, 47.0, 46.5, 46.5, 44.8, 44.4, 35.6, 35.5, 34.9, 33.6, 29.5, 26.0, 24.2, 22.9, 19.9, 18.6, 11.9.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{28}NaO$: 307.2032; found: 307.2047.

α-Methoxy Methyl Ester 15

Ester **12a** (16 mg, 0.036 mmol, 1.0 equiv) was dissolved in THF (0.36 mL), NaH (6 mg, 0.144 mmol, 4.0 equiv) was added, and the resulting mixture was stirred for 5 min at 25 °C. MeI (16 µL, 0.25 mmol, 7.0 equiv) was added and the mixture was stirred for 1 h at 25 °C. The mixture was cooled to 0 °C and quenched with sat. aq NH_4Cl (2 mL) and warmed to ambient temperature. The mixture was then extracted with EtOAc (3 × 2 mL), and the combined organic phases were washed sequentially with H_2O (3 mL) and sat. brine (3 mL), dried over $MgSO_4$, and filtered. All volatiles were removed under reduced pressure and the thus-obtained residue was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to yield **15** as a colorless oil.

Yield: 13 mg (0.03 mmol, 81%); $[\alpha]_D^{20}$ –18.9 (*c* 1.00, $CHCl_3$); R_f = 0.76 (*n*-hexane–EtOAc, 9:1, CAM [orange]).

IR (neat): 2951 (s), 2924 (s), 2866 (s), 2359 (w), 1740 (s), 1456 (m), 1379 (m), 1246 (m), 1215 (w), 1199 (w), 1152 (w), 1104 (m), 1053 (w), 970 (w), 793 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 5.21–5.16 (m, 2 H), 3.72 (s, 3 H), 3.20 (s, 3 H), 2.11 (t, *J* = 11.6 Hz, 1 H), 1.95 (dt, *J* = 12.9, 3.3 Hz, 1 H), 1.92–1.82 (m, 2 H), 1.75–1.63 (m, 4 H), 1.57–1.37 (m, 7 H), 1.19–1.03 (m, 3 H), 1.01 (d, *J* = 6.6 Hz, 3 H), 0.98–0.92 (m, 2 H), 0.91 (d, *J* = 6.9 Hz, 3 H), 0.89 (s, 3 H), 0.83 (d, *J* = 6.8 Hz, 3 H), 0.81 (d, *J* = 6.8 Hz, 3 H), 0.74 (dd, *J* = 8.6, 5.9 Hz, 1 H), 0.67 (d, *J* = 5.4 Hz, 1 H), 0.65 (s, 3 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 175.1, 135.9, 131.7, 87.8, 55.2, 55.1, 52.7, 51.8, 51.6, 51.4, 50.1, 49.6, 45.0, 42.8, 39.9, 39.0, 33.2, 33.1, 28.7, 25.7, 23.9, 23.8, 21.9, 21.1, 20.0, 19.6, 18.2, 17.6, 13.3, 12.6.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{30}H_{48}NaO_3$: 479.3496; found: 479.3497.

B-*nor*-*i*-Steroid Ketone 16a

Step 1 giving the corresponding diol: To ester **12a** (50 mg, 0.11 mmol, 1.0 equiv) in THF (4 mL) at 0 °C was added $LiAlH_4$ (17 mg, 0.45 mmol, 4.0 equiv). The resulting suspension was heated to 66 °C for 16 h. After cooling to ambient temperature, the reaction was quenched by addition of sat. aq potassium/sodium tartrate solution (2.5 mL) and stirred vigorously for 15 min. The phases were separated and the aqueous phase was extracted with EtOAc (2 × 5 mL). The combined organic phases were washed with sat. brine (5 mL), dried over $MgSO_4$,

and filtered. All volatiles were removed under reduced pressure to yield the corresponding diol as a colorless solid that was used immediately in the next step.

Yield: 42 mg (0.10 mmol, 92%); mp 88–90 °C ($CHCl_3$); $[\alpha]_D^{20}$ –5.7 (*c* 1.00, $CHCl_3$); R_f = 0.15 (*n*-hexane–EtOAc, 9:1, CAM [red]).

IR (neat): 3394 (b), 2954 (s), 2866 (s), 2360 (s), 2342 (m), 1456 (m), 1371 (m), 1275 (m), 1262 (m), 1159 (w), 970 (m), 749 (m) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 5.24–5.15 (m, 2 H), 3.41 (s, 2 H), 2.09–2.03 (m, 1 H), 2.00 (dt, *J* = 12.8, 3.1 Hz, 1 H), 1.88–1.80 (m, 2 H), 1.77–1.63 (m, 6 H), 1.51–1.37 (m, 4 H), 1.34–1.08 (m, 7 H), 1.03 (d, *J* = 6.7 Hz, 3 H), 0.91 (d, *J* = 6.8 Hz, 3 H), 0.85–0.81 (m, 9 H), 0.72–0.71 (m, 3 H), 0.47 (t, *J* = 5.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 136.0, 132.0, 78.4, 69.3, 55.4, 51.8, 51.3, 50.1, 49.1, 47.4, 44.9, 43.0, 40.1, 39.5, 33.5, 33.3, 29.0, 25.8, 24.9, 21.8 (2C), 21.3, 20.1, 19.8, 18.5, 17.8, 13.1, 9.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{46}NaO_2$: 437.3390; found: 437.3398.

Step 2 giving ketone ***16a***: To a solution of the diol (40 mg, 0.1 mmol, 1.0 equiv) in a mixture of THF (750 µL) and H_2O (250 µL) was added $NaIO_4$ (248 mg, 1.16 mmol, 5.0 equiv). The resulting suspension was stirred at 25 °C for 1.5 h. H_2O (4 mL) was added and the resulting mixture was extracted with EtOAc (3 × 3 mL). The combined organic phases were washed with sat. brine and dried over $MgSO_4$. All volatiles were removed under reduced pressure and the thus-obtained residue was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to yield **16a** as a colorless solid.

Yield: 83 mg (0.21 mmol, 90%; 82% over 2 steps); mp 133–134.5 °C (EtOAc); $[\alpha]_D^{20}$ –28.9 (*c* 1.00, $CHCl_3$); R_f = 0.65 (*n*-hexane–EtOAc, 9:1, CAM [blue]).

IR (neat): 2961 (s), 2940 (s), 2361 (s), 2338 (s), 1780 (s), 1463 (m), 1366 (m), 988 (w), 755 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 5.24–5.14 (m, 2 H), 2.18 (dd, *J* = 12.6, 10.3 Hz, 1 H), 2.09–2.00 (m, 3 H), 1.96–1.81 (m, 3 H), 1.78–1.69 (m, 2 H), 1.65–1.53 (m, 3 H), 1.51–1.41 (m, 2 H), 1.40–1.24 (m, 4 H), 1.23–1.11 (m, 3 H), 1.03 (d, *J* = 6.6 Hz, 3 H), 1.00 (s, 3 H), 0.91 (d, *J* = 6.8 Hz, 3 H), 0.89 (d, *J* = 5.4 Hz, 1 H), 0.83 (d, *J* = 6.8 Hz, 3 H), 0.82 (d, *J* = 6.8 Hz, 3 H), 0.69 (s, 3 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 217.0, 135.8, 132.1, 55.0, 51.8, 51.8, 50.7, 50.2, 48.1, 44.9, 43.0, 40.1, 39.4, 36.5, 35.0, 33.3, 29.2, 25.9, 23.9, 21.7, 21.4, 20.1, 19.8, 17.8, 17.7, 15.2, 12.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{42}NaO$: 405.3128; found: 405.3148.

B-*nor*-*i*-Steroid Ketone 16b

Step 1 giving the corresponding diol: To ester **12b** (190 mg, 0.41 mmol, 1.0 equiv) in THF (4 mL) at 0 °C was added $LiAlH_4$ (63 mg, 1.65 mmol, 4.0 equiv). The resulting suspension was heated to 66 °C for 16 h. After cooling to ambient temperature, the reaction was quenched by addition of sat. aq potassium/sodium tartrate solution (6 mL) and the mixture was stirred vigorously for 15 min. The phases were separated and the aqueous phase was extracted with EtOAc (2 × 5 mL). The combined organic phases were washed with sat. brine (5 mL), dried over $MgSO_4$, and filtered. All volatiles were removed under reduced pressure to yield the corresponding diol as a colorless solid that was used immediately in the next step.

Yield: 160 mg (0.37 mmol, 91%); mp 114–116 °C ($CHCl_3$); $[\alpha]_D^{20}$ +28.9 (*c* 1.00, $CHCl_3$); R_f = 0.24 (*n*-hexane–EtOAc, 9:1, CAM [blue]).

IR (neat): 3379 (b), 2965 (s), 2958 (s), 2864 (s), 2360 (m), 2341 (m), 1463 (m), 1376 (m), 1309 (w), 1266 (w), 1047 (w), 1020 (m), 747 (m) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 3.42 (d, *J* = 5.0 Hz, 2 H), 2.03 (dt, *J* = 12.8, 3.0 Hz, 1 H), 1.93–1.62 (m, 6 H), 1.50–0.96 (m, 19 H), 0.94 (d, *J* = 6.6 Hz, 3 H), 0.86 (s, 1 H), 0.84 (d, *J* = 1.6 Hz, 3 H), 0.83–0.82 (m, 6 H), 0.81 (d, *J* = 6.8 Hz, 3 H), 0.70 (s, 3 H), 0.47 (t, *J* = 5.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 78.3, 69.3, 55.3, 51.7, 51.2, 50.0, 49.1, 47.4, 45.9, 45.0, 39.6, 36.1, 34.1, 33.5, 29.2, 28.8, 26.1, 25.7, 24.8, 23.1, 21.8, 21.7, 19.9, 19.1, 19.0, 18.4, 12.7, 12.1, 9.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{50}NaO_2$: 453.3703; found: 453.3717.

Step 2 giving ketone ***16b***: To a solution of the diol (100 mg, 0.23 mmol, 1.0 equiv) in a mixture of THF (2 mL) and H_2O (500 µL) was added $NaIO_4$ (248 mg, 1.16 mmol, 5.0 equiv). The resulting suspension was stirred at 25 °C for 30 min. H_2O (4 mL) was added and the resulting mixture was extracted with EtOAc (3 × 3 mL). The combined organic phases were washed with sat. brine and dried over $MgSO_4$. All volatiles were removed under reduced pressure and the thus-obtained residue was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to yield **16b** as a colorless solid.

Yield: 83 mg (0.21 mmol, 90%; 82% over 2 steps); mp 75–76 °C ($CHCl_3$); $[\alpha]_D^{20}$ +8.8 (*c* 1.00, $CHCl_3$); R_f = 0.59 (*n*-hexane–EtOAc, 9:1, CAM [blue]).

IR (neat): 2953 (s), 2934 (s), 2867 (s), 2360 (s), 2341 (s), 1721 (s), 1540 (w), 1456 (m), 1383 (m), 1366 (m), 1290 (m), 1260 (m), 749 (s) cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 2.17 (dd, *J* = 12.4, 10.4 Hz, 1 H), 2.11–2.03 (m, 2 H), 1.96–1.79 (m, 2 H), 1.74 (dd, *J* = 12.9, 8.8 Hz, 2 H), 1.69–1.51 (m, 4 H), 1.47 (dd, *J* = 12.7, 3.6 Hz, 1 H), 1.43–1.08 (m, 15 H), 0.99 (s, 3 H), 0.93 (d, *J* = 6.5 Hz, 3 H), 0.89 (t, *J* = 5.3 Hz, 1 H), 0.84 (d, *J* = 7.6 Hz, 3 H), 0.83 (d, *J* = 6.8 Hz, 3 H), 0.80 (d, *J* = 6.8 Hz, 3 H), 0.68 (s, 3 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 217.1, 55.1, 51.8, 51.7, 50.6, 50.2, 48.1, 46.0, 44.9, 39.6, 36.5, 36.3, 35.0, 34.2, 29.3, 29.0, 26.3, 25.9, 23.9, 23.2, 21.7, 19.9, 19.2, 19.1, 17.7, 15.1, 12.3, 12.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{46}NaO$: 421.3441; found: 421.3454.

B-*nor*-3-Acetyl Ketone 17a

Ketone **16a** (24 mg, 0.06 mmol, 1.0 equiv) was dissolved in glacial AcOH (4.2 mL) and 2.5 M aq H_2SO_4 (1.1 mL) was added. The resulting solution was stirred at 95 °C for 48 h. After cooling to ambient temperature, the solution was neutralized with 25% aq NaOH and extracted with Et_2O (3 × 5 mL). The combined organic phases were washed with sat. brine (5 mL), dried over $MgSO_4$, and filtered. All volatiles were removed under reduced pressure and the thus-obtained residue was re-dissolved in pyridine (0.5 mL). To this solution were added sequentially DMAP (0.7 mg, 0.006 mmol, 0.1 equiv) and acetic anhydride (28 µL, 0.30 mmol, 5.0 equiv) and the mixture was stirred for 24 h at 25 °C. Afterwards, the reaction mixture was quenched with sat. aq NH_4Cl (1 mL) and extracted with Et_2O (3 × 3 mL). The combined organic phases were washed with sat. brine (5 mL), dried over $MgSO_4$, and filtered. All volatiles were removed under reduced pressure and the thus-obtained residue was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to yield **17a** as a colorless solid.

Yield: 22 mg (0.048 mmol, 80%, mixture of C5-epimers); mp 110.5–112 °C ($CHCl_3$); R_f = 0.44 (*n*-hexane–EtOAc, 9:1, CAM [blue]).

IR (neat): 2943 (s), 2939 (m), 2830 (s), 2359 (s), 2341 (s), 1450 (m), 1417 (m), 1115 (w), 1022 (s), 839 (m) cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.23–5.08 (m), 5.01 (t, *J* = 3.9 Hz), 4.35 (tq, *J* = 11.8, 4.4 Hz), 2.65–2.58 (m), 2.40–2.34 (m), 2.29 (ddt, *J* = 13.3, 4.3, 2.2 Hz), 2.23–2.16 (m), 2.16–2.04 (m), 2.02 (s), 1.99 (s), 1.98–1.20 (m), 1.17 (s), 1.04–1.02 (m), 1.03 (s), 1.01 (d, *J* = 6.6 Hz), 0.97 (d, *J* = 6.6 Hz), 0.90 (d, *J* = 6.8 Hz), 0.89 (d, *J* = 6.8 Hz), 0.82 (d, *J* = 6.9 Hz), 0.81 (d, *J* = 6.9 Hz), 0.80 (d, *J* = 6.8 Hz), 0.79 (d, *J* = 6.8 Hz), 0.65 (s), 0.51 (s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 207.6, 206.8, 170.2, 135.4, 132.0, 70.7, 68.4, 55.4, 54.8, 53.4, 52.2, 51.2, 50.4, 49.8, 47.6, 44.8, 44.1, 42.8, 42.8, 42.0, 40.2, 40.0, 39.2, 38.6, 38.0, 37.2, 33.1, 33.0, 32.8, 29.0, 27.9, 27.8, 27.1, 26.6, 25.0, 23.6, 23.6, 23.0, 21.8, 21.3, 21.3, 21.2, 21.1, 21.0, 20.7, 20.0, 19.9, 19.6, 17.6, 17.6, 17.6, 12.7, 12.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{46}NaO_3$: 465.3339; found: 465.3359.

B-*nor*-3-Acetyl Ketone 17b

Ketone **16b** (82 mg, 0.2 mmol, 1.0 equiv) was dissolved in glacial AcOH (16.7 mL) and 2.5 M aq H_2SO_4 (4.2 mL) was added. The resulting solution was stirred at 95 °C for 48 h. After cooling to ambient temperature, the solution was neutralized with 25% aq NaOH and extracted with Et_2O (3 × 15 mL). The combined organic phases were washed with sat. brine (15 mL), dried over $MgSO_4$, and filtered. All volatiles were removed under reduced pressure and the thus-obtained residue was re-dissolved in pyridine (4 mL). To this solution were added sequentially DMAP (2.5 mg, 0.02 mmol, 0.1 equiv) and acetic anhydride (95 µL, 1.0 mmol, 5.0 equiv) and the mixture was stirred for 24 h at 25 °C. Afterwards, the reaction mixture was quenched with sat. aq NH_4Cl (10 mL) and extracted with Et_2O (3 × 10 mL). The combined organic phases were washed with sat. brine (10 mL), dried over $MgSO_4$, and filtered. All volatiles were removed under reduced pressure and the thus-obtained residue was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to yield **17b** as a colorless solid (81 mg, 88%, mixture of C5-epimers). The mixture of epimers was re-subjected to column chromatography (silica gel, CH_2Cl_2–EtOAc–acetone 300:2:1) to yield an analytically pure sample of the less polar epimer.

Mixture of Epimers 17b

Yield: 81 mg (0.176 mmol, 88%, mixture of epimers); mp 115.5–116 °C ($CHCl_3$); R_f = 0.40 (*n*-hexane–EtOAc, 9:1, CAM [blue]).

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 5.04–5.00 (m), 4.37 (tt, *J* = 11.5, 4.4 Hz), 2.63 (t, *J* = 6.7 Hz), 2.38 (dt, *J* = 6.5, 2.1 Hz), 2.34–2.19 (m), 2.04 (s), 2.01 (s), 1.96–1.79 (m), 1.83 (s), 1.78–1.68 (m), 1.71–1.31 (m), 1.33 (s), 1.34–1.18 (m), 1.18 (s), 1.17–1.05 (m), 1.04 (s), 0.93 (d, *J* = 6.5 Hz), 0.89 (d, *J* = 6.5 Hz), 0.87–0.82 (m), 0.81 (d, *J* = 6.8 Hz), 0.65 (s), 0.52 (s).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 219.9, 170.6, 170.3, 70.9, 68.5, 55.6, 55.0, 53.5, 52.3, 51.4, 50.5, 50.0, 47.8, 47.6, 46.0, 45.9, 45.1, 44.2, 42.2, 39.5, 38.8, 38.2, 37.4, 36.4, 36.2, 34.1, 33.9, 33.0, 29.3, 29.2, 29.0, 28.1, 28.0, 27.7, 27.3, 26.7, 26.3, 26.2, 25.2, 23.8, 23.2, 23.2, 23.1, 22.0, 21.5, 21.4, 21.3, 20.9, 20.0, 19.9, 19.2, 19.2, 19.0, 19.0, 12.6, 12.3, 12.1.

Major, Less Polar Epimer 17b

Mp 122.5–123 °C ($CHCl_3$); $[\alpha]_D^{20}$ –24.9 (*c* 1.00, $CHCl_3$); R_f = 0.51 (*n*-hexane–EtOAc, 1:1, CAM [blue]).

IR (neat): 2954 (s), 2931 (s), 2869 (m), 2360 (w), 1733 (s), 1462 (m), 1375 (m), 1240 (s), 1140 (w), 1030 (m), 750 (s) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 4.37 (tt, *J* = 11.4, 4.4 Hz, 1 H), 2.62 (t, *J* = 6.7 Hz, 1 H), 2.37 (dt, *J* = 6.3, 2.1 Hz, 1 H), 2.30 (ddt, *J* = 12.9, 4.6, 2.3 Hz, 1 H), 2.25–2.17 (m, 1 H), 2.03 (t, *J* = 3.6 Hz, 1 H), 2.00 (s, 3 H), 1.89–1.79 (m, 2 H), 1.73 (dt, *J* = 13.2, 6.9 Hz, 1 H), 1.70–1.53 (m, 6 H), 1.54–1.21 (m, 9 H), 1.18 (s, 3 H), 1.16–0.98 (m, 6 H), 0.89 (d, *J* = 6.5 Hz, 3 H), 0.85–0.82 (m, 6 H), 0.80 (d, *J* = 6.8 Hz, 2 H), 0.51 (s, 3 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 219.9, 170.3, 70.9, 55.6, 53.5, 50.5, 47.8, 45.9, 44.2, 42.2, 38.9, 38.2, 36.4, 33.9, 33.0, 29.3, 27.7, 27.3, 26.7, 26.2, 23.2, 23.2, 22.0, 21.5, 20.9, 19.9, 19.2, 19.0, 12.6, 12.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{50}NaO_3$: 481.3652; found: 481.3675.

B-*nor*-3-Hydroxy Ketone 18a

To a solution of **17a** (20 mg, 0.044 mmol, 1.0 equiv) in MeOH–CH_2Cl_2 (10:1, 1.1 mL) was added KOH (12 mg, 0.22 mmol, 5.0 equiv). After stirring at 25 °C for 15 min, the reaction mixture was diluted with H_2O (5 mL) and neutralized with aq HCl (1.0 M). The aqueous layer was extracted with EtOAc (3 × 5 mL), and the combined organic phases were washed with sat. brine (5 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Column chromatography (silica gel, *n*-hexane–EtOAc, 3:1→1:1) gave **18a** as a colorless oil.

Yield: 15 mg (0.037 mmol, 83%); R_f = 0.59 (*n*-hexane–EtOAc, 1:1, CAM [blue]).

IR (neat): 3313 (b), 2947 (s), 2918 (m), 2359 (s), 2341 (s), 1711 (w), 1540 (m), 1507 (w), 1264 (m), 763 (m) cm^{-1}.

^{1}H NMR ($CDCl_3$, 401 MHz): δ = 5.26–5.08 (m), 4.10–4.05 (m), 3.39–3.28 (m), 2.64–2.57 (m), 2.38–1.22 (m), 1.17 (s), 1.03 (s), 1.02 (d, *J* = 6.6 Hz), 0.98 (d, *J* = 6.6 Hz), 0.91 (d, *J* = 6.8 Hz), 0.90 (d, *J* = 6.8 Hz), 0.84 (d, *J* = 1.6 Hz), 0.83 (d, *J* = 1.6 Hz), 0.82 (d, *J* = 1.6 Hz), 0.81 (d, *J* = 1.6 Hz), 0.66 (s), 0.53 (s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 197.2, 195.2, 135.6, 132.2, 76.8, 68.3, 65.4, 55.6, 53.9, 52.5, 50.6, 47.8, 44.2, 43.0, 42.1, 40.3, 40.1, 38.8, 38.2, 33.4, 33.2, 30.8, 30.7, 28.0, 23.2, 22.0, 21.2, 20.9, 20.1, 19.8, 17.7, 17.7, 12.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{46}NaO$: 423.6362 found: 423.6354.

B-*nor*-3-Hydroxy Ketone 18b

To a solution of **17b** (14 mg, 0.031 mmol, 1.0 equiv) in MeOH–CH_2Cl_2 (10:1, 0.7 mL) was added KOH (9 mg, 0.155 mmol, 5.0 equiv). After stirring at 25 °C for 15 min, the reaction mixture was diluted with H_2O (3 mL) and neutralized with aq HCl (1.0 M). The aqueous layer was extracted with EtOAc (3 × 3 mL), and the combined organic phases were washed with sat. brine (5 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Column chromatography (silica gel, *n*-hexane–EtOAc, 3:1→1:1) gave **18b** as a colorless solid.

Yield: 10 mg (0.024 mmol, 79%, mixture of C5-epimers); mp 115.5–116 °C ($CHCl_3$); R_f = 0.48 (*n*-hexane–EtOAc, 1:1, CAM [blue]).

IR (neat): 3389 (b), 2955 (s), 2932 (s), 2867 (s), 2360 (m), 2342 (m), 1729 (s), 1461 (m), 1379 (m), 1259 (m), 1204 (w), 1059 (m), 909 (m) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 5.04–5.00 (m), 4.37 (tt, *J* = 11.5, 4.4 Hz), 2.63 (t, *J* = 6.7 Hz), 2.38 (dt, *J* = 6.5, 2.1 Hz), 2.34–2.19 (m), 2.04 (s), 2.01 (s), 1.96–1.79 (m), 1.83 (s), 1.78–1.68 (m), 1.71–1.31 (m), 1.33 (s), 1.34–1.18 (m), 1.18 (s), 1.17–1.05 (m), 1.04 (s), 0.93 (d, *J* = 6.5 Hz), 0.89 (d, *J* = 6.5 Hz), 0.87–0.82 (m), 0.81 (d, *J* = 6.8 Hz), 0.65 (s), 0.52 (s).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 221.1, 68.3, 65.3, 55.6, 55.0, 53.9, 52.4, 51.2, 50.5, 50.0, 47.9, 45.9, 45.1, 44.1, 42.2, 38.9, 38.2, 37.4, 36.4, 36.2, 33.9, 33.4, 30.7, 30.7, 29.3, 27.7, 26.1, 23.9, 23.2, 22.0, 21.2, 20.9, 20.0, 19.2, 19.0, 12.6, 12.3, 12.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{48}NaO_2$: 439.3547; found: 439.3550.

***i*-Steroid Dione 22**

α-Hydroxy ketone **11g** (45 mg, 0.15 mmol, 1.0 equiv) was suspended in MeOH (3.8 mL) and CuCl (150 mg, 1.5 mmol, 10.0 equiv) was added. The resulting suspension was stirred at 50 °C for 16 h. After cooling to ambient temperature, the suspension was filtered through a plug of Celite, all volatiles were removed under reduced pressure, and the thus-obtained residue was purified by column chromatography (silica gel, *n*-hexane–EtOAc, 9:1) to give **22** (31 mg, 68%) as a colorless solid along with B-*nor*-α-hydroxy methyl ester **12g** (16 mg, 0.05 mmol, 21%).

Yield (**22**): 31 mg (0.1 mmol, 68%); $[\alpha]_D^{20}$ –25.9 (*c* 1.00, $CHCl_3$); R_f = 0.32 (*n*-hexane–EtOAc, 9:1, CAM [green]).

IR (neat): 2963 (m), 2922 (m), 2359 (m), 2342 (w), 1720 (m), 1693 (s), 1654 (w), 1455 (w), 1365 (w), 1293 (m), 1141 (w), 1100 (w), 991 (w), 876 (m) cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 4.70 (s, 1 H), 4.66 (s, 1 H), 2.77 (dd, *J* = 12.1, 10.4 Hz, 1 H), 2.58–2.49 (m, 1 H), 2.38–2.28 (m, 2 H), 2.00–1.41 (m, 10 H), 1.32–1.24 (m, 1 H), 1.23 (s, 3 H), 1.23–1.25 (m, 1 H), 1.19 (t, *J* = 10.5 Hz, 1 H), 1.10 (s, 1 H), 0.85 (s, 3 H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 198.2, 197.1, 159.7, 101.7, 50.5, 50.3, 48.7, 45.7, 45.4, 44.6, 40.9, 34.8, 34.1, 29.5, 25.8, 25.4, 23.0, 19.4, 18.6, 15.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{26}NaO_2$: 321.1825; found: 321.1811.

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Supporting Information

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