An Intramolecular Furan−Diene Diels−Alder Approach to 11-Oxo 10α-Steroids

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Dedicated to Professor John McMurry on the occasion of his 60th birthday

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The intramolecular cycloaddition of **14**, with dimethylaluminium chloride as a catalyst and under kinetic control, yielded the *exo* adduct **19a**. Opening of the oxygen bridge in the reduced adduct **20** gave intermediate **21**. Oxidation of the latter made it possible to introduce the methyl group at C-10, which exclusively afforded **23**, with the unnatural configuration. Further conversion resulted in the formation of D-homo-10-*epi*-adrenosterone (**25**).

Introduction

The development of novel reaction sequences to steroids, and 11-oxo steroids in particular, constitutes a longstanding challenge in total synthesis.[1] In this context, we have in the past been interested in a D → BCD → ABCD route that incorporates an intramolecular Diels−Alder reaction involving a furan−diene pair (IMDAF) for the construction of the BC ring system (Scheme 1).[2,3] In this strategy, which successfully provided (±)-adrenosterone,[4] the early introduction of the 11-carbonyl group had several functions: (1) activation of the dienophile **2** in the crucial cycloaddition step, (2) base-promoted opening of the oxa bridge in the adduct **3**, (3) the obtainment of the desired *trans* fusion of the BC ring system, and (4) indirect control of the configuration at the C-10 quaternary center. Here we wish to describe an analogous route that, when applied to the six-membered D-homo series, allows for the use of more elaborate dienophilic side chains. Further application of this approach resulted in the synthesis of a 10-*epi* derivative, (±)-D-homo-10α-androst-4-ene-3,11,17-trione (**25**),[5,6] the structure and peculiar geometry of which were determined by X-ray diffraction analysis.

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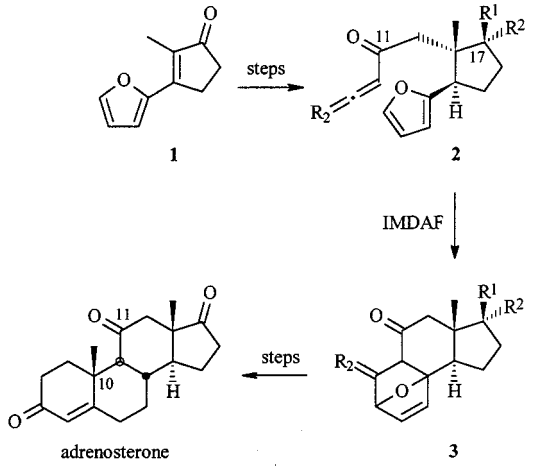


Scheme 1. The intramolecular furan−diene Diels−Alder strategy for the construction of the BC ring of adrenosterone

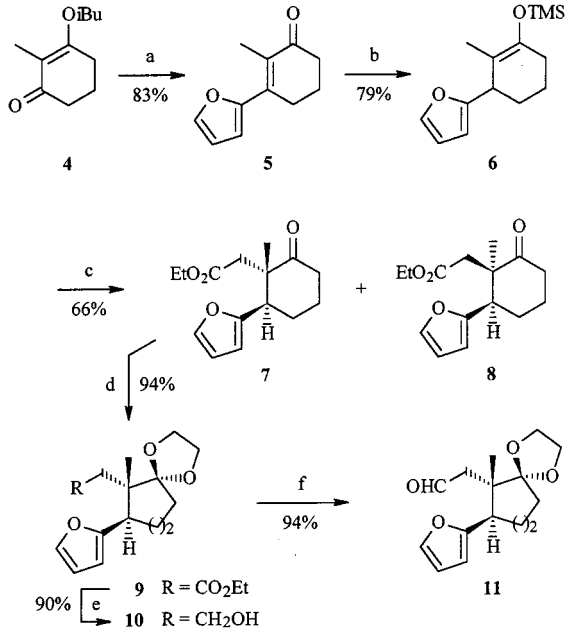
Results and Discussion

The Intramolecular Diels−Alder Strategy: Scope and Limitations

One important limitation of the IMDAF approach[7,8] as shown in Scheme 1 lies in the restrictions of the structure of the dienophile; so far, the successful cycloaddition of **2** has only been observed with two activated dienophilic side chains, involving the unsubstituted unsaturated enone (**2**, $R_2 = H_2$) and the allenic ketone (**2**, $R_2 = CH_2$). No Diels−Alder reaction took place in the case of an acetylenic

dienophile (cf. 9-yne derivative) or of β-substituted enones (cf. R_2 = H, alkyl). We also found the process to be sensitive to the nature of the D ring. In particular, the successful cycloadditions all involved an sp^3-hybridized C-17 (i.e., R^1 = OH, R^2 = H; R^1 = $OSiMe_2tBu$, R^2 = H; and R^1−R^2 = OCH_2CH_2O); the unsubstituted dienophilic enone **2** (R_2 = H_2), on the other hand, did not react when the D ring was a cyclopentanone (R^1, R^2 = O). The latter observation can be interpreted in terms of the low exothermicity of the reaction involving furan as a diene. The higher strain induced in the C ring upon adduct formation when the five-membered D ring is somewhat flattened may be responsible for a shift in the equilibrium (cf. change in hybridization at C-17 in *trans*-fused CD ring systems).[9] The outcome of the thermal cycloaddition process may thus depend on rather subtle structural features.[8]

After these observations we became interested in the study of an approach similar to the one described in Scheme 1, but involving a six-membered D ring. One might expect a broader range of dienophilic side-chains to be useful here, since less strain should be transmitted into the C ring upon cycloadduct formation than is the case with the five-membered D ring. Moreover, contraction of a six-membered D ring to provide the required five-membered ring size has been reported previously, providing a functionalized carbon atom that can be used for the construction of a classical pregnane side chain.[10] In this work we wish to describe the successful cycloaddition of β-substituted ynone **12**, and of β-substituted enones **13** and **14**, all characterized by the presence of a six-membered D ring.



Scheme 2. Synthesis of aldehyde **11**; reaction conditions: a) 2-furyllithium, THF, room temp.; NH_4Cl/HCl, −10 °C; b) Li, liq. NH_3, *t*BuOH, −78 °C; TMSCl, Et_3N, THF, −15 °C to 0 °C; c) MeLi, THF, 0 °C; $BrCH_2COOEt$, DMPU, room temp.; d) $HC(OMe)_3$, $HO(CH_2)_2OH$, *p*TsOH, room temp.; e) $LiAlH_4$, Et_2O, 0 °C; f) SO_3·py, DMSO, Et_3N, CH_2Cl_2, 0 °C

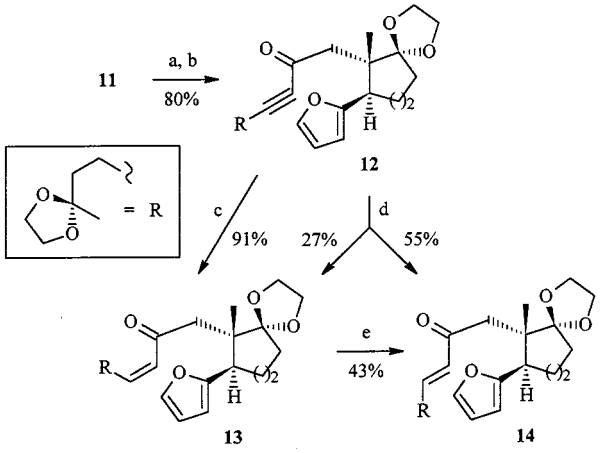
The Synthesis of Diels−Alder Precursors 12, 13, and 14

The Diels−Alder precursors **12**, **13**, and **14** were obtained from aldehyde **11** (Scheme 2). The synthesis of that compound involved a sequence similar to one followed in the five-membered D ring case.[2] Treatment of the known isobutyl enol ether **4**[11] (obtained from 2-methyl-1,3-cyclohexanedione in 96% yield; 2-methyl-1-propanol, *p*-toluenesulfonic acid, toluene) with 2-furyllithium, followed by controlled hydrolysis, provided cyclohexenone **5** in 83% yield. Subsequent dissolving-metal reduction (lithium, liquid ammonia, *tert*-butyl alcohol, −78 °C) generated the enolate anion, which was trapped with chlorotrimethylsilane and triethylamine to yield the silyl enol ether **6** in 79% yield. Regeneration of the enolate anion by treatment with methyllithium, followed by alkylation with ethyl bromoacetate, afforded a diastereomeric mixture consisting of cyclohexanone **7** and the corresponding *cis* derivative **8** (63% and 3%, respectively).[12] After protection of the carbonyl function in the *trans* derivative **7** as the acetal (trimethyl orthoformate, 1,2-ethanediol, *p*-toluenesulfonic acid; 94% yield), ester **9** was reduced with lithium aluminium hydride (90% yield) and the obtained alcohol **10** was oxidized to the corresponding aldehyde **11** (sulfur trioxide pyridine complex, dimethyl sulfoxide;[13] 94% yield).

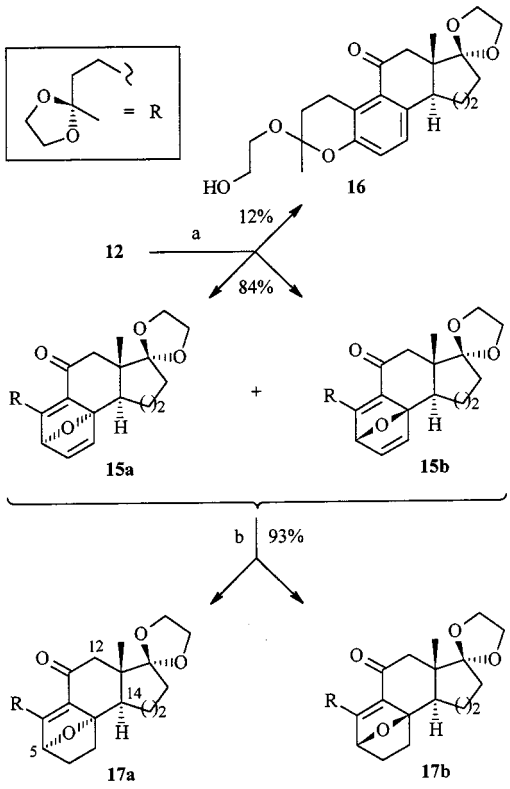
The further synthesis of the Diels−Alder precursors **13** and **14** is shown in Scheme 3. Treatment of aldehyde **11** with the lithium salt of the acetal derivative of 5-hexyn-2-one[14] gave a diastereomeric mixture of propargylic alcohols (ratio 2:1; 96% yield), which was further oxidized to the corresponding ynone **12** (sulfur trioxide pyridine complex, dimethyl sulfoxide;[13] 83% yield). Conversion of this to the (*Z*)-enone **13** was readily achieved by Lindlar hydrogenation (91% yield).[15] Obtention of the (*E*)-enone **14** proved more cumbersome: conjugate reduction with diisobutylaluminium hydride−hexamethylphosphoric triamide resulted in a mixture of **13** and the desired **14** (27% and 55% respectively).[16] The (*Z*)-enone **13** could be isomerized to the (*E*) derivative with lithium isopropyl thiolate (43% yield, together with recovered **13**).[17]

The Cycloadditions of Precursors 12, 13, and 14

Intramolecular Diels−Alder reactions involving furan−diene pairs (IMDAF) have been studied quite extensively on model derivatives.[8] The process has also successfully been applied in the total synthesis of various natural products.[18] The length of the tether that connects the furan and dienophile is most commonly three or four atoms, resulting in five- and six-membered ring formation upon cycloaddition. In general, when the dienophile is an alkene, the reaction involves an equilibrium situation. The position of the equilibrium depends on the substitution pattern of the dienophile, of the furan−diene pair, and the nature of the tether. In the past, several methods have been



Scheme 3. Synthesis of Diels−Alder precursors **12**, **13**, and **14**; reaction conditions: a) $CH_3C(OCH_2CH_2O)CH_2CH_2C{\equiv}CLi$, THF, −78 °C (96%; 2:1 diastereomeric mixture); b) SO_3·py, DMSO, Et_3N, CH_2Cl_2, 0 °C (83% yield); c) H_2, $Pd/CaCO_3$ poisoned with lead, toluene, room temp.; d) iBu$_2$AlH, HMPA, THF, 0 °C; e) iPrSLi, HMPA, THF, room temp.



Scheme 4. The Lewis acid catalyzed intramolecular Diels−Alder reaction of ynone **12**; reaction conditions: a) Me_2AlCl, CH_2Cl_2, −78 to −50 °C; b) H_2, $Pd/CaCO_3$ poisoned with lead, toluene, room temp.

applied to steer equilibria towards adduct formation; these include the use of β-cyclodextrin,[19] water,[19a] concentrated salt solutions,[20] and high pressure.[21] More recently, the effect of Lewis acids[22] in IMDAF processes involving six-membered ring formation with internally activated dienophiles was studied extensively by Keay;[23] in particular it was shown that the use of methylaluminium dichloride in dichloromethane at low temperature (0.1 and 1.1 equivalents) afforded high isolated yields in considerably reduced reaction times, also in the case of a β-monosubstituted dienophile.

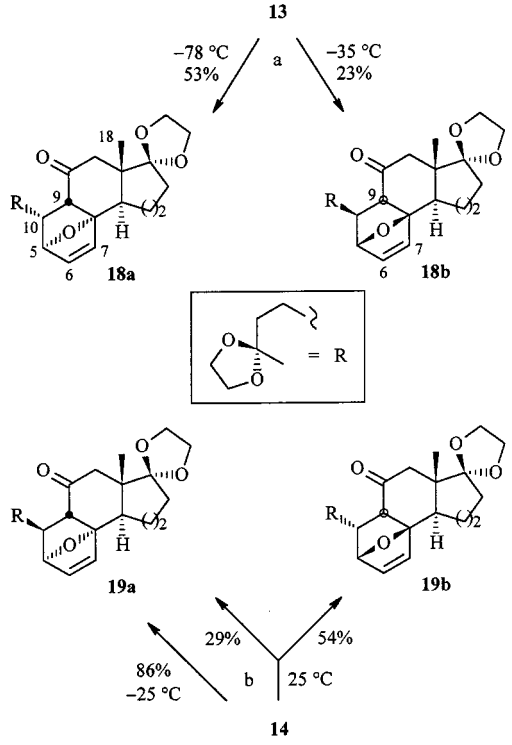
Use of these reaction conditions (1.1 equiv. of dimethylaluminium chloride in dichloromethane for 30 min at −78 °C, followed by 30 min at −50 °C) with ynone **12** (Scheme 4) resulted in a mixture of adducts **15a** and **15b** (ratio 1:1, 84% yield), together with some aromatized **16** (12% yield). Whereas separation of the two adducts was not successful at this stage, catalytic hydrogenation of the mixture of **15a** and **15b** (Lindlar catalyst, 93%) provided **17a** and **17b**, which could be obtained in pure form. The structural assignment of the two isomers was tentatively based on analysis of the ^{1}H NMR spectroscopic data (Table 1). In particular, the large geminal coupling constant (^2J = 17.8 Hz) observed for the protons at C-12 in **17b** was diagnostic of a smaller endocyclic torsion angle at bond C-11−C-12.[24] This was in line with force field calculations that showed the C ring adopting a flattened chair conformation in **17a** and a distorted boat geometry in **17b**, with associated endocyclic (C-11−C-12) dihedral angles of −37.7° and −28.7°, respectively.

When 0.1 equiv. of dimethylaluminium chloride was used in dichloromethane at −30 °C for 3 h (Scheme 5), the (*Z*)-enone **13** afforded a mixture of two adducts: **18a** (14%) and adduct **19a** (26%), together with starting material. The latter adduct must obviously result from the reaction of the corresponding (*E*)-enone **14**, formed on isomerization of the less stable (*Z*) derivative. Interestingly, the use of 1.1 equiv. of Lewis acid (−35 °C, 24 h) afforded the more stable adduct **18b** (23% isolated yield): under these conditions the process was under thermodynamic control (vide infra). On the other hand, when an excess of catalyst was used at −78 °C (two times 1 equiv., 2 h), only adduct **18a** was isolated (53% yield). The cycloaddition of (*E*)-enone **14** under kinetic control (0.1 equiv., −25 °C, 2 h) afforded a high yield (86% isolated) of *exo* adduct **19a**. At higher temperature (25 °C, 24 h) a mixture of **19a** (29% yield) and **19b** (54% yield) was formed, with the more stable adduct favored (cf. Table 3). The structural assignment of adducts **18a**, **18b**, **19a**, and **19b** was based on analysis of their ^{1}H NMR spectroscopic data, and in particular on the results of a series of NOE experiments (Table 2). The observation of an NOE effect on the protons at C-6/C-7 and on the 18-CH_3 group upon irradiation of the proton at C-9 was in agreement with

Table 1. Selected ^{1}H NMR spectroscopic data related to the B and C ring hydrogen atoms of **17a** and **17b**

Adduct		**17a**	**17b**
δ values	5-H	4.81	4.86
	12-H	2.67	2.44
	12-H	2.35	2.38
	14-H	2.62	2.36
J [Hz]	12-H,12-H	16.4	17.8

the relative α stereochemistry of the oxygen bridge (**18a**, **19a**); a similar effect upon irradiation of the proton at C-9 was only observed on protons at C-6 and C-7, indicating a β-oriented oxygen bridge (**18b**, **19b**). The relative orientation of the side chain at C-10 followed unambiguously from the magnitude of the vicinal coupling constant between the protons at C-5 and C-10: 0−1 Hz for a *cis* relationship (**18a**, **18b**) and 4−5 Hz for a *trans* relationship (**19a**, **19b**). Moreover, the *cis* and *trans* relationships between the protons at C-9 and C-10 directly follow from the magnitudes of the corresponding ^3J values: 8−9 Hz for a *cis* relationship (**18a**, **18b**) and 4−5 Hz for a *trans* relationships (**19a**, **19b**).



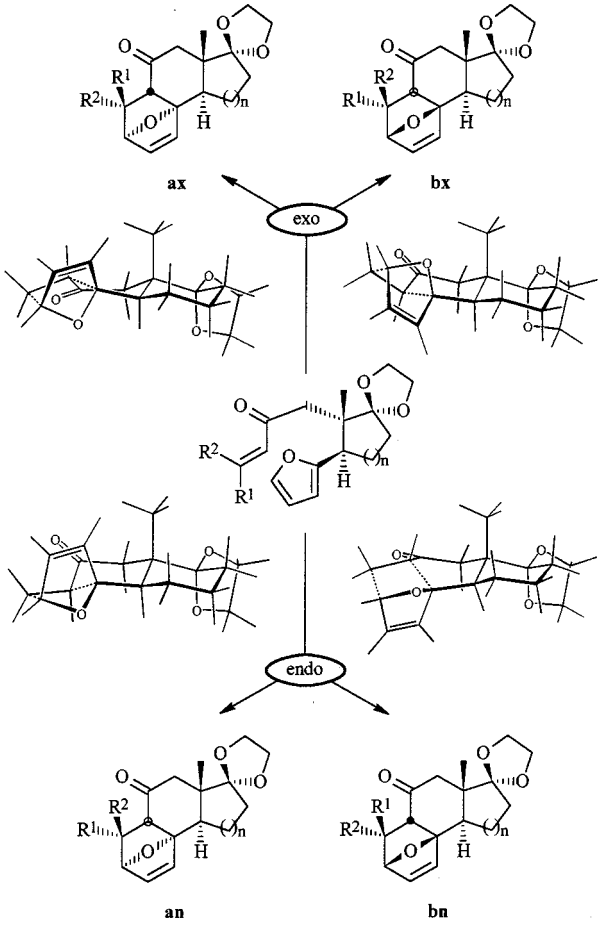
Scheme 5. The Lewis acid catalyzed intramolecular Diels−Alder reaction of enones **13** and **14**; reaction conditions: a) Me_2AlCl, CH_2Cl_2; b) Me_2AlCl, CH_2Cl_2

Table 2. ^{1}H NMR spectroscopic data related to the B and C ring hydrogen atoms of **18a**, **18b**, **19a**, and **19b**

Adduct		18a	18b	19a	19b
δ values	5-H	4.65	4.74	4.71	4.78
	6-H	6.25	6.24	6.37	6.25
	7-H	6.37	6.21	6.46	6.32
	9-H	2.23	2.09	1.95	[a]
	10-H	[a]	1.92	2.58	2.68
	12-H	2.52	2.53	2.69	2.63
	12-H	2.37	2.37	2.25	2.34
	14-H	2.42	[a]	2.14	2.58
	18-H	1.08	1.11	1.30	1.02
J [Hz]	12-H,12-H	16.3	15.6	18.7	12.7
	5-H,6-H	ca. 0	ca. 0	ca. 1	ca. 1
	6-H,7-H	5.8	5.7	5.8	5.7
	9-H,10-H	8.3	8.3	4.7	4.4
	5-H,10-H	ca. 0	ca. 0	4.2	4.4

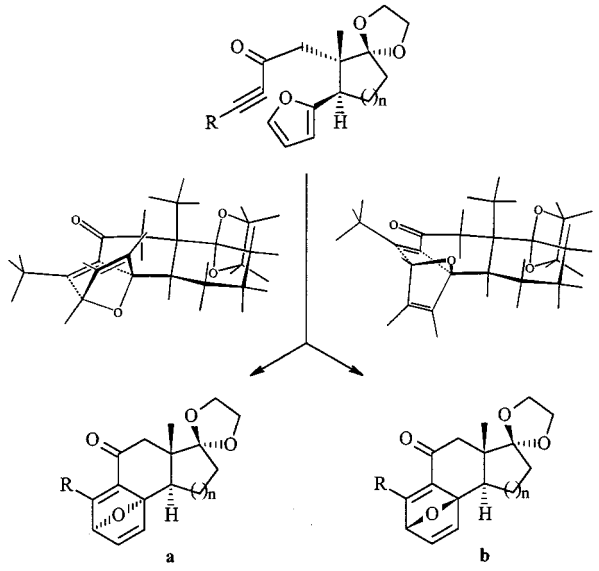
[a] Signal could not be assigned.

The stereochemical outcomes of the cycloaddition processes are outlined in Schemes 7. In the cases of the α,β-unsaturated enones **13** and **14**, four diastereomeric adducts may result. Among these, **ax** and **bx** result from *exo* addition and **an** and **bn** from the competitive *endo* addition (Scheme 6). In view of the expected asynchronicity of the reaction, one should, in the evaluation of the corresponding transition states, take account of the formation of the following ten-membered BC ring geometries: a boat-chair-boat conformation giving **ax**, a boat-chair-chair conformation giving **bx**, and distorted high-energy conformations giving the *endo* adducts. Since the boat-chair-boat form is the most stable one among those,[25] one may expect the preferred formation of **ax** adducts if the reaction proceeds under kinetic control. Under thermodynamic control, on the other hand, the **bx** adduct should predominate. Indeed, calculation of the relative steric energies of the four adducts conclusively pointed to adduct **bx** as the most stable one (Table 3).[26] The observed stereochemical outcomes of the cycloaddition reactions in the five-membered and six-membered D ring series were in full accord with the above analysis.



Scheme 6. Stereochemical outcomes of the Diels−Alder reactions of precursors with enone as dienophile (n = 1 or 2)

The cycloaddition of α,β-unsaturated ynone **12** can result in diastereoisomeric adducts **a** and **b** (Scheme 7). Calcula-



Scheme 7. Stereochemical outcomes of the Diels−Alder reactions of precursors with ynone as dienophile (n = 1 or 2)

Table 3. Relative steric energies [kJ mol^{-1}] of cycloadducts in the five-membered (n = 1) and six-membered (n = 2) D ring series according to Scheme 6

[a] Substrate	n = 1 ax	bx	an	bn	n = 2 ax	bx	an	bn
R^1 = H, R^2 = H	16.7	0.0	27.6	61.6	18.8	0.0	23.2	49.5
R^1 = Me, R^2 = H	16.4	0.0	26.1	60.1	18.5	0.0	21.5	47.7
R^1 = H, R^2 = Me	15.9	0.0	25.9	60.1	16.9	0.0	21.2	47.4

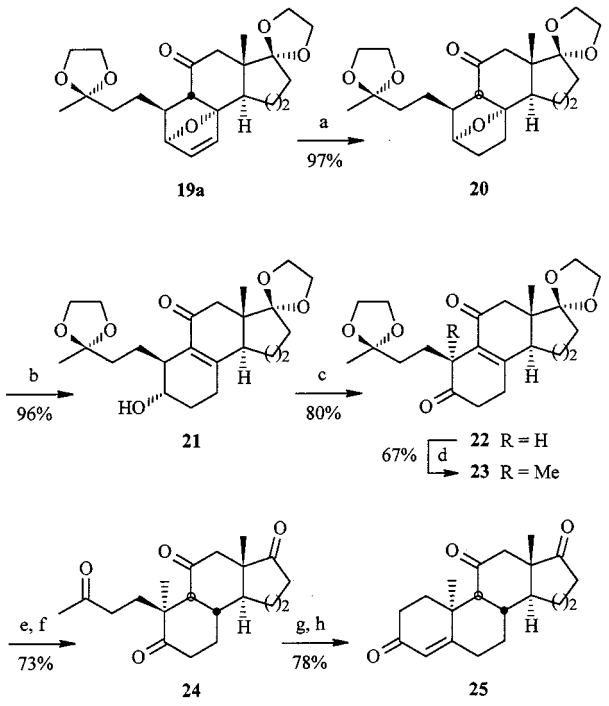
[a] Calculated by MacroModel.[26]

tion of their relative steric energies indicated only a small difference between both: 1 kJ·mol^{-1} in favor of **a** when R = Me.[26] This was also reflected in the process under kinetic control (vide supra).

The Synthesis of D-Homo-10-*epi*-adrenosterone (25)

From the above experimental work it was clear that **19a** was the most promising adduct for further work. Its conversion into a D-homo steroid derivative is shown in Scheme 8. The first part of the sequence was analogous to that that we had used in the synthesis of (±)-adrenosterone. It involved the catalytic hydrogenation of the strained double bond in **19a** (palladium on calcium carbonate, 97% yield), the opening of the oxa bridge in **20** under mild basic conditions (sodium methoxide, room temp., 96% yield), and oxidation of the resulting alcohol **21** to the corresponding enedione **22** (sulfur trioxide pyridine complex, dimethyl sulfoxide;[15] 80% yield).

In the context of the synthesis of natural steroid derivatives, the introduction of the methyl group at C-10 is a crucial step. From **22**, it involved the formation of the thermodynamic enolate anion and the stereoselective β introduction of the electrophile. After some experimentation, it was found that when equilibration conditions were used for the

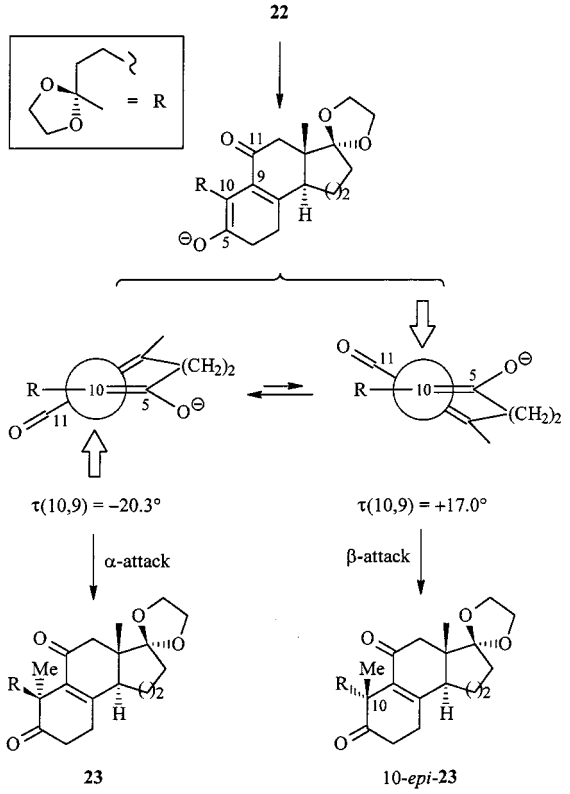


Scheme 8. Synthesis of 10-*epi*-D-homo adrenosterone (**25**); reaction conditions: a) H_2, $Pd/CaCO_3$, EtOAc, room temp.; b) NaOMe, MeOH, room temp.; c) SO_3·py, DMSO, Et_3N, CH_2Cl_2, room temp.; d) NaH (0.9 equiv.), THF, 0 °C, 4 h; MeI, room temp.; e) Li, liq. NH_3, *t*BuOH, THF, −33 °C; f) Jones' reagent, room temp.; g) KOH, MeOH, 40 °C; 37% HCl, 40 °C

enolate formation (0.9 equiv. of sodium hydride, 4 h), subsequent quaternization with iodomethane was achieved in fair yield (67%), but exclusively afforded **23**, with the unnatural configuration at C-10. The unambiguous structural assignment followed from X-ray diffraction analysis of the title compound (**25**).

A tentative explanation for the observed stereocontrol is presented in Scheme 9. Of the two B ring conformations of the intermediate enolate anion obtained from **22**, the more stable possessed an endocyclic torsion angle at the C-10−C-9 bond, characterized by a negative sign as illustrated in the Newman projection (τ = −20.3°). The conformation with the corresponding positive torsion angle (τ = +17.0°) was slightly less stable (steric energy difference of 2.2 kJ mol^{-1}).[27] The predominant destabilizing interaction in the enolate geometry was presumably the repulsive interaction between the alkyl chain R at C-10 and the carbonyl oxygen atom at C-11. One might expect perpendicular attack of the electrophile on the enolate system to occur preferentially, so as to minimize this repulsive interaction further. In the case of the more stable enolate conformation, this implied attack from the α side. Indeed, conversion of the C-10 center from sp^2 to sp^3 hybridization was accompanied by an enlargement of the dihedral angle between the C-10−C-1 and C-9−C-11 bonds. An analogous interpretation has been proposed by Stork in a similar situation.[1k]

The further conversion of **23** into the androstene derivative **25** occurred in two stages (Scheme 8). Firstly, the dissol-



Scheme 9. Stereochemical outcome of the alkylation of substrate **22**

ving-metal reduction of enone **23**, directly followed by Jones oxidation, afforded the expected more stable *trans*-fused BC ring system as present in the tetraketone **24** in 73% yield. Secondly, a classical two-step A ring annulation provided the D-homo derivative **25** in 78% yield. Final structural confirmation was obtained by X-ray diffraction analysis of **25**. A perspective view is shown in Figure 1.

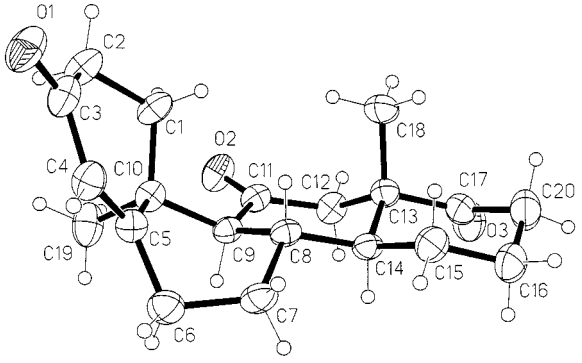


Figure 1. Perspective view of the crystal structure of **25** with atom numbering

Conclusion

This work describes the reactivity and stereochemical outcome of cycloadditions of the different precursors **12**, **13**, and **14**. The *exo* adduct **19a**, obtained with high selectivity from precursor **14**, proved to be useful for further conversion into the steroid skeleton, which resulted in the formation of D-homo-10-*epi*-adrenosterone (**25**).

Experimental Section

General: All reactions were carried out under argon with magnetic stirring. All solvents were purified or dried according to standard literature procedures. Solvent evaporations were carried out in a Rotavapor at 16 Torr. Flash chromatography was performed on SiO_2. HPLC separations were performed on Bio-Rad Bio-Sil D 90-10 columns (250 × 10 mm and 250 × 22 mm) with a Kontron 420 delivery system with RI detection. IR spectra were recorded with a Perkin−Elmer FTIR-1600 spectrometer, UV measurements with a Varian Cary 3E UV/Vis spectrometer, and mass spectra with an HP-5988 spectrometer. The ^{1}H NMR spectra were recorded at 500 MHz (Bruker AM 500), the ^{13}C NMR spectra at 50 MHz (Varian Gemini 200). The chemical shifts are expressed in ppm relative to TMS and coupling constants are in Hz. Elemental analyses were carried out by ICHOR, Université Pierre et Marie Curie (Paris, France).

3-(2′-Furanyl)-2-methyl-2-cyclohexen-1-one (5): A solution of *n*-butyllithium in hexane (1.6 M, 472 mL, 755 mmol) was added to a cooled solution (−20 °C) of furan (64.65 mL, 889 mmol) in dry tetrahydrofuran (474 mL). The mixture was stirred for 2 h at 0 °C, followed by the addition of a solution of **4** (45 g, 247 mmol) in tetrahydrofuran (80 mL). After stirring overnight at room temperature, the reaction mixture was cooled to −10 °C and treated with a mixture of a saturated NH_4Cl solution (200 mL) and HCl (44 mL−12 M) in water (40 mL). After this had stirred for 20 min, the organic phase was separated and the aqueous phase was extracted with diethyl ether. The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo, and the residue was purified by flash chromatography (from isooctane to isooctane/acetone, 9:1) followed by distillation of the residue in vacuo (Kugelrohr) to afford enone **5** (34.8 g, 83%); b.p. 130 °C/0.6 Torr. R_f = 0.58 (isooctane/ethyl acetate, 7:3). UV (MeOH): λ_{max} = 313 nm. IR (KBr): $\tilde{\nu}$ = 3118, 2946, 2867, 1650, 1593 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.03 (quint, *J* = 6.4 Hz, 2 H), 2.09 (t, *J* = 1.7 Hz, 3 H), 2.48 (br. t, *J* = 6.7 Hz, 2 H), 2.78 (dt, *J* = 1.7, 6.2 Hz, 2 H), 6.53 (dd, *J* = 1.7, 3.5 Hz, 1 H), 6.72 (d, *J* = 3.5 Hz, 1 H), 7.56 (d, *J* = 1.6 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 12.9 (CH_3), 22.0 (CH_2), 27.5 (CH_2), 37.7 (CH_2), 112.0 (CH), 114.3 (CH), 129.5 (C), 141.8 (C), 143.8 (CH), 153.0 (C), 199.4 (C). MS: *m*/*z* (%) = 176 (100) [M$^+$], 148 (48), 133 (17), 120 (74), 105 (16), 91 (78), 77 (28), 65 (22), 63 (16), 51 (29).

3-(2′-Furanyl)-2-methyl-1-trimethylsiloxy-1-cyclohexene (6): A solution of enone **5** (28.43 g, 161 mmol) in *tert*-butyl alcohol (12.17 mL, 129 mmol) and dry tetrahydrofuran (174 mL) was added at −78 °C to a suspension of lithium (3.36 g, 484 mmol) in liquid ammonia (1.2 L, distilled from sodium). After this had stirred for 30 min, isoprene was added to reduce the excess of unchanged lithium. The ammonia was evaporated in vacuo (KOH trap). The residue was dissolved in dry tetrahydrofuran (570 mL). The solution was cooled to −15 °C and treated with triethylamine (112 mL, 807 mmol) and dry chlorotrimethylsilane (102 mL, 807 mmol). After this had stirred for 30 min at −15 °C and 1 h at room temperature, pentane (600 mL) was added to the reaction mixture. After this had stirred for another 15 min, a saturated $NaHCO_3$ solution was added. After extraction with pentane, the organic phase was dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by distillation to afford **6** (31.9 g, 79%); b.p. 95 °C/0.1 Torr. R_f = 0.66 (isooctane/

ethyl acetate, 9:1). IR (KBr): $\tilde{\nu}$ = 2937, 2864, 1684 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.21 (s, 9 H), 1.54 (s, 3 H), 1.55−1.83 (m, 4 H), 2.02−2.12 (m, 2 H), 3.39 (m, 1 H), 5.95 (d, *J* = 3.2 Hz, 1 H), 6.27 (dd, *J* = 1.9, 3.1 Hz, 1 H), 7.31 (dd, *J* = 0.7, 1.8 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 0.8 (CH_3), 15.3 (CH_3), 19.9 (CH_2), 28.6 (CH_2), 30.2 (CH_2), 39.7 (CH), 105.8 (CH), 109.8 (CH), 111.8 (C), 140.7 (CH), 145.7 (C), 158.6 (C). MS: *m*/*z* (%) = 250 (19) [M^+], 235 (100), 178 (7), 107 (17), 84 (9), 73 (26).

Oxo Esters 7 and 8: A solution of methyllithium in diethyl ether (1.5 M, 40 mL, 59.9 mmol) was added to a cooled solution (0 °C) of silyl enol ether **6** (15 g, 59.9 mmol) in dry tetrahydrofuran. After deprotection of the enol ether (TLC), a mixture of ethyl bromoacetate (46.5 mL, 419 mmol) in DMPU (91 mL) was added. After stirring for 3 h at room temperature, the mixture was quenched with a saturated NH_4Cl solution. After extraction with diethyl ether, the organic phase was washed with dilute HCl solution (0.3 M), saturated $NaHCO_3$ solution, and brine. The organic phase was dried ($MgSO_4$) and concentrated in vacuo, and the residue was purified by flash chromatography and HPLC (isooctane/acetone, 9:1) to afford **7** (10 g, 63%) and **8** (0.5 g, 3%). Spectroscopic data of **7**: R_f = 0.39 (isooctane/acetone, 7:3). IR (KBr): $\tilde{\nu}$ = 2940, 2873, 1733, 1707 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.00 (s, 3 H), 1.27 (t, *J* = 7.2 Hz, 3 H), 1.86 (tq, *J* = 4.5, 13.1 Hz, 1 H), 1.95 (m, 1 H), 2.07 (m, 1 H), 2.17 (dq, *J* = 3.8, 13.0 Hz, 1 H), 2.39 (d, *J* = 17.0 Hz, 1 H), 2.47 (dddA*B*, *J* = 1.7, 3.0, 4.7, 15.5 Hz, 1 H), 2.55 (dd*A*B, *J* = 6.2, 13.2, 15.5 Hz, 1 H), 2.72 (d, *J* = 17.0 Hz, 1 H), 3.75 (dd, *J* = 3.8, 12.7 Hz, 1 H), 4.14 (q, *J* = 7.2 Hz, 2 H), 6.08 (d, *J* = 3.2 Hz, 1 H), 6.32 (dd, *J* = 1.9, 3.2 Hz, 1 H), 7.35 (d, *J* = 1.9 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 14.3 (CH_3), 20.8 (CH_3), 23.9 (CH_2), 25.7 (CH_2), 37.8 (CH_2), 40.2 (CH_2), 42.6 (CH), 50.7 (C), 60.2 (CH_2), 107.0 (CH), 109.9 (CH), 141.2 (CH), 155.2 (C), 171.9 (C), 212.8 (C). MS: *m*/*z* (%) = 264 (10) [M^+], 219 (22), 203 (22), 177 (100), 148 (11), 107 (61), 77 (25), 41 (22). $C_{15}H_{20}O_4$ (264.32): calcd. C 68.16, H 7.63; found C 68.16, H 7.66. Spectroscopic data of **8**: R_f = 0.35 (isooctane/acetone, 5:5). IR (KBr): $\tilde{\nu}$ = 2979, 2940, 1732, 1713 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.18 (s, 3 H), 1.18 (t, *J* = 7.2 Hz, 3 H), 1.74 (m, 1 H), 1.95 (m, 1 H), 2.11−2.19 (m, 2 H), 2.18 (d, *J* = 15.2 Hz, 1 H), 2.47 (ddd, *J* = 4.2, 4.9, 13.3 Hz, 1 H), 2.77 (ddd, *J* = 5.9, 12.1, 13.5 Hz, 1 H), 3.01 (d, *J* = 15.2 Hz, 1 H), 3.05 (dd, *J* = 3.7, 10.7 Hz, 1 H), 4.04 (q, *J* = 7.1 Hz, 2 H), 6.04 (d, *J* = 3.1 Hz, 1 H), 6.30 (dd, *J* = 1.9, 3.1 Hz, 1 H), 7.32 (br. d, *J* = 1.7 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 14.0 (CH_3), 21.0 (CH_3), 25.7 (CH_2), 26.0 (CH_2), 38.0 (CH_2), 39.4 (CH_2), 48.1 (CH), 51.1 (C), 60.5 (CH_2), 107.3 (CH), 110.0 (CH), 141.5 (CH), 154.4 (C), 171.4 (C), 212.4 (C). MS: *m*/*z* (%) = 264 (7) [M^+], 219 (16), 203 (12), 177 (50), 149 (4), (61), 121 (7), 79 (14), 41 (12).

Acetalization of Oxo Ester 7: A solution of oxo ester **7** (9.72 g, 36.8 mmol), ethylene glycol (10.8 mL, 195 mmol), trimethyl orthoformate (6.5 mL, 58.8 mmol), and *p*-toluenesulfonic acid (160 mg) was stirred for 24 h at room temperature. After quenching with a saturated $NaHCO_3$ solution and extraction with diethyl ether, the organic phase was dried (Na_2SO_4). After removal of the solvent in vacuo, the residue was purified by flash chromatography (isooctane/ethyl acetate, 8:2) to afford **9** (10.7 g, 94%). M.p. 38 °C (recrystallization from pentane). R_f = 0.58 (isooctane/acetone, 5:5). IR (KBr): $\tilde{\nu}$ = 2944, 2892, 1728 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.16 (s, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H), 1.56−1.70 (m, 5 H), 1.96 (dq, *J* = 3.8, 12.9 Hz, 1 H), 2.09 (A*B*, *J* = 13.5 Hz, 1 H), 2.27 (*A*B, *J* = 13.5 Hz, 1 H), 3.39 (dd, *J* = 3.3, 13.1 Hz, 1 H), 3.93 (m, 3 H), 4.04 (m, 1 H), 4.04 (q, *J* = 7.1 Hz, 2 H), 6.15 (d, *J* = 3.1 Hz, 1 H), 6.28 (dd, *J* = 1.9, 3.0 Hz, 1 H), 7.31 (br. d, *J* = 1.1 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 14.2 (CH_3), 17.5 (CH_3), 22.2 (CH_2), 25.8 (CH_2), 29.4 (CH_2), 39.9 (CH_2), 42.4 (CH), 46.7 (C), 59.7 (CH_2), 64.1 (CH_2), 64.4 (CH_2), 107.2 (CH), 109.8 (CH), 112.1 (C), 140.9 (CH), 156.5 (C), 172.7 (C). MS: *m*/*z* (%) = 308 (32) [M^+], 293 (5), 263 (10), 221 (58), 177 (16), 113 (65), 99 (100), 77 (32), 41 (48). $C_{17}H_{24}O_5$ (308.37): calcd. C 66.21, H 7.85; found C 66.22, H 7.84.

Reduction of Ester 9 to Alcohol 10: A solution of ester **9** (10.55 g, 34.2 mmol) in diethyl ether (125 mL) was added at 0 °C to a suspension of lithium aluminium hydride (2.60 g, 68.4 mmol) in dry diethyl ether (67 mL). After this had stirred for 1 h at 0 °C, sodium sulfate decahydrate was added portionwise. Stirring was continued at room temperature until a white suspension had formed. After filtration off of the solid, the solvent was evaporated in vacuo. The residue was lyophilized to afford **10** (8.2 g, 90%). R_f = 0.39 (isooctane/acetone, 5:5). IR (KBr): $\tilde{\nu}$ = 3388, 3114, 2952, 2888 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.08 (s, 3 H), 1.47−1.71 (m, 6 H), 1.76 (ddd, *J* = 7.6, 7.6, 14.8 Hz, 1 H), 1.87 (dq, *J* = 3.5, 13.6 Hz, 1 H), 1.98 (br. s, OH), 3.04 (dd, *J* = 3.3, 13.1 Hz, 1 H), 3.42 (m, 1 H), 3.59 (br. dt, *J* = 8.4, 8.4 Hz, 1 H), 3.95−4.04 (m, 4 H), 6.02 (d, *J* = 3.0 Hz, 1 H), 6.29 (dd, *J* = 1.9, 3.1 Hz, 1 H), 7.30 (br. d, *J* = 1.6 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 16.3 (CH_3), 22.2 (CH_2), 26.5 (CH_2), 29.3 (CH_2), 38.0 (CH_2), 43.9 (CH), 44.6 (C), 59.8 (CH_2), 64.0 (CH_2), 64.4 (CH_2), 106.6 (CH), 109.9 (CH), 112.7 (C), 140.6 (CH), 157.2 (C). MS: *m*/*z* (%) = 266 (21) [M^+], 221 (22), 157 (10), 122 (17), 113 (64), 99 (100), 77 (35), 41 (48).

Oxidation of Alcohol 10 to Aldehyde 11: Dry triethylamine (41 mL) was added at −10 °C to a solution of alcohol **10** (7.96 g, 29.9 mmol) in dry dichloromethane (74 mL) and dry dimethyl sulfoxide (74 mL). After 30 min, sulfur trioxide pyridine complex (28.5 g, 179 mmol) was added portionwise to the reaction mixture. After 1 h of stirring at −10 °C, stirring was continued at 0 °C for 4 h. The reaction mixture was purified by flash chromatography (from isooctane/ethyl acetate, 45:1 to isooctane/ethyl acetate, 9.5:0.5) to afford **11** (7.4 g, 94%). M.p. 64 °C (recrystallization from isooctane). R_f = 0.48 (isooctane/acetone, 5:5). IR (KBr): $\tilde{\nu}$ = 2950, 2892, 1711 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.18 (s, 3 H), 1.57−1.74 (m, 5 H), 1.93 (dq, *J* = 3.8, 12.9 Hz, 1 H), 2.08 (dA*B*, *J* = 3.2, 15.1 Hz, 1 H), 2.21 (d*A*B, *J* = 3.2, 15.1 Hz, 1 H), 3.32 (dd, *J* = 3.5, 13.1 Hz, 1 H), 3.77−3.94 (m, 4 H), 6.06 (d, *J* = 3.2 Hz, 1 H), 6.31 (dd, *J* = 1.9, 3.2 Hz, 1 H), 7.32 (br. d, *J* = 0.8 Hz, 1 H), 9.79 (dd, *J* = 3.5, 3.5 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 17.3 (CH_3), 22.2 (CH_2), 25.4 (CH_2), 29.5 (CH_2), 42.4 (CH), 47.2 (C), 49.4 (CH_2), 64.2 (CH_2), 64.3 (CH_2), 107.0 (CH), 110.0 (CH), 111.6 (C), 141.0 (CH), 156.2 (C), 201.4 (CH). MS: *m*/*z* (%) = 264 (9) [M^+], 221 (18), 113 (41), 99 (100), 77 (20), 41 (29).

Diels−Alder Precursor 12: A solution of *n*-butyllithium in hexane (2.5 M, 21 mL, 52.5 mmol) was added at −78 °C to a solution of the acetal derivative of 5-hexyn-2-one (7.36 g, 52.5 mmol) in dry tetrahydrofuran (41 mL). After 1 h at −78 °C, a solution of the aldehyde **11** (6.94 g, 26.2 mmol) in tetrahydrofuran (68 mL) was added. After a further 1 h of stirring at −78 °C, the reaction mixture was then further stirred at 0 °C for 1 h. The mixture was quenched with a saturated NH_4Cl solution. After extraction with diethyl ether, the organic phase was dried (Na_2SO_4), the solvent was removed in vacuo, and the residue was purified by flash chromatography (isooctane/acetone, 7:3) to afford a mixture of the propargylic diastereoisomeric alcohols (10.2 g, 96%) in 7:3 ratio. These were immediately further oxidized to ynone **12**. Dry triethylamine (35 mL) was added at −10 °C to a solution of the propargylic alco-

hols (9.94 g, 24.6 mmol) in dry dichloromethane (63 mL) and dry dimethyl sulfoxide (63 mL). After 30 min, sulfur trioxide pyridine complex (23.5 g, 147 mmol) was added portionwise to the reaction mixture. After 1 h of stirring at −10 °C, stirring was continued for 4 h at 0 °C. The reaction mixture was purified by flash chromatography (from isooctane/acetone, 45:1, to isooctane/acetone, 9:1, and to isooctane/acetone, 8.5:1.5) to afford ynone **12** (8.2 g, 83%). R_f = 0.52 (isooctane/acetone, 5:5). UV (MeOH): λ_{max} = 218 nm. IR (KBr): $\tilde{\nu}$ = 2933, 2889, 2215, 1659 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.24 (s, 3 H), 1.30 (s, 3 H), 1.52−1.69 (m, 5 H), 1.92 (m, 2 H), 1.95 (dq, *J* = 4.2, 13.8 Hz, 1 H), 2.26 (d, *J* = 13.1 Hz, 1 H), 2.42 (m, 2 H), 2.57 (d, *J* = 13.1 Hz, 1 H), 3.34 (dd, *J* = 3.4, 13.1 Hz, 1 H), 3.86−3.97 (m, 7 H), 4.05 (m, 1 H), 6.13 (d, *J* = 3.1 Hz, 1 H), 6.29 (dd, *J* = 1.9, 3.0 Hz, 1 H), 7.31 (br. d, *J* = 1.0 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 13.8 (CH_2), 17.6 (CH_3), 22.1 (CH_2), 23.8 (CH_3), 25.7 (CH_2), 29.0 (CH_2), 37.0 (CH_2), 43.0 (CH), 48.7 (C), 50.4 (CH_2), 63.7 (CH_2), 64.1 (CH_2), 64.8 (CH_2), 64.8 (CH_2), 82.7 (C), 91.3 (C), 107.2 (CH), 108.7 (C), 109.9 (CH), 111.8 (C), 140.9 (CH), 156.3 (C), 186.9 (C). MS: *m*/*z* (%) = 402 (2) [M^+], 220 (33), 177 (5), 148 (11), 87 (100), 43 (50). $C_{23}H_{30}O_6$ (402.49): calcd. C 68.64, H 7.51; found C 68.53, H 7.68.

Diels−Alder Precursor 13: A mixture of ynone **12** (1.01 g, 2.5 mmol) in toluene (24 mL) and Lindlar's catalyst (5% Pd/$CaCO_3$ poisoned with lead, 536 mg) was hydrogenated for 24 h at room temperature. After filtration through Celite, the solvent was removed in vacuo. The residue was purified by flash chromatography (isooctane/acetone, 9:1) to afford **13** (928 mg, 91%). R_f = 0.19 (isooctane/diethyl ether, 5:5). UV (MeOH): λ_{max} = 218 nm. IR (KBr): $\tilde{\nu}$ = 2986, 2953, 1682, 1614 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.21 (s, 3 H), 1.32 (s, 3 H), 1.50−1.68 (m, 5 H), 1.75 (t, *J* = 7.9 Hz, 2 H), 1.92 (br. dq, *J* = 3.7, 13.8 Hz, 1 H), 2.13 (d, *J* = 12.9 Hz, 1 H), 2.48 (d, *J* = 12.9 Hz, 1 H), 2.65 (br. dt, *J* = 7.6, 7.6 Hz, 2 H), 3.26 (dd, *J* = 3.2, 13.2 Hz, 1 H), 3.81−3.95 (m, 7 H), 4.03 (br. dt, *J* = 7.3, 7.3 Hz, 1 H), 5.93 (t*A*B, *J* = 7.2, 11.5 Hz, 1 H), 6.05 (*A*B, *J* = 11.5 Hz, 1 H), 6.11 (d, *J* = 3.0 Hz, 1 H), 6.28 (s, 1 H), 7.29 (br. s, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 18.1 (CH_3), 22.4 (CH_2), 24.2 (CH_3), 24.6 (CH_2), 26.4 (CH_2), 29.1 (CH_2), 38.9 (CH_2), 43.6 (CH), 48.6 (C), 49.4 (CH_2), 63.6 (CH_2), 64.1 (CH_2), 64.7 (CH_2), 64.7 (CH_2), 107.6 (CH), 110.2 (CH), 112.0 (C), 128.3 (CH), 129.6 (CH), 141.0 (C), 144.7 (CH), 157.2 (C), 199.6 (C). MS: *m*/*z* (%) = 404 (2) [M^+], 220 (32), 192 (5), 176 (6), 148 (13), 113 (29), 87 (100), 43 (45).

Diels−Alder Precursor 14: A solution of diisobutylaluminium hydride in hexane (1.0 M, 19.9 mL, 19.9 mmol) was added at 0 °C to a solution of dry tetrahydrofuran (50 mL) and hexamethylphosphoric triamide (HMPA, 10.5 mL). After 30 min of stirring at 0 °C, a solution of ynone **12** (4.03 g, 9.95 mmol) in dry tetrahydrofuran (14 mL) was added. After the reaction mixture had been stirred for 4 h at 0 °C, a 1 M HCl solution and diethyl ether were added. The organic phase was washed with a saturated $NaHCO_3$ solution and brine, and was then dried (Na_2SO_4). After removal of the solvent in vacuo, the residue, consisting of a mixture of **13** and **14**, was separated by HPLC (isooctane/diethyl ether, 5:5) to afford **13** (2.5 g, 61%) and **14** (1.1 g, 27%). R_f = 0.11 (isooctane/diethyl ether, 5:5). UV (MeOH): λ_{max} = 218 nm. IR (KBr): $\tilde{\nu}$ = 2952, 2889, 1688, 1625 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.20 (s, 3 H), 1.31 (s, 3 H), 1.52−1.70 (m, 5 H), 1.76 (m, 2 H), 1.94 (br. dq, *J* = 3.8, 13.8 Hz, 1 H), 2.25 (d, *J* = 13.0 Hz, 1 H), 2.23−2.30 (m, 2 H), 2.47 (d, *J* = 13.0 Hz, 1 H), 3.35 (dd, *J* = 3.4, 13.2 Hz, 1 H), 3.75 (br. dt, *J* = 6.9, 6.9 Hz, 1 H), 3.85−3.97 (m, 7 H), 6.08 (br. d, *J* = 15.5 Hz, 1 H), 6.15 (d, *J* = 3.1 Hz, 1 H), 6.28 (dd, *J* = 1.9, 2.9 Hz, 1 H), 6.68 (td, *J* = 6.9, 15.5 Hz, 1 H), 7.29 (s, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 17.8 (CH_3), 22.1 (CH_2), 24.0 (CH_3), 26.0 (CH_2), 26.8 (CH_2), 28.4 (CH_2), 37.6 (CH_2), 43.2 (CH), 45.1 (CH_2), 48.1 (C), 63.3 (CH_2), 63.8 (CH_2), 64.7 (CH_2), 64.7 (CH_2), 107.2 (CH), 109.4 (C), 109.9 (CH), 112.0 (C), 131.8 (CH), 140.8 (CH), 143.9 (CH), 156.6 (C), 199.6 (C). MS: *m*/*z* (%) = 404 (3) [M^+], 220 (53), 192 (12), 148 (23), 113 (43), 99 (100), 43 (72). $C_{23}H_{32}O_6$ (402.49): calcd. C 68.30, H 7.97; found C 68.21, H 8.04.

Conversion of Enone 13 into 14: A solution of *n*-butyllithium in hexane (2.5 M, 56.3 μL, 0.14 mmol) was added at 0 °C to a solution of 2-propanethiol (13.4 μL, 1.41 mmol) in dry tetrahydrofuran (4.5 mL). After 30 min of stirring, the reaction mixture was allowed to warm to room temperature and a solution of **13** (0.57 g, 1.41 mmol) in tetrahydrofuran (4.47 mL) was added. After this had stirred for 4 h at room temperature, a saturated NH_4Cl solution was added. The aqueous phase was extracted with diethyl ether, and the combined organic phases were dried (Na_2SO_4). After removal of the solvent in vacuo, the residue, a mixture of **13** and **14**, was separated by HPLC (isooctane/diethyl ether, 5:5) to afford **14** (245 mg, 43%).

Conversion of Ynone 12 into 17a and 17b: A solution of dimethylaluminium chloride in hexane (1.0 M, 8.47 mL, 8.5 mmol) was added at −78 °C to a solution of precursor **12** (3.1 g, 7.7 mmol) in dry dichloromethane (154 mL). After this had stirred for 30 min at −78 °C, the temperature was raised to −50 °C and stirring was continued for another 30 min. The reaction mixture was quenched with a saturated $NaHCO_3$ solution and allowed to warm slowly to room temperature. The aqueous phase was extracted with dichloromethane and the combined organic phases were dried (Na_2SO_4). After removal of the solvent in vacuo, the residue was purified by flash chromatography (isooctane/acetone, 8:2) to afford a mixture of **15a** and **15b** (2.6 g, 84%, ratio 1:1) and aromatized product **16** (372 mg, 12%). Spectroscopic data for **16**: R_f = 0.27 (isooctane/acetone, 7:3). IR (KBr): $\tilde{\nu}$ = 3451, 2946, 2880, 1672, 1589 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.90 and 0.92 (s, 3 H), 1.56 and 1.57 (s, 3 H), 7.00 (d, *J* = 8.6 Hz, 1 H), 7.15 and 7.17 (br. d, *J* = 8.3 Hz, 1 H). MS: *m*/*z* (%) = 87 (100), 43 (42). A mixture of adducts **15a** and **15b** (2.09 g, 5.2 mmol) in toluene (40 mL) and Lindlar's catalyst (5% Pd/$CaCO_3$ poisoned with lead, 1.11 g) was hydrogenated for 2 h at room temperature. After filtration through Celite, the solvent was removed in vacuo. The residue was purified by flash chromatography (isooctane/acetone, 8:2) to afford a mixture of **17a** and **17b** (1.95 g, 93%, ratio 1:1). The two products could be separated by HPLC (isooctane/acetone, 87:13).

Spectroscopic Data of 17a: M.p. 125 °C (recrystallization from isooctane/acetone). R_f = 0.19 (isooctane/acetone, 8:2). UV (MeOH): λ_{max} = 253 nm. IR (KBr): $\tilde{\nu}$ = 2948, 2872, 1673, 1622 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.07 (d, *J* = 0.8 Hz, 3 H), 1.27 (m, 1 H), 1.35 (m, 1 H), 1.34 (s, 3 H), 1.53−1.90 (m, 9 H), 1.98 (m, 1 H), 2.35 (d, *J* = 16.4 Hz, 1 H), 2.54 (ddd, *J* = 5.2, 11.3, 14.4 Hz, 1 H), 2.62 (dd, *J* = 3.5, 12.1 Hz, 1 H), 2.67 (d, *J* = 16.4 Hz, 1 H), 2.90 (ddd, *J* = 5.7, 11.2, 14.3 Hz, 1 H), 3.88−4.01 (m, 8 H), 4.81 (d, *J* = 5.1 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 17.4 (CH_3), 21.5 (CH_2), 21.5 (CH_2), 22.0 (CH_2), 23.8 (CH_3), 25.7 (CH_2), 26.2 (CH_2), 30.0 (CH_2), 36.5 (CH_2), 42.1 (CH), 44.3 (C), 47.6 (CH_2), 64.7 (CH_2), 65.0 (CH_2), 65.1 (CH_2), 65.3 (CH_2), 79.5 (CH), 89.7 (C), 109.4 (C), 111.5 (C), 136.8 (C), 160.6 (C), 197.2 (C). MS: *m*/*z* (%) = 376 (2), 112 (14), 87 (100), 43 (27). $C_{23}H_{32}O_6$ (404.50): calcd. C 68.30, H 7.97; found C 67.54, H 7.94.

Spectroscopic Data for 17b: R_f = 0.19 (isooctane/acetone, 8:2). IR (KBr): $\tilde{\nu}$ = 2946, 2878, 1674, 1622 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.09 (s, 3 H), 1.34 (s, 3 H), 1.33 (m, 2 H), 1.46−1.94

(m, 10 H), 2.36 (m, 1 H), 2.38 (A*B*, J = 17.8 Hz, 1 H), 2.44 (*A*B, J = 17.8 Hz, 1 H), 2.57 (ddd, J = 5.2, 10.9, 14.3 Hz, 1 H), 2.95 (ddd, J = 5.9, 10.8, 14.2 Hz, 1 H), 3.90−3.99 (m, 8 H), 4.86 (d, J = 5.1 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 16.1 (CH_3), 20.1 (CH_2), 21.7 (CH_2), 22.6 (CH_2), 23.8 (CH_3), 24.5 (CH_2), 29.8 (CH_2), 30.7 (CH_2), 36.3 (CH_2), 42.6 (CH), 44.0 (C), 47.6 (CH_2), 64.7 (CH_2), 64.8 (CH_2), 65.0 (CH_2), 65.1 (CH_2), 81.2 (CH), 88.3 (C), 109.3 (C), 111.6 (C), 137.6 (C), 161.1 (C), 196.4 (C). MS: *m*/*z* (%) = 376 (2), 112 (15), 87 (100), 43 (26).

Diels−Alder Adduct 18a: A solution of dimethylaluminium chloride in hexane (1.0 M, 0.51 mL, 0.51 mmol) was added at −78 °C to a solution of precursor **13** (204 mg, 0.51 mmol) in dry dichloromethane (10 mL). After this had stirred for 1 h at −78 °C, the same amount of catalyst was added and stirring was continued for another 1 h at −78 °C. The reaction mixture was then quenched with a saturated $NaHCO_3$ solution and allowed to warm slowly to room temperature. The aqueous phase was extracted with dichloromethane and the combined organic phases were dried (Na_2SO_4). After removal of the solvent in vacuo, the residue was purified by flash chromatography (isooctane/acetone, 8:2) to afford **18a** (108 mg, 53%). M.p. 109 °C (recrystallization from isooctane/acetone). R_f = 0.17 (isooctane/acetone, 8:2). IR (KBr): $\tilde{\nu}$ = 2932, 2872, 1697cm^{-1}. ^{1}H NMR/H,H-COSY (500 MHz, $CDCl_3$): δ = 1.08 (s, 3 H), 1.08−1.16 (m, 1 H), 1.30 (s, 3 H), 1.59−1.75 (m, 8 H), 1.94−2.05 (m, 2 H), 2.23 (d, J = 8.3 Hz, 1 H), 2.37 (A*B*, J = 16.3 Hz, 1 H), 2.42 (dd, J = 2.7, 12.1 Hz, 1 H), 2.52 (*A*B, J = 16.3 Hz, 1 H), 3.87−3.98 (m, 8 H), 4.65 (s, 1 H), 6.25 (d, J = 5.8 Hz, 1 H), 6.37 (d, J = 5.8 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 16.7 (CH_3), 22.7 (CH_2), 23.8 (CH_3), 24.0 (CH_2), 24.6 (CH_2), 29.9 (CH_2), 37.7 (CH_2), 42.4 (CH), 43.4 (C), 44.1 (CH), 48.4 (CH_2), 52.5 (CH), 64.6 (CH_2), 64.6 (CH_2), 65.2 (CH_2), 65.2 (CH_2), 79.0 (CH), 91.4 (C), 110.0 (C), 111.5 (C), 134.8 (CH), 138.1 (CH), 212.1 (C). MS: *m*/*z* (%) = 404 (2) [M$^+$], 220 (46), 176 (8), 148 (16), 113 (19), 99 (48), 87 (100), 43 (78). $C_{23}H_{32}O_6$ (404.50): calcd. C 68.30, H 7.97; found C 68.19, H 8.07.

Diels−Alder Adduct 18b: A solution of dimethylaluminium chloride in hexane (1.0 M, 0.55 mL, 0.55 mmol) was added at −35 °C to a solution of precursor **13** (216.8 mg, 0.54 mmol) in dry dichloromethane (11 mL). After stirring for 24 h at −35 °C, the reaction mixture was quenched with a saturated $NaHCO_3$ solution and allowed to warm slowly to room temperature. The aqueous phase was extracted with dichloromethane and the organic phases were dried (Na_2SO_4). After removal of the solvent in vacuo, the residue was purified by flash chromatography (isooctane/acetone, 8:2) to afford **18b** (50 mg, 23%). M.p. 133 °C (recrystallization from isooctane/acetone). R_f = 0.15 (isooctane/acetone, 8:2). IR (KBr): $\tilde{\nu}$ = 2933, 2872, 1703 cm^{-1}. ^{1}H NMR/H,H-COSY (500 MHz, $CDCl_3$): δ = 1.11 (s, 3 H), 1.34 (s, 3 H), 1.58−1.84 (m, 10 H), 1.92 (ddd, J = 3.3, 8.5, 11.6 Hz, 1 H), 2.09 (d, J = 8.3 Hz, 1 H), 2.37 (A*B*, J = 15.6 Hz, 1 H), 2.45 (m, 1 H), 2.53 (*A*B, J = 15.6 Hz, 1 H), 3.87−4.00 (m, 8 H), 4.74 (br. s, 1 H), 6.21 (A*B*, J = 5.7 Hz, 1 H), 6.24 (d*A*B, J = 1.6, 5.7 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 17.4 (CH_3), 22.4 (CH_2), 22.6 (CH_2), 23.9 (CH_3), 24.3 (CH_2), 29.6 (CH_2), 38.6 (CH_2), 41.6 (CH), 42.8 (CH), 47.4 (C), 48.4 (CH_2), 52.4 (CH), 64.8 (CH_2), 65.1 (CH_2), 65.2 (CH_2), 65.3 (CH_2), 81.7 (CH), 91.7 (C), 110.2 (C), 111.9 (C), 134.7 (CH), 140.0 (CH), 210.1 (C). MS: *m*/*z* (%) = 404 (1) [M$^+$], 220 (20), 176 (3), 148 (8), 113 (10), 99 (40), 87 (100), 43 (53). $C_{23}H_{32}O_6$ (404.50): calcd. C 68.30, H 7.97; found C 68.17, H 8.12.

Diels−Alder Adduct 19a: A solution of dimethylaluminium chloride (1.0 M, 0.5 mL, 0.55 mmol) in hexane was added at −25 °C to a solution of **14** (2.0 g, 4.98 mmol) in dry dichloromethane (100 mL). After 2 h of stirring at −25 °C, the reaction mixture was quenched with a saturated $NaHCO_3$ solution and allowed to warm slowly to room temperature. The aqueous phase was extracted with dichloromethane and the combined organic phases were dried (Na_2SO_4). After removal of the solvent in vacuo, the residue was purified by flash chromatography (isooctane/acetone, 8:2) to afford **19a** (1.7 g, 86%). M.p. 116 °C (recrystallization from isooctane/acetone). R_f = 0.17 (isooctane/acetone, 8:2). IR (KBr): $\tilde{\nu}$ = 2984, 2948, 2884, 1705 cm^{-1}. ^{1}H NMR/H,H-COSY (500 MHz, $CDCl_3$): δ = 1.27 (s, 3 H), 1.30 (s, 3 H), 1.25−1.31 (m, 1 H), 1.52−1.73 (m, 9 H), 1.95 (d, J = 4.7 Hz, 1 H), 2.14 (dd, J = 3.3, 11.9 Hz, 1 H), 2.25 (d, J = 18.7 Hz, 1 H), 2.58 (tt, J = 4.5, 7.9 Hz, 1 H), 2.69 (d, J = 18.7 Hz, 1 H), 3.87−3.99 (m, 8 H), 4.71 (dd, J = 1.0, 4.2 Hz, 1 H), 6.37 (A*B*, J = 5.8 Hz, 1 H), 6.46 (*A*B, J = 5.8 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 18.3 (CH_3), 22.2 (CH_2), 23.8 (CH_3), 24.2 (CH_2), 27.1 (CH_2), 29.4 (CH_2), 37.9 (CH_2), 41.6 (CH), 42.8 (CH), 43.1 (C), 46.0 (CH_2), 57.4 (CH), 64.6 (CH_2), 64.6 (CH_2), 64.8 (CH_2), 65.1 (CH_2), 79.2 (CH), 93.3 (C), 109.6 (C), 111.7 (C), 134.9 (CH), 137.1 (CH), 210.4 (C). MS: *m*/*z* (%) = 404 (3) [M$^+$], 220 (52), 176 (10), 148 (16), 113 (27), 99 (100), 87 (68), 43 (67). $C_{23}H_{32}O_6$ (404.50): calcd. C 68.30, H 7.97; found C 68.11, H 8.13.

Diels−Alder Adduct 19b: A solution of dimethylaluminium chloride in hexane (1.0 M, 16 μL, 0.016 mmol) was added at room temperature to a solution of **14** (63.9 mg, 0.16 mmol) in dry dichloromethane (3 mL). After stirring for 24 h at room temperature, the reaction mixture was quenched with a saturated $NaHCO_3$ solution. The aqueous phase was extracted with dichloromethane and the combined organic phases were dried (Na_2SO_4). After removal of the solvent in vacuo, the residue was separated by HPLC (isooctane/acetone, 8:2) to afford **19b** (34.5 mg, 54%) and **19a** (18.5 mg, 29%). M.p. 108 °C (recrystallization from isooctane). R_f = 0.17 (isooctane/acetone, 8:2). IR (KBr): $\tilde{\nu}$ = 2933, 2872, 1708 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.02 (s, 3 H), 1.27 (s, 3 H), 1.23−1.29 (m, 2 H), 1.74 (br. d, J = 3.9 Hz, 1 H), 1.50−1.79 (m, 8 H), 2.34 (d, J = 12.7 Hz, 1 H), 2.58 (dd, J = 2.3, 12.3 Hz, 1 H), 2.63 (d, J = 12.7 Hz, 1 H), 2.68 (tt, J = 4.4, 8.1 Hz, 1 H), 3.86−3.92 (m, 6 H), 3.93−4.01 (m, 2 H), 4.78 (dd, J = 0.8, 4.4 Hz, 1 H), 6.25 (A*B*, J = 5.7 Hz, 1 H), 6.32 (d*A*B, J = 1.4, 5.7 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 16.6 (CH_3), 22.4 (CH_2), 22.7 (CH_2), 23.7 (CH_3), 27.1 (CH_2), 29.8 (CH_2), 37.9 (CH_2), 42.1 (CH), 42.3 (CH), 46.3 (CH_2), 47.3 (C), 58.2 (CH), 64.6 (CH_2), 64.6 (CH_2), 65.1 (CH_2), 65.2 (CH_2), 81.4 (CH), 94.3 (C), 109.7 (C), 111.8 (C), 134.4 (CH), 139.4 (CH), 209.7 (C). MS: *m*/*z* (%) = 404 (3) [M$^+$], 220 (36), 176 (11), 148 (16), 113 (16), 99 (62), 87 (100), 43 (76). $C_{23}H_{32}O_6$ (404.50): calcd. C 68.30, H 7.97; found C 68.08, H 8.12.

Hydrogenation of 19a: A mixture of **19a** (2.20 g, 5.4 mmol) and palladium calcium carbonate (10% Pd, 145 mg) in ethyl acetate (89 mL) was hydrogenated for 24 h at room temperature. After filtration through Celite, the solvent was removed in vacuo. The residue was purified by flash chromatography (isooctane/acetone, 7:3) to afford **20** (2.1 g, 97%). M.p. 111 °C (recrystallization from isooctane/acetone). R_f = 0.43 (isooctane/acetone, 5:5). IR (KBr): $\tilde{\nu}$ = 2949, 2882, 1705 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.25 (s, 3 H), 1.30 (s, 3 H), 1.42 (m, 2 H), 1.50−1.71 (m, 10 H), 1.85 (m, 2 H), 1.96 (d, J = 6.4 Hz, 1 H), 2.14 (d, J = 18.6 Hz, 1 H), 2.22 (dd, J = 3.6, 12.1 Hz, 1 H), 2.45 (m, 1 H), 2.67 (d, J = 18.6 Hz, 1 H), 3.88−4.01 (m, 8 H), 4.26 (t, J = 5.1 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 18.9 (CH_3), 22.0 (CH_2), 23.8 (CH_3), 23.8 (CH_2), 24.6 (CH_2), 25.8 (CH_2), 29.3 (CH_2), 32.2 (CH_2), 37.8 (CH_2), 42.6 (CH), 43.1 (C), 43.6 (CH), 45.9 (CH_2), 61.1 (CH), 64.7 (CH_2), 64.7 (CH_2), 65.0 (CH_2), 65.0 (CH_2), 77.3 (CH), 90.0 (C), 109.7 (C),

111.8 (C), 211.2 (C). MS: *m*/*z* (%) = 406 (7) [M$^+$], 362 (11), 344 (7), 304 (14), 112 (63), 99 (98), 87 (92), 55 (44), 44 (100). $C_{23}H_{34}O_6$ (406.52): calcd. C 67.96, H 8.43; found C 67.89, H 8.58.

Opening of the Oxygen Bridge in 20: A solution of **20** (2.06 g, 5.06 mmol) in methanol was added to a solution of sodium (233 mg, 10.12 mmol) in dry methanol (73 mL). After stirring for 2 h at room temperature, the reaction mixture was concentrated in vacuo and the residue was dissolved in water. After extraction with diethyl ether, the organic phase was dried (Na_2SO_4). After removal of the solvent in vacuo, the residue was purified by flash chromatography (isooctane/acetone, 7:3) to afford **21** (2.0 g, 96%). M.p. 155 °C (recrystallization from isooctane/acetone). R_f = 0.40 (isooctane/acetone, 5:5). UV (MeOH): λ_{max} = 252 nm. IR (KBr): nu (tilde) = 3444, 2949, 2882, 1657, 1614 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.00 (s, 3 H), 1.20 (m, 1 H), 1.30 (s, 3 H), 1.32 (m, 1 H), 1.56−1.60 (m, 4 H), 1.67−1.83 (m, 6 H), 1.89 (m, 1 H), 2.23 (m, 2 H), 2.33 (A*B*, *J* = 16.7 Hz, 1 H), 2.58 (*A*B, *J* = 16.7 Hz, 1 H), 2.69 (br. s, OH), 2.80 (d, *J* = 11.9 Hz, 1 H), 3.91−3.98 (m, 9 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 15.1 (CH_3), 22.5 (CH_2), 22.9 (CH_2), 23.5 (CH_3), 23.7 (CH_2), 24.6 (CH_2), 28.8 (CH_2), 29.2 (CH_2), 36.7 (CH_2), 39.3 (CH), 44.3 (CH), 44.3 (C), 44.4 (CH_2), 64.4 (CH_2), 64.5 (CH_2), 65.0 (CH_2), 65.2 (CH_2), 67.3 (CH), 110.0 (C), 111.3 (C), 132.7 (C), 155.8 (C), 198.3 (C). MS: *m*/*z* (%) = 292 (3), 274 (3), 115 (27), 87 (100), 43 (30). $C_{23}H_{34}O_6$ (406.52): calcd. C 67.96, H 8.43; found C 67.81, H 8.56.

Oxidation of 21: Dry triethylamine (7 mL) was added at 0 °C to a solution of alcohol **21** (2.06 g, 5.06 mmol) in dry dichloromethane (13 mL) and dry dimethyl sulfoxide (13 mL). Sulfur trioxide pyridine complex (4.83 g, 30.4 mmol) was added portionwise. After stirring for 1 h at 0 °C, the reaction mixture was purified by flash chromatography (from isooctane to isooctane/acetone, 8:2) to afford **22** (1.6 g, 80%). M.p. 108 °C (recrystallization from isooctane/acetone). R_f = 0.45 (isooctane/acetone, 5:5). UV (MeOH): λ_{max} = 251 nm. IR (KBr): ṽ = 2951, 2876, 1710, 1665, 1620 cm^{-1}. ^{1}H NMR/H,H-COSY (500 MHz, $CDCl_3$): δ = 1.06 (s, 3 H), 1.25 (s, 3 H), 1.37 (qd, *J* = 3.8, 13.1 Hz, 1 H), 1.49−1.66 (m, 5 H), 1.73 (m, 1 H), 1.80 (m, 1 H), 1.94 (m, 2 H), 2.30 (m, 1 H), 2.39 (A*B*, *J* = 16.2 Hz, 1 H), 2.54−2.67 (m, 3 H), 2.59 (*A*B, *J* = 16.2 Hz, 1 H), 2.87 (d, *J* = 12.6 Hz, 1 H), 3.40 (m, 1 H), 3.83−3.97 (m, 8 H). ^{1}H NMR (500 MHz, C_6D_6): δ = 0.81 (m, 1 H), 1.02 (d, *J* = 0.7 Hz, 3 H), 1.27 (s, 3 H), 1.31 (m, 2 H), 1.48 (m, 3 H), 1.65 (m, 1 H), 1.76−1.97 (m, 5 H), 2.20 (ddd, *J* = 4.0, 6.4, 15.1 Hz, 1 H), 2.34 (tt, *J* = 5.1, 12.3 Hz, 1 H), 2.49 (dA*B*, *J* = 0.8, 16.2 Hz, 1 H), 2.51 (m, 1 H), 2.52 (*A*B, *J* = 16.2 Hz, 1 H), 3.30 (m, 2 H), 3.38 (m, 2 H), 3.44−3.54 (m, 4 H), 3.72 (t, *J* = 5.7 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 15.1 (CH_3), 22.1 (CH_2), 22.6 (CH_2), 23.6 (CH_3), 27.1 (CH_2), 27.2 (CH_2), 29.3 (CH_2), 35.8 (CH_2), 36.3 (CH_2), 44.2 (CH_2), 44.8 (CH), 45.0 (C), 45.3 (CH), 64.5 (CH_2), 64.6 (CH_2), 65.1 (CH_2), 65.3 (CH_2), 109.6 (C), 111.1 (C), 133.4 (C), 155.9 (C), 197.0 (C), 212.0 (C). MS: *m*/*z* (%) = 290 (4), 115 (9), 87 (100), 43 (19).

Conversion of 22 into 23: A solution of **22** (547 mg, 1.35 mmol) in tetrahydrofuran (5 mL) was added at 0 °C to a suspension of sodium hydride (60% in mineral oil, 48.7 mg, 1.22 mmol) in dry tetrahydrofuran (5 mL). After this had stirred for 4 h at 0 °C, methyl iodide (67 μL, 10.8 mmol) was added. After 30 min, the reaction mixture was brought to room temperature and was stirred for another 3 h. The reaction mixture was quenched with a saturated NH_4Cl solution. Extraction was performed with diethyl ether and the organic phase was dried (Na_2SO_4). After removal of the solvent in vacuo, the residue was purified by flash chromatography and HPLC (isooctane/acetone, 8.5:1.5) to afford **23** (378 mg, 67%). M.p. 167 °C (recrystallization from isooctane/acetone). R_f = 0.26 (isooctane/acetone, 7:3). UV (MeOH): λ_{max} = 251 nm. IR (KBr): ṽ = 2954, 2880, 1715, 1664, 1597 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.05 (s, 3 H), 1.16 (m, 1 H), 1.28 (s, 3 H), 1.32 (m, 1 H), 1.38 (s, 3 H), 1.58 (m, 3 H), 1.76 (m, 2 H), 1.95 (m, 1 H), 2.15 (ddA*B*, *J* = 4.8, 12.8, 12.8 Hz, 1 H), 2.28 (dd*A*B, *J* = 4.1, 12.9, 12.9 Hz, 1 H), 2.33 (A*B*, *J* = 15.2 Hz, 1 H), 2.41 (*A*B, *J* = 15.2 Hz, 1 H), 2.42 (m, 1 H), 2.56−2.65 (m, 3 H), 2.91 (m, 1 H), 3.82−3.99 (m, 8 H). ^{1}H NMR (500 MHz, C_6D_6): δ = 0.76 (m, 1 H), 1.06 (s, 3 H), 1.28 (m, 1 H), 1.36 (m, 1 H), 1.44 (s, 3 H), 1.42−1.49 (m, 3 H), 1.54 (m, 1 H), 1.58 (s, 3 H), 1.65 (m, 1 H), 1.74 (m, 2 H), 2.11 (m, 2 H), 2.49 (A*B*, *J* = 15.1 Hz, 1 H), 2.53 (*A*B, *J* = 15.1 Hz, 1 H), 2.57 (m, 1 H), 2.68 (ddA*B*, *J* = 5.1, 12.6, 12.6 Hz, 1 H), 2.77 (dd*A*B, *J* = 4.0, 12.9, 12.9 Hz, 1 H), 3.29 (m, 2 H), 3.37 (m, 2 H), 3.48−3.56 (m, 3 H), 3.61 (m, 1 H). ^{13}C NMR/DEPT (50 MHz, C_6D_6): δ = 15.5 (CH_3), 22.0 (CH_2), 23.1 (CH_2), 24.0 (CH_3), 26.0 (CH_3), 28.4 (CH_2), 29.8 (CH_2), 30.7 (CH_2), 35.6 (CH_2), 36.1 (CH_2), 45.0 (C), 46.1 (CH), 46.7 (CH_2), 50.8 (C), 64.6 (CH_2), 64.6(CH_2), 65.1 (CH_2), 65.2 (CH_2), 110.2 (C), 111.2 (C), 135.8 (C), 155.8 (C), 197.4 (C), 211.4 (C). MS: *m*/*z* (%) = 403 (2), 304 (20), 99 (100). $C_{24}H_{34}O_6$ (418.53): calcd. C 68.88, H 8.19; found C 68.69, H 8.33.

The Dissolving-Metal Reduction of Enone 23: A solution of **23** (163 mg, 0.39 mmol) in dry tetrahydrofuran (3 mL) and *tert*-butyl alcohol (38 μL) was added to a solution of lithium (16.2 mg, 2.34 mmol) in liquid ammonia (13 mL, distilled from sodium). After stirring for 1 h at −33 °C, the reaction mixture was quenched with NH_4Cl. After evaporation of the ammonia, the residue was dissolved in water and extracted with diethyl ether. The organic phase was dried (Na_2SO_4). After removal of the solvent in vacuo, the residue was dissolved in acetone (12 mL) and treated at 0 °C with Jones' reagent. After this had stirred overnight at room temperature, excess reagent was destroyed with 2-propanol and solid sodium carbonate was added. The mixture was stirred for 15 min and filtered, and the precipitate was washed with diethyl ether and acetone. The combined organic phases were concentrated in vacuo. The residue was dissolved in water and extracted with diethyl ether. After the usual workup the residue was purified by flash chromatography and HPLC (isooctane/acetone, 8:2) to afford **24** (95 mg, 73%). M.p. 128 °C (recrystallization from isooctane/acetone). R_f = 0.18 (isooctane/acetone, 7:3). IR (KBr): ṽ = 2959, 2864, 1710 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.13 (s, 3 H), 1.20 (s, 3 H), 1.43 (m, 1 H), 1.55−1.75 (m, 4 H), 1.90−2.10 (m, 4 H), 2.12 (s, 3 H), 2.18 (m, 1 H), 2.19 (d, *J* = 11.8 Hz, 1 H), 2.31−2.40 (m, 3 H), 2.43 (A*B*, *J* = 13.3 Hz, 1 H), 2.53 (*A*B, *J* = 13.3 Hz, 1 H), 2.47−2.67 (m, 3 H). ^{1}H NMR/H,H-COSY (500 MHz, C_6D_6): δ = 0.61 (s, 3 H), 0.64 (m, 1 H), 0.78 (dq, *J* = 4.0, 12.8 Hz, 1 H), 0.91 (m, 1 H), 1.12 (m, 2 H), 1.38 (s, 3 H), 1.50 (m, 2 H), 1.56 (s, 3 H), 1.60 (d, *J* = 11.8 Hz, 1 H), 1.75 (m, 2 H), 2.01−2.14 (m, 5 H), 2.23 (dt, *J* = 6.3, 14.1 Hz, 1 H), 2.29 (d, *J* = 13.2 Hz, 1 H), 2.52 (d, *J* = 13.2 Hz, 1 H), 2.69 (ddd, *J* = 4.9, 10.4, 13.9 Hz, 1 H). ^{13}C NMR/DEPT (50 MHz, C_6D_6): δ = 17.6 (CH_3), 19.3 (CH_3), 23.9 (CH_2), 25.9 (CH_2), 26.2 (CH_2), 30.1 (CH_3), 31.9 (CH_2), 37.3 (CH_2), 37.7 (CH_2), 37.8 (CH), 38.8 (CH_2), 50.3 (CH), 51.0 (CH_2), 51.6 (C), 52.2 (C), 63.0 (CH), 206.8 (C), 208.1 (C), 210.7 (C), 211.7 (C). MS: *m*/*z* (%) = 332 (3) [M$^+$], 314 (3), 275 (14), 43 (100). $C_{20}H_{28}O_4$ (332.44): calcd. C 72.26, H 8.49; found C 72.08, H 8.69.

(±)-D-Homo-10α-androst-4-ene-3,11,17-trione (25): Tetraketone **24** (26.7 mg, 0.08 mmol) was dissolved in a KOH/methanol solution (4%, 0.4 mL). The reaction mixture was heated at 40 °C for 3 h. At the same temperature, a 37% HCl solution was added until pH = 1 was reached. After 4 h, the mixture was neutralized with a saturated $NaHCO_3$ solution and concentrated in vacuo. The residue was

dissolved in water, extracted with diethyl ether, and dried (Na_2SO_4). After removal of the solvent in vacuo, the residue was purified by flash chromatography and HPLC (isooctane/acetone, 8.5:1.5) to afford **25** (19.7 mg, 78%). M.p. 165 °C (recrystallization from ethyl acetate). R_f = 0.21 (isooctane/acetone, 7:3). IR (KBr): $\tilde{\nu}$ = 2938, 2865, 1705, 1667 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.01 (d, *J* = 0.9 Hz, 3 H), 1.48 (s, 3 H), 1.50 (m, 1 H), 1.60−1.69 (m, 3 H), 1.75 (m, 2 H), 1.90 (m, 1 H), 2.02 (m, 1 H), 2.14 (m, 1 H), 2.16 (d, *J* = 11.1 Hz, 1 H), 2.24 (dd, *J* = 8.7, 13.1 Hz, 1 H), 2.29 (m, 1 H), 2.39 (A*B*, *J* = 15.6 Hz, 1 H), 2.41 (m, 2 H), 2.52 (*A*B, *J* = 15.6 Hz, 1 H), 2.56−2.63 (m, 3 H), 5.75 (s, 1 H). ^1H NMR/H,H-COSY (500 MHz, C_6D_6): δ = 0.47 (s, 3 H), 0.66−0.91 (m, 3 H), 1.23 (s, 3 H), 1.06−1.36 (m, 6 H), 1.53 (m, 2 H), 1.69 (m, 1 H), 2.02 (m, 2 H), 2.20 (br. d, *J* = 15.4 Hz, 1 H), 2.31 (m, 1 H), 2.42 (ddd, *J* = 5.5, 13.9, 19.4 Hz, 1 H), 2.50 (ddd, *J* = 2.0, 5.3, 12.9 Hz, 1 H), 2.64 (d, *J* = 15.6 Hz, 1 H), 5.73 (s, 1 H). ^{13}C NMR/DEPT (50 MHz, $CDCl_3$): δ = 16.9 (CH_3), 23.0 (CH_3), 23.8 (CH_2), 26.0 (CH_2), 28.1 (CH_2), 28.8 (CH_2), 30.6 (CH_2), 34.3 (CH_2), 34.6 (CH), 36.9 (CH_2), 40.1 (C), 49.8 (CH_2), 49.9 (C), 51.0 (CH), 57.0 (CH), 125.1 (CH), 170.0 (C), 197.0 (C), 207.8 (C), 210.4 (C). MS: *m*/*z* (%) = 314 (16) [M^+], 286 (4), 179 (14), 161 (18), 122 (100), 91 (38), 77 (29), 55 (45).

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