Dialkylation of Various Butane-2,3-diacetals Using Allylsilane and 1,8-Bis(trimethylsilyl)-2,6-octadiene

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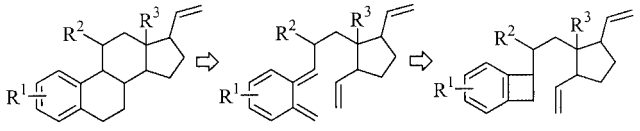
We report in this paper a greatly improved procedure for the formation of a range of 1-acetyl-1-methyl-2,5-divinylcyclopentanes from 1,8-bis(trimethylsilyl)octa-2,6-diene (BISTRO) and 1,2-diacetals prepared directly from biacetyl. These 1-acetyl-1-methyl-2,5-divinylcyclopentanes are building blocks for the synthesis of 2- and 3-methoxy-12-oxo-17β-vinylestranes.

Introduction

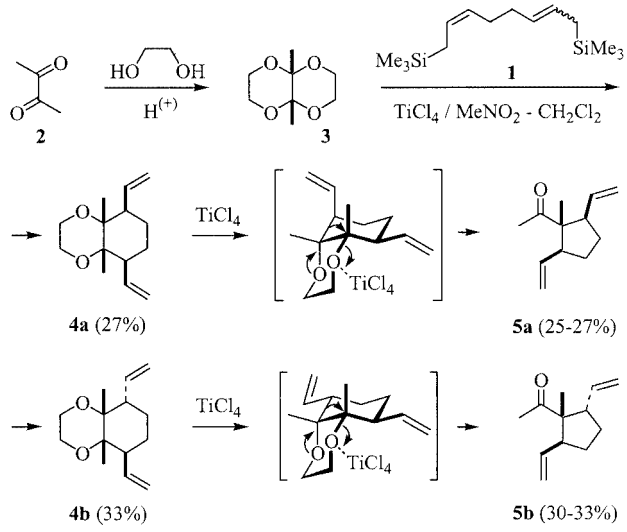
In the course of a program directed towards the development of new steroids that might exhibit improved therapeutic actions over existing drugs, we have adopted a convergent steroid synthesis,[1] based on the approach A + D → AD → ABCD, which involves the use of the intramolecular cycloaddition of *o*-xylylenes that was developed independently by Oppolzer[2] and Kametani[3] for the generation of the BC ring system (Scheme 1).



Scheme 1

The required substituted divinylcyclopentanes result from the addition of 1,8-bis(trimethylsilyl)octa-2,6-diene (BISTRO, **1**) to various electrophilic reagents (anhydrides,[4] ethyleneketals,[5] benzaldehyde,[6] and acyl chlorides[7]). The reaction of BISTRO with the ketal **3** (derived from **2**), which leads to **5** via **4** through a pinacol-type rearrangement (Scheme 2), has attracted much current interest.[8]

Our past studies have shown that divinylcyclopentanes **5** can lead to 12-oxo-17β-vinylsteroids in good yields.[9] This present account describes the synthesis of ten steroids obtained in three steps from **5a** or **5b**, as outlined in Scheme 3.



Scheme 2

The *trans-anti-trans* steroids, obtained from **5a**, are of prime interest. To enhance the selectivity of the reactions of both BISTRO and allylsilane[10] with the ketals, we studied the reactivity of some ketals of the 2,3-butanedione other than **3**. In particular, we investigated the mixed ketals obtained from methanol and optically active diols, such as (+)-*trans*-1,2-cyclohexanol, (+)-1-phenyl-1,2-ethanediol, and L-(+)-dimethyl tartrate, or triols, such as glycerol protected by the Ley procedure.[11] Thus, **15** was prepared from **2** in 80% yield; the reaction of L-(+)-dimethyl tartrate with **2** in methanol in the presence of trimethyl orthoformate gave the dioxane derivative (−)-**16** in 93% yield.[12,13] The same procedure led to (−)-**17** (95% yield) from (+)-*trans*-1,2-cyclohexanol,[11b] (−)-**18** (98% yield) from (+)-1-phenyl-1,2-ethanediol,[14] and **19** (98% yield) from glycerol[14,15] (Scheme 4).

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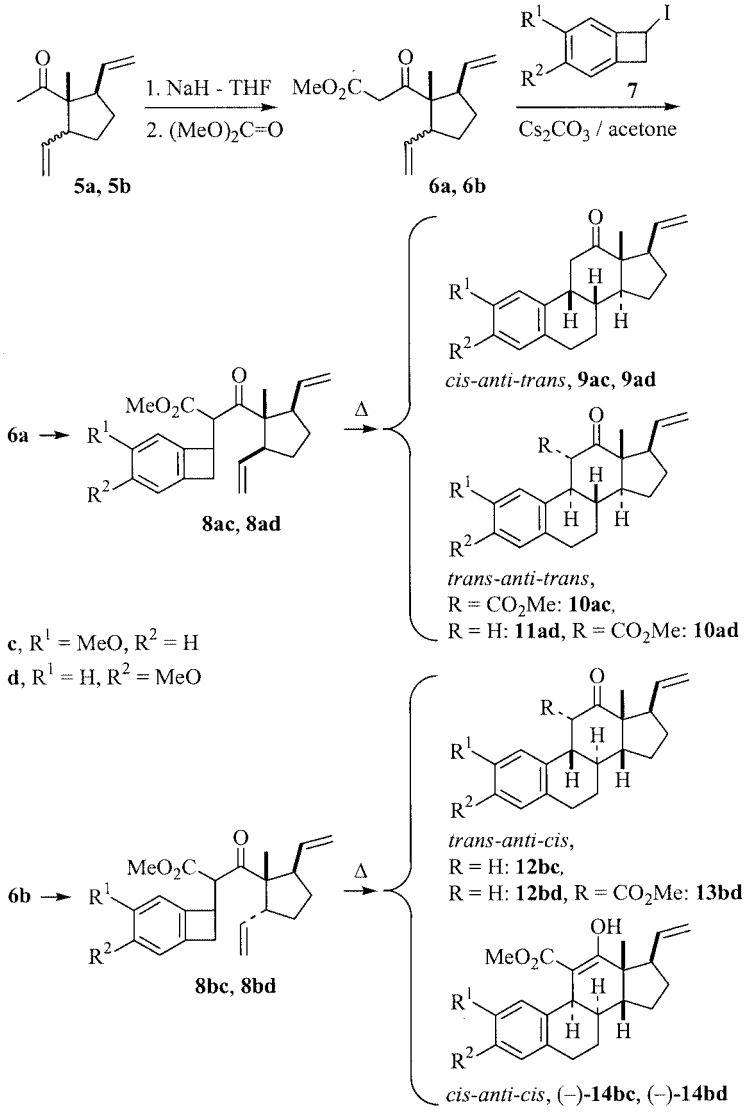
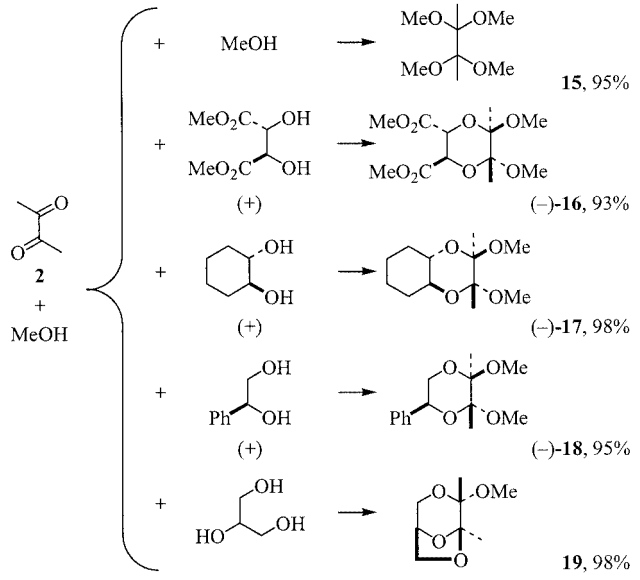


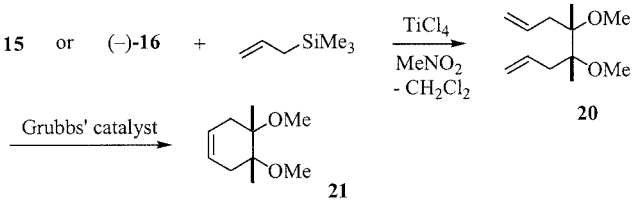
Scheme 3



Scheme 4

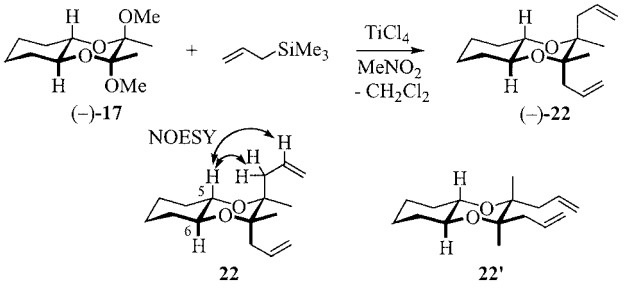
Results and Discussion

First, we studied the generally clean $TiCl_4$-mediated addition of allylsilanes to the acetals using CH_2Cl_2 as solvent and 4 equiv. of nitromethane.[16] Compound **20** was produced from **15**, in the presence of 3 equiv. of allylsilane, in 43% yield and from (−)-**16** in 60% yield. The structure of **20** was established by its ring closing metathesis using the Grubbs catalyst[17] to form (1*R*,2*S*)-1,2-dimethyl-1,2-dimethoxycyclohex-4-ene (**21**) in 90% yield. As indicated in Scheme 5, the chirality of the (−)-**16** moiety is lost.



Scheme 5

In the case of (−)-**17**, substitution of the methoxyl groups was observed and the optically active dioxadecalin (−)-**22** was obtained in 68% yield as the sole product (> 98% *de*, > 99% *ee*). Analysis of the ^1H and ^{13}C NMR spectra proved that the C_2 axis of symmetry is maintained. Only two structures having such a C_2-axis of symmetry, **22** and **22′**, are possible. Nevertheless, the NOESY spectrum of **22** shows two diagnostic cross peaks between the H(5) or H(6) protons and the allylic protons. Moreover, all attempts to apply ring closing metathesis to **22** failed,[11] leading us to propose that structure **22** results from a substitution that occurs with retention of configuration (Scheme 6).



Scheme 6

The Lewis acid-mediated addition of carbon nucleophiles to acetals is a common reaction in organic synthesis; it is used widely for the formation of carbon−carbon bonds.[18] The Hosomi−Sakurai allylation of acetals is a seminal example of these reactions.[19]

Mechanistic hypotheses involving either synchronous (S_N2-like) or dissociative (S_N1-like) substitution processes have been proposed, as well as the involvement of equilibrating ion pairs.[20]

With regard to the use of asymmetric acetals in organic synthesis, a general view has emerged that a reaction mechanism continuum exists with its extremes being an S_N2-type invertive displacement and a dissociative S_N1-type process proceeding via a free oxocarbenium ion and followed by rapid nucleophilic attack.[21]

The double retention of configuration observed in the case of (−)-**17** could result from the participation of one methoxyl group assisting the departure of the other so that the first substitution occurs with retention. The anomerically assisted ionization[22] of the second methoxyl group in accordance with the lone-pair-electron hypothesis[23] then leads to an oxocarbenium species that is attacked axially by allylsilane, as shown in Scheme 7.[24]

We have investigated the structure of the oxocarbenium ion at the B3LYP/6-311G (d,p) level by using Gaussian 98, revision A.11.4.[25] These calculations indicate that the oxygen atom of the methoxyl group contributes to the stabilization of the positive charge. In particular, the C(2)−C(3)−O(7) angle is reduced to 100.4° and the O(7) atom is positioned nearer to the C(2) center than to either the C(10) or O(4) atoms (Figure 1).

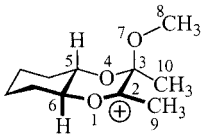
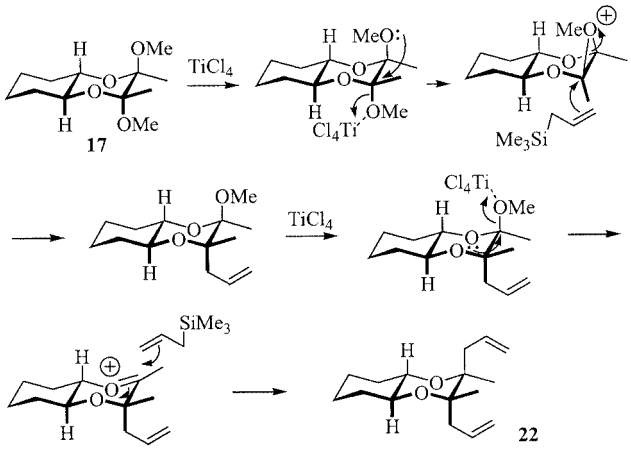
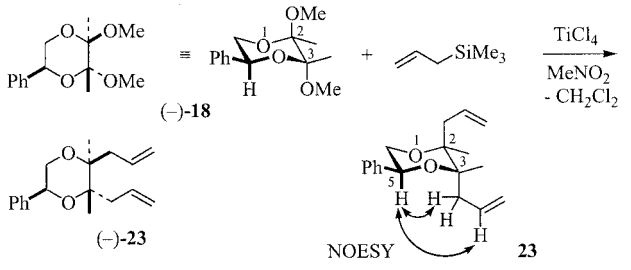


Figure 1. Optimized geometry of the oxocarbenium ion at the B3LYP/6.311G (d,p) level; selected bond lengths (A): O(1)−C(2), 1.258; O(1)−C(6), 1.530; C(2)−C(3), 1.549; C(2)−C(9), 1.475; C(3)−O(4), 1.404; C(3)−O(7), 1.406; O(4)−C(5), 1.437; C(5)−C(6), 1.506; O(7)−C(8), 1.445; C(2)−O(7), 2.27; O(4)−O(7), 2.34; C(10)−O(7), 2.48; selected bond angles (°): O(1)−C(2)−C(3), 121.9; O(1)−C(2)−C(9), 116.9; C(3)−C(2)−C(9), 121.2; C(2)−C(3)−O(7), 100.4; O(4)−C(3)−O(7), 112.9; O(7)−C(3)−C(10), 115.2; selected dihedral angle (°): O(1)−C(2)−C(3)−O(4), −5.0; O(1)−C(2)−C(3)−O(7), 114.9; C(2)−C(3)−O(7)−C(8), 173.3; C(9)−C(2)−C(3)−O(7), −64.2; selected total atomic charges: O(1), 0.175; C(2), 0.398; C(9), −0.468; C(3), −0.709; O(4), 0.127; O(7), 0.001; C(8), −0.173; the HOMO (MO, 54; E = −11.76 eV) is centered on O(7) and the LUMO (MO, 55; E = −6.98 eV) is centered on C(2); total energy: −656.201(90) hartrees

Similarly, the dioxane (−)-**23** was obtained in 60% yield from (−)-**18**; again, no ring closing metathesis was observed when using the Grubbs catalyst. NOESY data allowed us to confirm the identity of structure **23**. We observed two cross peaks in the NOESY spectrum of **23** that reveal an NOE between H(5) and both protons of the proximal allylic group. In contrast, the NOESY spectrum does not shown any NOE between H(5) and the distal allylic moiety or the two methyl groups. Again, we note that the allylic substitution occurs with a double retention of configuration. All attempts to observe the monoallylation failed; we obtained **23** only when we used one equiv. of allylsilane (Scheme 8).



Scheme 7



Scheme 8

We studied the coordination of the two methoxyl groups of **18** in the presence of 0.25 equiv. of titanium tetrachloride by 400-MHz ^{1}H NMR spectroscopy at room temperature;[26] the spectra revealed that the ratio of the one doubly and two singly coordinated species [i.e., through either the C(2) methoxyl or C(3) methoxyl groups] to the free ketal was ca. 2.1:1.6:1.15:1.

Two oxocarbenium ions **A** and **B** could result from the departure of the methoxyl group of **18**. Our calculations indicated that the departure of the C(3) methoxyl group led to the more-stable oxocarbenium ion **A** (Figure 2).

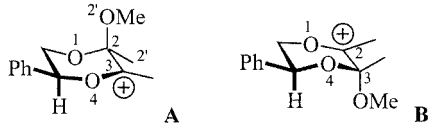
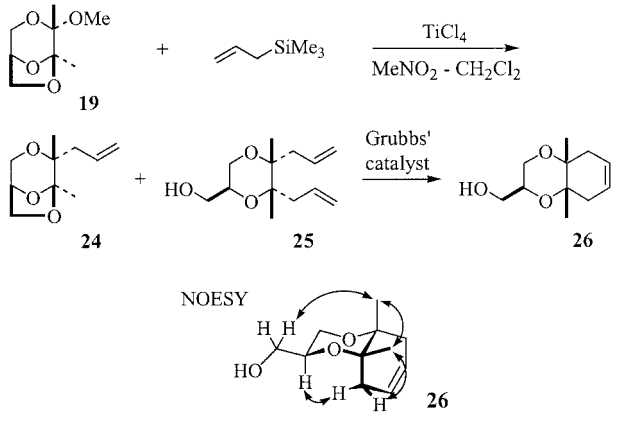


Figure 2. Optimized geometry of the oxocarbenium ions at the B3LYP/6.31G(d,p) level; total energy (hartrees): **A**, −731.060(41); **B**, −731.056(84); energy difference: 2.24 kcal/mol; **A**, selected bond lengths (Å): O(4)−C(3), 1.26; C(2)−O(2′), 1.41; C(3)−O(2′), 2.27; selected bond angles (°): C(3)−C(2)−O(2′), 100.5; O(1)−C(2)−O(2′), 113.1; O(2′)−C(2)−C(2′), 115.5

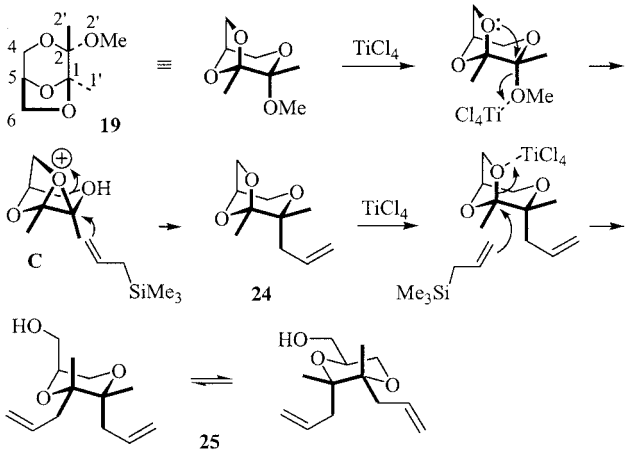
For the asymmetric dioxane **19**, in the presence of one equiv. of allylsilane, the first reaction is a substitution of the methoxyl group with overall retention of configuration followed by an invertive ("S_N2-like") substitution on the mixed ketal moiety.

Again, the stereochemistry of **25** has been confirmed by performing a ring closing metathesis using the Grubbs catalyst; it led to a *cis* ring junction dioxadecalin, **26**. Moreover, NOESY experiments were in agreement with the proposed structure (Scheme 9).



Scheme 9

For the substitution occurring with retention of configuration, the most reasonable interpretation is that, after coordination of titanium tetrachloride to the oxygen atom of the methoxyl group, an oxygen atom participation occurred to give an oxonium ion **C**, which was attacked by allylsilane to give an overall retention of configuration. Subsequently, the coordination of titanium tetrachloride to the oxygen atom of the bridge is postulated to induce the substitution occurring with inversion. In each case, the more reactive C−O bond is in an axial position (Scheme 10).



Scheme 10

A 400-MHz ^{1}H NMR spectroscopy study of the coordination of titanium tetrachloride with **19** showed that the Lewis acid is bound mainly to the methoxyl group. When 0.25 equiv. of titanium tetrachloride was added to a solution of **19** in deuterated chloroform at room temperature, the signal of the methoxyl group shifts from δ = 3.27 to 4.63 ppm (broad singlet, $W_{1/2}$ = 27 Hz). In the ^{13}C NMR spectra, the number of signals doubled [δ, ppm: C(1), 106.8 and 107.5; C(1′), 18.2 and 19.1; C(2), 99.0 and 104.0; C(2′), 18.5 and 27.4; C(6), 64.2 and 66.5].

We have investigated the structure of the oxocarbenium ion **C** at the B3LYP/6-311G (d,p) level. These calculations indicate that the oxygen atom of the bridge contributes to the stabilization of the positive charge. In particular, the O(7)−C(1)−C(2) angle is reduced to 90.7° and the O(7) atom is positioned near the C(2) center (Figure 3).

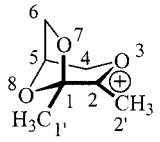
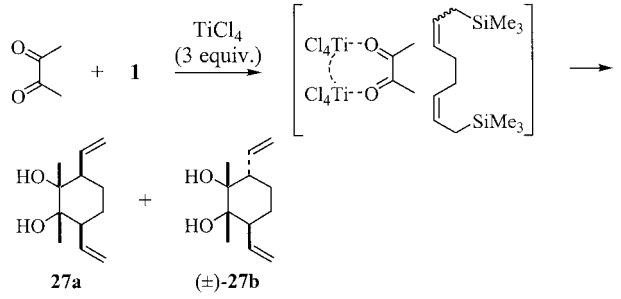


Figure 3. Optimized geometry of the oxocarbenium ion at the B3LYP/6.311G (d,p) level; selected bond lengths (Å): C(1)−O(8), 1.400; C(1)−O(7), 1.429; C(1)−C(2), 1.542; C(1)−C(1′), 1.505; C(2)−O(3), 1.270; C(2)−C(2′), 1.471; O(3)−C(4), 1.498; C(2)−O(7), 2.27; selected bond angles (°): O(7)−C(1)−C(2), 90.7; O(8)−C(1)−C(2), 108.6; O(7)−C(1)−O(8), 107.0; O(7)−C(1)−C(1′), 112.7; C(1)−C(2)−O(3), 119.3; C(1)−C(2)−C(2′), 123.8; C(2′)−C(2)−O(3), 116.8; selected dihedral angles (°): O(8)−C(1)−C(2)−O(3), 30.3; C(1′)−C(1)−C(2)−C(2′), −27.3; C(1)−C(2)−O(3)−C(4), −3.0; selected total atomic charges: C(1), −1.078; C(1′), −0.577; C(2), 0.770; C(2′), −0.686; O(3), 0.104; O(7), 0.063; O(8), 0.018; the HOMO (MO, 38; E = −12.36 eV) is centered on O(7) and the LUMO (MO, 39; E = −7.42 eV) is centered on C(2); total energy: −498.883(61) hartrees

The addition of BISTRO to various mixed ketals **15**−**19** was less stereoselective than the addition of allylsilane. In most cases, we obtained a mixture of **5a** and **5b**, but, interestingly, in some cases, **5a** or **5b** was the major product.

At first, we added BISTRO to biacetyl, which led to the creation of a 1:1 mixture of **27a** and (±)-**27b** in 50% yield. We note that these compounds could result from the addition of a chelated biacetyl, but the use of a large excess of $TiCl_4$ should exclude the formation of chelated complexes (Scheme 11).



Scheme 11

The structure of **27** was established by analysis of the NOESY spectra; it was confirmed by X-ray crystallographic analysis of (±)-**27b** (Figure 4). Unfortunately, we were unable to rearrange **27**, obtained in fair yields, into the corresponding acetylcyclopentanes **5**.

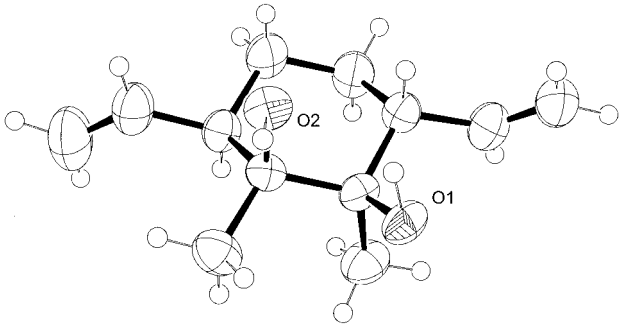
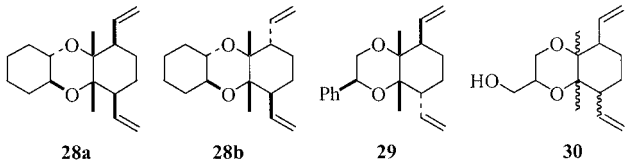


Figure 4. ORTEP diagram of diol (±)-**27b**

Next, we examined the addition of BISTRO to the ketals **15**−**19** (Table 1).

Table 1. Addition of BISTRO to ketals **15**−**19**

Ketals	$TiCl_4$ equiv.	Temp. (°C)	Dioxane yield (%)	**5** yield (%)
15	3	−90 → −60	−	**5a**, 55; (±)-**5b**, 23
15	4	−90 → −60	−	**5a**, 45; (±)-**5b**, 19
(−)-**16**	4	−90 → −60	−	**5a**, 42; (±)-**5b**, 28
(−)-**16**	3	−90 → −10	−	**5a**, 45; (±)-**5b**, 30
(−)-**17**	3	−90 → −60	**28a**, 15; **28b**, 36	trace
(−)-**17**	3	−90 → rt	**28a**, 4; **28b**, 10	**5a**, 13; (−)-(*S*,*S*)-**5b**, 31
(+)-**18**	4	−90 → −60	−	**5a**, 7; (+)-(*R*,*R*)-**5b**, 60
(+)-**18**	2	−90 → −60	**29** (28)	**5a**, 8; (+)-(*R*,*R*)-**5b**, 32
19	4	−90 → −60	**30** (9)	**5a**, 45; (±)-**5b**, 19



As is evident from Table 1, the best yields of **5** were obtained from the more-common ketal **15**, which also gave the highest proportion of **5a** (70%).

The stereochemistries of the dioxanes **28a** and **28b** were confirmed by NOESY analyses (Figure 5).

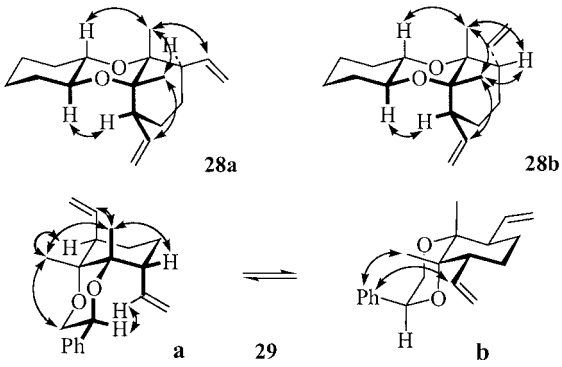


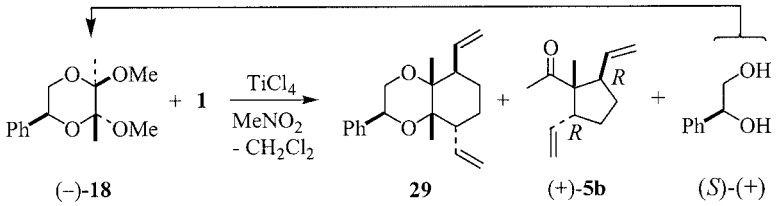
Figure 5. NOESY analyses of **28a**, **28b**, and **29**

We have determined that the dioxanes **28a** or **28b**, when treated with $TiCl_4$, rearrange to acetylcyclopentanes **5a** and (−)-(*S*,*S*)-**5b**, respectively.

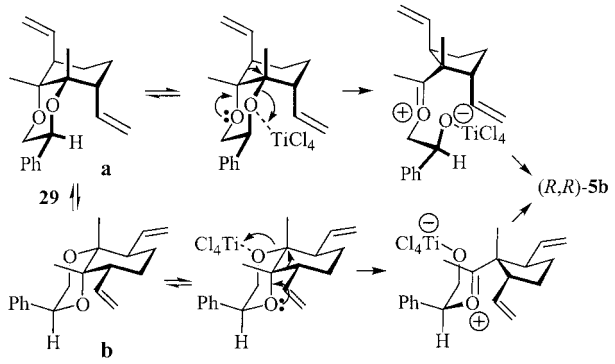
A more interesting result was observed with the dioxane (−)-**18**, obtained from (*S*)-(+)-1-phenyl-1,2-ethanediol (98% *ee*), which led mainly to (+)-(*R*,*R*)-**5b** (98% *ee*).[27] Using 3 equiv. of $TiCl_4$, we obtained mainly the non-racemic dioxane **29**. The ^{13}C NMR spectra of **29** reveals a conformationally mobile system at room temperature, which is in accordance with a *cis* ring junction (signals duplicated so that 35 resonances appear instead of the 20 expected). According to semi-empirical calculations undertaken using the PM3-method,[28] conformation **b** is slightly more stable than that of **a** [ΔH_f (kcal mol^{-1}), **a**: −4915.70; **b**: −4916.04].[29] The structure was established by a series of 1D NMR spectroscopy and NOESY experiments (Figure 5).

The use of 4 equiv. of $TiCl_4$ led directly to (+)-(*R*,*R*)-**5b** and (*S*)-(+)-1-phenyl-1,2-ethanediol (35% isolated yield). The enantiomeric excess of the recovered diol was determined by its transformation into (−)-**18** (Scheme 12). Comparison with the starting material showed that no racemization occurred during either the BISTRO addition or the pinacol-like rearrangement. In either case, the O−C and C−C bonds that are involved have the antiperiplanar relationship required for 1,2-migration (Scheme 13).[30]

The reaction of BISTRO with **19** occurred with poor stereoselectivity; **30** was formed as a mixture of diastereoisomers.



Scheme 12



Scheme 13

Starting from **5a**, we have prepared five new steroids according to procedures we have reported previously (Scheme 3). Compound **5a** was acylated and the resulting compound, **6a**, was alkylated with **7c** (R^1 = MeO, R^2 = H) or **7d** (R^1 = H, R^2 = MeO).[4e] Interestingly, we obtained only one racemic stereoisomer **8ac** or **8ad**. Upon heating at 215 °C, **8ac** was converted into steroids **9ac** (40%) and **10ac** (40%) and **8ad** into steroids **9ad** (40%) and **11ad** (40%). In the latter case, and as already mentioned,[9] heating at 215 °C leads to an in situ demethoxycarbonylation of **10ad** and the formation of **11ad** (40%). Upon heating at 200 °C, **8ad** was converted into steroids **9ad** (40%) and **10ad** (40%). The structures of **10ac**, **9ad**, and **11ad** have been confirmed unambiguously by X-ray diffractometry (see Figure 6, Figure 7, Figure 8, Figure 9).

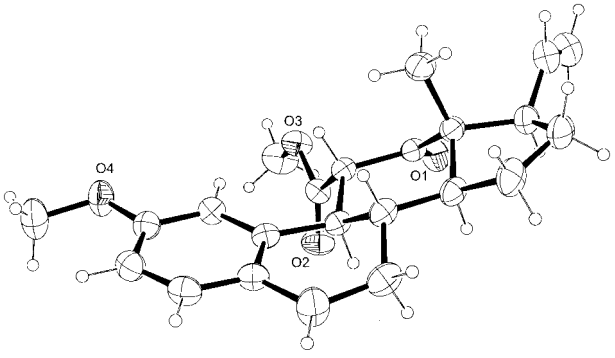


Figure 6. ORTEP diagram of steroid **10ac**

Heating of **8bc** or **8bd** led to five steroids that exhibit a *cis* C/D ring junction. Upon heating at 215 °C, **8bc** was cyclized into **12bc** (27%) and **14bc** (63%) and **8bd** into **12bd** (25%) and **14bd** (55%). In contrast, heating of **8bd** at 200 °C led to **13bd** (25%) and **14bd** (55%). The structure of **14bc** was confirmed by X-ray diffractometry (Figure 9). The enantiomeric excesses of **14bc** (93%) and **14bd** (98%) correspond to the optical purity of the L-(+)-mandelic acid used for the preparation of (−)-**18**.

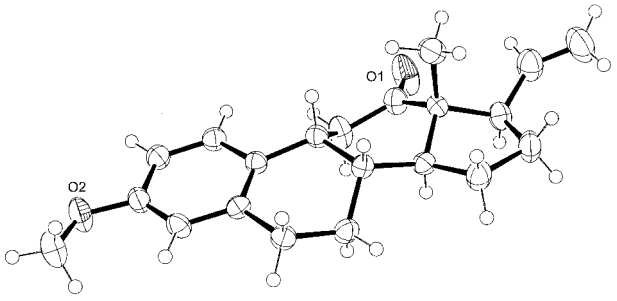


Figure 7. ORTEP diagram of steroid **9ad**

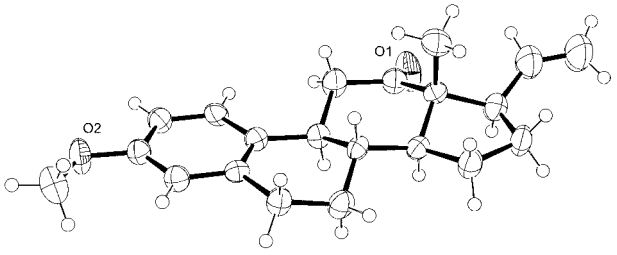


Figure 8. ORTEP diagram of steroid **11ad**

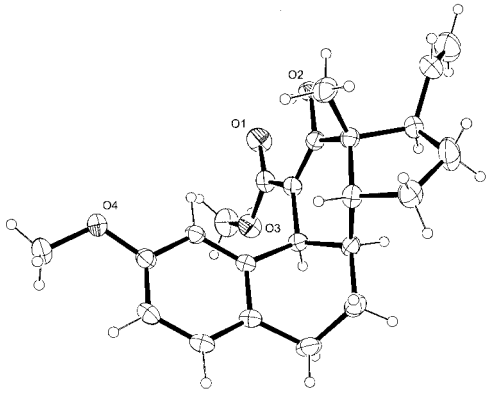
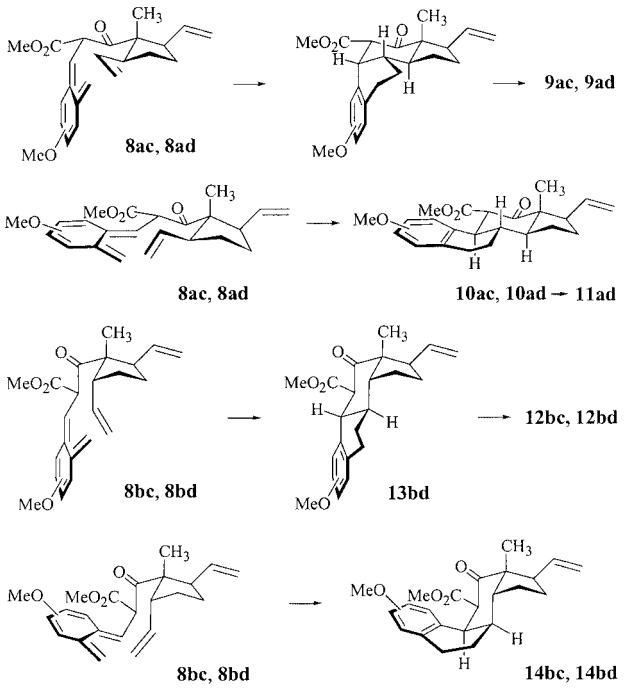


Figure 9. ORTEP diagram of steroid **14bc**

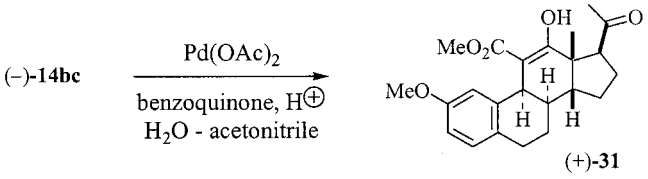
From the structures of the various steroids, it was easy to predict the structures of the transition states of the Diels−Alder reactions. Steroids bearing a *cis* B/C ring junction, such as **9ac**, **9ad**, **14bc**, and **14bd**, arise from an *endo* transition state involving the formation of an *E*-*o*-xylylene.

In contrast, **10ac**, **10ad**, **11ad**, **12bc**, **12bd**, and **13bd**, each of which exhibits a *trans* B/C ring junction, result from *exo* transition states, which imply, again, the formation of an (*E*)-*o*-xylylene (Scheme 14).



Scheme 14

As an illustration of the possibility of functionalizing the 17β position, we performed the oxidation of the vinyl group by the Wacker process.[4e,31] The corresponding 17β-acetyl steroid (+)-**31** was obtained in 55% yield (Scheme 15).



Scheme 15

Conclusion

We have shown that allylsilane and BISTRO can react with ketals with high stereoselectivity. In fact, the formation of discrete oxocarbenium ions, stabilized by the anomeric effect and the proximal methoxyl group, seems to be the major process of the various allylic substitution reactions.[32] The high stereoselectivities of these reactions allow the synthesis of divinylacetylcyclopentanes **5**, which are key molecules for the stereoselective synthesis of various 12-oxosteroids.

Experimental Section

General: All reactions were performed under argon in oven-dried glassware. TLC was performed on silica gel 60 F_{254}. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ solutions at 500, 400, and 300 and 125, 100, and 75 MHz, respectively. Carbon−proton couplings were determined by DEPT sequence experiments. Mass spectra (electron impact ionization, 70 eV) were recorded by GC/MS (Varian−Saturn 2100 T; Chrompack column, CP-Sil 8CB, 30 m × 0.25 mm, DF = 0.25 μm). THF was distilled before use from sodium/benzophenone; CH_2Cl_2 from P_2O_5. The enantiomeric excesses of ketals and ketones were determined by GC (Chrompack CP7502 WCOT fused silica column and CP-Chirasil-Dex CB as the stationary phase) and those of the steroids by chiral HPLC (Daicel, 250 × 4.6 mm; **14bc**: Chiralcel OD-H [cellulose *tris*(3,5-dimethylphenylcarbamate)], mobile phase: hexane/2-PrOH, 95:5; **14bd**: Chiralpak AD [amylose *tris*(3,5-dimethylphenylcarbamate)], mobile phase: hexane/ethanol, 95:5). Flash chromatography was performed on silica gel (230−400 mesh) obtained from Macherey−Nagel & Co.

For the preparation of iodobenzocyclobutenes **7**, see ref.[4e]; for compounds **8** and steroids **9**−**11** ($R^1 = R^2 = H$), see ref.[9]

General Procedure for the Formation of *trans* Acetals: Camphorsulfonic acid (0.1 equiv.) was added to a solution of diol (0.9 equiv.), 2,3-butanedione (1 equiv.), and trimethyl orthoformate (3 equiv.) in dry methanol (1.75 mL/mmol of biacetyl). The mixture was heated under reflux for 72 h. The reaction was neutralized by the addition of triethylamine and then the solvents were evaporated under reduced pressure. The residue was purified by flash chromatography to give the diacetals **16**, **17**, **18**, and **19**.

General Procedure for the Condensation of Silylated Derivatives on Ketals: A 250-mL flask equipped with a thermometer, septum cap, magnetic stirring bar, and argon outlet was charged with anhydrous CH_2Cl_2 (100 mL) and anhydrous nitromethane (4.4 mL, 80 mmol). The solution was cooled to −70 °C; $TiCl_4$ (11.4 g, 6.6 mL, 60 mmol) was added, followed by the slow addition of the ketal (20 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred 0.5 h. at this temperature, then cooled to −90 °C; a solution of allyltrimethylsilane (6.9 g, 9.6 mL, 60 mmol) or BISTRO (10.2 g, 40 mmol) in CH_2Cl_2 (30 mL) was then added over 15 min. The mixture was stirred for 2 h. at −90 °C. When BISTRO was used, the solution was slowly warmed to −60 °C. After a certain time, the reaction was quenched by addition of saturated aqueous NH_4Cl and then the mixture was stirred for 0.5 h. before being extracted with CH_2Cl_2. The organic layer was washed with water, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was subjected to flash chromatography.

(4*R*,5*S*)-4,5-Dimethoxyocta-4,5-dimethyl-1,7-diene (20): Synthesized from **15** (3.56 g) or **16** (5.84 g) and allyltrimethylsilane (2 h. at −90 °C). The crude product was purified by flash chromatography (petroleum ether/Et_2O, 98:2) to give **20** [1.70 g from **15** (43%) or 2.40 g from **16** (60%)] as an oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 5.88 (ddt, *J* = 16.9, 10.9, 7.1 Hz, 2 H), 4.97 (m, 4 H), 3.25 (s, 6 H), 2.49 (1/2AB, br. d, *J* = 14.7, 7.1 Hz, 1 H), 2.24 (1/2AB, dt, *J* = 14.7, 7.6, 1.2 Hz, 1 H), 1.14 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 136.0 (d), 116.3 (t), 81.9 (s), 51.0 (q), 39.6 (t), 18.0 (q) ppm. MS: *m*/*z* (%) = 157 (44, M^+ − allyl), 125 (25), 116 (22), 101 (34), 99 (100), 98 (22), 89 (55), 73 (21), 67 (45), 43 (30), 41 (29).

(−)-(2*S*,3*S*,5*S*,6*S*)-2,3-Diallyl-2,3-dimethoxyoctahydrobenzo[1,4]-dioxine (22): Synthesized from (−)-**17** (4.61 g) and allyltrimethylsilane (2 h at −90 °C). The crude product was purified by flash chro-

matography (petroleum ether/Et_2O, 98:2) to give **22** (3.40 g, 68%) as an oil; *ee* > 99%. $[\alpha]_D^{25} = -108.4$ ($CHCl_3$, 0.92). ^1H NMR ($CDCl_3$, 300 MHz): δ = 5.77 (dddd, *J* = 16.6, 10.8, 8.0, 5.9 Hz, 2 H), 5.11 (br. d, *J* = 10.8 Hz, 2 H), 5.10 (br. d, *J* = 16.6 Hz, 2 H), 3.29 (m, 2 H), 3.16 (1/2AB, d, *J* = 14.8, 5.8 Hz, 2 H), 1.97 (1/2AB, d, *J* = 14.8, 8.0 Hz, 2 H), 1.72 (m, 4 H), 1.25 (m, 4 H), 1.0 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 133.8 (d), 117.8 (t), 77.4 (s), 72.7 (d), 35.5 (t), 30.2 (t), 24.4 (t), 21.1 (q) ppm. MS: *m*/*z* (%) = 210 (17), 209 (100, M^+ − allyl), 153 (10), 123 (11), 111 (28), 93 (14), 83 (24), 81 (32), 69 (15), 67 (36), 43 (70), 41 (16). $C_{16}H_{26}O_2$ (250.38): calcd. C 76.75, H 10.47; found C 76.82, H 10.32.

(−)-(2*S*,3*S*,5*S*)-2,3-Diallyl-2,3-dimethyl-5-phenyl-1,4-dioxane (23): Synthesized from (+)-**18** (5.05 g) and allyltrimethylsilane (2 h. at −90 °C). The crude product was purified by flash chromatography (petroleum ether/Et_2O, 98:2) to give **23** (3.27 g, 60%) as an oil; *ee* > 99%. $[\alpha]_D^{25} = -77.9$ ($CHCl_3$, 1.05). ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.21 (m, 5 H), 5.75 (m, 2 H), 5.05 (m, 4 H), 4.70 (dd, *J* = 9.9, 5.1 Hz, 1 H), 3.48 (m, 2 H), 3.20 (1/2AB, d, *J* = 14.9, 5.9 Hz, 2 H), 1.99 (1/2AB, d, *J* = 14.9, 7.7 Hz, 2 H), 0.99 (s, 3 H), 0.95 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 139.0 (s), 133.8 (d), 133.6 (d), 128.5 (d, 2C), 128.0 (d), 126.4 (d, 2C), 118.2 (t), 118.0 (t), 77.4 (s), 76.0 (s), 70.2 (t), 65.6 (t), 35.3 (t), 35.0 (t), 21.3 (q), 20.8 (q) ppm. MS: *m*/*z* (%) = 231 (18, M^+ − allyl), 188 (11), 104 (100), 78 (19), 43 (29). $C_{18}H_{24}O_2$ (272.38): calcd. C 79.37, H 8.88; found C 79.28, H 9.02.

(1*S,2*R**,5*R**)-2-Allyl-1,2-dimethyl-3,7,8-trioxabicyclo[3.2.1]octane (24):** Synthesized from **19** (3.48 g) and allyltrimethylsilane (3.2 mL, 0.2 mmol) (2 h. at −90 °C). The crude product was purified by flash chromatography (petroleum ether/Et_2O, 95:5 to 70:30) to give **24** (0.74 g, 21%) and **25** (1.18 g, 26%). **24**, oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 5.81 (dddd, *J* = 16.9, 10.3, 7.7, 6.6 Hz, 1 H), 5.09 (m, 1 H), 5.08 (m, 1 H), 4.39 (br. t, *J* = 6.6 Hz, 1 H), 4.11 (d, *J* = 6.6 Hz, 1 H), 3.99 (br 1/2AB, *J* = 11.6 Hz, 1 H), 3.86 (td, *J* = 6.0, 1.3 Hz, 1 H), 3.41 (1/2AB, d, *J* = 11.6, 1.2 Hz, 1 H), 3.00 (1/2AB, d, *J* = 14.6, 6.6 Hz, 1 H), 1.97 (1/2AB, d, *J* = 14.6, 7.7 Hz, 1 H), 1.32 (s, 3 H), 1.10 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 133.2 (d), 117.6 (t), 109.2 (s), 78.6 (s), 74.8 (d), 67.7 (t), 65.1 (t), 29.8 (t), 21.3 (q), 19.6 (q) ppm.

(2*R,3*S**,5*S**)-2,3-Diallyl-5-(hydroxymethyl)-2,3-dimethyl-1,4-dioxane (25):** Synthesized from **20** (3.48 g) and allyltrimethylsilane (2 h at −90 °C). The crude product was purified by flash chromatography (petroleum ether/Et_2O, 95:5 to 80:20) to give **25** (3.26 g, 72%) as an oil. ^1H NMR ($CDCl_3$, 500 MHz): δ = 5.86 (m, 2 H), 5.17 (m, 2 H,), 5.10 (m, 2 H), 3.90 (m, 1 H), 3.70 (1/2AB, d, *J* = 11.6, 11.4 Hz, 1 H,), 3.59 (m, 1 H), 3.95 (m, 1 H), 3.53 (1/2AB, d, *J* = 11.6, 3.6 Hz, 1 H), 3.48 (m, 1 H), 3.20 (1/2AB, d, *J* = 14.7, 6.2 Hz, 1 H), 2.26 (1/2AB, d, *J* = 13.9, 5.6 Hz, 1 H), 2.04 (m, 2 H), 1.32 (s, 3 H), 1.06 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 133.9 (d), 133.6 (d), 118.1 (t), 117.6 (t), 76.9 (s), 76.8 (s), 68.1 (d), 62.8 (t), 61.0 (t), 41.8 (t), 35.0 (t), 21.6 (q), 17.6 (q) ppm. MS: *m*/*z* (%) = 185 (37, M^+ − allyl), 117 (17), 85 (10), 84 (11), 83 (13), 69 (19), 55 (15), 43 (100). $C_{13}H_{22}O_3$ (226.31): calcd. C 68.99, H 9.8; found C 68.84, H 10.01.

General Procedure for the RCM Reaction: $Cl_2(PCy_3)_2Ru{=}CHPh$ (124 mg, 0.151 mmol) was added to a solution of **20** (300 mg, 1.51 mmol) or **25** (342 mg, 1.51 mmol) in dry CH_2Cl_2 (18 mL). The mixture was stirred at room temp. (for **20**: 1.15 h; for **25**: 24 h). The solution was concentrated and the residue was purified by flash chromatography (**21**: petroleum ether/Et_2O, 100:0 to 90:10; **26**: 90:10 to 60:40) to give **21** (231 mg, 90%) or **26** (263 mg, 88%).

(1*R*,2*S*)-1,2-Dimethoxy-1,2-dimethylcyclohex-4-ene (21): Oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 5.53 (br. s, 2 H), 3.23 (s, 6 H), 2.44 (1/2AB, d, *J* = 16.3 Hz, 2 H), 1.96 (1/2AB, d, *J* = 16.3 Hz, 2 H), 1.13 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 124.8 (d), 78.0 (s), 49.8 (q), 33.8 (t), 17.8 (q) ppm. MS: *m*/*z* (%) = 170 (14, M^+), 111 (100), 81 (30), 79 (33), 73 (21).

(1*S,3*S**,6*R**)-3-(Hydroxymethyl)-1,6-dimethyl-2,5-dioxabicyclo-[4.4.0]dec-8-ene (26):** Oil. ^1H NMR ($CDCl_3$, 500 MHz): δ = 5.65 (m, 1 H), 5.45 (m, 1 H), 4.07 (dddd, *J* = 11.7, 4.8, 4.4, 3.4 Hz, 1 H), 3.82 (1/2AB, d, *J* = 11.9, 11.7 Hz, 1 H), 3.62 (1/2AB, d, *J* = 11.7, 3.4 Hz, 1 H), 3.53 (1/2AB, d, *J* = 11.9, 4.4 Hz, 1 H), 3.49 (1/2AB, d, *J* = 11.7, 4.8 Hz, 1 H), 3.13 (1/2AB, *J* = 17.2 Hz, 1 H), 2.23 (br. s, 1 H), 2.00 (br. s, 1 H), 1.73 (1/2AB, d, *J* = 17.2, 5.2 Hz, 1 H), 1.34 (s, 3 H), 1.06 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 124.5 (d), 122.5 (d), 74.4 (s), 73.1 (s), 67.3 (d), 62.8 (t), 61.2 (t), 39.3 (t), 30.8 (t), 24.0 (q), 19.1 (q) ppm. MS: *m*/*z* (%) = 144 (100, M^+ − 1,3-butadiene), 43 (53).

(1*S,2*R**,3*R**,6*S**)-1,2-Dimethyl-3,6-divinylcyclohexan-1,2-diol (27a) and (1*S**,2*R**,3*S**,6*S**)-1,2-Dimethyl-3,6-divinylcyclohexan-1,2-diol [(±)-27b]:** Compounds were synthesized from biacetyl (20 mmol, 1.72 g) and BISTRO (12 h. at room temp.) according to the general procedure. The crude product was purified by flash chromatography (petroleum ether/Et_2O, 98:2 to 80:20) to give **27a** (1.02 g, 26%) and then (±)-**27b** (0.98 g, 25%).

27a: Oil. ^1H NMR ($CDCl_3$, 500 MHz): δ = 5.89 (ddd, *J* = 17.3, 10.5, 8.4 Hz, 2 H), 5.09 (br. d, *J* = 10.5 Hz, 2 H), 5.06 (br. d, *J* = 17.3 Hz, 2 H), 2.42 (ddd, *J* = 11.9, 8.4, 3.2 Hz, 2 H), 1.63 (m, 3 H), 1.43 (m, 3 H), 1.21 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 139.9 (d), 116.4 (t), 74.8 (s), 45.9 (d), 26.7 (t), 21.9 (q) ppm. MS: *m*/*z* (%) = 168 (17), 153 (12), 135 (21), 109 (34), 93 (23), 88 (30), 69 (31), 43 (100).

(±)-27b: White crystals, m.p. 64−65 °C (hexane). ^1H NMR ($CDCl_3$, 300 MHz): δ = 5.90 (m, 2 H), 5.11 (m, 2 H), 5.04 (m, 2 H), 2.54 (ddd, *J* = 11.7, 7.5, 3.6 Hz, 1 H), 2.09 (ddd, *J* = 11.9, 8.2, 3.8 Hz, 1 H), 1.67 (m, 2 H), 1.39 (m, 1 H), 1.32 (dq, *J* = 4.0, 0.9 Hz, 1 H), 1.16 (s, 3 H), 1.05 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 139.4 (d), 139.3 (d), 116.6 (t), 116.0 (t), 75.8 (s), 75.4 (s), 48.3 (d), 46.8 (d), 27.3 (t), 27.1 (t), 22.4 (q), 17.8 (q) ppm. MS: *m*/*z* (%) = 168 (28), 153 (15), 135 (35), 109 (38), 95 (29), 88 (44), 69 (22), 43 (100).

(1*R*,3*S*,8*S*,10*S*,11*S*,14*R*)-1,10-Dimethyl-11,14-divinyl-2,9-dioxatricyclo[8.4.0.0^{3,8}]tetradecane (28a) and (1*R*,3*S*,8*S*,10*S*,11*S*,14*S*)-1,10-Dimethyl-11,14-divinyl-2,9-dioxatricyclo[8.4.0.0^{3,8}]tetradecane (28b): Synthesized from **17** (4.61 g) and BISTRO (12 h. at −60 °C) according to the general procedure. The crude product was purified by flash chromatography (petroleum ether/Et_2O, 100:0 to 98:2) to give **28b** (2.00 g, 36%) and then **28a** (0.83 g, 15%).

28a: Oil. ^1H NMR ($CDCl_3$, 200 MHz): δ = 5.98 (m, 2 H), 5.06 (m, 4 H), 3.50 (m, 2 H), 2.36 (m, 1 H), 2.07 (m, 1 H), 1.78 (m, 4 H), 1.50 (m, 4 H), 1.32 (s, 3 H), 1.29 (m, 4 H), 0.93 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 139.4 (d), 138.9 (d), 116.7 (t), 114.4 (t), 78.2 (s), 78.1 (s), 73.4 (d), 71.5 (d), 51.3 (d), 38.8 (d), 30.7 (t), 30.5 (t), 26.2 (t), 24.6 (t, 2C), 23.5 (t), 19.4 (q), 18.9 (q) ppm.

28b: Oil. ^1H NMR ($CDCl_3$, 500 MHz): δ = 6.15 (ddd, *J* = 17.5, 10.7, 5.7 Hz, 1 H), 5.98 (ddd, *J* = 17.2, 10.2, 9.0 Hz, 1 H), 5.14 (d, *J* = 10.7 Hz, 1 H), 5.06 (d, *J* = 17.5 Hz, 1 H), 5.01 (m, 2 H), 3.89 (td, *J* = 10.1, 4.0 Hz, 1 H), 3.80 (td, *J* = 10.1, 4.0 Hz, 1 H), 2.66 (m, 1 H), 2.03 (m, 2 H), 1.97 (m, 1 H), 1.75 (m, 2 H), 1.69 (m, 2 H), 1.35 (m, 2 H), 1.25 (s, 3 H), 1.23 (m, 2 H), 1.21 (m, 2 H), 1.01 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 139.6 (d), 139.5 (d), 115.0 (t), 114.6 (t), 79.2 (s), 77.4 (s), 74.8 (2C, d), 52.1 (d), 49.3

(d), 33.4 (t), 32.8 (t), 28.0 (t), 27.3 (q), 26.8 (t), 24.2 (t, 2C), 19.2 (q) ppm. MS: *m*/*z* (%) = 169 (16), 168 (100, $M^+ - C_8H_{12}$), 99 (15), 81 (28), 79 (15), 67 (24), 43 (23), 41 (10). $C_{18}H_{28}O_2$ (276.41): calcd. C 78.21, H 10.21; found C 78.27, H 10.17.

(1*S*,3*S*,6*R*,7*R*,10*R*)-1,6-Dimethyl-3-phenyl-7,10-divinyl-2,5-dioxabicyclo[4.4.0]decane (29): Synthesized from (−)-**18** (5.05 g) and BISTRO (1 h. at −60 °C) according to the general procedure using 2 equiv. of $TiCl_4$ (7.6 g, 4.4 mL). The crude product was purified by flash chromatography (petroleum ether/Et_2O, 100:0 to 98:2) to give **29** (1.67 g, 28%) and then **5** (1.43 g, 40%).

29: Oil. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.48 (d, *J* = 7.3 Hz, 1 H), 7.44 (d, *J* = 7.3 Hz, 1 H), 7.33 (d, *J* = 7.3 Hz, 1 H), 7.31 (d, *J* = 7.3 Hz, 1 H), 7.25 (m, 1 H), 6.04 (m, 1 H), 5.96 (m, 1 H), 5.04 (m, 4 H), 4.85 (m, 1 H), 4.14 (m, 2 H), 3.19 (m, 1 H), 2.83 (m, 1 H), 2.05 (m, 2 H), 1.74 (m, 2 H), 1.43 (s, 3 H), 1.05 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 142.3 (s), 141.4 (s), 139.5 (d), 139.1 (d), 138.9 (d), 128.4 (d), 128.3 (d), 127.8 (d), 127.7 (d), 127.2 (d), 127.0 (d), 115.5 (t), 115.3 (t), 115.0 (t), 114.3 (t), 79.3 (s), 77.4 (s), 77.1 (s), 76.4 (s), 71.6 (d), 70.9 (d), 64.1 (t), 61.4 (t), 51.8 (d), 51.4 (d), 46.0 (d), 42.8 (d), 28.0 (t), 27.5 (t), 26.73 (t), 26.66 (t), 25.0 (q), 24.0 (q), 18.9 (q), 18.2 (q) ppm. MS: *m*/*z* (%) = 190 (21, $M^+ - C_8H_{12}$), 163 (10), 120 (21), 109 (14), 104 (100), 91 (25), 78 (29), 43 (52). $C_{20}H_{26}O_2$ (298.42): calcd. C 80.50, H 8.78; found C 80.46, H 8.83.

(+)-(2*R*,5*R*)-1-Acetyl-1-methyl-2,5-divinylcyclopentane (5b): Synthesized from (−)-**18** (5.05 g) and BISTRO according to the general procedure using 4 equiv. of $TiCl_4$ (15.2 g, 8.8 mL); the reaction mixture was stirred 12 h. at −60 °C. The crude product was purified by flash chromatography (petroleum ether/Et_2O, 100:0 to 98:2) to give **5** (2.40 g, 67%) as a mixture of **5a** and **5b** (10:90).[9] **5b:** *ee* > 98%. $[\alpha]_D^{25}$ = +13.1 ($CHCl_3$, 1.1). ^1H NMR ($CDCl_3$, 300 MHz): δ = 5.68 (m, 2 H), 4.97 (m, 4 H), 3.17 (br. q, *J* = 9.1 Hz, 1 H), 2.44 (br. q, *J* = 7.4 Hz, 1 H), 2.01 (s, 3 H), 1.80 (m, 2 H), 1.55 (m, 2 H), 1.11 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 212.5 (s), 139.6 (d), 138.7 (d), 115.3 (t), 114.8 (t), 61.6 (s), 46.6 (d), 45.5 (d), 29.8 (t), 28.2 (t), 28.2 (q), 19.7 (q) ppm.

(2*S*,5*R*)-1-Acetyl-1-methyl-2,5-divinylcyclopentane (5a): Synthesized from **15** (3.56 g) and BISTRO according to the general procedure using 3 equiv. of $TiCl_4$ (11.4 g, 6.6 mL); the reaction mixture was stirred 12 h. at −60 °C. Compound **5** (2.78 g, 78%) was obtained as a mixture of **5a** and **5b** (70:30). **5a:** Oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 5.64 (ddd, *J* = 16.8, 10.6, 7.8 Hz, 2 H), 4.99 (br. d, *J* = 10.6 Hz, 2 H), 4.97 (br. d, *J* = 16.8 Hz, 2 H), 2.87 (q, *J* = 7.2 Hz, 2 H), 2.09 (s, 3 H), 1.91 (m, 2 H), 1.62 (m, 2 H), 0.93 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 212.7 (s), 137.8 (d), 116.2 (t), 62.0 (s), 52.0 (d), 27.9 (t), 27.1 (q), 11.1 (q) ppm.

4-Hydroxymethyl-1,6-dimethyl-7,10-divinyl-2,5-dioxabicyclo[4.4.0]decane (30): Synthesized from **19** (3.48 g) and BISTRO (12 h. at −60 °C) according to the general procedure using 4 equiv. of $TiCl_4$ (15.2 g, 8.8 mL). The crude product was purified by flash chromatography (petroleum ether/Et_2O, 100:0 to 98:2 then 70:30) to give **5** (2.28 g, 64%) and then **30** (0.45 g, 9%; inseparable mixture of two diastereoisomers). **30:** Oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.30−5.1 (m, 2 H), 5.1−5.8 (m, 4 H), 4.2−3.9 (m, 2 H), 3.7−3.5 (m, 3 H), 2.80−2.70 (m, 2 H), 1.8 (m, 2 H), 1.5 (m, 2 H), 1.30−1.28 (m, 3 H), 0.89−0.86 (m, 3 H) ppm. MS: *m*/*z* (%, first/second eluted isomer) = 178 (12/3, $M^+ - C_3H_6O_2$), 163 (34/27), 135 (78/36), 124 (31/47), 119 (21/9), 109 (90/100), 107 (61/47), 91 (67/48), 79 (97/66), 43 (100).

Methoxycarbonylation of 5: A 250-mL flask equipped with a thermometer, septum cap, magnetic stirring bar, and argon outlet was charged with anhydrous THF (100 mL), NaH (55% dispersion in oil, 587 mg, 13.5 mmol), and dimethyl carbonate (1 mL, 11.8 mmol). The mixture was heated under reflux and then **5** (800 mg, 4.49 mmol) was added. The solution was heated under reflux for 12 h and then cooled to room temp.; acetic acid (4 mL) was added slowly, followed by water (13.2 mL). After extraction with diethyl ether (3 × 10 mL), the organic phases were washed with water (2 × 5 mL) and brine (5 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was subjected to flash chromatography (petroleum ether/Et_2O, 100:0 to 98:2) to give **6a** and then **6b** (827 mg, 78% of overall yield).

(2*S*,5*R*)-1-[2-(Methoxycarbonyl)ethan-1-on-1-yl]-1-methyl-2,5-divinylcyclopentane (6a): Synthesized from **5a**. **6a:** ^1H NMR ($CDCl_3$, 300 MHz): δ = 5.66 (ddd, *J* = 16.5, 10.8, 7.9 Hz, 2 H), 5.0 (m, 4 H), 3.69 (s, 3 H), 3.48 (s, 2 H), 2.91 (br. q. *J* = 6.8 Hz, 2 H), 1.94 (m, 2 H), 1.64 (m, 2 H), 0.95 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 206.7 (s), 168.2 (s), 137.3 (d, 2C), 116.9 (t, 2C), 62.1 (s), 52.3 (q), 51.6 (t, 2C), 46.0 (t), 27.8 (t, 2C), 11.0 (q) ppm.

(+)-(2*R*,5*R*)-1-[2-(Methoxycarbonyl)ethan-1-on-1-yl]-1-methyl-2,5-divinylcyclopentane (6b): Synthesized from (+)-**5b**. (+)-**6b**: $[\alpha]_D^{25}$ = +33.1 ($CHCl_3$, 1.16). ^1H NMR ($CDCl_3$, 300 MHz): δ = 5.65 (m, 2 H), 5.00 (m, 4 H), 3.68 (s, 3 H), 3.49 (1/2AB, *J* = 16.0 Hz, 1 H), 3.36 (1/2AB, *J* = 16.0 Hz, 1 H), 3.14 (br. q, *J* = 8.0 Hz, 1 H), 2.43 (br. q, *J* = 8.5 Hz, 1 H), 1.94 (m, 2 H), 1.57 (m, 2 H), 1.12 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 205.5 (s), 168.0 (s), 138.5 (d), 138.1 (d), 115.7 (t), 115.67 (t), 61.6 (s), 55.7 (q), 52.0 (d), 47.0 (t), 46.9 (d), 29.8 (t), 28.3 (t), 19.3 (q) ppm.

General Procedure for the Alkylation of 6: Cesium carbonate (2.44 g, 7.5 mmol) and 4- or 5-methoxy-1-iodobenzocyclobutene (1.95 g, 7.5 mmol) were added to a solution of **6** (1.18 g, 5 mmol) in anhydrous acetone (25 mL). The mixture was stirred vigorously and then heated under reflux for 24 h. After cooling, the mixture was filtered through Celite®. The filtrate was concentrated under reduced pressure and the residue was subjected to flash chromatography.

1-[2-(5-Methoxybenzocyclobuten-1-yl)-2-(methoxycarbonyl)-1-oxoethyl]-1-methyl-2,5-divinylcyclopentane (8ac): ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.88 (d, *J* = 8.1 Hz, 1 H), 6.69 (dd, *J* = 8.1, 2.1 Hz, 1 H), 6.45 (d, *J* = 2.1 Hz, 1 H), 5.63 (ddd, *J* = 17.4, 10.6, 7.0 Hz, 1 H), 5.54 (ddd, *J* = 17.2, 10.2, 8.1 Hz, 1 H), 4.94 (m, 2 H), 4.79 (dd, *J* = 10.3, 0.9 Hz, 1 H), 4.54 (d, *J* = 17.0 Hz, 1 H), 3.98 (1/2AB, dd, *J* = 11.0, 5.0, 2.1 Hz, 1 H), 3.85 (1/2AB, *J* = 11.0 Hz, 1 H), 3.66 (s, 3 H), 3.63 (s, 3 H), 3.19 (1/2AB, d, *J* = 13.9, 5.0 Hz, 1 H), 3.16 (m, 1 H), 2.89 (1/2AB, d, *J* = 13.9, 2.1 Hz, 1 H), 2.69 (br. q, *J* = 8.4 Hz, 1 H), 1.85 (m, 2 H), 1.56 (m, 2 H), 0.93 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 207.5 (s), 168.8 (s), 159.0 (s), 147.0 (s), 137.2 (d), 134.5 (s), 123.8 (d), 116.8 (t), 115.9 (t), 115.1 (d, 2C), 108.6 (d), 61.9 (s), 59.8 (q), 55.3 (q), 52.6 (d), 52.2 (d), 50.2 (d), 41.8 (d), 33.3 (t), 28.2 (t), 26.8 (t), 11.0 (q) ppm.

1-[2-(4-Methoxybenzocyclobuten-1-yl)-2-(methoxycarbonyl)-1-oxoethyl]-1-methyl-2,5-divinylcyclopentane (8ad): ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.85 (1/2AB, *J* = 8.1 Hz, 1 H), 6.69 (1/2AB, d, *J* = 8.1, 1.7 Hz, 1 H), 6.61 (br. s, 1 H), 5.69−5.59 (m, 2 H), 4.96 (m, 4 H), 4.03 (1/2AB, dd, *J* = 10.6, 5.1, 1.9 Hz, 1 H), 3.89 (1/2AB, *J* = 10.6 Hz, 1 H), 3.70 (s, 3 H), 3.67 (s, 3 H), 3.29 (1/2AB, d, *J* = 14.4, 5.1 Hz, 1 H), 3.12 (br. q, *J* = 7.9 Hz, 1 H), 2.85 (br. q, *J* = 7.9 Hz, 1 H), 2.60 (1/2AB, *J* = 14.4 Hz, 1 H), 1.88 (m, 2 H), 1.59 (m, 2 H), 0.99 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 207.2 (s),

168.6 (s), 160.2 (s), 143.5 (s), 137.3 (d), 137.0 (d), 123.6 (d), 116.6 (t), 116.0 (t), 113.6 (d), 108.6 (d), 62.0 (s), 59.0 (q), 55.2 (q), 53.2 (d), 52.0 (d), 51.2 (d), 41.9 (d), 35.6 (t), 28.3 (t), 27.0 (t), 10.8 (q) ppm.

1-[2-(5-Methoxybenzocyclobuten-1-yl)-2-(methoxycarbonyl)-1-oxoethyl]-1-methyl-2,5-divinylcyclopentane (8bc): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.02 (1/2AB, *J* = 7.7 Hz, 1 H), 6.86 (br. s, 1 H), 6.85 (1/2AB, *J* = 7.7 Hz, 1 H,), 5.69−5.58 (m, 2 H), 5.05−4.74 (m, 4 H), 3.76 (s, 3 H), 3.68 (s, 3 H), 3.51 (1/2AB, d, *J* = 13.6, 4.7 Hz, 1 H), 3.23 (br. d, *J* = 13.6 Hz, 1 H), 2.95 (m, 2 H), 1.86 (m, 2 H), 1.62 (m, 2 H), 0.76 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 173.8 (s), 166.0 (s), 159.5 (s), 146.2 (s), 137.7 (d), 134.0 (s), 124.2 (d), 117.0 (d), 116.8 (d), 115.7 (t, 2C), 109.1 (d), 79.7 (d), 55.6 (q), 55.2 (s), 51.1 (d), 50.2 (d), 39.6 (t), 27.0 (t), 26.7 (t), 12.7 (q) ppm.

1-[2-(4-Methoxybenzocyclobuten-1-yl)-2-(methoxycarbonyl)-1-oxoethyl]-1-methyl-2,5-divinylcyclopentane (8bd): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.14 (d, *J* = 8.3 Hz, 1 H), 6.74 (d, *J* = 8.3 Hz, 1 H), 6.69 (br. s, 1 H), 5.87−5.57 (m, 2 H), 5.26−4.71 (m, 4 H), 3.75 (s, 3 H), 3.67 (s, 3 H), 3.55 (1/2AB, d, *J* = 14.6, 4.1 Hz, 1 H), 3.28 (1/2AB, *J* = 14.6 Hz, 1 H), 2.95 (m, 2 H), 1.85 (m, 2 H), 1.60 (m, 2 H), 0.74 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 206.7 (s), 169.2 (s), 160.2 (s), 143.8 (s), 139.3 (s), 138.6 (d), 124.0 (d), 115.6 (t), 115.5 (t), 113.6 (d), 113.5 (d), 108.5 (d), 61.6 (s), 56.7 (q), 55.3 (q), 52.1 (d), 51.9 (d), 48.4 (d), 41.5 (d), 35.4 (t), 30.8 (t), 28.4 (t), 19.1 (q) ppm.

General Procedure for the Thermolysis of 8: A solution of **8** in anhydrous 1,2,4-trichlorobenzene (10 mL/mmol) was heated at 200 °C or 215 °C for 6 h (the progress of the reaction was followed by TLC analysis). The solvent was evaporated under reduced pressure and the residue was subjected to flash chromatography (petroleum ether/Et_2O, 98:2 to 95:5) to give the corresponding steroid.

(±)-(8β,9β,14α)-2-Methoxy-17β-vinylestra-1,3,5(10)-trien-12-one (9ac): Obtained by heating **8ac** at 215 °C (40% yield); white crystals, m.p. 109 °C (acetonitrile). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.97 (d, *J* = 8.1 Hz, 1 H), 6.82 (br. s, 1 H), 6.66 (br. d, *J* = 8.1 Hz, 1 H), 6.02 (ddd, *J* = 18.1, 9.80, 5.9 Hz, 1 H), 5.04 (m, 2 H), 3.76 (s, 3 H), 3.45 (br. q, *J* = 5.9 Hz, 1 H), 2.89 (1/2AB, d, *J* = 15.4, 6.1 Hz, 1 H), 2.79 (1/2AB, d, *J* = 15.4, 5.9 Hz, 1 H), 2.62 (m, 3 H), 2.33 (br. sext, *J* = 5.6 Hz, 1 H), 1.93−1.60 (m, 6 H), 1.45 (m, 1 H), 1.01 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 214.1 (s), 158.1 (s), 139.0 (d), 138.4 (s), 129.6 (d), 129.5 (s), 115.1 (t), 112.8 (d), 112.0 (d), 55.3 (q), 55.2 (s), 48.9 (d), 46.6 (d), 42.4 (t), 39.5 (d), 33.9 (d), 26.1 (t), 25.9 (t), 24.8 (t), 24.1 (t), 13.1 (q) ppm. MS: *m*/*z* (%) = 310 (100) [M^+], 292 (29), 267 (18), 159 (21). $C_{21}H_{26}O_2$ (310.43): calcd. C 81.25, H 8.44; found C 81.32, H 8.34.

(±)-(8β,9α,14α)-2-Methoxy-11α-methoxycarbonyl-17β-vinylestra-1,3,5(10)-trien-12-one (10ac): Obtained by heating **8ac** at 215 °C (40% yield); white crystals, m.p. 168−169 °C (acetonitrile). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.03 (d, *J* = 8.3 Hz, 1 H), 6.70 (dd, *J* = 8.3, 2.2 Hz, 1 H), 6.49 (br. d, *J* = 2.2 Hz, 1 H), 5.89 (ddd, *J* = 17.3, 10.6, 6.2 Hz, 1 H), 5.12 (dt, *J* = 17.3, 1.0 Hz, 1 H), 5.07 (d, *J* = 10.6 Hz, 1 H), 3.94 (d, *J* = 11.7 Hz, 1 H), 3.84 (s, 3 H), 3.72 (s, 3 H), 3.25 (t, *J* = 10.9 Hz, 1 H), 2.85 (m, 3 H), 1.97 (m, 1 H), 1.89 (m, 1 H), 1.85 (m, 1 H), 1.76 (m, 1 H), 1.64 (m, 1 H), 1.58 (m, 1 H), 1.45 (m, 2 H), 0.94 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 209.0 (s), 172.0 (s), 157.9 (s), 140.6 (s), 138.2 (d), 129.6 (d), 129.1 (s), 115.9 (t), 111.8 (d), 109.7 (d), 57.6 (d), 56.4 (s), 55.2 (q), 54.0 (d), 52.6 (q), 47.8 (d), 46.8 (d), 37.1 (d), 27.3 (t), 27.2 (t), 25.1 (t), 24.1 (t), 12.5 (q) ppm. MS: *m*/*z* (%) = 368 (16) [M^+], 310 (21), 309 (100, $M^+ - CO_2Me$), 200 (17), 109 (12).

(±)-(8β,9β,14α)-3-Methoxy-17β-vinylestra-1,3,5(10)-trien-12-one (9ad): Obtained by heating **8ad** at 215 °C (40% yield); white crystals, m.p. 163 °C (acetonitrile). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.20 (d, *J* = 8.7 Hz, 1 H), 6.70 (dd, *J* = 8.7, 2.4 Hz, 1 H), 6.60 (br. d, *J* = 2.4 Hz, 1 H), 6.00 (ddd, *J* = 18.2, 9.7, 5.9 Hz, 1 H), 5.04 (m, 2 H), 3.74 (s, 3 H), 3.42 (br. q, *J* = 5.7 Hz, 1 H), 2.88 (1/2AB, d, *J* = 15.2, 6.1 Hz, 1 H), 2.78 (1/2AB, d, *J* = 15.2, 5.4 Hz, 1 H), 2.67 (m, 2 H), 2.55 (m, 1 H), 2.34 (sext. *J* = 5.5 Hz, 1 H), 1.94−1.40 (m, 7 H), 1.00 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 214.2 (s), 157.7 (s), 139.1 (d), 138.7 (s), 129.3 (s), 128.5 (d), 115.1 (t), 113.8 (d), 112.1 (d), 55.3 (s), 55.26 (q), 48.7 (d), 46.6 (d), 42.3 (t), 39.1 (d), 34.1 (d), 27.1 (t), 25.6 (t), 24.7 (t), 24.1 (t), 13.1 (q) ppm. MS: *m*/*z* (%) = 310 (100) [M^+], 292 (15), 267 (15), 199 (31), 160 (21), 115 (13), 91 (18).

(±)-(8β,9α,14α)-3-Methoxy-17β-vinylestra-1,3,5(10)-trien-12-one (11ad): Obtained by heating **8ad** at 215 °C (40% yield); white crystals, m.p. 146 °C (acetonitrile). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.02 (d, *J* = 8.5 Hz, 1 H), 6.70 (br. d, *J* = 8.5 Hz, 1 H), 6.65 (br. s, 1 H), 5.98 (ddd, *J* = 17.4, 10.6, 5.8 Hz, 1 H), 5.14 (d, *J* = 17.4 Hz, 1 H), 5.11 (m, 1 H), 3.76 (s, 3 H), 2.90 (m, 3 H), 2.68 (1/2AB, *J* = 12.9 Hz, 1 H), 2.61 (1/2AB, *J* = 12.9 Hz, 1 H), 2.00−1.40 (m, 8 H), 0.93 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 213.7 (s), 158.0 (s), 139.0 (d), 137.8 (s), 131.2 (s), 126.0 (d), 115.3 (t), 114.1 (d), 111.7 (d), 56.8 (s), 55.3 (q), 54.8 (d), 46.4 (d), 45.5 (d), 42.8 (t), 38.3 (d), 29.8 (t), 27.3 (t), 24.9 (t), 23.6 (t), 13.1 (q) ppm. MS: *m*/*z* (%) = 310 (100) [M^+], 292 (62), 277 (64), 238 (12), 199 (11), 159 (31), 115 (16), 91 (31).

(±)-(8β,9α,14α)-3-Methoxy-11α-methoxycarbonyl-17β-vinylestra-1,3,5(10)-trien-12-one (10ad): Obtained by heating **8ad** at 200 °C (40% yield); white crystals, m.p. 196 °C (acetonitrile). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.80 (d, *J* = 8.3 Hz, 1 H), 6.67 (br. s, 1 H), 6.65 (dd, *J* = 8.3, 2.6 Hz, 1 H), 5.89 (ddd, *J* = 17.3, 10.4, 6.3 Hz, 1 H), 5.1 (d, *J* = 17.3 Hz, 1 H), 5.06 (d, *J* = 10.4 Hz, 1 H), 3.90 (d, *J* = 11.9 Hz, 1 H), 3.82 (s, 3 H), 3.74 (s, 3 H), 3.20 (br. d, *J* = 11.9, 9.8 Hz, 1 H), 2.88 (m, 3 H), 2.00−1.40 (m, 8 H), 0.93 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 209.0 (s), 172.0 (s), 158.1 (s), 138.5 (s), 138.2 (d), 131.6 (s), 124.4 (d), 115.8 (t), 114.4 (d), 111.1 (d), 57.8 (d), 56.4 (s), 55.2 (q), 53.8 (d), 52.5 (q), 47.2 (d), 46.7 (d), 37.4 (d), 28.4 (t), 27.1 (t), 25.0 (t), 25.0 (t), 24.0 (t), 12.4 (q) ppm. MS: *m*/*z* (%) = 368 (1) [M^+], 310 (26), 309 (100, $M^+ - CO_2Me$), 292 (23), 266 (18), 159 (38), 91 (30).

(±)-(8α,9β,14β)-2-Methoxy-17β-vinylestra-1,3,5(10)-trien-12-one (12bc): Obtained by heating **8bc** at 215 °C (27% yield); oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.98 (d, *J* = 8.3 Hz, 1 H), 6.68 (dd, *J* = 8.3, 2.5 Hz, 1 H), 6.62 (d, *J* = 2.5 Hz, 1 H), 5.71 (ddd, *J* = 17.6, 9.6, 8.1 Hz, 1 H), 5.01 (m, 2 H), 3.75 (s, 3 H), 3.35 (m, 1 H), 3.03 (dt, *J* = 8.1, 7.0 Hz, 1 H), 2.74 (m, 2 H), 2.66 (m, 2 H), 2.04 (m, 1 H), 1.99−1.82 (m, 2 H), 1.82 (m, 1 H), 1.58 (m, 1 H), 1.25 (m, 1 H), 0.98 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 215.0 (s), 157.8 (s), 140.2 (s), 138.3 (d), 130.1 (d), 128.0 (s), 115.6 (t), 112.8 (d), 112.7 (d), 56.2 (s), 55.3 (q), 52.5 (d), 50.0 (d), 42.6 (t), 38.2 (d), 37.4 (d), 30.3 (t), 29.0 (t), 27.9 (t), 26.0 (t), 21.1 (q) ppm. MS: *m*/*z* (%) = 310 (100) [M^+], 292 (23), 266 (18), 159 (38), 91 (30). $C_{21}H_{26}O_2$ (310.43): calcd. C 81.25, H 8.44; found C 81.48, H 8.39.

(−)-(8α,9α,14β)-2-Methoxy-11-methoxycarbonyl-17β-vinylestra-1,3,5(10),11-tetraen-12-ol (14bc): Obtained by heating **8bc** at 215 °C (63% yield); white crystals, m.p. 112 °C (acetonitrile). $[\alpha]_D^{25}$ = −21.9 ($CHCl_3$, 1.0). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 12.91 (s, 1 H), 6.99 (d, *J* = 8.2 Hz, 1 H), 6.66 (dd, *J* = 8.2, 2.2 Hz, 1 H), 6.48 (br. s, 1 H), 6.19 (ddd, *J* = 17.1, 10.6, 6.6 Hz, 1 H), 5.04 (m, 1 H),

5.01 (d, J = 17.1 Hz, 1 H), 3.75 (s, 3 H), 3.72 (s, 3 H), 2.68 (m, 3 H), 2.07 (sext., J = 6.8 Hz, 1 H), 1.91 (m, 3 H), 1.72 (m, 1 H), 1.65 (m, 1 H), 1.55 (m, 2 H), 1.43 (m, 1 H), 0.86 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 181.0 (s), 173.8 (s), 157.9 (s), 141.4 (s), 139.6 (d), 129.7 (s), 128.3 (d), 114.5 (t), 113.5 (d), 110.3 (d), 98.3 (s), 55.3 (q), 51.7 (q), 50.5 (d), 48.9 (s), 47.7 (d), 37.8 (d), 37.2 (d), 28.6 (t), 27.5 (t), 26.2 (t), 25.5 (t), 21.8 (q) ppm. MS: *m/z* (%) = 310 (100, $M^+ - CO_2Me$), 292 (22), 267 (21), 159 (34), 109 (29).

(±)-(8α,9β,14β)-3-Methoxy-17β-vinylestra-1,3,5(10)-trien-12-one (12bd): Obtained by heating **8bd** at 215 °C (25% yield); oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.01 (d, J = 8.5 Hz, 1 H), 6.68 (dd, J = 8.5, 2.6 Hz, 1 H), 6.61 (d, J = 2.6 Hz, 1 H), 5.70 (ddd, J = 15.9, 11.5, 7.9 Hz, 1 H), 5.01 (br. d, J = 11.5 Hz, 1 H), 4.98 (br. d, J = 15.9 Hz, 1 H), 3.75 (s, 3 H), 3.34 (m, 1 H), 3.03 (dt, J = 7.9, 7.7 Hz, 1 H), 2.80 (m, 2 H), 2.74 (m, 1 H), 2.66 (1/2AB, d, J = 15.9, 6.4 Hz, 1 H), 2.10−1.80 (m, 6 H), 1.65−1.55 (m, 2 H), 0.95 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 215.0 (s), 157.9 (s), 138.3 (d), 137.3 (s), 131.2 (s), 129.0 (d), 115.6 (t), 113.9 (d), 112.1 (d), 56.3 (s), 55.2 (q), 52.3 (d), 50.0 (d), 42.7 (t), 37.6 (d), 37.5 (d), 30.1 (t), 28.9 (t), 28.8 (t), 25.7 (t), 20.8 (q) ppm. MS: *m/z* (%) = 310 (100) [M^+], 292 (20), 277 (25), 187 (22), 174 (39), 160 (74), 115 (21), 91 (27).

(−)-(8α,9α,14β)-3-Methoxy-11-methoxycarbonyl-17β-vinylestra-1,3,5(10),11-tetraen-12-ol (14bd): Obtained by heating **8bd** at 215 °C (55% yield); white crystals, m.p. 111 °C (hexane/ethanol, 95:5). $[\alpha]_D^{25}$ = −62.1 ($CHCl_3$, 1.3). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 12.87 (s, 1 H), 6.79 (d, J = 8.1 Hz, 1 H), 6.64 (d, J = 8.1 Hz, 1 H), 6.62 (br. s, 1 H), 6.18 (ddd, J = 16.9, 11.0, 6.5 Hz, 1 H), 5.02 (m, 1 H), 4.99 (d, J = 16.9 Hz, 1 H), 3.74 (br. s, 6 H), 3.72 (m, 1 H), 2.72 (m, 3 H), 2.06 (sext., J = 6.9 Hz, 1 H), 1.9 (m, 3 H), 1.75 (m, 1 H), 1.69−1.58 (m, 4 H), 1.41 (m, 1 H), 0.82 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 180.8 (s), 174.0 (s), 157.6 (s), 139.7 (d), 138.4 (s), 132.1 (s), 128.1 (d), 114.5 (t), 113.0 (d), 111.3 (d), 98.9 (s), 55.2 (q), 51.7 (q), 50.5 (d), 48.9 (d), 47.2 (d), 37.6 (d), 37.0 (d), 28.6 (t), 27.6 (t), 26.5 (t), 25.9 (t), 22.0 (q) ppm. MS: *m/z* (%) = 368 (3) [M^+], 311 (24), 310 (100, $M^+ - CO_2CH_2$), 292 (25), 267 (29), 187 (30), 160 (75), 115 (21), 91 (34). $C_{23}H_{28}O_4$ (368.47): calcd. C 74.97, H 7.66; found C 74.82, H 7.54.

(8α,9β,14β)-3-Methoxy-11α-methoxycarbonyl-17β-vinylestra-1,3,5(10)-trien-12-one (13bd): Obtained by heating **8bd** at 200 °C (25% yield); oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.81 (d, J = 8.5 Hz, 1 H), 6.65 (m, 2 H), 5.90 (ddd, J = 17.4, 10.5, 6.2 Hz, 1 H), 5.11 (d, J = 17.4 Hz, 1 H), 5.01 (d, J = 10.5 Hz, 1 H), 3.90 (d, J = 11.9 Hz, 1 H), 3.83 (s, 3 H), 3.74 (s, 3 H), 3.20 (t, J = 10.8 Hz, 1 H), 2.95−2.75 (m, 3 H), 2.25−1.35 (m, 8 H), 0.93 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 209.1 (s), 172.1 (s), 158.2 (s), 138.6 (s), 138.2 (d), 131.7 (s), 124.5 (d), 115.9 (t), 114.4 (d), 111.1 (d), 57.9 (d), 56.5 (s), 55.3 (d), 53.9 (d), 52.6 (d), 47.2 (d), 46.8 (d), 37.5 (d), 28.5 (t), 27.1 (t), 25.1 (t), 24.0 (t), 12.5 (q) ppm. MS: *m/z* (%) = 310 (24), 309 (100, $M^+ - CO_2Me$), 109 (10). $C_{23}H_{28}O_4$ (368.47): calcd. C 74.97, H 7.66; found C 75.02, H 7.64.

Wacker-Type Oxidation of 14bc: Water (1.5 mL) and $HClO_4$ (70%; 0.3 mL) were added successively to a solution of $Pd(OAc)_2$ (22.4 mg, 0.1 mmol, 0.1 equiv.) and benzoquinone (97 mg, 0.9 mmol, 0.9 equiv.), in acetonitrile (10 mL). The mixture was stirred for 1 h at room temp. under argon. A solution of **14bc** (368 mg, 1 mmol) in acetonitrile (2 mL) was then added and the mixture was stirred at room temp. for 5 h [(the progress of the reaction was followed by TLC analysis (petroleum ether/Et_2O, 50:50)]. The mixture was poured into diethyl ether and washed with 30% aqueous NaOH. The aqueous layer was extracted with diethyl ether. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (petroleum ether/Et_2O, 95:5) to give **31** (211 mg, 55%).

(+)-(8α,9α,14β)-17β-Acetyl-2-methoxy-11-(methoxycarbonyl)estra-1,3,5(10),11-tetraen-12-ol (31): Oil. $[\alpha]_D^{25}$ = +4.7 ($CHCl_3$, 1.1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 12.91 (s, 1 H), 6.98 (br. d, J = 8.1 Hz, 1 H), 6.64 (br. d, 1 Hd, J = 8.1, 2.7 Hz), 6.45 (br. d, J =

Table 2. Crystal data and structure refinement for **27b**, **10ac**, **9ad**, **11ad**, and **14bc**

	27b	**10ac**	**9ad**	**11ad**	**14bc**
Empirical formula	$C_{12}H_{20}O_2$	$C_{23}H_{28}O_4$	$C_{21}H_{26}O_2$	$C_{21}H_{26}O_2$	$C_{23}H_{28}O_4$
Formula mass	196.29	368.47	310.43	310.43	368.47
Crystal color	colorless	colorless	colorless	colorless	colorless
Crystal size/mm^3	0.3 × 0.2 × 0.1	0.5 × 0.5 × 0.5	0.3 × 0.15 × 0.05	0.4 × 0.3 × 0.3	0.4 × 0.4 × 0.3
Crystal system	monoclinic	monoclinic	orthorhombic	orthorhombic	monoclinic
Space group	$P2_1/c$	$P2_1/c$	$P2_12_12_1$	$P2_12_12_1$	$P2_1/c$
a (Å)	12.6130 (7)	12.0682(7)	7.8381 (3)	7.9300 (4)	10.9790 (3)
b (Å)	12.2233 (5)	17.0040 (5)	12.4579 (8)	12.536 (1)	9.8450 (4)
c (Å)	7.5992 (3)	9.6948 (5)	17.1470 (10)	17.203 (1)	18.2470 (7)
β (°)	99.860 (2)	96.795 (4)			90.274 (2)
V [A^3]	1154.3(1)	1975.5(2)	1674.3(2)	1710.2(2)	1972.3(1)
Z	4	4	4	4	4
D_c/g·cm^{-3}	1.13	1.24	1.23	1.205	1.24
μ(Mo-K_α)/cm^{-1}	0.7	0.9	0.8	0.78	0.84
Number of unique data	2245	3757	1856	1915	3909
Number of parameters refined	127	244	208	208	244
Number of refl. in refinement	1630	2620	1611	1900	3728
R	0.049 [$F^2 > 4.5\sigma F^2$]	0.051 [$F^2 > 3\sigma F^2$]	0.05 [$F^2 > 3\sigma F^2$]	0.084 [$F^2 > 3\sigma F^2$]	0.053 [$F^2 > 3\sigma F^2$]
wR	0.061[a]	0.066[a]	0.048[a]	0.24[b]	0.149[c]
Goodness of fit	1.561	1.387	1.373	1.17	1.15
Residual Fourier/e Å^{-3}	−0.21; 0.21	−0.19; 0.21	−0.21; 0.21	−0.254; 0.23	−0.335; 0.302

[a] $w = 1/[\sigma^2(F_o^2) + (0.03F_o^2]$. [b] $w = 1/[\sigma^2(F_o^2) + (0.094P)^2 + 2.8716P]$ where $P = (F_o^2 + 2F_c^2)/3$. [c] $w = 1/[\sigma^2(F_o^2) + (0.08684P)^2 + 0.5489P]$ where $P = (F_o^2 + 2F_c^2)/3$.

2.7 Hz, 1 H), 3.80 (s, 3 H), 3.80 (m, 1 H), 3.75 (s, 3 H), 3.09 (dd, J = 8.9, 7.5 Hz, 1 H), 2.71 (t, J = 6.9 Hz, 2 H), 2.28 (s, 3 H), 2.09 (m, 1 H), 2.02−1.82 (m, 6 H), 1.58 (m, 1 H), 0.93 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 210.9 (s), 179.0 (s), 173.7 (s), 158.0 (s), 140.9 (s), 129.5 (s), 128.4 (d), 113.5 (d), 110.5 (d), 98.8 (s), 56.7 (q), 55.3 (q), 51.9 (d), 51.2 (s), 48.4 (d), 37.7 (d), 36.7 (d), 32.8 (q), 28.0 (t), 27.6 (t), 26.1 (t), 25.4 (t), 22.8 (q) ppm. $C_{23}H_{28}O_5$ (384.47): calcd. C 71.85, H 7.34; found C 71.80, H 7.44.

X-ray Crystallography: CCDC-225808 [for (±)-**27b**], -225809 (for **10ac**), -225810 (for **9ad**), -225811 (for **11ad**), and -225812 (for **14bc**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223-336-033; or E-mail: deposit@ccdc.cam.ac.uk]. A summary of the crystal data, data collection, and refinements is given in Table 2.

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