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Versatile Use of Hindered Oxalates for the Stereoselective Preparation of Novel 11-Modified Androst-5-ene Derivatives

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Abstract: The 11α- and 11*β*-modified androst-5-ene derivatives **3a**,**b** as well as the exo- and endocyclic dehydrated compounds **4a**−**c** and **5b**−**c** were produced using the oxalate derivatives of the highly hindered 11*β*-hydroxyandrost-5-enes **1a**−**c**. The 11-tetrahydrofuran derivative **6** was produced for the first time with good diastereoselectivity by an intramolecular 5-exo cyclization under radical conditions from the corresponding oxalate as precursor.

Our group is involved in the preparation of modified androstanes at the C-11 position. To date, it has been possible to prepare several 11α-substituted 11*β*-hydroxyandrost-5-enes **1** with various kinds of substituents (aryl,[1] alkyl,[1] and allyl;[2] see Scheme 1). The importance of that position, especially at C-11*β*, in the biological implications of these hormones has been shown,[3] but new series of C-11 modified androstanes are still needed to extensively explore their structure−activity relationships. Furthermore, the study of such a hindered position is challenging from the modern chemistry point of view.

To reduce **1**, some classical methods were first tried (among others, ionic hydrogenation, derivatization to sulfonates followed by addition of hydride, and Barton−McCombie deoxygenation), but were unsuccessful.[4]

However, an oxalate moiety can be introduced into hindered systems, and under free-radical conditions, oxalates are also known to produce deoxygenated compounds.[5] Thus, we present here a study of the reactivity of hindered oxalates, derived from 11-modified androst-5-enes **1a**−**c** under free-radical and thermolytic conditions. The oxalate derivatives **2a**−**c** were quantitatively prepared, by a one-pot procedure, by deprotonation of **1a**−**c** with *n*-BuLi and treatment with methyl chlorooxoacetate (Scheme 2)

SCHEME 1. 11-Modified Androstanes of Type 1

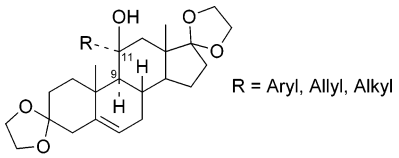

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TABLE 1. Reactivity of Oxalates 2a−c under Free-Radical Conditions

entry[a]	substrate	*T* (°C)	*t* (h)	reduction[b] (%) *R*-**3a**−**c**	reduction[b] (%) *S*-**3a**−**c**	elimination[b] (%)	**6**[b] (%)	**1a**−**c**[b] (%)
1	**2a**	110	2	28	0	46 (**4a**)		26
2	**2a**	110	22	28	0	46 (**4a**)		26
3	**2a**	80	2	33 (17)	0	33 (**4a**)		34
4[c]	**2a**	rt	3	0	0	0		100
5	**2b**	110	1	24 (21)	38 (31)	0	38 (27)	0
6	**2b**	80	1	22	40	0	38	0
7[c]	**2b**	rt	2	0	0	0	0	100
8	**2c**	110	2	0	0	45 (**4c**)/ 55 (**5c**)		0
9[c]	**2c**	rt	2	0	0	0		100

[a] *n*-Bu_3SnH 2 equiv, radical initiator (AIBN 20 mol % unless otherwise specified), toluene. [b] Conversion determined by means of ^1H NMR using the integration for H-6 of the crude mixtures. When determined, the isolated yield is given in parentheses. [c] Air−Et_3B as radical initiator.

The results concerning the reduction of **2a**−**c** with *n*-Bu_3SnH in the presence of a radical precursor under different conditions are presented in Table 1.

The deoxygenation of **2a** and **2b** was observed at 110 °C with AIBN as initiator (Table 1, entries 1 and 5). In the case of **2a**, only *R*-**3a** was observed with a relative retention of configuration (17% isolated yield, see the Experimental Section), but in the case of **2b**, the two possible diastereoisomers *R*- and *S*-**3b** were produced (21% and 31% isolated yield for *R*-**3b** and *S*-**3b**, respectively, see the Experimental Section). The deoxygenation of **2c** was not observed (Table 1, entry 8).

At temperatures above 80 °C, the elimination of the oxalate moiety of **2a** and **2c** was observed, leading to the unsaturated compounds **4a**, **4c**, and **5c**. The elimination occurred exclusively from cis-hydrogens. At room temperature, no elimination occurred, but the starting alcohols **1a**−**c** were recovered quantitatively (Table 1, entries 4, 7, and 9).

In the case of **2b**, a cyclization compound identified as the 11-tetrahydrofuran derivative **6** was formed during the course of the reaction at temperatures above 80 °C (Table 1, entries 5 and 6). Compound **6** was produced as a 1/0.4/0.2 mixture of three of the four possible diastereomers in 27% isolated yield.

The configuration of the deoxygenated compounds *R*-**3a** and *R*- and *S*-**3b** was determined by NMR methods. Compounds *R*-**3b** and *S*-**3b** showed ^1H NMR chemical shifts for H-9 at δ 1.06 (t, J = 10.2 Hz, 1H) and δ 1.47−1.55 (m, 1H), respectively. The multiplicity of the NMR signal of H-9 for *R*-**3b** was attributed to an equivalent axial-axial coupling between H-9 and H-11 and H-8,

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(1) Lecomte, V.; Stéphan, E.; LeBideau, F.; Jaouen, G. *Tetrahedron* **2003**, *59*, 2169−2176.
(2) Lecomte, V.; Stéphan, E.; Vaissermann, J.; Jaouen, G. *Steroids* **2004**, *69*, 17−21.
(3) Cleve, A.; Fritzemeier, K.-H.; Heinrich, N.; Klar, U.; Müller-Fahrnow, A.; Neef, G.; Ottow, E.; Schwede, W. *Tetrahedron* **1996**, *52*, 1529−1542. See also for modification of the symmetrical position 7: Zheng, Y.; Li, Y. *J. Org. Chem.* **2003**, *68*, 1603−1606.
(4) The failure of the Barton−McCombie reaction was due to the fact that the formation of the starting xanthate did not work by literature methods on this substrate (see: Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574−1585).
(5) Dolan, S. C.; McMillan, J. *J. Chem. Soc., Chem. Commun.* **1985**, 1588−1589.

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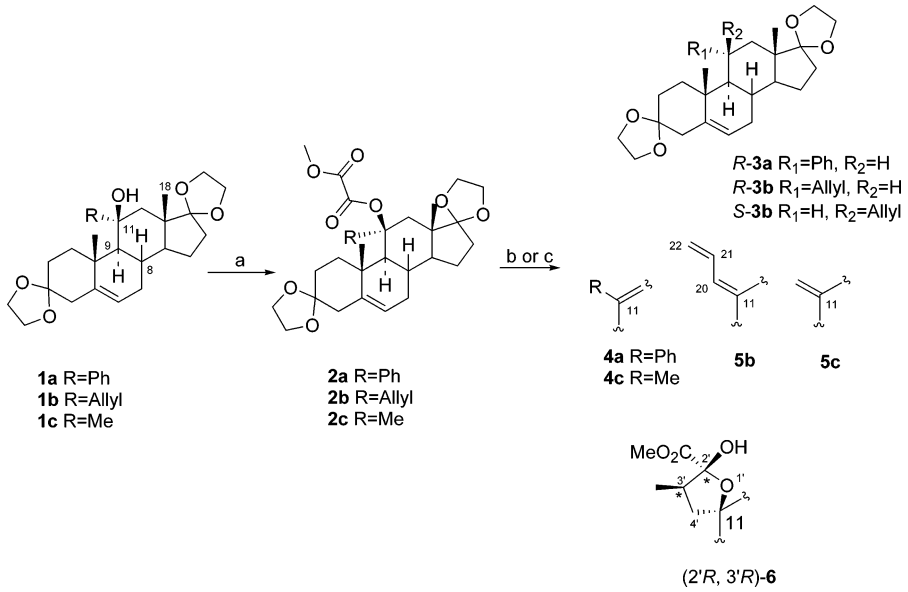
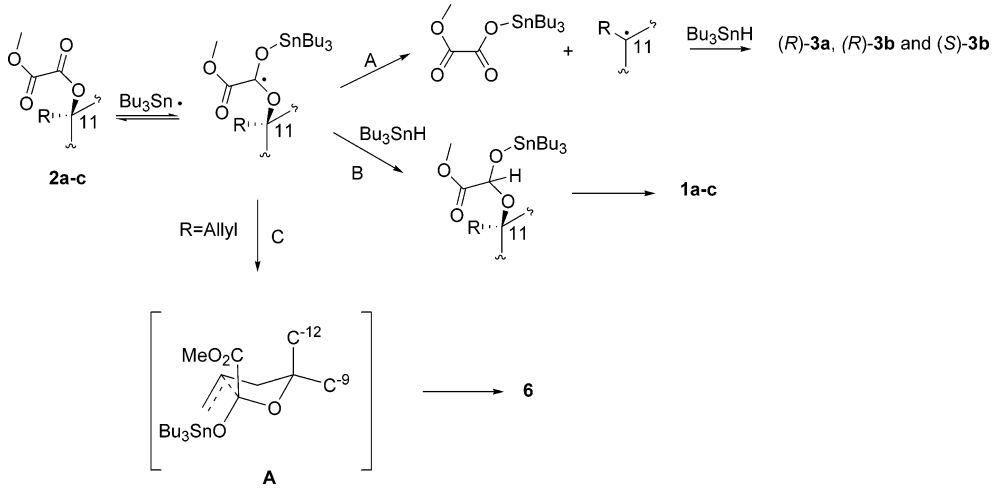
SCHEME 2. Products Formed under Free-Radical and Thermolytic Conditions[a]



[a] Key: (a) *n*-BuLi, −78 °C, then $Cl(CO)_2OMe$, −70 to −50 °C; (b) *n*-Bu_3SnH, radical initiator, $PhCH_3$; (c) refluxing toluene or mesitylene.

SCHEME 3. Proposed Mechanism for the Deoxygenation of 2a−c



indicating the *R* configuration. This configuration was confirmed by cross-peaks in the NOESY spectrum of *R*-**3b** between H-18 and H-11. The stereochemistry of *R*-**3a** was determined by the same method using benzylic H-11 showing a chemical shift at δ 2.91 (ddd, J = 12.5, 10.4, 4.7 Hz, 1H) due to two axial−axial couplings with H-9 and H-12_{ax} and an equatorial−axial coupling with H-12_{eq}.

The major epimer of **6** was isolated and its configuration was determined by NMR methods as well. This epimer showed ^{1}H NMR chemical shifts for H-3′ and CH_3-ester at δ 2.95 (m, sep, 1H) and δ 3.83 (s, 3H), respectively. Cross-peaks in the NOESY spectrum between H-3′ and H-12 were observed indicating the (*R*) configuration at C-3′ of the THF residue. Moreover, cross-peaks between H of CH_3-ester and H-12 were also observed indicating a cis relation between substituents at C-3′ and C-2′ and thus the (*R*) configuration at C-2′ of the THF residue (see Scheme 2).

To date, no detailed study of the mechanism of the radical deoxygenation of oxalates has been available. In Scheme 3, a mechanism for the formation of *R*- and *S*-**3a**,**b** as well as for the formation of **6**, inspired by the Barton−McCombie deoxygenation[6] is proposed. The first step would be a reversible addition of the stannyl radical to the oxalate moiety,[7] followed by 3 possible competitive pathways. In path A, a homolytic cleavage can lead to **3a**−**c**. In the case of **2c**, the stability of the radical centered on C-11 would be too low to yield **3c**. Path B shows the competitive abstraction leading to alcohols **1a**−**c**. In the case of **2c**, path C shows the intramolecular 5-exo cyclization leading to **6**. According to literature reports,[8] the chairlike transition state **A** bearing the larger groups C-9 and −$OSnBu_3$ in pseudoequatorial

(6) Barton, D. H. R.; Jang, D. O.; Jaszberenyi, J. C. *Tetrahedron Lett.* **1990**, *31*, 3991−3994.

(7) The addition may reversibly occur on both of the carbonyls of the oxalate, but no cyclization product from the furthest carbone of the oxalate has been detected.

(8) Beckwith, A. L. J.; Zimmermann, J. *J. Org. Chem.* **1991**, *56*, 5791−5796. Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925−3941. Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073−3100.

TABLE 2. Thermolysis of Oxalates 2a−c

entry[a]	substrate	conversion[c] (%)	isolated yield (%)
1	**2a**	100 (**4a**)	76 (**4a**)
2	**2b**	100 (**5b**)	42 (**5b**)
3	**2c**	45 (**4c**)/55 (**5c**)	
4[b]	**2c**	65 (**4c**)/35 (**5c**)	36 (**4c**)/14 (**5c**)

[a] Refluxing toluene until disappearance of the starting material. [b] Mesitylene as solvent (bp 162−164 °C). [c] Conversion determined by means of ^{1}H NMR.

positions is proposed to explain the stereochemistry of the major epimer observed.

To date, the thermolysis of an oxalate moiety has never been reported. As shown in Table 2, when the oxalate derivatives **2a**−**c** were stirred in refluxing toluene, **2a** yielded exclusively the endo cyclic compounds **4a** (Table 2, entry 1) and **2b** the exo cyclic compound **5b**[9] (Table 2, entry 2). **2c** led to a nonstatistical 45/55 mixture of endo- and exocyclic compounds **4c** and **5c**, respectively (Table 2, entry 3). In that case, as the temperature was increased, the ratio **4c**/**5c** was also increased (Table 2, entry 4). We assumed this increase, and the fact that the ratio was far from the statistical 25/75 proportion, could be explained by the lower stability of an exocyclic compound versus an endocyclic one, as is the case for the Chugaev pyrolysis of xanthates,[10] but at lower temperature (100−200 °C is usually required for the thermolysis of xanthates). No other unsaturated product was detected (namely no double bond in the 9(11) position).

The elimination of 11α-methyl-11β-hydroxy androst-5-enes derivatives, such as **1c**, under acidic (formic or perchloric acid)[11] or basic conditions (thionyl chloride−pyridine)[12] was described in the literature. Mixtures of endo- (position 9(11)) or exocyclic unsaturated compounds were obtained, but no mention was found of any elimination in position 11(12). In our case, such a regioselectivity could be explained by an E_i mechanism involving a six-membered cyclic transition state requiring cis hydrogen. Such a transition state was proposed for the similar Chugaev thermolysis of xanthates.[10]

Free-radical cyclization is a widely used method to prepare substituted tetrahydrofuran derivatives occurring in many natural products,[13] but no report was found on the use of homoallylic oxalates as precursors for such compounds. However, as shown in Table 1, they may be considered as new tools for stereoselective access to 2,2,5,5-tetrasubstituted 3-methyltetrahydrofuran.

In summary, we have developped a novel approach to highly hindered 11α- and 11β-modified androst-5-ene, as well as to 11-modified androstadiene, starting with the oxalate derivatives **2a**−**c** obtained in quantitative yields. This method will especially make 11β derivatives more easily obtainable than before. The availability of 11-modified steroids will provide opportunities to study their structure−activity relationships. Moreover, this paper extends the use of oxalate derivatives to radical cyclization in order to produce valuable tetrahydrofuran derivatives, such as **6**. The scope and limitations of this reaction is under study in our group.

Experimental Section

General Conditions for the Preparation of 2a−c. To a solution of alcohol **1a**−**c** (2.1 mmol) in THF at −60 °C (20 mL) was slowly added a commercial solution of *n*-BuLi 2.1 M (1.6 mL, 3.36 mmol). The solution was stirred for 5 min at −60 °C followed by addition of methyl chlorooxoacetate (4 mL, 4.2 mmol) at −60 °C. The mixture was stirred at −60 °C for 30 min, the temperature was slowly raised to rt, and the mixture was stirred at rt for 2 h. The mixture was then diluted with ethyl acetate (50 mL), and water was added (50 mL). The organic phase was separated, washed with water and brine, and dried over magnesium sulfate. The solvent was removed under vacuum to afford a yellowish powder (99% conversion) which was further used without purification.

If desired, an analytical sample of **2b** and **2c**[14] can be obtained by purification on silica gel chromatographic column using a 100/1 dichloromethane/ethyl acetate mixture.

11α-Allyl-11β-(*O*-methyloxoacetate)-3,3,17,17-(ethylenedioxy)androst-5-ene (2b): mp 72 °C; ^{1}H NMR ($CDCl_3$) δ 0.85 (4H, m), 0.92 (3H, s), 1.25 (5H, m), 1.42 (3H, s), 1.61−2.17 (16H, m), 2.63 (1H, m), 2.65 (1H, d, J = 15.0 Hz), 2.91 (1H, dd, J = 15.0, 6.0 Hz), 3.48 (1H, dd, J = 15.0, 6.0 Hz), 3.86 (3H, s, CH_3−O), 3.81−3.96 (8H, m), 5.14 (1H, d, J_{trans} = 17.4 Hz), 5.16 (1H, d, J_{cis} = 10.5 Hz), 5.31 (1H, bs), 5.82 (1H, m); ^{13}C NMR ($CDCl_3$) δ 14.3, 21.5, 23.5, 31.0, 31.9, 32.9, 34.1, 36.8, 38.0, 41.1, 41.7, 44.2, 44.7, 50.3, 52.4, 53.2, 64.2, 64.5, 64.6, 65.1, 94.1, 108.5, 119.5, 119.7, 121.4, 134.1, 141.8, 156.6, 158.8; MS (*m*/*z*) 516 $[M]^+$ (3), 457 $[M - CO_2Me]^+$ (5), 413 (9), 99 (100); IR (KBr) cm^{-1} 1737, 1763. Anal. Calcd for $C_{29}H_{40}O_8$: C, 67.42; H, 7.80. Found: C, 67.28; H, 7.99.

11α-Methyl-11β-(*O*-methyloxoacetate)-3,3,17,17-(ethylenedioxy)androst-5-ene (2c):. mp 82 °C; ^{1}H NMR ($CDCl_3$) δ 0.91 (3H, s), 1.28−1.47 (4H, m), 1.38 (3H, s), 1.60−2.21 (21H, m), 1.90 (3H, s), 2.61 (1H, bd, J = 14.8 Hz), 2.69 (1H, d, J = 14.9 Hz), 3.86 (3H, s), 3.82−3.96 (8H, m), 5.35 (1H, m); ^{13}C NMR ($CDCl_3$) δ 14.5, 21.0, 23.3, 31.1, 31.3, 32.1, 32.4, 34.2, 38.4, 40.4, 41.6, 41.8, 44.6, 51.2, 53.2, 59.4, 64.2, 64.4, 64.6, 65.1, 90.8, 108.6, 119.3, 121.5, 141.0, 156.4, 158.8; MS (*m*/*z*) 490 $[M]^+$ (1), 431 $[M - CO_2Me]^+$ (1), 387 (4), 99 (100); IR (KBr) cm^{-1} 1740, 1764. Anal. Calcd for $C_{27}H_{38}O_8$: C, 66.10; H, 7.81. Found: C, 65.58; H, 8.08.

11α-Phenyl-3,3,17,17-(ethylenedioxy)androst-5-ene (*R*-3a). A solution of **2a** (0.18 mmol, 100 mg), Bu_3SnH (0.36 mmol, 0.09 mL), and AIBN (20 mol %, 5 mg) in dry and degassed toluene (2.2 mL) was heated at 80 °C for 2 h. The solvent was evaporated, and the crude mixture was chromatographed with petroleum ether/ethyl acetate 9/1 to afford *R*-**3a** (13.8 mg, 17% yield): mp 91 °C; ^{1}H NMR ($CDCl_3$) δ 0.70−0.91 (3H, m), 0.98 (3H, s), 1.16 (3H, s), 1.21−1.85 (20H, m), 2.01−2.08 (3H, m), 2.48 (1H, dq, J = 13.7, 3.6 Hz), 2.99 (1H, ddd, J = 12.5, 10.4, 4.7 Hz), 3.71−3.94 (8H, m), 5.41 (1H, bs), 7.03−7.21 (5H, m); ^{13}C NMR ($CDCl_3$) δ 14.5, 18.4, 23.4, 31.1, 31.7, 33.6, 34.3, 38.0, 39.8, 40.7, 42.3, 43.7, 45.6, 49.4, 53.0, 64.0, 64.3, 64.5, 65.1, 68.2, 77.2, 108.9, 119.1, 119.5, 122.4, 125.6, 128.4, 140.6, 149.2; MS *m*/*z* 451 $[M^+ + H]$ (100), 389 (32); HRMS calcd for $C_{29}H_{39}O_4$ $(M^+ + H)$ 451.2848, found 451.2849.

11α-Allyl-3,3,17,17-(ethylenedioxy)androst-5-ene (*R*-3b), 11β-Allyl-3,3,17,17-(ethylenedioxy) androst-5-ene (*S*-3b), and Spiro[3,3,17,17-(ethylenedioxy)androst-5-ene-11,5′-tetrahydrofuran-3′-methyl-2′-hydroxy-2′-methyl acetate] (*6*). A solution of **2b** (200 mg, 0.39 mmol), Bu_3SnH (0.21 mL, 0.77

(9) Only one elimination product with an exocyclic double bond was formed, as shown by ^{13}C NMR of the crude mixture, but its stereochemistry could not have been determined. However, on the basis of the supposed E_i mechanism favoring the most stable alkene, we assumed that its configuration was *s-trans*.

(10) Nace, H. R. *Org. React.* **1962**, *12*, 57−100.

(11) Elks, J. *J. Chem. Soc.* **1960**, 3333−3339.

(12) Kirk, D. N.; Petrow, V. *J. Chem. Soc.* **1961**, 2091−2098.

(13) For recent reviews on the preparation of oxygen heterocycles, see, for example: Elliott, M. C. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2301−2323; Elliott, M. C.; Williams, E. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2303−2340.

(14) The intermediate **2a** can be stored in air without noticeable degradation but cannot be purified by silica gel column chromatography. However, its formation was confirmed by ^{1}H NMR of the crude mixture showing chemical shifts for CH_3-18 and -19 and CO_2CH_3 at δ 1.01 (3H, s), 1.37 (3H, s), and 3.94 (3H, s), respectively.

mmol), and AIBN (10 mg, 20 mol %) in dry and degassed toluene (4.8 mL) was refluxed for 1 h. The solution was cooled, and water was added. The organic phase was separated, washed, and dried on magnesium sulfate. The solvent was evaporated under vacuum, and the crude was chromatographed on silica gel, first neutralized with a 5% v/v NEt_3 solution in petroleum ether, to afford *R*-**3b** (34 mg, 21% yield) [mp 132 °C; ^{1}H NMR ($CDCl_3$) δ 0.84 (3H, s), 1.06 (1H, t, J = 10.2 Hz), 1.15 (3H, s), 1.19−1.29 (1H, m), 1.35−1.47 (5H, m), 1.61−1.71 (3H, m), 1.74−1.97 (5H, m), 2.03−2.22 (3H, m), 2.42 (1H, dm, J = 14.7 Hz), 2.58 (1H, dq, J = 14.0, 2.6 Hz), 3.81−3.98 (8H, m), 4.97 (1H, bd, J_{trans} = 15.9 Hz), 4.98 (1H, bd, J_{cis} = 11.5 Hz), 5.43 (1H, bd, J = 5.6 Hz), 5.73−5.82 (1H, m); ^{13}C NMR ($CDCl_3$) δ 14.8, 17.7, 23.4, 31.3, 31.6, 32.7, 34.2, 37.9, 38.3, 39.9, 41.5, 42.7, 45.3, 49.4, 52.2, 64.3, 64.4, 64.6, 65.2, 109.0, 116.1, 119.7, 122.8, 137.0, 140.7; *m*/*z* 414 [M^+] (1), 99 (100). Anal. Calcd for $C_{26}H_{38}O_4$ C, 75.32; H, 9.24. Found: C, 74.97; H, 9.44], *S*-**3b** (50 mg, 31% yield) [mp 132 °C; ^{1}H NMR ($CDCl_3$) δ 0.95 (3H, s), 1.15 (3H, s), 1.19−1.30 (1H, m), 1.35−1.42 (1H, m), 1.46−1.55 (3H, m), 1.63−1.78 (7H, m), 1.85 (1H, dt, J = 13.1, 3.6 Hz), 1.97−2.03 (1H, m), 2.09−2.25 (4H, m), 2.48−2.52 (1H, m), 2.56 (1H, dq, J = 14.0, 2.6 Hz), 3.81−3.98 (8H, m), 4.96−5.02 (2H, m), 5.16−5.17 (1H, m), 5.68−5.78 (1H, m); ^{13}C NMR ($CDCl_3$) δ 16.0, 21.6, 22.9, 29.4, 30.9, 31.8, 32.2, 34.2, 34.7, 36.9, 37.2, 40.8, 45.6, 52.4, 53.4, 64.2, 64.5, 64.6, 65.1, 109.0, 115.6, 119.8, 120.9, 139.7, 141.7; MS *m*/*z* 414 [M^+] (1), 99 (100); HRMS calcd for $C_{26}H_{37}O_4$ (M^+ − H) 413.2692, found 413.2690], and **6** (49 mg, 27% yield) [mp 132 °C; ^{1}H NMR ($CDCl_3$) δ 0.86 (3H, s), 0.96 (3H, d, J = 6.7 Hz), 1.19−1.31 (1H, m), 1.37 (3H, s), 1.36−1.45 (1H, m), 1.50−1.60 (3H, m), 1.65−1.86 (7H, m), 1.96−2.03 (2H, m), 2.09 (1H, dd, J = 14.5, 3.2 Hz), 2.16 (1H, d, J = 13.6 Hz), 2.57 (1H, dd, J = 14.5, 2.9 Hz), 2.58 (1H, t, J = 12.5 Hz), 2.74 (1H, dt, J = 12.2, 3.5 Hz), 2.95 (1H, sep), 3.83 (3H, s), 3.86−3.98 (8H, m), 5.29−5.31 (1H, m); ^{13}C NMR ($CDCl_3$) δ 13.0, 13.7, 20.7, 23.9, 31.1, 34.0, 36.6, 37.9, 41.7, 41.9, 44.3, 45.2, 48.0, 49.7, 53.0, 53.3, 64.2, 64.3, 64.4, 65.0, 89.0, 102.9, 108.9, 119.8, 121.4, 142.9, 172.7; MS (ICP/NH_3) *m*/*z* 536 [M + NH_4]$^+$ (7.5), 519 [M + H]$^+$ (100), 501 [M − H_2O + NH_4]$^+$ (70); IR (KBr) cm^{-1} 1744 (C═O). Anal. Calcd for $C_{29}H_{42}O_8$: C, 67.16; H, 8.16. Found: C, 66.78; H, 8.30].

11-Phenyl-3,3,17,17-(ethylenedioxy)androsta-5,11(12)-diene (4a). A solution of **2a** (604 mg, 1.09 mmol) in dry toluene (30 mL) was refluxed overnight. The organic phase was washed with water and dried on magnesium sulfate. The solvent was evaporated under vacuum, and the crude was chromatographed with a mixture petroleum ether/ethyl acetate 85/15 to afford **4a** (374 mg, 76% yield): mp 211 °C; ^{1}H NMR ($CDCl_3$) δ 0.77 (1H, dt, J = 13.3), 1.00 (1H, dt, J = 13.7), 1.06 (6H, s), 1.23−1.52 (4H, m), 1.74 (1H, m), 1.82−2.12 (8H, m), 2.41 (1H, dq, J = 13.7), 2.60 (1H, m), 3.75−3.95 (8H, m), 5.52 (1H, bs), 5.80 (1H, d, J = 1.5 Hz), 7.13−7.29 (5H, m); ^{13}C NMR ($CDCl_3$) δ 17.6, 18.5, 21.9, 31.9, 33.6, 35.0, 38.2, 41.4, 42.3, 46.4, 47.5, 55.6, 64.0, 64.1, 64.3, 65.2, 77.2, 109.0, 118.5, 123.4, 125.9, 126.9, 127.6, 128.1, 128.4, 136.9, 140.9, 141.9, 146.7; MS *m*/*z* 448 [M^+] (9), 386 (1), 99 (100); IR (KBr) cm^{-1} 759, 694. Anal. Calcd for $C_{29}H_{36}O_4$: C, 77.64; H, 8.09. Found: C, 77.48; H, 8.16.

11-(Vinylmethylidene)-3,3,17,17-(ethylenedioxy)androst-5-ene (5b). A solution of **2b** (100 mg, 0.19 mmol) in dry toluene (2 mL) was refluxed overnight. The organic phase was washed with water and dried on magnesium sulfate. The solvent was evaporated under vacuum, and the crude was chromatographed with a mixture petroleum ether/ethyl acetate 9/1 to afford **5b** (33 mg, 42% yield): mp 110 °C; ^{1}H NMR ($CDCl_3$) δ 0.91 (3H, s), 1.08 (3H, s), 1.18−1.37 (3H, m), 1.51 (1H, dt, J = 13.8, 3.9 Hz), 1.66−2.03 (13H, m), 2.13 (1H, dd, J = 13.8, 3.3 Hz), 2.25 (1H, dt, J = 13.2, 3.6 Hz), 2.48 (1H, bd, J = 13.8 Hz), 2.84 (2H, m), 3.90−4.01 (8H, m), 5.01 (1H, bd, J_{trans} = 17.4 Hz), 5.02 (1H, bd, J_{cis} = 10.2 Hz), 5.51 (1H, bd, J = 5.7 Hz), 5.76 (2H, m); ^{13}C NMR ($CDCl_3$) δ 17.5, 17.7, 21.9, 30.9, 31.3, 33.9, 35.0, 37.5, 41.0, 42.6, 42.7, 46.5, 47.3, 55.9, 64.3, 64.3, 64.4, 65.3, 108.9, 115.9, 118.7, 123.6, 133.5, 137.4, 137.5, 141.7; MS (ICP/NH_3) *m*/*z* 430 [M + NH_4] (100). Anal. Calcd for $C_{26}H_{36}O_4$: C, 75.69; H, 8.80. Found: C, 75.53; H, 8.97.

11-Methyl-3,3,17,17-(ethylenedioxy)androst-5,11(12)-diene (4c) and 11-Methylidene-3,3,17,17-(ethylenedioxy)-androst-5-ene (5c). A solution of **2c** (613 mg, 1.25 mmol) in dry mesitylene was refluxed for 2 h. The organic phase was washed and dried on magnesium sulfate. The solvent was evaporated under vacuum, and the crude was chromatographed with a mixture petroleum ether/ethyl acetate 9/1 to afford **4c** (173 mg, 36% yield) [mp 80 °C; ^{1}H NMR ($CDCl_3$) δ 0.92 (3H, s), 1.07 (3H, s), 1.30 (2H, m), 1.48 (1H, dt, J = 13.8, 3.9 Hz), 1.66 (2H, m), 1.81 (3H, s), 1.75−1.97 (10H, m), 2.14 (1H, dd, J = 13.7, 3.0 Hz), 2.31 (1H, dt, J = 13.1, 3.6 Hz), 2.52 (1H, dq, J = 13.7, 2.1 Hz), 3.87−4.01 (8H, m), 5.51 (1H, bd, J = 6.0 Hz), 5.70 (1H, s); ^{13}C NMR ($CDCl_3$) δ 17.6, 18.0, 22.1, 27.6, 30.9, 31.3, 33.7, 34.9, 37.4, 40.5, 42.6, 46.7, 47.1, 56.7, 64.2, 64.3, 64.4, 65.2, 109.0, 118.7, 123.4, 133.3, 135.0, 141.7; MS (*m*/*z*) 386 [M]$^+$ (5), 99 (100). Anal. Calcd for $C_{24}H_{34}O_4$: C, 74.58; H, 8.87. Found: C, 74.55; H, 8.96] and **5c** (69 mg, 14% yield) [mp 234 °C; ^{1}H NMR ($CDCl_3$) δ 0.77 (3H, s), 1.23 (1H, m), 1.29 (3H, s), 1.38 (1H, dt, J = 14.1, 3.9 Hz), 1.55−1.98 (11H, m), 2.14 (1H, dt, J = 14.1, 3.0 Hz), 2.38 (1H, bd, J = 12.0 Hz), 2.47 (1H, dt, J = 13.8, 3.7 Hz), 2.61 (1H, dq, J = 14.4, 2.9 Hz), 3.83−3.99 (8H, m), 4.98 (2H, bd, J = 8.4), 5.30 (1H, bs); ^{13}C NMR ($CDCl_3$) δ 14.4, 18.7, 23.1, 31.1, 32.0, 33.5, 34.5, 34.9, 37.4, 41.9, 45.6, 46.6, 51.1, 54.1, 64.2, 64.4, 64.5, 65.2, 109.1, 113.5, 119.0, 120.7, 141.6, 145.0; MS (*m*/*z*) 387 [M + H]$^+$ (100). Anal. Calcd for $C_{24}H_{34}O_4$: C, 74.58; H, 8.87. Found: C, 74.54; H, 8.95.]

Supporting Information Available: Characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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