A Very Short Synthesis of Steroids from 1,3-Butadiene and Benzocyclobutenes

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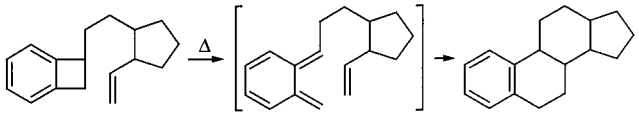
Received July 21, 2000

Lewis acid mediated addition of 1,8-bis(trimethylsilyl)octa-2,6-diene (BISTRO) **1** to succinic anhydride led to spirolactone **2** [(±)-6,9-divinyl-1-oxaspiro[4.4]nonan-2-one]. Methoxycarbonylation followed by stereoselective alkylation by various benzocyclobutenes afforded the substituted benzocyclobutene steroid precursors **5**. Thermolysis of **5** gave rise to steroids (±)-**6** with a *trans-anti-cis* configuration in five steps and in a highly stereoselective manner. Modifications of the sequence allowed the preparation of steroids (±)-**11** with *trans-anti-trans* configuration.

Steroids are compounds of enormous therapeutic importance, and it is estimated that fully one-third of all prescription drugs contain a steroid drug substance.[1] 19-Norsteroids, also known as gestogens,[2] are of significant importance because many of these compounds exhibit pronounced biological activity as compared to their methylated analogues.[3] In the course of a program directed toward developing novel steroids with improved therapeutic indices over existing drugs,[4] we developed a convergent steroid synthesis[5] based on the approach A + D → AD → ABCD. This strategy involves the use of intramolecular cycloaddition of *o*-xylylenes to generate the BC ring system, which was developed by Oppolzer[6] and Kametani[7] (Scheme 1). Although this route provides

Scheme 1



the most efficient access to the steroid tetracyclic skeleton, the difficulties encountered in the synthesis of the 3-vinyl cyclopentane moiety has always prevented it from becoming an efficient large-scale process. In the past few years, we have introduced 1,8-bis(trimethylsilyl)octa-2,6-diene (BISTRO) **1** and extensively studied its reactivity toward electrophiles.[8] BISTRO is a readily available[9] and very convenient annulation reagent to form divinylcyclopentane derivatives.[10] Acylation of **1** with methyl 3-chloroformylpropionate or succinic anhydride gave the (±)-spirolactone **2** as a single product in 80% yield.[11] Initial alkylation attempts of the lactone **2** with various alkyl iodides required large excess (10 equiv) of electrophile and was unsuitable for an efficient synthesis. With the aim of enhancing the nucleophilic character of the enolate, the lactone **2** was acylated with dimethyl carbonate to provide **3** (98% yield).[12] Thus, the alkylation of the malonic derivative **3** was carried out in refluxing

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(1) (a) Makin, H. L. J.; Trafford, D. J. H.; Nolan, J. *Mass Spectra and GC Data of Steroids*; Wiley-VCH: Weinheim, 1998. (b) Zeelen, F. J. *Medicinal Chemistry of Steroids*; Elsevier: Amsterdam, 1990.

(2) (a) Djerassi, C. *Science* **1966**, *151*, 1055−1060. (b) Morand, P.; Lyall, J. *Chem. Rev.* **1968**, *68*, 85−124. (c) Coffey, S. In *Rodd's Chemistry of Carbon Compounds*, 2nd ed.; Elsevier: Amsterdam, 1970; Vol. II, Part D, p 230. (d) Dore, J.-C.; Gilbert, J.; Ojasoo, T.; Raynaud, J.-P. *J. Med. Chem.* **1986**, *29*, 54−60. (e) Crocq, V.; Masson, C.; Winter, J.; Richard, C.; Lemaitre, G.; Lenay, J.; Vivat, M.; Buendia, J.; Prat, D. *Org. Process Res. Dev.* **1997**, *1*, 2−13.

(3) Anstead, G. M.; Carlson, K. E.; Katzenellenbogen, J. A. *Steroids* **1997**, *62*, 268−303.

(4) (a) Pellissier, H.; Santelli, M. *Tetrahedron* **1996**, *52*, 9093−9100. (b) Burtin, G.; Pellissier, H.; Santelli, M. *Tetrahedron* **1998**, *54*, 4913−4922. (c) Burtin, G.; Pellissier, H.; Santelli, M. *Tetrahedron* **1998**, *54*, 8065−8074. (d) Wilmouth, S.; Pellissier, H.; Santelli, M. *Tetrahedron* **1998**, *54*, 10079−10088. (e) Wilmouth, S.; Pellissier, H.; Santelli, M. *Tetrahedron* **1998**, *54*, 13805−13812. (f) Cachoux, F.; Ibrahim-Ouali, M.; Santelli, M. *Tetrahedron Lett.* **2000**, *41*, 1767−1769. (g) Cachoux, F.; Ibrahim-Ouali, M.; Santelli, M. *Synlett* **2000**, *3*, 418−420.

(5) (a) Akhrem, A. A.; Titov, Y. A. *Total Steroid Synthesis*; Plenum Press: New York, 1970. (b) Blickenstaff, R. T.; Ghoosh, A. C.; Wolf, G. C. *Total Steroid Synthesis*; Academic Press: New York, 1974.

(6) (a) Oppolzer, W. *J. Am. Chem. Soc.* **1971**, *93*, 3833−3834, 3834−3835. (b) Oppolzer, W.; Keller, K. *J. Am. Chem. Soc.* **1971**, *93*, 3836−3837. (c) Oppolzer, W. *Tetrahedron Lett.* **1974**, 1001−1004. (d) Oppolzer, W. *Ang. Chem., Int. Ed. Engl.* **1977**, *16*, 10−22. (e) Oppolzer, W.; Petrzilka, M.; Bättig, K. *Helv. Chim. Acta* **1977**, *60*, 2964−2967. (f) Oppolzer, W.; Bättig, K.; Petrzilka, M. *Helv. Chim. Acta* **1978**, *61*, 1945−1947.

(7) (a) Kametani, T.; Fukumoto, K. *Heterocycles* **1975**, *3*, 29−56. (b) Kametani, T.; Kato, Y.; Honda, T.; Fukumoto, K. *Heterocycles* **1976**, *4*, 241−246. (c) Kametani, T.; Nemoto, H.; Ishikawa, H.; Shiroyama, K.; Fukumoto, K. *J. Am. Chem. Soc.* **1976**, *98*, 3378−3379. (d) Kametani, T.; Matsumoto, H.; Nemoto, H.; Fukumoto, K. *J. Am. Chem. Soc.* **1978**, *100*, 6218−6220.

(8) (a) Pellissier, H.; Toupet, T.; Santelli, M. *J. Org. Chem.* **1994**, *59*, 1709−1713. (b) Pellissier, H.; Faure, R.; Santelli, M. *J. Chem. Soc., Chem. Commun.* **1995**, 1847−1848. (c) Pellissier, H.; Toupet, L.; Santelli, M. *J. Org. Chem.* **1998**, *63*, 2148−2153.

(9) Tubul, A.; Santelli, M. *Tetrahedron* **1988**, *44*, 3975−3982.

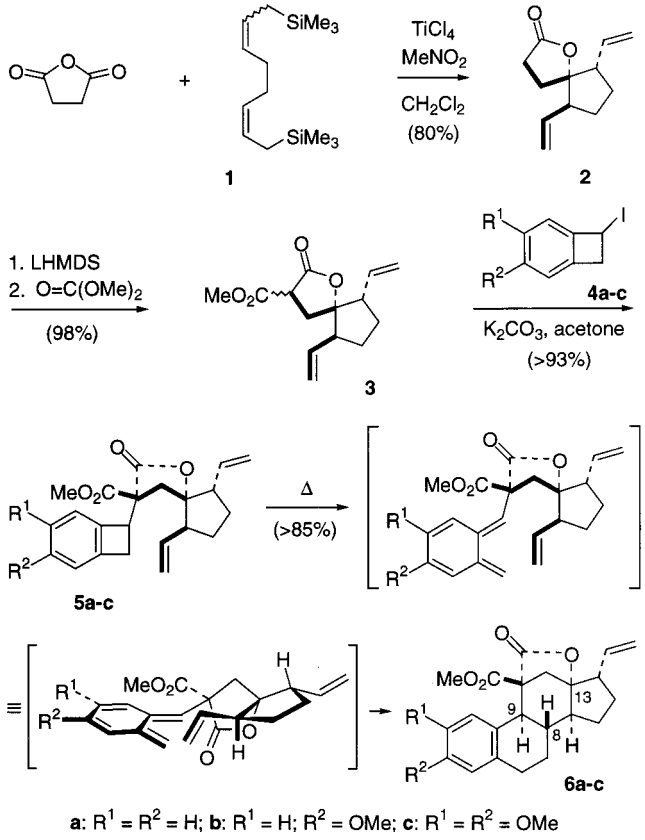
(10) (a) Tubul, A.; Ouvrard, Ph.; Santelli, M. *Synthesis* **1991**, 173−176. (b) Tubul, A.; Ouvrard, Ph.; Santelli, M. *Bull. Soc. Chim. Fr.* **1992**, *129*, 265−269. (c) Ouvrard, Ph.; Tubul, A.; Santelli, M. *Tetrahedron Lett.* **1992**, *33*, 7519−7520. (d) Pellissier, H.; Wilmouth, S.; Santelli, M. *Tetrahedron Lett.* **1996**, *37*, 5107−5110. (e) Burtin, G.; Pellissier, H.; Santelli, M. *Tetrahedron* **1998**, *54*, 2075−2086.

(11) Pellissier, H.; Wilmouth, S.; Santelli, M. *Bull. Soc. Chim. Fr.* **1995**, *132*, 627−641.

(12) (a) House, H. O. *Modern Synthetic Reactions*, 2d ed.; W. A. Benjamin: Menlo Park, CA, 1972; pp 734−765. (b) Fray, A. H.; Kaye, R. L.; Kleinman, E. F. *J. Org. Chem.* **1986**, *51*, 4828−4833.

10.1021/jo001106f CCC: $20.00
Published on Web 12/05/2000

Scheme 2



a: $R^1 = R^2 = H$; **b**: $R^1 = H$; $R^2 = OMe$; **c**: $R^1 = R^2 = OMe$

acetone in the presence of anhydrous potassium carbonate and only 1.3 mole equiv of iodobenzocyclobutene using the very simple Claisen procedure.[13] A mixture of two cyclobutene diastereoisomers **5** (2.5:1) was isolated in 93% yield. The stereoselectivity of the reaction is such that the attack takes place on the face of the enolate bearing the vinyl group *anti* to the lactone ring−oxygen linkage.[14] Upon thermolysis of **5a**−**c**, only one vinyl group is involved in the course of the intramolecular Diels−Alder reaction, and the steroids (±)-**6a**−**c** are produced in almost quantitative yield. The cycloadducts result from an *exo* approach of the (*E*)-*o*-xylylene intermediate during the cyclization and the relative configuration of six stereogenic centers is controlled during the cycloaddition process. *Steroids **6a**−**c** were obtained in five steps from 1,3-butadiene with an overall yield of ca. 27−33%* (Scheme 2). The structures of steroids **6a**−**c** were characterized on the basis of their spectroscopic properties (including a series of COSY and HMQC NMR experiments, 400 MHz) and X-ray crystallography. The stereochemistry of the B/C ring was established using ^{1}H NMR, while the C/D ring junction was determined by X-ray crystallography. For example, steroid **6b** displayed a doublet at 3.04 ppm for the proton $H^{(9)}$ with a coupling constant $J_{H^{(8)}-H^{(9)}} = 11.0$ Hz, which indicated a *trans* relationship for the B/C ring junction. Moreover, COSY experiments on $H^{(9)}$ showed that the signal of $H^{(8)}$ at 1.22 ppm was a double quadruplet corresponding to three J_{trans} coupling constants ($J = 11.0$ Hz) and one J_{cis} coupling constant ($J = 7.5$ Hz). The C-13 configuration was then rigorously

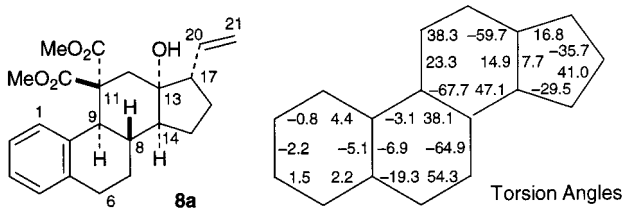


Figure 1.

established by X-ray crystallographic analysis of steroid **8a**, obtained by treatment of **6a** with methanol in the presence of catalytic amounts of BF_3-OEt_2.[15]

The structure of **8a**, along with torsion angles, is depicted in Figure 1 and reveals unexpected structural and conformational properties.[16] (An ORTEP drawing and table of bond lengths and angles is available in Supporting Information.) The A-ring is not planar but rather exists as a distorted "boat" conformation with $H^{(1)}$ as bowsprit. The B ring has a half-chair conformation with atoms C(7)α and C(8)*β* displaced on opposite sides of the medium plane of atoms C(6), C(5), C(9), and C(10).[17] As predicted,[18] repulsive interactions between the C(11)-substituents and the hydrogen atom on C(1) open the C(10)−C(9)−C(11) valence angle to 114.7° and the C(1)−C(10)−C(9)−C(11) torsion angle to 52.6°. The latter differs by more than 15° from the average of four crystallographically independent observations of estrone, 28.1°, 33.1°, 32.9°, and 35.0°.[19] Moreover, the bond length of C(9)−C(11) (1.584 Å) is significantly longer than those reported for estradiol analogues (1.526 Å in 3,17*β*-estradiol,[20] 1.529 Å in 11-ketoestrone[21]). One way to achieve this result is to relieve the unfavorable interactions by putting ring C into a boat-twist conformation, with $H^{(12\alpha)}$ as bowsprit.[22] The D ring conformation is a distorted 16α-envelope and can be described by the parameters $\Delta = 158°$ and $\varphi_m = 41°$.[23]

Although, the configuration *trans-syn-cis* has often been described because it is present in natural cardioactive steroids,[24] to the best of our knowledge, the only structural analogue of **8a** (*trans-anti-cis* structure) is *d,l*-3-methoxy-14*β*-hydroxy-8α,9*β*-estra-1,3,5(10)-trien-17-one.[25] However, this structure was not confirmed by X-ray analysis.[26]

Demethoxycarbonylation of diester **6a**−**c**, according to the Krapcho procedure,[27] led to the α-bridged steroids **7a**−**c**. The same compounds could also be obtained in two

(13) (a) Barco, A.; Benetti, S.; Pollini, G. P. *Synthesis* **1973**, 316. (b) Kataoka, H.; Yamada, T.; Goto, K.; Tsuji, J. *Tetrahedron* **1987**, *43*, 4107−4112.

(14) Pellissier, H.; Michellys, P.-Y.; Santelli, M. *J. Org. Chem.* **1997**, *62*, 5588−5591.

(15) In our preliminary report, the use of NMR did not allow us to securely determine the C-13 configuration and the wrong stereochemistry was assigned to the C/D ring junction, see: Michellys, P.-Y.; Pellissier, H.; Santelli, M. *Tetrahedron Lett.* **1993**, *34*, 1931−1934.

(16) Duax, W. L.; Weeks, C. M.; Rohrer, D. C. *Top. Stereochem.* **1976**, *9*, 271−383.

(17) Geise, H. J.; Altona, C.; Romers, C. *Tetrahedron* **1967**, *23*, 439−463.

(18) Liang, C. D.; Baran, J. S.; Allinger, N. L.; Yuh, Y. *Tetrahedron* **1976**, *32*, 2067−2069; erratum, **1977**, *33*, 594.

(19) Busetta, B.; Courseille, Ch.; Hospital, M. *Acta Crystallogr.* **1973**, *B29*, 298−313.

(20) Busetta, B.; Hospital, M. *Acta Crystallogr.* **1972**, *B28*, 560−567.

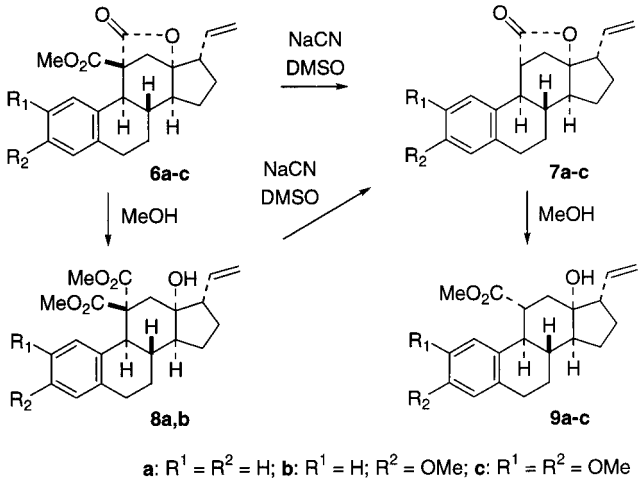
(21) Segaloff, A.; Gabbard, R. B.; Flores, A.; Borne, R. F.; Baker, J. K.; Duax, W. L.; Strong, P. D.; Rohrer, D. C. *Steroids* **1980**, *35*, 335−349.

(22) Kellie, G. M.; Riddel, F. G. *Top. Stereochem.* **1974**, *8*, 225−269.

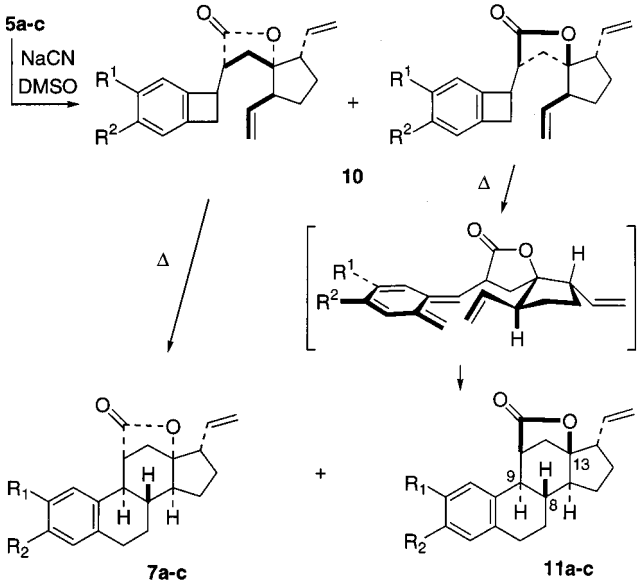
(23) Altona, C.; Geise, H. J.; Romers, C. *Tetrahedron* **1968**, *24*, 13−32.

(24) (a) Kálmán, A.; Argay, G.; Scharfenberg-Pfeiffer, D.; Höhne, E.; Ribár, B. *Acta Crystallogr.* **1991**, *B47*, 68−77. (b) Cho, C. K.; Secco, A. S. *Acta Crystallogr.* **1991**, *B47*, 492−498.

Scheme 3

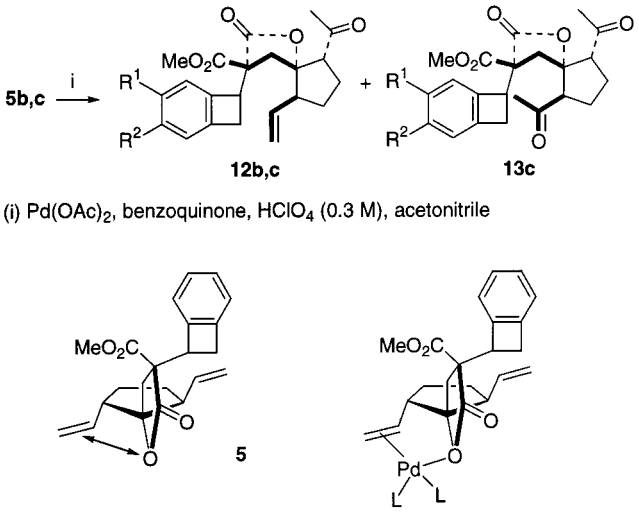


Scheme 4



steps: first methanolysis of **6a**−**c**, followed by demethoxycarbonylation. Methanolysis of **7a**−**c** gave rise to 13-hydroxy steroids **9a**−**c** in excellent yields (Scheme 3). With an aim to access steroids with a *trans-anti-trans* configuration, we first performed a demethoxycarbonylation of **5**. Epimerization occurred and an inseparable mixture of two precursors **10** was obtained. Cyclization of **10** on heating gave rise, in similar proportion, to two isomeric steroids (±)-**7a**−**c** and (±)-**11a**−**c** with *trans-anti-cis* and *trans-anti-trans* configurations, respectively (Scheme 4). Again, the cycloadducts **11a**−**c** result from an *exo* approach of the (*E*)-*o*-xylylene intermediate during

Scheme 5



cyclization. The structures of steroids **11a**−**c** were determined using a series of NMR experiments (COSY and phase NOESY, 400 MHz). For example, the ^{1}H NMR spectrum of **11b** in C_6D_6 displayed a doublet at 2.17 ppm for $H^{(9)}$ with a coupling constant $J_{H^{(8)}}-J_{H^{(9)}} = 11.1$ Hz. In addition, a COSY experiment on $H^{(9)}$ showed that the signal of $H^{(8)}$ at 1.54 ppm was a double quadruplet corresponding to three J_{trans} coupling constants ($J = 11.1$ Hz) and one J_{cis} coupling constant ($J = 3.2$ Hz). The combination of these observations confirmed the *trans* B/C ring junction. Finally, phase mode NOESY experiments confirm the vicinal relationship between $H^{(8)}$ and $H^{(17)}$ and also between $H^{(9)}$, $H^{(11)}$, $H^{(12\alpha)}$, and $H^{(14)}$ indicating the C/D *trans* ring junction.

Wacker oxidation of the 17α-vinyl groups afforded the corresponding 17α-acetyl or 17α-(2-oxoethyl)-steroids. Derivatives bearing the lactonic bridge on the *β*-face, as is the case for **11**, afforded the expected acetyl derivatives. In contrast, when the lactonic bridge (**6** or **7**) or a hydroxyl group (**8** or **9**) was present on the α-face (*syn* relationship), aldehydes resulting from an anti-Markovnikov hydroxypalladation were obtained in appreciable yields.[28] We have rationalized these results by an intramolecular coordination of the palladium with the oxygen atom present in the α-face. This chelation induced an increase of the coefficient of the complexed *π**-orbital at the end of the double bond and increased the overall rate of the oxidation reaction.[29] This result was confirmed by Wacker oxidation of the benzocyclobutene derivatives **5b,c** according to the Miller and Wayner procedure.[30] The major products **12b,c** arise from the selective oxidation of the vinyl group, which was activated by the presence of the oxygen atom of the lactonic linkage (**12b**, 54%; **12c**, 53%, **13**c, 10%) (Scheme 5). Thermolysis of **12c** afforded the expected major product, steroid **14** (*trans-anti-cis* geometry) resulting from an *exo* transition state. The steroid **15**, having a *cis-anti-cis* geometry, was isolated in minor amounts and result from an *endo* transition state. Elimination followed by decarboxylation of **14** explains the formation of **16** (Scheme 6).

(25) (a) Zakharychev, A. V.; Hora, I.; Ananchenko, S. N.; Torgov, I. V. *Tetrahedron Lett.* **1966**, 3585−3590. (b) Dzhafarov, M. Kh.; Dodonov, M. V.; Ananchenko, S. N.; Ionov, S. P.; Torgov, I. V. *Bioorg. Khim.* **1988**, *14*, (5), 675−680. (c) Dzhafarov, M. Kh.; Timofeeva, T. V.; Struchkov, Yu. T. *J. Org. Chem. USSR* **1989**, *25*, 306−311.

(26) For an X-ray analysis of the (*dl*)-3-methoxy-8*β*,9α-estra-1,3,5-(10)-trien-14*β*-ol-17-one (*trans-syn-cis* structure), see: Dzhafarov, M. Kh.; Lindeman, S. V.; Struchkov, Yu. T.; Karamyan, S. Kh.; Ananchenko, S. N. *Bull. Acad. Sci. USSR* **1991**, *40*, 2511−2515 and for the (*dl*)-3-methoxy-8*β*,9α-estra-1,3,5(10)-trien-14α-ol-17-one (*trans-anti-trans* structure), see: Dzhafarov, M. Kh.; Lindeman, S. V. *Bioorg. Khim.* **1987**, *13*, 679−684.

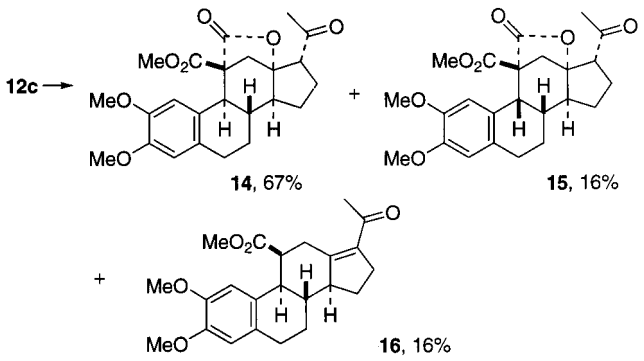
(27) (a) Krapcho, A. P.; Glynn, G. A.; Grenon, B. J. *Tetrahedron Lett.* **1967**, 215−217. (b) Krapcho, A. P. *Synthesis* **1982**, 805−822. (c) Krapcho, A. P. *Synthesis* **1982**, 893−914.

(28) Pellissier, H.; Michellys, P.-Y.; Santelli, M. *Tetrahedron* **1997**, *53*, 7577−7586.

(29) Pellissier, H.; Michellys, P.-Y.; Santelli, M. *Tetrahedron* **1997**, *53*, 10733−10742.

(30) Miller, D. G.; Wayner, D. D. M. *J. Org. Chem.* **1990**, *55*, 2924−2927.

Scheme 6



Conclusion

We have proposed a new strategy for the synthesis of unnatural steroids in a highly stereoselective and efficient manner. The construction of the D ring system, employing Lewis acid mediated addition of BISTRO to succinic anhydride, provides an effective route to the synthesis of various steroids. This strategy is of particular interest, since it allows a quick and facile access to compounds possessing many structural features present in natural steroids, such as the aromatic cycle A of estrone, the oxygenated bridge of aldosterone, or the 17-acetyl group of progesterone. These compounds can be used as templates for the attachment of virtually any functional groups on these positions. Only a few cases of steroids possessing an 11,13-bridge and its influence on biological activity have been reported in the literature. Moreover, only four 13-hydroxy steroids are described in the literature.[31]

Experimental Section

General. All reactions were run under argon in oven-dried glassware. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ solutions. Chemical shift (δ) are reported in ppm with tetramethylsilane as internal standard. Flash chromatography was performed on silica gel (230−400 mesh) and TLC on silica gel.

1-Iodobenzocyclobutene (4a) is generated through a six-step sequence. According to literature procedure, anthranilic acid is easily converted into 1,1-dichlorobenzocyclobutene and then benzocyclobutenone,[32] which was quantitatively reduced by $LiAlH_4$ in THF into benzocyclobutenol.[33] This alcohol is transformed into the corresponding mesylate ($ClSO_2Me$, NEt_3, CH_2Cl_2). The crude mixture is directly treated by NaI (in refluxed acetone)[34] to give expected iodobenzocyclobutene.[35] The overall yield of the sequence is 29% from anthranilic acid.

(±)-6,9-Divinyl-1-oxaspiro[4.4]nonan-2-one (2) was prepared by acylation of BISTRO **1** with succinic anhydride (80% yield).[11]

1-Iodo-4-methoxybenzocyclobutene (4b) was prepared from 4-methoxybenzocyclobutenol[36] according to the following procedure.[37] In a two-necked flask equipped with a magnetic stirring bar and an argon outlet and charged with anhydrous toluene (500 mL) and iodine (21.3 g, 84 mmol) was added triphenylphosphine (19.1 g, 73 mmol). After 5 min of stirring, imidazole was added (11.4 g, 168 mmol). The mixture was stirred at room temperature for 10 min and 4-methoxybenzocyclobutenol (8.4 g, 56 mmol) in toluene (100 mL) was added. The solution was heated at 50 °C for 45 min and then was cooled to room temperature. A saturated solution of $NaHCO_3$ and $Na_2S_2O_3$ was added. The reaction mixture was extracted with petroleum ether. The organic layer was dried ($MgSO_4$), filtered, and concentrated under vacuo. The solid was extracted with pentane, and after filtration the pentane solution was concentrated in vacuo to give **4b** (11.8 g, 45 mmol, 81%): ^{1}H NMR ($CDCl_3$) δ 6.99 (1H, d, J = 8.1 Hz), 6.83 (1H, dd, J = 8.1, 1.5 Hz), 6.59 (1H, d, J = 1.5 Hz), 5.46 (1H, dd, J = 4.5, 1.8 Hz), 3.82 (1H, dd, J = 14.9, 4.5 Hz), 3.76 (3H, s), 3.44 (1H, dd, J = 14.9, 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 161.4 (s), 142.6 (s), 138.8 (s), 123.8 (d), 115.3 (d), 108.2 (d), 55.4 (q), 44.1 (t), 15.1 (d).

1-Iodo-4,5-dimethoxybenzocyclobutene (4c) was obtained from 4,5-dimethoxybenzocyclobutenol,[38] which was treated as for the preparation of **4a**. **4c**: ^{1}H NMR ($CDCl_3$) δ 6.78 (1H, s), 6.68 (1H, s), 5.30 (1H, dd, J = 4.2, 1.5 Hz, 3.80 (6H, s), 3.72 (1H, dd, J = 13.6, 4.2 Hz), 3.28 (1H, dd, J = 13.6, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 151.7 (s), 150.0 (s), 135.8 (s), 132.7 (s), 106.2 (d), 105.4 (d), 53.1 (t), 42.4 (d). Anal. Calcd for $C_{10}H_{11}IO_2$: C, 41.4; H, 3.82. Found: C, 41.9; H, 3.78.

3-Methoxycarbonyl-6,9-divinyl-1-oxaspiro[4.4]nonan-2-one (3). To a solution of 2.1 g (0.011 mmol, 2.2 equiv) of lithium hexamethyldisilazide in 13 mL of THF at −80 °C was slowly added lactone **2** (0.96 g, 5 mmol, 1 equiv) in 2 mL of THF. The mixture was stirred for 0.5 h and then a solution of dimethyl carbonate (4.21 mL, 4.5 g, 50 mmol, 10 equiv) in 3 mL of THF was slowly added. The solution was stirred for 12 h at −60 °C and the mixture was allowed to warm to room temperature. The reaction was quenched by the addition of 20 mL of a saturated aqueous NH_4Cl solution and then extracted with diethyl ether. The organic layer was dried ($MgSO_4$) and evaporated. The yellow oil was flash chromatographed on silica gel eluting with a pentane/diethyl ether (85:15) affording 1.22 g (4.9 mmol, 98%) of lactone as an inseparable diastereoisomeric yellow mixture (60:40): ^{1}H NMR ($CDCl_3$) δ 5.76−5.48 (2H, m), 5.20−5.05 (4H, m), 3.72 (3H, s), 3.71−3.52 (1H, m), 2.81−2.62 (1H, m), 2.45−2.33 (2H, m), 2.16−2.06 (1H, m), 2.02−1.50 (4H, m); ^{13}C NMR ($CDCl_3$) δ 171.3 (s), 168.4 (s), 137.4 (d), 135.4 (d), 119.1 (t), 117.6 (t), 96.3 (s), 53.4 (d or q), 53.0 (d or q), 52.9 (d or q), 47.2 (d), 30.9 (t), 28.6 (t), 28.4 (t). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.23; H, 7.30.

General Procedure for the Alkylation of the Lactone 3. The lactone **3** (5 g, 20 mmol) was dissolved in 200 mL of acetone, and K_2CO_3 (3.56 g, 26 mmol) and iodobenzocyclobutene (26 mmol) were successively added. The mixture was brought to reflux under argon. The progress of the reaction was followed by TLC analysis. The reaction was cooled to room temperature, filtered and then evaporated under vacuum. The residue was chromatographed on silica gel (pentane/diethyl ether, 85:15) to give the expected compound **5** as an inseparable diastereoisomeric mixture (70:30) (6.54 g, 18.6 mmol, 93% for **5a**; 6.62 g, 18.8 mmol, 94% for **5b**; 8 g, 19.4 mmol, 97% for **5c**).

3-(Benzocyclobuten-1-yl)-3-methoxycarbonyl-6,9-divinyl-1-oxaspiro[4.4]nonan-2-one (5a). ^{1}H NMR ($CDCl_3$) δ 7.16 (4H, m), 5.51 (1H, dt, J = 17.8, 8.9 Hz), 5.12 (3H, m), 4.72 (1H, dd, J = 9.9, 1.3 Hz), 4.13 (1H, d, J = 17.9 Hz), 3.80 (1H, m), 3.76 (3H, s), 3.35 (1H, m), 2.94 (1H, m), 2.43−1.48 (8H, m); ^{13}C NMR ($CDCl_3$) δ 172.3 (s), 169.5 (s), 143.6 (s), 142.2 (s), 136.5 (d), 134.7 (d), 127.9 (d), 126.5 (d), 122.2 (d), 121.6

(31) (a) Janot, M.-M.; Lusinchi, X.; Goutarel, R. *C. R. Acad. Sci. Fr.* **1964**, *258*, 4780−4782. (b) Janot, M.-M.; Lusinchi, X.; Labler, L.; Goutarel, R. *Bull. Soc. Chim. Fr.* **1966**, 3276−3281. (c) Bascoul, J.; Reliaud, C.; Guinot, A.; Crastes de Paulet, A. *Bull. Soc. Chim. Fr.* **1968**, 4074−4079. (d) Mincione, E.; Feliziani, F. *Ann. Chim. (Rome)* **1975**, *65*, 209−223.

(32) Dürr, H.; Nickels, H.; Pacala, L. A.; Jones, M., Jr. *J. Org. Chem.* **1980**, *45*, 973−980.

(33) Kündig, E. P.; Leresche, J.; Saudan, L.; Bernardinelli, G. *Tetrahedron* **1996**, *52*, 7363−7378.

(34) Funk, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1980**, *102*, 5253−5261.

(35) DeCamp, M. R.; Viscogliosi, L. A. *J. Org. Chem.* **1981**, *46*, 3918−3920.

(36) Honda, T.; Ueda, K.; Tsubuki, M.; Toya, T.; Kurozumi, A. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1749−1754.

(37) Ireland, R. E.; Gleason, J. L.; Gegnas, L. D.; Highsmith, T. K. *J. Org. Chem.* **1996**, *61*, 6856−6872.

(38) Charlton, J. L.; Koh, K.; Plourde G. L. *Can. J. Chem.* **1990**, *68*, 2028−2032.

(d), 117.1 (t), 116.4 (t), 93.0 (s), 56.5 (q), 55.5 (s), 52.0 (d), 51.7 (d), 45.7 (d), 32.6 (t), 29.5 (t), 27.4 (t); MS (EI) *m*/*z* (relative intensity) 352 (4), 324 (13), 221(78), 103 (100); HRMS calcd 352.1674, found 352.1689. Anal. Calcd for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 75.03; H, 6.75.

3-(4-Methoxybenzocyclobuten-1-yl)-3-methoxycarbonyl-6,9-divinyl-1-oxaspiro[4.4]nonan-2-one (5b). Yellow oil, ^{1}H NMR ($CDCl_3$) δ 6.90 (1H, d, J = 8.2 Hz), 6.73 (1H, dd, J = 8.2, 2.2 Hz), 6.63 (1H, d, J = 2.2 Hz), 5.68 (1H, ddd, J = 17.8, 9.5, 8.9 Hz), 5.18 (1H, ddd, J = 17.0, 10.0, 9.4 Hz), 5.03 (4H, m), 4.71 (1H, dd, J = 10.2, 1.7 Hz), 4.21 (1H, dq, J = 17.0, 0.8 Hz), 4.06 (1H, dd, J = 5.1, 2.1 Hz), 3.74 (3H, s), 3.71 (3H, s), 3.22 (1H, $^1/_2$AB, d, J = 14.9, 5.2 Hz), 2.82 (1H, $^1/_2$AB, d, J = 14.9, 2.4 Hz), 2.31 (1H, q, J = 9.0 Hz), 2.25 (1H, $^1/_2$AB, J = 14.3 Hz), 2.13 (1H, $^1/_2$AB, J = 14.3 Hz), 2.08−2.05 (1H, m), 1.84 (1H, dtd, J = 13.3, 9.0, 4.3 Hz), 1.71 (1H, ddt, J = 17.0, 10.6, 6.6 Hz), 1.43 (1H, dddd, J = 13.1, 9.4, 6.6, 3.7 Hz);^{13}C NMR ($CDCl_3$) δ 173.7 (s), 170.6 (s), 160.8 (s), 144.8 (s), 137.2 (d), 135.4 (d), 134.3 (s), 123.8 (d), 118.1 (t), 117.3 (t), 114.0 (t), 108.7 (t), 94.2 (s), 57.5 (s), 55.5 (d), 53.3 (d or q), 53.0 (d or q), 52.8 (d or q), 45.7 (d), 32.7 (t), 30.2 (t), 28.2 (t), 27.8 (t); HRMS calcd for $C_{23}H_{26}O_5$, 382.1780, found 382.1781.

3-(4,5-Dimethoxybenzocyclobuten-1-yl)-3-methoxycarbonyl-6,9-divinyl-1-oxaspiro[4.4]nonan-2-one (5c). Major diastereomer, white crystals, mp 89 °C; ^{1}H NMR ($CDCl_3$) δ 6.65 (1H, s), 6.57 (1H, s), 5.70 (1H, dt, J = 17.8, 9.2 Hz), 5.20 (1H, dt, J = 17.2, 9.6 Hz), 5.05 (2H, m), 4.73 (1H, dd, J = 10.2, 1.4 Hz), 4.29 (1H, d, J = 17.0 Hz), 4.08 (1H, dd, J = 4.8, 2.0 Hz), 3.82 (3H, s), 3.78 (3H, s), 3.73 (3H, s), 3.20 (1H, dd, J = 14.3, 4.9 Hz), 2.79 (1H, dd, J = 14.3, 2.0 Hz), 2.35 (1H, q, J = 9.3 Hz), 2.27 (1H, $^1/_2$AB, J = 14.3 Hz), 2.16 (1H, $^1/_2$AB, J = 14.3 Hz), 2.06 (1H, m), 1.86 (2H, m), 1.71 (1H, m), 1.45 (1H, m); ^{13}C NMR ($CDCl_3$) δ 174.0 (s), 170.6 (s), 151.0 (s), 150.1 (s), 137.1 (d), 135.5 (d), 135.3 (s), 133.7 (s), 118.2 (t), 117.4 (t), 107.1 (d), 106.6 (d), 94.3 (s), 57.6 (s), 56.4 (d or q), 56.3 (d or q), 53.5 (d or q), 53.0 (d or q), 52.9 (d or q), 45.9 (d), 32.6 (t), 30.2 (t), 28.3 (t), 27.8 (t). Anal. Calcd for $C_{24}H_{28}O_6$: C, 69.89; H, 6.84. Found: C, 69.92; H, 6.88. Minor diastereomer, white crystals, mp 110 °C; ^{1}H NMR ($CDCl_3$) δ 6.65 (1H, s), 6.57 (1H, s), 5.70 (1H, dt, J = 17.8, 9.2 Hz), 5.49 (1H, dt, J = 17.8, 9.2 Hz), 5.06 (4H, m), 4.08 (1H, dd, J = 4.9, 1.8 Hz), 3.73 (3H, s), 3.82 (3H, s), 3.79 (3H, s), 3.20 (1H, dd, J = 14.3, 4.9 Hz), 2.78 (1H, dd, J = 14.3, 1.8 Hz), 2.37−1.38 (9H, m); ^{13}C NMR ($CDCl_3$) δ 172.8 (s), 169.6 (s), 150.4 (s), 149.3 (s), 136.4 (d), 134.7 (d), 134.5 (s), 132.9 (s), 117.2 (t), 116.4 (t), 106.5 (d), 105.8 (d), 93.2 (s), 56.7 (s), 55.5 (q), 55.4 (q), 52.7 (q), 52.1 (d), 51.8 (d), 44.9 (d), 31.8 (t), 29.4 (t), 27.5 (t), 27.0 (t).

General Procedure for the Thermolysis of 5. The benzocyclobutenic precursor **5** (1 mmol) was dissolved in 10 mL of 1,2,4-trichlorobenzene and boiled under argon. The progress of the reaction was followed by TLC analysis. After cooling at room temperature, the mixture was concentrated under vacuum. The residue was chromatographed on silica gel (petroleum ether/diethyl ether) to give the expected compound **6** in 85−87% yield.

(±)-(8*β*,9α,14α)-11α,13α-*γ*-Carbolactone-11*β*-methoxycarbonyl-17α-vinylgona-1,3,5(10)-triene (6a). White crystals, mp 112 °C; ^{1}H NMR ($CDCl_3$) δ 7.09 (3H, m), 6.83 (1H, d, J = 6.3 Hz), 5.86 (1H, dt, J = 17.6, 8.3 Hz), 5.13 (2H, m), 3.71 (3H, s), 3.09 (1H, d, J = 10.9 Hz), 2.82 (2H, m), 2.75 (1H, d, J = 12.2 Hz), 2.47 (1H, dt, J = 11.8, 7.1 Hz), 2.22 (1H, d, J = 12.2 Hz), 1.99 (4H, m), 1.63 (2H, m), 1.23 (1H, m), 0.90 (1H, dq, J = 11.9, 5.5 Hz); ^{13}C NMR ($CDCl_3$) δ 175.3 (s), 170.2 (s), 142.0 (s), 137.6 (s), 134.8 (d), 128.5 (d), 125.9 (d), 125.5 (d), 120.6 (d), 116.9 (t), 93.1 (s), 54.9 (s), 53.1 (q), 52.4 (d), 50.5 (d), 42.9 (d), 42.6 (d), 35.3 (t), 31.6 (t), 30.5 (t), 27.0 (t), 25.8 (t); MS (EI) *m*/*z* (relative intensity) 352 (85), 308 (52), 306 (70), 276 (59), 154 (65), 129 (100), 128 (85); HRMS calcd for $C_{22}H_{24}O_4$, 352.1674, found, 352.1674. Anal. Calcd for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 74.50; H, 7.02.

(±)-(8*β*,9α,14α)-11α,13α-*γ*-Carbolactone-3-methoxy-11*β*-methoxycarbonyl-17α-vinylgona-1,3,5(10)-triene (6b). White crystals, mp 98 °C; ^{1}H NMR ($CDCl_3$) δ 6.74 (1H, d, J = 8.4 Hz), 6.71 (1H, d, J = 2.6 Hz), 6.61 (1H, dd, J = 8.4, 2.6 Hz), 5.87 (1H, ddd, J = 16.7, 10.6, 8.2 Hz), 5.12 (1H, d, J = 16.7 Hz), 5.11 (1H, d, J = 10.6 Hz), 3.75 (3H, s), 3.71 (3H, s), 3.04 (1H, d, J = 11.0 Hz), 2.83 (1H, br. q, J = 8.2 Hz), 2.74 (1H, td, J = 8.3, 3.0 Hz), 2.70 (1H, d, J = 12.4 Hz), 2.47 (1H, br. dt, J = 11.8, 7.4 Hz), 2.22 (1H, d, J = 12.3 Hz), 2.04 (1H, quint., J = 6.0 Hz), 1.90 (2H, m), 1.88 (1H, dd, J = 12.9, 7.4 Hz), 1.65 (1H, qd, J = 12.2, 5.4 Hz), 1.54 (1H, qm, J = 10.8 Hz), 1.22 (1H, qd, J = 11.0, 7.5 Hz), 0.94 (1H, qd, J = 12.1, 5.5 Hz); ^{13}C NMR ($CDCl_3$) δ 175.6 (s), 170.5 (s), 157.8 (s), 139.3 (s), 135.0 (d), 134.3 (s), 121.9 (d), 117.2 (t), 114.6 (d), 110.4 (d), 93.2 (s), 55.2 (s), 55.2 (q), 53.2 (q), 52.7 (d), 50.8 (d), 43.4 (d), 42.3 (d), 35.6 (t), 31.8 (t), 30.7 (t), 27.7 (t), 26.0 (t); HRMS calcd for $C_{23}H_{26}O_5$, 382.1780, found, 382.1761.

(±)-(8*β*,9α,14α)-11α,13α-*γ*-Carbolactone-2,3-dimethoxy-11*β*-methoxycarbonyl-17α-vinylgona-1,3,5(10)-triene (6c). White crystals, mp 137−138 °C; ^{1}H NMR ($CDCl_3$) δ 6.65 (1H, s), 6.50 (1H, s), 5.88 (1H, ddd, J = 17.6, 9.6, 8.2 Hz), 5.12 (2H, m), 3.83 (3H, s), 3.77 (3H, s), 3.68 (3H, s), 3.05 (1H, d, J = 11.2 Hz), 2.80−2.73 (3H, m), 2.62 (1H, d, J = 12.3 Hz), 2.48 (1H, dt, J = 11.5, 7.5 Hz), 2.31 (1H, d, J = 12.3 Hz), 2.05 (1H, br. q, J = 5.9 Hz), 1.95−1.87 (4H, m), 1.66 (1H, qd, J = 12.2, 5.5 Hz), 1.54−1.47 (2H, m), 1.34 (1H, qd, J = 11.1, 6.7 Hz), 1.00 (1H, dq, J = 12.0, 5.7 Hz); ^{13}C NMR ($CDCl_3$) δ 175.2 (s), 171.0 (s), 147.0 (s), 146.8 (s), 135.1 (d), 133.0 (s), 129.7 (s), 117.2 (t), 112.3 (d), 106.5 (d), 92.7 (s), 56.1 (q), 55.9 (q), 55.1 (s), 52.9 (d or q), 52.6 (d or q), 51.0 (d), 43.4 (d), 43.0 (d), 36.1 (t), 31.8 (t), 30.5 (t), 27.5 (t), 26.5 (t); MS (EI) *m*/*z* (relative intensity) 412 (100), 205 (36), 189 (29), 163 (38); HRMS calcd for $C_{24}H_{28}O_6$, 412.1885, found, 412.1894.

General Procedure for the Demethoxycarbonylation. A mixture of **6** (5 mmol), 40 mL of DMSO, and NaCN (735 mg, 15 mmol) was heated at 90 °C under argon. The progress of the reaction was followed by TLC analysis. After cooling at room temperature, the mixture was poured in water and then extracted with CH_2Cl_2. The organic layer was washed with water, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel and then recrystallized in diethyl ether to give **7** (1.04 g, 3.55 mmol, 71% for **7a**, 1.02 g, 3.14 mmol, 63% for **7b**, 1.61 g, 4.55 mmol, 91% for **7c**).

(±)-(8*β*,9α,14α)-11α,13α-*γ*-Carbolactone-17α-vinylgona-1,3,5(10)-triene (7a). White crystals, mp 95 °C; ^{1}H NMR ($CDCl_3$) δ 7.30 (1H, d, J = 6.8 Hz), 7.16 (2H, m), 7.11 (1H, d, J = 6.9 Hz), 5.91 (1H, ddd, J = 17.6, 9.6, 8.2 Hz), 5.15−5.07 (2H, m), 3.24 (1H, br. s), 2.90 (2H, m), 2.75 (1H, d, J = 10.9 Hz), 2.46 (1H, dt, J = 11.4, 7.5 Hz), 2.14 (1H, quint.m, J = 4.9 Hz), 2.05 (1H, s), 2.04 (1H, s), 2.01 (1H, m), 1.93 (1H, m), 1.90 (1H, m), 1.66 (1H, qd, J = 12.1, 5.5 Hz), 1.58−1.49 (2H, m), 1.09 (1H, qd, J = 12.1, 5.7 Hz); ^{13}C NMR ($CDCl_3$) δ 180.6 (s), 138.6 (s), 137.0 (s), 135.8 (d), 129.4 (d), 126.5 (d),125.9 (d), 124.3 (d), 116.5 (t), 94.5 (s), 52.2 (d), 51.5 (d), 41.4 (d), 40.5 (d), 40.2 (d), 33.0 (t), 31.7 (t), 29.9 (t), 29.0 (t), 27.2 (t); MS (EI) *m*/*z* (relative intensity) 294 (100), 265 (36), 249 (15), 222 (38), 156 (32), 141 (42), 128 (52); HRMS calcd for $C_{20}H_{22}O_2$, 294.1620, found, 294.1619. Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.55; H, 7.59.

(±)-(8*β*,9α,14α)-11α,13α-*γ*-Carbolactone-3-methoxy-17α-vinylgona-1,3,5(10)-triene (7b). White crystals, mp 134 °C; ^{1}H NMR ($CDCl_3$) δ 7.20 (1H, d, J = 8.5 Hz), 6.72 (1H, dd, J = 8.5, 2.5 Hz), 6.65 (1H, d, J = 2.5 Hz), 5.91 (1H, ddd, J = 16.4, 10.8, 8.4 Hz), 5.08 (1H, d, J = 16.4 Hz), 5.08 (1H, d, J = 10.8 Hz), 3.76 (3H, s), 3.17 (1H, s), 2.87 (2H, m), 2.70 (1H, d, J = 11.3), 2.45 (1H, dt, J = 11.5, 7.4 Hz), 2.15−1.85 (3H, m), 1.65 (1H, qd, J = 12.0, 6.4 Hz), 1.55−1.45 (2H, m), 1.08 (1H, qd, J = 11.9, 5.6 Hz); ^{13}C NMR ($CDCl_3$) δ 180.6 (s), 158.1 (s), 138.3 (s), 135.9 (d), 130.7 (s), 125.6 (d), 116.5 (t), 114.7 (d), 111.3 (d), 94.5 (s), 55.3 (q), 52.1 (d), 51.5 (d), 41.0 (d), 40.8 (d), 40.5 (d), 33.0 (t), 31.7 (t), 29.9 (t), 29.5 (t), 27.3 (t); HRMS calcd for $C_{21}H_{24}O_3$, 324.1725, found 324.1726.

(±)-(8*β*,9α,14α)-11α,13α-*γ*-Carbolactone-2,3-dimethoxy-17α-vinylgona-1,3,5(10)-triene (7c). White crystals, mp 196 °C; ^{1}H NMR ($CDCl_3$) δ 6.79 (1H, s), 6.59 (1H, s), 5.91 (1H, ddd, J = 17.6, 9.6, 8.2 Hz), 5.15−5.05 (2H, m), 3.87 (3H, s), 3.83 (3H, s), 3.12 (1H, d, J = 3.7 Hz), 2.89−2.80 (2H, m), 2.72 (1H, d, J = 10.2 Hz), 2.46 (1H, br. dt, J = 11.2, 7.2 Hz), 2.12 (1H, m), 2.08 (1H, $^1/_2$AB, J = 11.9 Hz), 2.03 (1H, $^1/_2$ABd, J = 11.9, 4.3 Hz), 1.94−1.86 (2H, m), 1.66 (1H, qd, J = 12.0, 5.4 Hz),

1.57−1.48 (3H, m), 1.10 (1H, qd, J = 12.0, 5.7 Hz); ^{13}C NMR ($CDCl_3$) δ 180.5 (s), 147.6 (s), 147.1 (s), 135.8 (d), 130.1 (s), 128.8 (s), 116.5 (t), 112.4 (d), 108.6 (d), 94.5 (s), 56.2 (q), 55.9 (q), 51.8 (d), 51.5 (d), 41.3 (d), 41.2 (d), 40.4 (d), 33.0 (t), 31.7 (t), 29.8 (t), 29.1 (t), 27.5 (t); MS (EI) *m*/*z* (relative intensity) 354 (74), 279 (16), 190 (18), 167 (27) 149 (71), 57 (100); HRMS calcd for $C_{22}H_{26}O_4$, 354.1831, found, 354.1822.

General Procedure for the Transesterification of 6. The steroid **6** (2 mmol) was dissolved in 20 mL of dry methanol and boiled under argon for 48 h. After cooling at room temperature, the mixture was concentrated under vacuum. The residue was recrystallized in diethyl ether to give **8** (0.545 g, 1.42 mmol, 71% for **8a**, 0.561 g, 1.35 mmol, 68% for **8b**).

(±)-(8*β*,9α,14α)-11,11-Bis(methoxycarbonyl)-17α-vinylgona-1,3,5(10)-trien-13α-ol (8a). White crystals, mp 174 °C; ^{1}H NMR ($CDCl_3$) δ 7.41 (1H, m), 7.01 (3H, m), 5.80 (1H, ddd, J = 17.2, 10.5, 7.5 Hz), 5.21 (1H, dd, J = 10.5, 1.1 Hz), 5.15 (1H, dt, J = 17.2, 1.2 Hz), 3.85 (3H, s), 3.72 (1H, d, J = 11.5 Hz), 3.19 (3H, s), 2.84−2.70 (2H, m), 2.74 (1H, d, J = 14.3 Hz), 2.18 (2H, d, J = 14.3 Hz), 2.16 (1H, quint., J = 6.4 Hz), 2.0 (1H, dquint., J = 12.8, 2.4 Hz), 1.76−1.69 (2H, m), 1.63−1.54 (3H, m), 1.36 (1H, qd, J = 12.5, 4.5 Hz), 1.18 (1H, qd, J = 12.3, 5.9 Hz); ^{13}C NMR ($CDCl_3$) δ 174.8 (s), 172.3 (s), 138.1 (s), 136.9 (s), 136.4 (d), 128.8 (d), 128.5 (d), 125.6 (d), 125.3 (d), 118.5 (t), 79.4 (s), 59.5 (s), 55.8 (q), 54.9 (d), 53.0 (q), 51.9 (d), 44.7 (d), 42.5 (t), 40.3 (d), 30.8 (t), 30.7 (t), 29.3 (t), 27.9 (t). Anal. Calcd for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 71.92; H, 7.28.

(±)-(8*β*,9α,14α)-11,11-Bis(methoxycarbonyl)-3-methoxy-17α-vinylgona-1,3,5(10)-trien-13α-ol (8b). Yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.36 (1H, d, J = 8.8 Hz), 6.59 (1H, dd, J = 8.8, 2.7 Hz), 6.54 (1H, d, J = 2.7 Hz), 5.80 (1H, ddd, J = 17.3, 10.3, 7.5 Hz), 5.21 (1H, ddd, J = 10.3, 1.0, 0.7 Hz), 5.15 (1H, ddd, J = 17.3, 1.2, 0.5 Hz), 3.84 (3H, s), 3.73 (3H, s), 3.64 (1H, d, J = 11.4 Hz), 3.23 (3H, s), 2.83−2.66 (2H, m), 2.72 (1H, d, J = 14.3 Hz), 2.18 (1H, d, J = 14.3 Hz), 2.18−2.12 (2H, m), 1.98 (1H, dquint., J = 12.7, 2.1 Hz), 1.74−1.53 (4H, m), 1.34 (1H, qd, J = 12.3, 4.5 Hz), 1.22−1.12 (2H, m); ^{13}C NMR ($CDCl_3$) δ 174.8 (s), 172.3 (s), 157.2 (s), 139.6 (s), 136.4 (d), 129.8 (d), 129.0 (s), 118.4 (t), 113.3 (d), 111.3 (d), 79.4 (s), 59.5 (s), 55.8 (d or q), 55.1 (q), 55.0 (q), 52.9 (d), 52.0 (d), 44.2 (d), 42.4 (t), 40.4 (d), 31.1 (t), 30.8 (t), 29.3 (t), 27.9 (t); HRMS calcd for $C_{24}H_{30}O_6$, 414.2042, found 414.2043.

Transesterification of 7. The procedure was the same as before, except for the purification of the crude product. In this case, the residue was chromatographed on silica gel (petroleum ether/diethyl ether, 80:20 for **9a,b**; petroleum ether/ethyl acetate, 70:30 for **9c**) to give **9** (0.58 g, 1.78 mmol, 89% for **9a**, 0.58 g, 1.64 mmol, 82% for **9b**, 0.66 g, 1.72 mmol, 86% for **9c**).

(±)-(8*β*,9α,14α)-11α-Methoxycarbonyl-17α-vinylgona-1,3,5(10)-trien-13α-ol (9a). White wax; ^{1}H NMR ($CDCl_3$) δ 7.08 (3H, m), 6.99 (1H, m), 5.88 (1H, m), 5.58 (1H, m), 5.12 (1H, ddd, J = 17.2, 1.7, 1.2 Hz), 3.77 (3H, s), 3.07 (1H, dd, J = 11.7, 9.4 Hz), 2.88 (1H, td, J = 9.0, 6.3 Hz), 2.79 (2H, m), 2.29 (1H, dt, J = 8.4, 7.8 Hz), 2.15 (1H, dddd, J = 13.8, 10.4, 7.4, 4.1 Hz), 2.07 (1H, dd, J = 14.0, 6.3 Hz), 1.99 (1H, m), 1.95 (1H, dd, J = 14.0, 6.5 Hz), 1.73 (3H, m), 1.49 (1H, ddd, J = 16.2, 9.6, 6.8 Hz), 1.29 (1H, m), 1.18 (1H, m); ^{13}C NMR ($CDCl_3$) δ 177.9 (s), 140.4 (s), 137.6 (s), 136.9 (d), 128.3 (d), 125.9 (d), 125.8 (d), 125.2 (d), 117.2 (t), 80.3 (s), 54.1 (q), 52.3 (d), 52.1 (d), 44.0 (d), 41.0 (d), 40.4 (d), 36.5 (t), 29.1 (t), 28.6 (t), 28.2 (t)(2C); MS (EI) *m*/*z* (relative intensity) 352; HRMS calcd for $C_{21}H_{26}O_3$, 308.17762, found, 308.17760. Anal. Calcd for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03. Found: C, 77.34; H, 7.97.

(±)-(8*β*,9α,14α)-3-Methoxy-11α-methoxycarbonyl-17α-vinylgona-1,3,5(10)-trien-13α-ol (9b). Colorless oil; ^{1}H NMR ($CDCl_3$) δ 6.91 (1H, d, J = 8.4 Hz), 6.66 (1H, dd, J = 8.4, 2.7 Hz), 6.61 (1H, d, J = 2.7 Hz), 5.87 (1H, ddd, J = 17.2, 10.4, 7.6 Hz), 5.17 (1H, ddd, J = 10.4, 1.8, 0.8 Hz), 5.12 (1H, ddd, J = 17.2, 1.8, 1.2 Hz), 3.76 (3H, s), 3.75 (3H, s), 3.00 (1H, dd, J = 11.5, 9.4 Hz), 2.85−2.76 (3H, m), 2.28 (1H, td, J = 10.6, 7.8 Hz), 2.18−2.04 (1H, m), 2.05 (1H, $^1/_2$AB,d, J = 14.0, 6.3 Hz), 2.00 (1H, m), 1.93 (1H, $^1/_2$AB,d, J = 14.0, 6.4 Hz), 1.79−1.67 (3H, m), 1.46 (1H, m), 1.29 (1H, m), 1.16 (1H, qd, J = 11.5, 4.3 Hz); ^{13}C NMR ($CDCl_3$) δ 178.1 (s), 157.6 (s), 138.9 (s), 136.9 (d), 132.6 (s), 126.5 (d), 117.4 (t), 113.5 (d), 111.6 (d), 80.4 (s), 55.2 (q), 54.5 (q), 54.5 (d), 52.4 (d), 44.4 (d), 41.0 (d), 40.9 (d), 36.5 (t), 29.6 (t), 28.8 (t), 28.3 (t)(2C); HRMS calcd for $C_{22}H_{28}O_4$, 356.1988, found, 356.2004.

(±)-(8*β*,9α,14α)-3,4-Dimethoxy-11α-methoxycarbonyl-17α-vinylgona-1,3,5(10)-trien-13α-ol (9c). White crystals, mp 140 °C; ^{1}H NMR ($CDCl_3$) δ 6.59 (1H, s), 6.56 (1H, s), 5.88 (1H, ddd, J = 17.4, 10.4, 7.6 Hz), 5.16 (1H, dq, J = 10.4, 1.6 Hz), 5.11 (1H, dd, J = 17.4, 0.9 Hz), 3.82 (3H, s), 3.77 (3H, s), 3.76 (3H, s), 3.02 (1H, t, J = 10.3 Hz), 2.84 (1H, dt, J = 9.2, 6.3 Hz), 2.74 (2H, q, J = 4.0 Hz), 2.27 (1H, dt, J = 10.3, 7.8 Hz), 2.14 (1H, m), 2.05 (1H, ?ABd, J = 14.2, 6.0 Hz), 1.93 (1H, ?ABd, J = 14.2, 6.6 Hz), 1.76−1.65 (3H, m), 1.44 (1H, br. quint., J = 10.3 Hz), 1.28 (1H, dq, J = 12.2, 8.0 Hz), 1.17 (1H, dq, J = 11.4, 3.8 Hz); ^{13}C NMR ($CDCl_3$) δ 178.5 (s), 147.1 (s)(2C), 137.0 (d), 132.0 (s), 129.6 (s), 117.3 (t), 111.5 (d), 109.5 (d), 80.3 (s), 55.9 (q), 55.8 (q), 54.5 (q), 52.8 (d), 52.4 (d), 44.8 (d), 41.6 (d), 41.0 (d), 36.5 (t), 29.1 (t), 29.0 (t), 28.5 (t)(2C). Anal. Calcd for $C_{23}H_{30}O_5$: C, 71.48; H, 7.82. Found: C, 71.55; H, 7.72.

Demethoxycarbonylation of Precursors 5a−c. A mixture of benzocyclobutenic derivative **5** (20 mmol), 150 mL of DMSO, and NaCN (2.94 g, 60 mmol) was heated at 90 °C. The progress of the reaction was followed by TLC analysis. After the usual work up, the residue was chromatographed on silica gel (petroleum ether/diethyl ether) to give **10** as an inseparable mixture of four diastereoisomers (5.30 g, 18 mmol, 90% for **10a**, 5.38 g, 16.6 mmol, 83% for **10b**, 6.23 g, 17.6 mmol, 88% for **10c**).

3-(Benzocyclobuten-1-yl)-6,9-divinyl-1-oxaspiro[4.4]-nonan-2-one (10a). Mixture of isomers, ^{1}H NMR ($CDCl_3$) δ 7.16 (4H, m), 5.65 (2H, m), 4.99 (4H, m), 3.79 (1H, m), 3.39 (1H, m), 2.68 (1H, m), 2.35 (1H, m), 2.25 (2H, m), 2.20−1.47 (6H, m); ^{13}C NMR ($CDCl_3$) δ 176.5 (s), 145.6 (s), 143.0 (s), 137.9 (d), 135.5 (d), 127.9 (d), 127.0 (d), 122.9 (d), 122.2 (d), 118.2 (t), 116.5 (t), 94.4 (s), 53.4 (d), 52.1 (d), 43.0 (d), 42.4 (d), 33.8 (t), 29.2 (t), 28.4 (t), 27.9 (t). Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.48; H, 7.60.

3-(4-Metoxybenzocyclobuten-1-yl)-6,9-divinyl-1-oxaspiro[4.4]nonan-2-one (10b). Mixture of isomers, ^{1}H NMR ($CDCl_3$) δ 6.86 (1H, d, J = 8.1 Hz), 6.70 (1H, dd, J = 8.1, 2.2 Hz), 6.65 (1H, d, J = 2.2 Hz), 5.72−5.56 (2H, m), 5.19−4.94 (4H, m), 3.75 (1.5H, s), 3.74 (1.5H, s), 3.35 (1H, dd, J = 14.6, 5.4 Hz), 2.98−2.86 (2H, m), 2.77−2.67 (1H, m), 2.29 (1H, dd, J = 13.0, 8.8 Hz), 2.18−1.69 (5H, m), 1.55−1.46 (2H, m); ^{13}C NMR ($CDCl_3$) δ 177.4 (s), 160.2 (s), 144.3 (s), 138.5 (d), 137.0 (s), 135.6 (d), 123.5 (d), 118.1 (t), 116.8 (t), 113.5 (d), 108.7 (d), 94.6 (s), 55.4 (q), 52.9 (d), 52.4 (d), 43.1 (d), 41.9 (d), 34.2 (t), 29.3 (t), 28.9 (t), 28.8 (t).

3-(4,5-Dimethoxybenzocyclobuten-1-yl)-6,9-divinyl-1-oxaspiro[4.4]nonan-2-one (10c). Mixture of isomers, ^{1}H NMR ($CDCl_3$) δ 6.59 (1H, s), 6.58 (1H, s), 5.65 (2H, m), 5.0 (4H, m), 3.83 (3H, s), 3.81 (3H, s), 3.58 (1H, m), 3.25 (1H, m), 2.79 (2H, m), 2.40−1.04 (8H, m); ^{13}C NMR ($CDCl_3$) δ 177.5 (s), 150.3 (s), 149.8 (s), 137.9 (d), 135.9 (d), 135.8 (s), 134.5 (s), 118.4 (t), 116.9 (t), 107.5 (d), 106.6 (d), 94.9 (s), 57.8 (q), 56.7 (q), 53.6 (d), 52.8 (d), 43.2 (d), 42.1 (d), 33.4 (t), 29.6 (t), 29.5 (t), 29.0 (t). Anal. Calcd for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39. Found: C, 74.61; H, 7.34.

Cyclization of 10. Synthesis of Steroids 7 and 11. Benzocyclobutenic derivative **10** was dissolved in 150 mL of 1,2,4-trichlorobenzene and boiled under argon. The progress of the reaction was followed by TLC analysis. After cooling at room temperature, the mixture was concentrated under vacuum. In the case of **11a**, the residue was first crystallized in diethyl ether in order to partially remove compound **7a**. Then, mother liquors were purified by chromatography on silica gel (petroleum ether/ethyl acetate, 90:10) providing expected steroid **11a** as a pure form. The two diastereoisomers were quantitatively obtained in a 57/43 ratio in favor of **7a**. In the case of **11b**, the residue was first crystallized in diethyl ether/methanol (3:1) in order to partially remove compound **7b**. The mother liquors were purified by chromatography on silica gel (petroleum ether/diethyl ether, 90:10) providing expected steroid **11b** as a pure form (60/40 ratio in favor of

7b). In the case of **11c**, the crude was directly chromatographed on silica gel (petroleum ether/ethyl acetate, 85:15) allowing the complete separation of the two diastereoisomers **7c** and **11c**. These latter were quantitatively obtained in a 53/47 ratio in favor of **7c**. Overall yields were higher than 95%.

(±)-(8*β*,9α,14α)-11*β*,13*β*-*γ*-Carbolactone-17α-vinylgona-1,3,5(10)-triene (11a). White crystals, mp 107 °C; ^{1}H NMR ($CDCl_3$) δ 7.42 (1H, d, J = 7.6 Hz), 7.23 (2H, m), 7.06 (1H, dd, J = 6.9, 6.7 Hz), 5.64 (1H, ddd, J = 17.0, 10.0, 9.0 Hz), 5.11 (2H, m), 3.50 (1H, dd, J = 5.4, 1.4 Hz), 2.90 (2H, m), 2.86 (1H, m), 2.70 (1H, d, J = 10.0 Hz), 2.48 (1H, dd, J = 11.7, 5.4 Hz), 2.23 (1H, m), 2.02 (1H, m), 1.78 (1H, d, J = 11.7 Hz), 1.70 (1H, m), 1.61 (3H, m), 1.46 (1H, m); ^{13}C NMR ($CDCl_3$) δ 175.7 (s), 137.3 (d), 136.3 (s), 135.5 (s), 128.9 (d), 126.1 (d), 125.3 (d), 124.8 (d), 116.2 (t), 95.9 (s), 49.1 (d), 48.9 (d), 44.0 (d), 41.8 (d), 40.7 (d), 38.6 (t), 29.3 (t), 28.7 (t), 27.3 (t), 26.9 (t); MS (EI) *m*/*z* (relative intensity) 294 (100), 265 (26), 222 (34), 193 (33), 141 (32), 129 (42); HRMS calcd for $C_{20}H_{22}O_2$, 294.1620, found, 294.1619. Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.60; H, 7.54.

(±)-(8*β*,9α,14α)-11*β*,13*β*-*γ*-Carbolactone-3-methoxy-17α-vinylgona-1,3,5(10)-triene (11b). White crystals, mp 129 °C; ^{1}H NMR ($CDCl_3$) δ 7.31 (1H, d, J = 8.6 Hz), 6.72 (1H, dd, J = 8.6, 2.6 Hz), 6.60 (1H, d, J = 2.6 Hz), 5.63 (1H, ddd, J = 17.1, 10.1, 8.8 Hz), 5.12 (1H, d, J = 17.1 Hz), 5.08 (1H, d, J = 10.1 Hz), 3.74 (3H, s), 3.43 (1H, d, J = 5.3 Hz), 2.92−2.82 (3H, m), 2.62 (1H, d, J = 10.0 Hz), 2.46 (1H, dd, J = 11.7, 5.4 Hz), 2.22 (1H, m), 2.03−1.96 (3H, m), 1.76 (1H, d, J = 11.7 Hz), 1.72−1.53 (3H, m), 1.45 (1H, q, J = 10.4 Hz); ^{13}C NMR ($CDCl_3$) δ 176.2 (s), 158.2 (s), 138.0 (s), 137.7 (d), 126.2 (d), 116.6 (t), 114.5 (d), 111.4 (d), 96.4 (s), 55.2 (q), 49.5 (d), 49.3 (d), 44.2 (d), 42.5 (d), 41.5 (d), 39.2 (t), 29.7 (t), 29.5 (t), 27.8 (t), 27.2 (t); HRMS calcd for $C_{21}H_{24}O_3$, 324.1725, found 324.1745.

(±)-(8*β*,9α,14α)-11*β*,13*β*-*γ*-Carbolactone-2,3-dimethoxy-17α-vinylgona-1,3,5(10)-triene (11c). White crystals, mp 137 °C; ^{1}H NMR ($CDCl_3$) δ 6.87 (1H, s), 6.55 (1H, s), 5.63 (1H, ddd, J = 17.0, 9.8, 9.2 Hz), 5.12 (1H, d, J = 17.0 Hz), 5.08 (1H, d, J = 9.8 Hz), 3.87 (3H, s), 3.80 (3H, s), 3.40 (1H, d, J = 5.5 Hz), 2.84 (2H, m), 2.79 (1H, m), 2.63 (1H, br. d, J = 9.8 Hz), 2.47 (1H, dd, J = 11.7, 5.5 Hz), 2.23 (1H, m), 2.01 (2H, m), 1.77 (1H, d, J = 11.7 Hz), 1.70−1.57 (4H, m), 1.45 (1H, quint, J = 10.4 Hz); ^{13}C NMR ($CDCl_3$) δ 176.1 (s), 147.7 (s), 146.9 (s), 137.6 (d), 128.8 (s), 127.6 (s), 116.5 (t), 112.2 (d), 108.9 (d), 96.4 (s), 56.1 (q), 55.9 (q), 49.4 (d), 49.2 (d), 44.4 (d), 42.8 (d), 41.4 (d), 39.2 (t), 29.6 (t), 29.0 (t), 27.9 (t), 27.1 (t); HRMS calcd for $C_{22}H_{26}O_4$, 354.1831, found, 354.1834. Anal. Calcd for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39. Found: C, 74.42; H, 7.48.

Wacker-Type Oxidation of 5b,c. To a solution of 0.1 mmol of $Pd(OAc)_2$ (22.4 mg, 0.1 equiv) and 0.9 mmol of benzoquinone (97 mg, 0.9 equiv) in 10 mL of acetonitrile, were successively added 3.1 mL of water and 0.65 mL of $HClO_4$ (70%). The mixture was stirred 0.5 h at room temperature under argon. Then a solution of **5** (1 mmol) in 12 mL of acetonitrile was added and stirred at room temperature for 4 h (the progress of the reaction was followed by TLC analysis). The mixture was poured in diethyl ether and washed with a solution of NaOH (30%). The aqueous layer was extracted with diethyl ether. The combined organic layers were dried on $MgSO_4$, filtrated, and concentrated under vacuum. The crude product was purified by chromatography on silica gel (petroleum ether/ethyl acetate) to give **12b** (214 mg,0.54 mmol, 54%) or a separable mixture of **12c** (226 mg, 0.53 mmol, 53%) and **13c** (44 mg, 0.1 mmol, 10%).

6-Acetyl-3-(4-methoxybenzocyclobuten-1-yl)-3-methoxycarbonyl-9-vinyl-1-oxaspiro[4.4]nonan-2-one (12b). Colorless oil; ^{1}H NMR ($CDCl_3$) δ 6.92 (1H, d, J = 8.1 Hz), 6.75 (1H, dd, J = 8.1, 1.9 Hz), 6.65 (1H, d, J = 1.9 Hz), 5.13 (1H, ddd, J = 17.0, 10.3, 8.3 Hz), 4.75 (1H, dq, J = 10.3, 0.5), 4.43 (1H, dt, J = 17.0, 1.3 Hz), 4.18 (1H, dd, J = 5.0, 2.2 Hz), 3.87 (3H, s), 3.75 (3H, s), 3.24 (1H, dd, J = 14.9, 5.1 Hz), 2.91 (1H, dd, J = 9.4, 7.5 Hz), 2.77 (1H, dd, J = 14.8, 2.4 Hz), 2.44 (1H, d, J = 14.1 Hz), 2.13 (3H, s), 2.09 (1H, d, J = 14.1 Hz), 2.03 (3H, m), 1.57 (2H, m); ^{13}C NMR ($CDCl_3$) δ 207.9 (s), 173.5 (s), 171.0 (s), 160.9 (s), 144.6 (s), 135.5 (d), 134.3 (s) 124.1 (d), 118.1 (t), 114.1 (d), 108.7 (d), 91.1 (s), 58.5 (q), 57.8 (d or q), 55.5 (d or q), 53.3 (d), 51.3 (d), 45.8 (d), 32.6 (t), 30.9 (t), 30.5 (q), 26.0 (t), 24.3 (t); HRMS calcd for $C_{23}H_{26}O_6$, 398.1729, found 398.1732.

6-Acetyl-3-(4,5-dimethoxybenzocyclobuten-1-yl)-3-methoxycarbonyl-9-vinyl-1-oxaspiro[4.4]nonan-2-one (12c). White crystals, mp 91−92 °C; ^{1}H NMR ($CDCl_3$) δ 6.66 (1H, s), 6.56 (1H, s), 5.16 (1H, m), 4.76 (1H, d, J = 17.5 Hz), 4.49 (1H, d, J = 9.3 Hz), 4.18 (1H, dd, J = 4.8, 1.6 Hz), 3.88 (3H, s), 3.83 (3H, s), 3.78 (3H, s), 3.21 (1H, dd, J = 14.3, 4.8 Hz), 2.95 (1H, J = 8.8 Hz), 2.68 (1H, dd, J = 14.3, 1.6 Hz), 2.42 (1H, d, J = 14.1 Hz), 2.14 (3H, s), 2.12 (1H, d, J = 14.1 Hz), 1.79 (5H, m); ^{13}C NMR ($CDCl_3$) δ 207.9 (s), 173.7 (s), 170.9 (s), 151,0 (s), 150.0 (s), 135.3 (d), 134.9 (s), 133.6 (s), 118.2 (t), 107.0 (d), 106.8 (d), 91.2 (s), 58.4 (d), 57.7 (s), 56.3 (q), 51.2 (q), 51.2 (d), 45.8 (d), 32.5 (t), 30.8 (t), 30.7 (q), 25.9 (t), 24.2 (t). Anal. Calcd for $C_{24}H_{28}O_7$: C, 67.28; H, 6.59. Found: C, 67.35; H, 6.48.

6,9-Diacetyl-3-(4,5-dimethoxybenzocyclobuten-1-yl)-3-methoxycarbonyl-1-oxaspiro[4.4]nonan-2-one (13c). White crystals, mp 93 °C; ^{1}H NMR ($CDCl_3$) δ 6.62 (1H, s), 6.59 (1H, s), 4.13 (1H, dd, J = 5.0, 1.8 Hz), 3.85 (3H, s), 3.78 (3H, s), 3.14 (1H, m), 3.12 (1H, dd, J = 14.5, 5.0 Hz), 2.84 (1H, d, J = 14.5 Hz), 2.69 (1H, m), 1.98 (3H, s), 1.59 (3H, s); ^{13}C NMR ($CDCl_3$) δ 209.3 (s), 207.0 (s), 173.7 (s), 170.4 (s), 151.1 (s), 150.0 (s), 135.4 (s), 133.7 (s), 107.2 (d), 106.6 (d), 90.1 (s), 59.7 (d), 59.3 (d), 56.9 (s), 56.6 (q), 56.3 (q), 53.3 (q), 46.7 (d), 32.2 (t), 31.2 (q), 30.9 (t), 29.9 (q), 25.6 (t), 25.4 (t). Anal. Calcd for $C_{24}H_{28}O_8$: C, 64.85; H, 6.35. Found: C, 64.92; H, 6.41.

Thermolysis of 12c. Compound **12c** (118 mg, 0.257 mmol) in 1,2,4-trichlorobenzene was refluxed for 16 h (the progress of the reaction was followed by TLC analysis). The solvent was removed under vacuo and the residue was flash chromatographed on silica gel to give **14** (79 mg, 0.186 mmol, 67%), **15** (19 mg, 0.044 mmol, 16%), and **16** (17 mg, 0.043 mmol, 16%).

(±)-(8*β*,9α,14α)-17α-Acetyl-11α,13α-*γ*-carbolactone-2,3-dimethoxy-11*β*-methoxycarbonylgona-1,3,5(10)-triene (14). White crystals, mp 137−138 °C; ^{1}H NMR ($CDCl_3$) δ 6.63 (1H, s), 6.52 (1H, s), 3.82 (3H, s), 3.77 (3H, s), 3.65 (3H, s), 3. 07 (1H, d, J = 11.1 Hz), 2.91 (1H, dd, J = 10.2, 7.1 Hz), 2.79 (1H, d, J = 12.5 Hz), 2.75 (2H, t, J = 6.6 Hz), 2.57 (1H, d, J = 12.5 Hz), 2.24 (3H, s), 2.15 (2H, m), 1.96 (1H, ddd, J = 11.1, 7.1, 5.5 Hz), 1.87 (2H, m), 1.50, (1H, m), 1.41 (1H, qd, J = 11.1, 5.5 Hz), 1.04 (1H, m); ^{13}C NMR ($CDCl_3$) δ 204.3 (s), 173.9 (s), 169.8 (s), 147.0 (s), 146.7 (s), 131.4 (s), 129.5 (s), 112.2 (d), 106.8 (d), 91.1 (s), 57.7 (d), 56.3 (s), 55.9 (q), 55.8 (q), 52.5 (q or d), 51.9 (d or q), 43.5 (d), 42.4 (d), 37.4 (t), 30.7 (q), 29.6 (t), 27.2 (t), 26.7 (t), 26.5 (t). Anal. Calcd for $C_{24}H_{28}O_7$: C, 67.28; H, 6.59. Found: C, 67.15; H, 6.65.

(±)-(8*β*,9*β*,14α)-17α-Acetyl-11α,13α-*γ*-carbolactone-2,3-dimethoxy-11*β*-methoxycarbonylgona-1,3,5(10)-triene (15). White crystals, mp 117 °C; ^{1}H NMR ($CDCl_3$) δ 7.34 (1H, s), 6.42 (1H, s), 4.29 (1H, d, J = 7.1 Hz), 3.79 (3H, s), 3.49 (3H, s), 3.48 (3H, s), 2.56 (1H, d, J = 11.9 Hz), 2.49 (1H, m), 2.29 (1H, m), 2.22 (1H, dd, J = 10.4, 6.9 Hz), 2.06 (1H, d, J = 11.9 Hz), 1.99 (1H, m), 1.93 (1H, m), 1.87 (3H, s), 1.72 (1H, m), 1.52 (3H, m), 1.37 (1H, dddd, J = 14.9, 6.7, 6.6, 1.9 Hz), 0.49 (1H, dq, J = 11.8, 6.4 Hz); ^{13}C NMR ($CDCl_3$) δ 204.9 (s), 172.0 (s), 171.3 (s), 147.5 (s), 146.6 (s), 128.9 (s), 124.5 (s), 112.3 (d), 111.3 (d), 90.6 (s), 58.6 (d), 55.9 (q), 55.8 (q), 55.2 (s), 52.8 (d), 45.2 (q), 41.7 (d), 39.4 (d), 35.1 (t), 30.6 (t), 30.1 (t), 26.9 (q), 25.1 (t), 24.3 (t). Anal. Calcd for $C_{24}H_{28}O_7$: C, 67.28; H, 6.59. Found: C, 67.19; H, 6.68.

(±)-(8*β*,9α,14α)-17-Acetyl-2,3-dimethoxy-11*β*-methoxycarbonylgona-1,3,5(10),13(17)-tetraene (16). White crystals, mp 156−157 °C; ^{1}H NMR ($CDCl_3$) δ 6.76 (1H, s), 6.52 (1H, s), 3.90 (1H, m), 3.81 (3H, s), 3.80 (3H, s), 3.59 (1H, m), 3.43 (3H, s), 2.71 (5H, m), 2.23 (6H, m), 2.22 (3H, s), 1.43 (2H, m); ^{13}C NMR ($CDCl_3$) δ 198.8 (s), 172.3 (s), 153.9 (s), 147.2 (s), 134.9 (s), 129.5 (s), 128.7 (s), 125.1 (s), 112.1 (d), 109.3 (d), 56.1 (q), 55.8 (q), 53.8 (q or d), 51.4 (d or q), 44.2 (d), 43.0 (d), 42.6 (d), 33.2 (t), 32.3 (q), 30.3 (t), 29.7 (t), 28.5 (t), 27.3 (t). Anal. Calcd for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 71.77; H, 7.42.

Acknowledgment. We thank Dr. H. Darbon and Dr R. Faure for their assistance in NMR measurements. P.Y.M. and Ph.M. are grateful to the Ministère de l'Education Nationale, de la Recherche et de la Technologie for a grant. We are indebted to Dr. B. Vacher (Pierre Fabre Médicaments, Castres, France) for helpful comments.

Supporting Information Available: ^{13}C NMR spectra for **2**, **4b**−**12b**, **6c** and **7c**; ORTEP view and selected bond lengths and angles for **8a**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO001106F