added and the reaction mixture refluxed for 17 h. The mixture was then diluted with CH_2Cl_2, poured into 0.1 N HCl, and exhaustively extracted with CH_2Cl_2. The combined organic extracts were washed with $NaHCO_3$, dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (silica gel) (eluted with 2:1 EtOAc/hexanes) yielded 110 mg of olefin **2** (44% two-step yield), mp 117–118 °C (recrystallized from EtOAc/hexanes).

^1H NMR (270 MHz, $CDCl_3$) δ $CHCl_3$: 2.22–2.47 (2 H, m), 3.73 (3 H, s), 3.74 (3 H, s), 3.96 (1 H, s), 4.18 (1 H, s), 4.23 (1 H, $^1/_2$ AB q, J = 14.62 Hz), 4.44 (2 H, s), 14.60 (1 H, $^1/_2$ AB q, J = 14.62 Hz), 4.87 (1 H, s), 4.99 (1 H, s), 6.77–7.13 (8 H, m). IR (NaCl, neat): 2923, 2825, 1690, 1605, 1503, 1437, 1240, 1021 cm^{-1}. Anal. ($C_{23}H_{24}N_2O_4$) Calcd: C, 70.39; H, 6.16; N, 7.14. Found: C, 70.21; 5.87; 7.09.

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Registry No. 1, 109392-75-8; 2, 109392-76-9; 3, 79074-03-6; 4, 109392-77-0; 5, 109164-76-3; 6, 109164-77-4; 7, 109392-78-1; 8, 109392-79-2; 9, 109392-80-5; 10 (isomer 1), 109392-81-6; 10 (isomer 2), 109392-84-9; 11 (isomer 1), 109392-82-7; 11 (isomer 2), 109525-98-6; 12, 109392-83-8; *N*-(*p*-methoxybenzyl)glycine ethyl ester, 60857-16-1; *p*-methoxybenzyl chloride, 824-94-2; trimethylsulfoxonium iodide, 1774-47-6.

Synthesis from Pregnenolone of Fluorescent Cholesterol Analogue Probes with Conjugated Unsaturation in the Side Chain

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Fluorescent sterol probes which resemble cholesterol closely in both molecular geometry and amphipathic nature have been synthesized by the introduction of hydrophobic side chains embodying aryl diene or triene units. A direct synthesis of one of these fluorescent cholesterol analogues **6a** was possible by a phosphonate Wittig reaction on pregnenolone protected at C-3. However, the other cholesterol analogues **7a** and **8a** were prepared by phosphorane and phosphonate Wittig reactions on the more reactive and less sterically hindered 20(22)*E*-α,β-unsaturated aldehyde **5a**, which could be obtained by two different routes. The first route involved a Grignard reaction with vinylmagnesium bromide followed by oxidative rearrangement with pyridinium chlorochromate, which resulted in an 80:20 ratio of the diastereomeric aldehydes **5a**/**5b**. A more stereoselective synthesis of **5a** over **5b** (96:4) was achieved by a phosphonate Wittig reaction of pregnenolone protected at C-3 with the carbanion generated from diethyl [2-(cyclohexylimino)vinyl]phosphonate. Yields and ratios of all Wittig reactions performed are presented as are preliminary absorption and fluorescence data for the cholesterol analogue probes.

Introduction

Cholesterol is an important lipid component of many membranes, but its role in influencing the structure and function of membranes is not fully understood.[1] This is in part due to the very few methods that can be used to follow the properties of cholesterol when it is in such an inhomogeneous environment as a membrane. Hence, an external material with an easily measurable property is usually added to the system under question in order to probe the effect of cholesterol on the system.

Fluorescence is one of the most sensitive probe techniques available. Very little external probe material needs to be added, thereby minimizing any possible perturbations of the system by the probe. Many fluorescent probes bearing no resemblance to natural membrane constituents have been utilized in cholesterol/membrane studies, particularly the olefin diphenylhexatriene (DPH).[2] The latter has been found to partition into the lipid acyl chain region of a membrane. For our projected cholesterol/membrane studies, we wished to have a probe molecule which would partition into the cholesterol-rich domains of a membrane. To achieve this, it was decided to synthesize a fluorescent probe molecule with a structure as close as possible to that of cholesterol and retaining cholesterol's amphipathic nature.

Three main classes of fluorescent cholesterol-like probes have previously been synthesized: those derivatized[3] in the 3β-OH position (e.g., **1a**), those containing extra unsaturation in the ring system[4] (e.g., **2a** and **2b**), and those with a modified C-17 side chain[5] (e.g., **1b**). In some of the 3β-substituted cholesterol derivatives the amphipathic property[3c] is lost, while in all cases the interaction of the 3β-substituent with the head group of the phospholipids in membranes is significantly different from that of a 3β-hydroxy group. The ring unsaturated cholesterol-type molecules suffer from having a different geometry than

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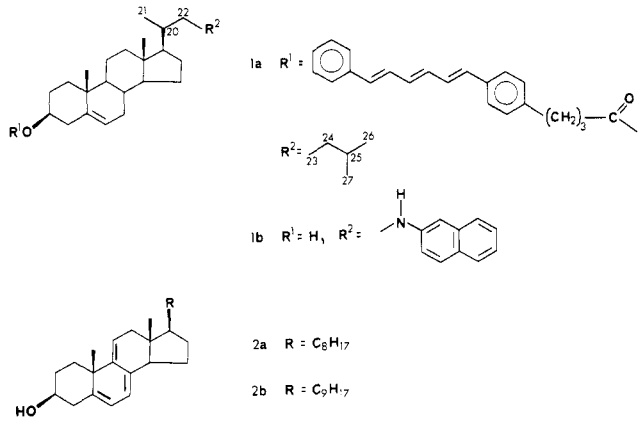


cholesterol with respect to the ring system and the angular methyl groups. These probes will interact differently from cholesterol with the lipid acyl chains in a membrane. Those cholesterol-type fluorescent probes that have previously been synthesized with modified side chains all contain heteroatoms in the side chain, greatly altering its hydrophobic character.

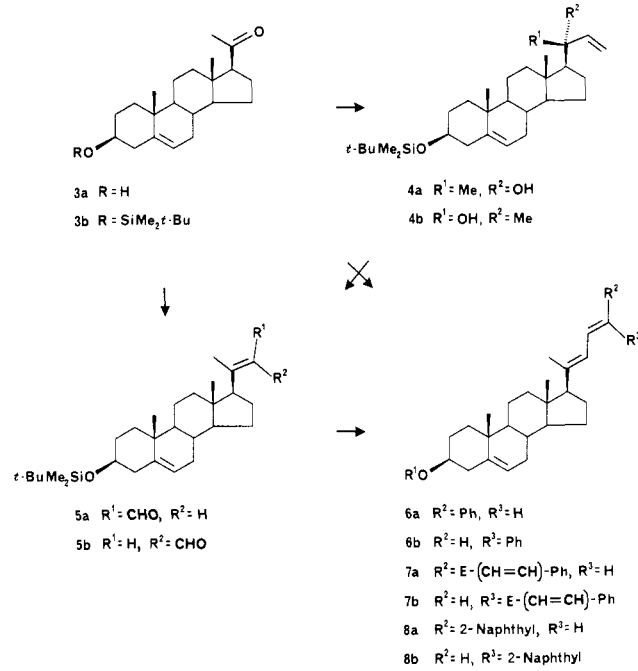
It was decided to synthesize fluorescent cholesterol analogues modified in the side chain with hydrophobic fluorophores, namely, by introduction of conjugated unsaturation.[6] Such fluorescent cholesterol-type molecules should resemble cholesterol more closely in both geometry and amphipathic nature and hence should partition into membranes in the cholesterol-rich domains and report on the membrane environment of the cholesterol.

A Wittig-type reaction on pregnenolone **3a** suitably protected at C-3 could furnish the desired polyunsaturated side chains directly. A survey of the literature shows several applications of *phosphorane* Wittig reactions on pregnenolone derivatives[7] but none with ylides bearing unsaturated groups. Only two cases of successful *phosphonate* Wittig reactions on pregnenolone have been reported, and these are with the activated carbanions, diethyl (cyanomethyl)phosphonate[8a-d] and, recently, ethyl (diethylphosphinyl)acetate[8e] after a number of unsuccessful attempts.[8a,c,9] Initially, it was decided to proceed with a Wittig reaction on pregnenolone by using an appropriately substituted phosphorane reagent.

Results and Discussion

The 3β-*tert*-butyldimethylsilyl ether of pregnenolone **3b** was treated with (*E*)-cinnamyltriphenylphosphonium bromide in order to obtain the *E,E*-diene phenyl compound **6a** (R^1 = $SiMe_2$-*t*-Bu). Despite the use of a number of combinations of base and solvent (lithium ethoxide and ethanol, potassium *tert*-amylate and toluene, *n*-butyllithium and tetrahydrofuran, sodium hydride with dimethyl sulfoxide and tetrahydrofuran), no reaction was observed. Considering the precedents for phosphorane Wittig reactions on pregnenolone, this lack of reactivity is probably due to the low nucleophilicity of the phosphorane ylide (the negative charge being delocalized through the conjugated unsaturation).

Despite the history of unsuccessful phosphonate Wittig reactions on pregnenolone and other 20-ketones, the 3β-*tert*-butyldimethylsilyl ether of pregnenolone **3b** was then treated with the carbanion generated from diethyl (*E*)-cinnamylphosphonate. Using *n*-butyllithium as the base and tetrahydrofuran as the solvent, the desired *E,E*-diene phenyl compound **6a** (R^1 = $SiMe_2$-*t*-Bu) was obtained, albeit in a relatively low yield of 35%. The ratio of isomers formed was 90:10 favoring the *E,E*-isomer, as determined by high-resolution NMR. However, it was the 23(24) double bond about which the isomers were formed as determined by Nuclear Overhauser Effect (NOE) experiments.[10] Failure to observe a *Z* isomer about the 20(22) double bond which was formed in the reaction could be rationalized by steric hindrance from the steroid nucleus to 20(22)*Z* double bond formation given the bulk of the side chain being added. On the other hand, observation of the diastereomers about the 23(24) double bond suggests that the negative charge of the phosphonate carbanion was delocalized over the allylic system, resulting in loss of geometrical integrity about the eventual 23(24) double bond.



A similar reaction of the 3β-*tert*-butyldimethylsilyl ether of pregnenolone **3b** with a 90:10 mixture of the diethyl (2*E*,4*E*)- and (2*Z*,4*E*)-2,4-pentadienylphosphonate carbanion was unsuccessful. The explanation for this may be that the introduction of one extra double bond into the phosphonate reagent stabilizes the carbanion to such an extent as to make it unreactive toward the rather sterically hindered 20-keto group of pregnenolone.

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Table I. Ratios of 20(22)*E*/20(22)*Z*-Aldehydes (5a/5b) Obtained after Oxidative Rearrangement of Various Ratios of 20*R*/20*S*-Alcohols (4a/4b) with Pyridinium Chlorochromate

4a/4b	5a/5b	4a/4b	5a/5b
10:90	80(±1):20(±1)[a]	0:100	78(±2):22(±2)[b]
100:0	98(±1):2(±1)[b]	10:90	80(±2):20(±2)[c]

[a] Determined by 300-MHz ^{1}H NMR. [b] Determined by HPLC. [c] Calculated from observed ratios of aldehydes obtained by starting from pure **4a** and pure **4b**.

A more reactive carbonyl compound was needed in order to arrive at the desired olefinic sterol derivatives **7a** and **8a**. It was decided to synthesize the 20(22)*E*-α,β-unsaturated aldehyde **5a**. Apart from having a more reactive carbonyl function than the 20-keto group of pregnenolone, this aldehyde is less sterically hindered for reaction with a Wittig reagent, and hence it should react with both phosphorane ylides and phosphonate carbanions.

Synthesis of the analogous 3β-acetoxy aldehyde has been reported,[11] the more efficient route involving a Grignard reaction and then a rearrangement of the tertiary alcohol and subsequent oxidation.[11a] We adopted this route except that use of pyridinium chlorochromate[12] enabled us to perform the rearrangement and oxidation in one step.

The *tert*-butyldimethylsilyl ether of pregnenolone **3b** was treated with vinyl magnesium bromide to obtain the epimeric C-20 alcohols **4a** and **4b**. The ratio of alcohols obtained was determined to be 1:9 by integration of the C-23 ^{1}H NMR peaks centered at δ 5.22 and 5.00 and at δ 5.15 and 4.96. The major isomer was assigned the 20*S* configuration (**4b**) in keeping with the stereochemical preference reported for other Grignard reactions on C-20 steroidal ketones.[11a,13] The 9:1 ratio of 20*S*/20*R* alcohols (**4b**/**4a**) is in good agreement with that observed for the analogous 3β-acetoxy compound (11:1).[11a]

Treatment of the 9:1 mixture of 20*S*,20*R*-alcohols **4b** and **4a** with pyridinium chlorochromate resulted in an 80:20 mixture of the 20(22)*E*- and 20(22)*Z*-α,β-unsaturated aldehydes **5a** and **5b**, respectively. The 20(22)*E*- and 20(22)*Z*-aldehydes were assigned on the basis of their C-21 ^{1}H NMR resonances:[14] 20(22)*E*-isomer **5a**, δ 2.22; 20(22)*Z*-isomer **5b**, δ 1.99. The 80:20 ratio of the aldehydes was determined by integration of the C-23 ^{1}H NMR peaks at δ 10.07 [20(22)*E*] and 9.97 [20(22)*Z*] and of the C-22 proton peaks at δ 6.05 [20(22)*Z*] and 5.95 [20(22)*E*].

In order to obtain some insight into the mechanism of this oxidative rearrangement, the pure 20*R*- and 20*S*-alcohols (**4a** and **4b**) were each treated with pyridinium chlorochromate, and the resulting ratios of 20(22)*E*/20(22)*Z*-aldehydes determined by HPLC. The results are given in Table I.

It can be seen that the 20*R*-alcohol **4a** gives the 20(22)*E*-aldehyde **5a** in a highly stereoselective manner, in contrast to the 20*S*-alcohol **4b**. This difference in behavior can be attributed to the relative arrangement of the functional groups on C-20 with respect to the D ring of the steroid nucleus. From an X-ray crystallographic study[13] on the analogous 20*S*-ethyl compound, the position of the ethyl group was determined to be close to 180° from C-13 (when looking along the C-17,C-20 bond). The C-20 C–O bond lies over the D ring while the 21-methyl group points out the back of the molecule. If we assume that likewise the ethylene group of the 20*S*- and 20*R*-alcohols (**4b** and **4a**) adopts an ~180° conformation from C-13 in solution, then the higher stereoselectivity of the 20*R*-alcohol oxidative rearrangement can be rationalized. The hydroxyl group of the 20*R*-alcohol **4a** would be pointing out the back of the molecule and hence it could be envisaged that the oxidative rearrangement occurs mainly by a concerted mechanism as there is little steric hindrance from neighboring nuclei. On the other hand, the hydroxyl group of the 20*S*-alcohol **4b** would lie over the D ring of the steroid nucleus as in the 20*S*-ethyl compound, and there would be some steric hindrance to a concerted oxidative rearrangement.

The difference in stereoselectivities of the oxidative rearrangement of the epimeric alcohols can be seen to account for the ratio difference between the reactants and products (20*S*/20*R*-alcohols in 9:1 ratio → 20(22)*E*/20(22)*Z*-aldehydes in 4:1 ratio). As shown in Table I, if 90% of the resultant ratio from the 20*S* alcohol **4b** oxidative rearrangement is added to 10% of the product ratio from the 20*R*-alcohol **4a** oxidative rearrangement, an aldehyde ratio is arrived at (80:20), which is the same as that found experimentally for the 20*S*/20*R*-alcohol (9:1) oxidative rearrangement reaction.

Another route to the isomeric aldehydes **5a** and **5b** was investigated with the aim of synthesizing the 20(22)*E*-aldehyde **5a** more stereoselectively. It was decided to treat the *tert*-butyldimethylsilyl ether of pregnenolone **3b** with diethyl [2-(cyclohexylimino)vinyl]phosphonate, which has been shown to react with 3-keto and 17-keto steroids,[15] followed by hydrolysis of the cyclohexylimino function. This phosphonate Wittig reaction was expected[16] to yield predominantly the 20(22)*E*-aldehyde **5a**, and this proved to be the case (a ratio of 96:4 favoring **5a** over **5b** was determined by HPLC).

Both phosphorane and phosphonate Wittig reactions were successfully carried out on the 20(22)*E*-aldehyde **5a**. For example, when **5a** was treated with the ylide generated from (*E*)-cinnamyltriphenylphosphonium bromide in tetrahydrofuran, the expected *E*,*E*,*E*- and *E*,*Z*,*E*-trienes **7a** and **7b** (R^1 = $SiMe_2$-*t*-Bu) were formed in 75% yield. After removal of the *tert*-butyldimethylsilyl protecting group at C-3, the ratio of **7a**/**7b** (R^1 = H) was determined by 500-MHz ^{1}H NMR to be 40:60.[10]

In order to improve the stereoselectivity of *E*,*Z*,*E*-triene **7b** formation, the above experiment was repeated in a 1:9 ratio of hexamethylphosphoramide (HMPA)/tetrahydrofuran as solvent. Use of HMPA as a cosolvent has been shown[17] to increase *Z* stereoselectivity of Wittig reactions. It has been postulated that this is due to the ability of HMPA to act as a lithium cation complexing agent, hence accelerating the formation of olefin from the betaine–lithium bromide complex, producing the more kinetically favored (*Z*)-olefin. The ratio of conjugated trienes formed under these conditions was determined by HPLC to be 1:99 (**7a**/**7b**, R^1 = $SiMe_2$-*t*-Bu).

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Table II. Yields and E/Z Ratios for Various Wittig Reactions on Compounds 3b and 5a

RR'CO	method[a]		product	yield, %	E/Z ratio[b,c]
		$(EtO)_2P(O)CH_2R''$			
3b	III	R'' = (*E*)-(CH=CH)Ph[d]	**6a,b**	35	90:10[b,e]
3b	III	R'' = $(CH=CH)_2Ph$[f]	no reaction		
3b	III	R'' = $CH=NC_6H_{11}$[g]	**5a,b**	45	96:4[c]
5a	III	R'' = (*E*)-(CH=CH)Ph	**7a,7b**	40	83:17[c]
5a	III	R'' = 2-$(C_{10}H_7)$[h]	**8a,b**	55	90:10[b]
		$Ph_3P^+CH_2R''$ X^-			
3b	I	R'' = (*E*)-(CH=CH)Ph	no reaction		
5a	I	R'' = Ph	**6a,b**	75	40:60[b]
5a	I	R'' = (*E*)-(CH=CH)Ph	**7a,b**	75	40:60[b]
5a	II	R'' = (*E*)-(CH=CH)Ph	**7a,b**		1:99[c]

[a] Method I: phosphorane ragent, THF, reflux for 12 h. Method II: phosphorane reagent, 9:1 THF/HMPA, room temperature for 24 h. Method III: phosphonate reagent, THF, room temperature for 24 h. [b] Determined by 500-MHz ^1H NMR. [c] Determined by HPLC. [d] See ref 18. [e] About C-23 (24) double bond, see text. [f] 90:10 mixture of 2*E*,4*E*/2*Z*,4*E*-isomers. [g] See ref 15 and 19. [h] See ref 20.

A more stereoselective synthesis of the *E,E,E*-triene **7a** was achieved by treating the 20(22)*E*-aldehyde **5a** with the carbanion generated from diethyl (*E*)-cinnamylphosphonate in tetrahydrofuran. The ratio of conjugated trienes **7a/7b** (R^1 = $SiMe_2$-*t*-Bu) obtained by this method was found to be 83:17 by HPLC analysis. See Table II for yields and E/Z ratios of all Wittig-type reactions performed on the aldehyde **5a** and on the 3β-*tert*-butyldimethylsilyl ether of pregnenolone **3b**.

All of the polyunsaturated sidechain analogues reported here resemble cholesterol very closely in amphipathic nature. Inspection of space-filling models shows that the *E,E*-diene phenyl isomer **6a** (R^1 = H) has the closest geometrical structure to that of cholesterol.

A number of observations in the literature lend support to the idea that the sterol probes **6a**, **7a**, and **8a** will prove to be close analogues of cholesterol in membranes. First, deuterium NMR studies[21] of various deuteriated cholesterol derivatives incorporated into model dimyristoylphosphatidyl choline (DMPC) membranes have shown that the side chain of cholesterol, up to C-22, is as rigid as the ring system, as measured by the molecular order parameter S_{mol} = 0.80. Even at C-24, the side chain was found to be highly ordered with S_{mol} = 0.66. Second, X-ray crystallographic studies[22] of anhydrous cholesterol have shown that at around physiological temperatures, cholesterol undergoes a phase transition in which the side chain conformation changes from gauche-trans to the more favorable trans-trans geometry.

It would appear then that the presence of unsaturation in the side chains of the sterol probes **6a**, **7a**, and **8a** should not lead to a significant difference in their side chain order with respect to that of cholesterol, when incorporated in membranes. Furthermore, as the preferred side chain conformation of crystalline anhydrous cholesterol is trans-trans, the all-trans geometry of the olefinic side chains of **6a**, **7a**, and **8a** should render these sterols close analogues of cholesterol.

Absorption and fluorescence maxima of the fluorescent analogues are summarized in Table III. Results of our studies on the fluorescence properties of these compounds in model membrane bilayers and in various density lipoprotein fractions will be reported elsewhere.

Experimental Section

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Spectra were obtained on the following instruments: Bruker AM-500 and AM-200 and Varian XL300 (^1H and ^{13}C NMR), Varian Cary 219 (UV), Perkin-Elmer MPF-44A (fluorescence), Perkin-Elmer 23 polarimeter (rotations), and a Vacuum Generator VG 7070E (MS). The ionizing voltage for MS was 70 eV. Elemental analyses were performed by Mr. H. Séguin, Division of Biological Sciences, National Research Council, Ottawa, Canada.

Table III. Absorption and Fluorescence Maxima of Cholesterol Analogue Probes 6a, 7a, and 8a

compd (with R^1 = H)	λ_{max}^{abs}, nm[a]	λ_{max}^{em}, nm[a,b]
6a	295	352
7a	332	390
8a	271,332	407

[a] For solvent used, see Experimental Section. [b] For excitation wavelength, see Experimental Section.

For flash column chromatography Terochem silica gel 1918 (equivalent to Merck 9385, 20–45 μm) was used. Thin-layer chromatography (TLC) was done on Merck 60 nonfluorescent silica gel plates, which were visualized by spraying with 5% sulfuric acid in ethanol and heating. Analytical and preparative high-performance liquid chromatography (HPLC) was performed on a Varian Vista 5500 liquid chromatograph with a Varian DS604 data system.

Preparation of Phosphonates. Diethyl (*E*)-Cinnamylphosphonate. Equimolar amounts of triethyl phosphite and (*E*)-cinnamyl bromide were heated under reflux at 160 °C for 10 h. The ethyl bromide evolved was condensed in an acetone/dry ice cold finger, and the reaction mixture was distilled to give pure diethyl (*E*)-cinnamylphosphonate: bp 147.0–148.5 °C (1.0 mm); ^1H NMR (300 MHz) δ 1.29 (t, 6 H, *J* = 7.1 Hz, OCH_2CH_3), 2.74 (d of d of d, 2 H, *J* = 1.2, 7.5, 22.1 Hz, CH_2P), 4.10 (m, 4 H, OCH_2CH_3), 6.15 (m, 1 H, $CH=CHCH_2P$), 6.51 (d of d, 1 H, *J* = 5.0, 15.7 Hz, $CH=CHCH_2P$), 7.18 → 7.35 (m, 5 H, Ar protons). Anal. Calcd for $C_{13}H_{19}O_3P$: C, 61.41; H, 7.53. Found: C, 61.19; H, 7.39.

Diethyl (2-Naphthylmethyl)phosphonate. This phosphonate was prepared by a reported[20] method: bp 168.0–169.0 °C (1.2 mm); ^1H NMR (300 MHz) δ 1.22 (t, 6 H, *J* = 7.1 Hz, OCH_2CH_3), 3.30 (d, 2 H, *J* = 21.7 Hz, CH_2P), 4.00 (m, 4 H, OCH_2CH_3), 7.40 → 7.47, (m, 3 H, Ar protons), 7.73 → 7.81 (m, 4 H, Ar protons).

Diethyl (2*E*,4*E*)- and (2*Z*,4*E*)-2,4-Pentadienylphosphonate. This phosphonate was prepared from (*E,E*)-cinnamylideneacetic acid as outlined below.

Methyl (*E,E*)-5-Phenyl-2,4-pentadien-1-oate. (*E,E*)-Cinnamylideneacetic acid (Pfitzer and Bauer, 10.0 g) was dissolved in anhydrous MeOH (200 mL), and dry HCl (~10 g) was added. The reaction mixture was stirred at room temperature for 20 h, and then the MeOH was evaporated under reduced pressure. The product was extracted with *n*-pentane through a thimble and allowed to crystallize. Total yield of the ester was 96% (10.4 g) after two crops of crystals: mp 67.0–68.0 °C (lit.[23] mp 71 °C); MS, *m/z* 188 (M^+), 157 ($M^+ - OCH_3$), 129 ($M^+ - CO_2CH_3$); ^1H NMR

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(300 MHz) δ 3.80 (s, 3 H, CO_2CH_3), 6.03 (d, 1 H, J = 15.9 Hz, H-2), 6.86 → 6.92 (m, 2 H, H-4, H-5), 7.33 → 7.52 (m, 6 H, 5 Ar protons and H-3). Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.53; H, 6.43.

(*E*,*E*)-5-Phenyl-2,4-pentadien-1-ol. The 1-methyl ester from above (0.94 g) was added to benzene (Na dried, 11 mL) under nitrogen, and then diisobutylaluminum hydride (1.0 M solution in toluene, 10.0 mL, 2.0 equiv) was added slowly over 1 h. The reaction mixture was then heated at 45 °C for 3 h until no starting material remained. After the mixture was cooled, dry MeOH (1.04 mL in 1.14 mL of toluene, 6.0 equiv) and then H_2O (0.55 mL in 1.14 mL of MeOH, 6.0 equiv) were added. The gel which formed upon addition of H_2O was filtered, washed with MeOH, evaporated to dryness, extracted through a thimble with *n*-pentane, and allowed to crystallize to yield 0.70 g of the alcohol (87% yield): mp 79.5–81.5 °C (lit.[24a] mp 80–81 °C, lit.[24b] mp 73–78 °C); MS, m/z 160 (M^+), 142 ($M^+ - H_2O$); ^1H NMR (300 MHz) δ 4.26 (d of d, J = 7, 2 Hz, CH_2OH). Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.21; H, 7.43.

1-Bromo-5-phenyl-2,4-pentadiene. (*E*,*E*)-5-Phenyl-2,4-pentadien-1-ol (0.95 g) was dissolved in dry ether (20 mL) and cooled to 0 °C, and phosphorus tribromide (1.62 mL, 1.05 equiv) was added dropwise. After being stirred at 0 °C for 1.5 h, the reaction mixture was poured onto ice, extracted with ether, washed with $NaHCO_3$, and dried over $MgSO_4$. After evaporation of the solvent under reduced pressure, the cream-colored residue was ground to a powder and dried under vacuum (over KOH) to give 1.06 g (80% yield) of slightly contaminated 1-bromo-5-phenyl-2,4-pentadiene, which was used within 3 days in the following reaction: MS, m/z (under chemical ionization conditions) 225, 223 (MH^+), 224, 222 (M^+); ^1H NMR (300 MHz) δ 4.09 (d of d, J = 7.7, 2.0 Hz, CH_2Br).

Diethyl 5-Phenyl-2,4-pentadien-1-ylphosphonate. The slightly contaminated 1-bromo-5-phenyl-2,4-pentadiene (3.48 g) was heated at 160 °C with triethyl phosphite (3.00 mL, 1.12 equiv) for 20 h. The reaction mixture was distilled [153–158 °C (0.1 mm)] to give 2.06 g (47% yield) of a 90:10 mixture of the 2*E*,4*E*/2*Z*,4*E* isomers as determined by 200-MHz ^1H NMR. This mixture of isomers is suspected to have originated from the bromination reaction above.

2*E*,4*E*-Isomer: ^1H NMR (200 MHz) δ 1.26 (t, 6 H, J = 7.1 Hz, OCH_2CH_3), 2.64 (d of d, 2 H, J = 22.9, 7.7 Hz, CH_2P), 4.05 (m, 4 H, OCH_2CH_3), 5.72 (m, 1 H, H-2), 6.28 (d of d of d, 1 H, J = 15.1, 10.2, 5.0 Hz, H-3), 6.44 (d of d, 1 H, J = 15.7, 2.4 Hz, H-5), 6.71 (d of d, 1 H, J = 15.5, 10.4 Hz, H-4), 7.14 → 7.38 (m, Ar protons).

2*Z*,4*E*-Isomer: ^1H NMR (200 MHz) δ 2.79 (d of d, J = 23, 8 Hz, CH_2P), 5.48 (d of d, J = 11, 8 Hz, *H*-2), 6.96 (d of d, J = 15, 10 Hz, H-4).

General Conditions of Phosphorane Wittig Reaction (Method I). To a cooled solution (−78 °C) of the phosphorane (1.1 equiv) in THF was added *n*-BuLi (1.1 equiv), and after the mixture was stirred for 45 min, a solution of the carbonyl compound in THF was added. The reaction mixture was stirred at −78 °C for a further 45 min, allowed to come to room temperature, and then refluxed for 12 h. The solvent was evaporated and the residue taken up in ether and worked up in the usual way. Chromatography of the crude product on silica gel (hexane) gave a mixture of (*E*/*Z*)-olefins (see Table II). After deprotection, the (*E*)- and (*Z*)-olefins were separated by HPLC (Beckman Ultrasphere ODS column, 10 mm × 25 cm, 3 mL/min, 95% MeOH/5% H_2O).

General Conditions of Phosphorane Wittig Reaction for Stereoselective Synthesis of (*Z*)-Olefins (Method II). The above procedure was followed except that the solvent for the reaction was 90% THF/10% hexamethylphosphoramide (HMPA) and the reaction mixture was not refluxed but kept stirring at room temperature for 24 h (see Table II for isomer ratios).

General Conditions of Phosphonate Wittig Reaction for Stereoselective Synthesis of (*E*)-Olefins (Method III). The procedure was identical with that of method I except that the appropriate phosphonate was used instead of the phosphorane and the reaction mixture was not refluxed but kept stirring at room temperature for 24 h (see Table II for isomer ratios).

Pregnenolone 3β-*tert*-Butyldimethylsilyl Ether (3b) from **3a.** Pregnenolone (**3a**, 22.6 g) was treated with *tert*-butyldimethylsilyl chloride (13.1 g, 1.2 equiv) and imidazole (11.9 g, 2.4 equiv) in dry DMF for 20 h at room temperature. The resulting precipitate was filtered and recrystallized from $CHCl_3$ to give pure **3b**. The filtrate was extracted with ether, washed with H_2O, and dried over $MgSO_4$ and the solvent removed under reduced pressure. The resulting white powder was chromatographed on silica gel (hexane/ethyl acetate, 98:2) to give more protected pregnenolone **3b** (total yield 28.3 g, 92%): mp 164.5–165.0 °C (lit.[25] mp 162–164 °C); MS, m/z 415 ($M^+ - CH_3$), 373 ($M^+ - C(CH_3)_3$); $[\alpha]^{25}_D$ +23° (*c* 1.29, CH_2Cl_2); ^1H NMR (300 MHz) δ 0.06 (s, 6 H, $Si(CH_3)_2$), 0.63 (s, 3 H, C-18 methyl), 0.89 (s, 9 H, $C(CH_3)_3$), 1.00 (s, 3 H, C-19 methyl), 2.12 (s, 3 H, C-21 methyl), 3.48 (m, 1 H, H-3α), 5.34 (br d, 1 H, H-6); ^{13}C NMR (75 MHz) δ −4.61 ($Si(CH_3)_2$), 25.90 ($C(CH_3)_3$), 209.58 (C-20). Anal. Calcd for $C_{27}H_{46}O_2Si$: C, 75.27; H, 10.77. Found: C, 75.02; H, 10.79.

General Deprotection Procedure. The *tert*-butyldimethylsilyl ether derivatives of the unsaturated alcohols **6a,b**, **7a,b**, and **8a,b** were treated with tetra-*n*-butylammonium fluoride[26] (1.0 M solution in THF, 4 equiv) in dry THF for 20 h at room temperature. After removal of the solvent, the residue was taken up in ethyl acetate, washed with water, and dried over $MgSO_4$ and the ethyl acetate evaporated under reduced pressure. The crude solid was chromatographed over silica gel (hexane/ethyl acetate, 88:12) to give quantitative yields of the corresponding C-3 alcohols.

(20*R*)- and (20*S*)-20-Vinylpregn-5-ene-3β,20-diol 3β-*tert*-Butyldimethylsilyl Ether (4a and 4b) from 3b. To a cooled solution (−78 °C) of the *tert*-butyldimethylsilyl ether of pregnenolone (**3b**, 15.7 g) in THF was added vinylmagnesium bromide (1 M solution in THF, 90 mL, 2.5 equiv), and the reaction mixture was stirred at −78 °C for 1 h and then at room temperature for 24 h. Hydrolysis with a saturated solution of NH_4Cl (0 °C), extraction with ether, and working up in the usual way[11a] gave the crude product, which was purified by chromatography on silica gel (hexane, hexane/ethyl acetate, 98.5:1.5). The fractions containing solely the 20*R*- and 20*S*-isomers **4a** and **4b**, respectively, were combined separately; total yield of C-20 alcohol was 14.6 g (87%). ^1H NMR (300 MHz) on partially purified reaction product (starting material removed) determined the ratio of the epimers to be 1:9 by integration of the H-23 peaks ($RCH{=}CH_2$) centered at δ 5.22 and 5.15 and at δ 5.00 and 4.96. The major isomer was assigned the 20*S* configuration (**4b**) in line with reported epimer ratios[11a,13] for other Grignard reactions on 20-keto steroids.

20*R*-Epimer 4a: mp 192–194.5 °C; MS, m/z 443 ($M^+ - CH_3$), 401 ($M^+ - C(CH_3)_3$); $[\alpha]^{22}_D$ −26° (*c* 0.24, $CHCl_3$); ^1H NMR (500 MHz) δ 0.053 (s, 6 H, $Si(CH_3)_2$), 0.770 (s, 3 H, C-18 methyl), 0.886 (s, 9 H, $C(CH_3)_3$), 0.983 (s, 3 H, C-19 methyl), 1.538 (s, 3 H, C-21 methyl), 3.48 (m, 1 H, H-3α), 5.00 (d, 1 H, J = 10.7 Hz, H-23), 5.22 (d, 1 H, J = 17.2 Hz, H-23), 5.31 (br d, 1 H, H-6), 6.03 (d of d, 1 H, J = 17.3, 10.7 Hz, H-22); ^{13}C NMR (125 MHz) δ 13.35 (C-18), 22.40 (C-16), 29.93 (C-21), 58.98 (C-17), 75.42 (C-20), 109.78 (C-23), 146.24 (C-22). Anal. Calcd for $C_{29}H_{50}O_2Si$: C, 75.90; H, 10.99. Found: C, 75.75; H, 11.01.

20*S*-Epimer 4b: mp 157–158 °C; MS, m/z 443 ($M^+ - CH_3$), 401 ($M^+ - C(CH_3)_3$); $[\alpha]^{25}_D$ −52° (*c* 1.07, CH_2Cl_2); ^1H NMR (500 MHz) δ 0.055 (s, 6 H, $Si(CH_3)_2$), 0.830 (s, 3 H, C-18 methyl), 0.888 (s, 9 H, $C(CH_3)_3$), 0.999 (s, 3 H, C-19 methyl), 1.542 (s, 3 H, C-21 methyl), 3.48 (m, 1 H, H-3α), 4.96 (d of d, 1 H, J = 10.8, 1.3 Hz, H-23), 5.15 (d of d, 1 H, J = 17.3, 1.2 Hz, H-23), 5.31 (br d, 1 H, H-6), 5.98 (d of d, 1 H, J = 17.3, 10.8 Hz, H-22); ^{13}C NMR (125 MHz) δ 13.80 (C-18), 23.21 (C-16), 28.78 (C-21), 59.47 (C-17), 75.73 (C-20), 110.22 (C-23), 146.12 (C-22). Anal. Calcd for $C_{29}H_{50}O_2Si$: C, 75.90; H, 10.99. Found: C, 75.80; H, 11.11.

(20(22)*E*)- and (20(22)*Z*)-24-Norchola-5,20(22)-dien-23-al, 3β-*tert*-Butyldimethylsilyl Ether (5a and 5b) from 4a and 4b. To a suspension of pyridinium chlorochromate (12.0 g, 2 equiv) and sodium acetate (4.5 g, 2 equiv) in CH_2Cl_2 was added a solution of the 1:9 mixture of the 20*R*/20*S*-alcohols **4a** and **4b** (12.9 g) in CH_2Cl_2. After the mixture was stirred at room temperature for

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20 h, the solvent was evaporated and the residue taken up in ether, washed with saturated $NaHCO_3$ and brine, and dried over $MgSO_4$. The crude solid obtained after removal of the solvent was chromatographed on silica gel (hexane, hexane/ethyl acetate, 99:1). Those fractions containing solely the 20(22)*Z*- or 20(22)*E*-isomers were combined separately, giving a total yield of aldehydes of 88% (**5a**, **5b**, 11.3 g). The *E*- and *Z*-aldehydes were assigned on the basis of their ^1H and ^{13}C 21-methyl NMR resonances: δ 2.20 (*E*) and 1.99 (*Z*);[14] δ 19.36 (*E*) and 24.54 (*Z*). The ratio of diastereomeric aldehydes was determined by integration of the H-23 peaks at δ 10.07 (*E*) and 9.97 (*Z*) and the H-22 peaks at δ 6.05 (*Z*) and 5.95 (*E*) to be 80 ± 1/20 ± 1 as *E*/*Z*.

The oxidation procedure described above was carried out on both the pure 20*R*-alcohol **4a** and on the pure 20*S*-alcohol **4b** and the ratio of resultant aldehydes determined on the crude products by HPLC (Varian MCH-5NCAP column, 4.6 mm × 15 cm, 100% MeOH, 254 nm). The results are summarized in Table I.

(20(22)*E*)- and (20(22)*Z*)-Norchola-5,20(22)-dien-23-al, 3β-*tert*-Butyldimethylsilyl Ether (5a and 5b) from **3b**. The *tert*-butyldimethylsilyl ether of pregnenolone (**3b**, 2.9 g) was treated with diethyl-2-(cyclohexylimino)vinyl phosphonate[15,19] (1.1 equiv) and NaH (50% dispersion in oil, 1.1 equiv) in THF initially at 0 °C and then at reflux temperature for 12 h. A yellow-green color developed upon heating. The reaction mixture was diluted with water and extracted with ether. Hydrolysis of the crude product and chromatography on silica gel (hexane, hexane/ethyl acetate, 96:4) gave a 45% yield of the diastereomeric 20(22)*E*/20(22)*Z*-aldehydes (**5a** and **5b**, 1.40 g). The ratio of aldehydes was determined by HPLC (Varian SPC-18 column, 4.6 mm × 15 cm, 100% CH_3CN, 250 nm) to be 20(22)*E*/20(22)*Z* = 96:4.

20(22)*E*-Isomer (5a): mp 145–146.5 °C; MS, *m*/*z* 456 (M^+), 441 ($M^+ - CH_3$), 399 ($M^+ - C(CH_3)_3$); UV λ_{max}^{abs} 248 nm ($CHCl_3$); ^1H NMR (300 MHz) δ 0.06 (s, 6 H, $Si(CH_3)_2$), 0.62 (s, 3 H, C-18 methyl), 0.89 (s, 9 H, $C(CH_3)_3$), 1.01 (s, 3 H, C-19 methyl), 2.20 (s, 3 H, C-21 methyl), 3.49 (s, 1 H, H-3α), 5.35 (br d, 1 H, H-6), 5.95 (d, 1 H, *J* = 7.8 Hz, H-22), 10.07 (d, 1 H, *J* = 8.0 Hz, H-23); ^{13}C NMR (125 MHz) δ 19.36 (C-21), 127.99 (C-22), 164.24 (C-20). Anal. Calcd for $C_{29}H_{48}O_2Si$: C, 76.32; H, 10.53. Found: C, 75.80; H, 10.72.

20(22)*Z*-Isomer (5b): mp 118–119 °C; MS, *m*/*z* 456 (M^+), 441 ($M^+ - CH_3$), 399 ($M^+ - C(CH_3)_3$); $[\alpha]^{25}_D$ −102° (*c* 0.66, $CHCl_3$); ^1H NMR (500 MHz) δ 0.059 (s, 6 H, $Si(CH_3)_2$), 0.698 (s, 3 H, C-18 methyl), 0.890 (s, 9 H, $C(CH_3)_3$), 1.009 (s, 3 H, C-19 methyl), 1.992 (s, 3 H, C-21 methyl), 3.48 (m, 1 H, H-3α), 5.33 (br d, 1 H, H-6), 6.05 (d, 1 H, *J* = 8.0 Hz, H-22), 9.97 (d, 1 H, *J* = 8.3, H-23); ^{13}C NMR (125 MHz) δ 24.54 (C-21), 131.59 (C-22), 164.11 (C-20), 191.16 (C-23). Anal. Calcd for $C_{29}H_{48}O_2Si$: C, 76.32; H, 10.53. Found: C, 76.06; H, 10.65.

(20(22)*E*,23*E*)-24-Phenylchola-5,20(22),23-trien-3β-ol (6a, R^1 = H): mp 141.0–142.5 °C; MS, *m*/*z* 416 (M^+); $[\alpha]^{25}_D$ −30° (*c* 0.19, CH_2Cl_2); UV λ_{max}^{abs} 280, *295*, 306 nm (MeOH), λ_{max}^{em} 352 nm (MeOH, λ_{ex} = 300 nm); ^1H NMR (500 MHz) δ 0.598 (s, 3 H, C-18 methyl), 1.009 (s, 3 H, C-19 methyl), 1.896 (s, 3 H, C-21 methyl), 3.526 (m, 1 H, H-3α) 5.365 (br d, 1 H, H-6), 6.074 (br d, 1 H, *J* = 11.0 Hz, H-22), 6.466 (d, 1 H, *J* = 15.6 Hz, H-24), 7.083 (d of d, 1 H, *J* = 11.0, 15.6 Hz, H-23), 7.182 (t, 1 H, H-4′), 7.295 (t, 2 H, H-3′ and H-5′), 7.400 (d, 2 H, H-2′ and H-6′); ^{13}C NMR (125 MHz) δ 13.05 (C-18), 18.71 (C-21), 19.44 (C-19), 121.60 (C-6), 125.73 (C-22, C-24), 126.08 (C-2′, C-6′), 126.90 (C-4′), 128.54 (C-3′, C-5′), 130.03 (C-23), 138.18 (C-1′), 139.91 (C-20), 140.84 (C-5). Anal. Calcd for $C_{30}H_{40}O$: C, 86.48; H, 9.68. Found: C, 86.24; H, 9.78.

(20(22)*E*,23*Z*)-24-Phenylchola-5,20(22),23-trien-3β-ol (6b, R^1 = H): MS, *m*/*z* 416 (M^+); ^1H NMR (500 MHz) δ 0.614 (s, 3 H, C-18 methyl), 1.014 (s, 3 H, C-19 methyl), 1.869 (s, 3 H, C-21 methyl), 3.491 (m, 1 H, H-3α), 5.357 (br d, 1 H, H-6), 6.343 (br d, 1 H, *J* = 11.3 Hz, H-22), 6.444 (d, 1 H, *J* = 11.3 Hz, H-24), 6.506 (d of d, 1 H, *J* = 11.3, 11.3 Hz, H-23), 7.211 (t, 1 H, H-4′), 7.32 (t, 2 H, H-3′, and H-5′), 7.34 (d, 2 H, H-2′ and H-6′); ^{13}C NMR (125 MHz) δ 13.17 (C-18), 18.58 (C-21), 19.44 (C-19), 121.60 (C-6), 121.84 (C-22), 126.52 (C-2′, C-6′), 127.36 (C-4′), 128.13 (C-3′, C-5′), 129.13 (C-23, C-24), 138.06 (C-1′), 140.84 (C-5), 141.49 (C-20). Anal. Calcd for $C_{30}H_{40}O$: C, 86.48; H, 9.68. Found: C, 86.09; H, 9.70.

(20(22)*E*,23*E*,25*E*)-26-Phenyl-27-norcholesta-5,20(22),23,25-tetraen-3β-ol (7a, R^1 = H): mp 171.5–173.0 °C; MS, *m*/*z* 442 (M^+); $[\alpha]^{25}_D$ −7° (*c* 0.15, CH_2Cl_2); UV λ_{max}^{abs} 319, *332*, 347 nm (THF), λ_{max}^{em} 390 nm (THF, λ_{ex} 332 nm); ^1H NMR (500 MHz) δ 0.589 (s, 3 H, C-18 methyl), 1.013 (s, 3 H, C-19 methyl), 1.848 (s, 3 H, C-21 methyl), 3.530 (m, 1 H, H-3α), 5.361 (br d, 1 H, H-6), 6.007 (br d, 1 H, *J* = 11.1 Hz, H-22), 6.322 (d of d, 1 H, *J* = 10.1, 14.7 Hz, H-24), 6.507 (d, 1 H, *J* = 15.2 Hz, H-26), 6.641 (d of d, 1 H, *J* = 11.1, 14.7 Hz, J-23), 6.883 (d of d, 1 H, *J* = 10.1, 15.2 Hz, H-25), 7.189 (t, 1 H, H-4′), 7.299 (t, 2 H, H-3′ and H-5′), 7.389 (d, 2 H, H-2′ and H-6′); ^{13}C NMR (125 MHz) δ 13.05 (C-18), 18.67 (C-21), 19.44 (C-19), 121.59 (C-6), 125.77 (C-22), 126.17 (C-2′, C-6′), 127.13 (C-4′), 128.59 (C-3′, C-5′), 129.85 (C-25), 130.28 (C-23), 130.88 (C-24), 130.93 (C-26), 137.74 (C-1′), 140.20 (C-20), 140.84 (C-5). Anal. Calcd for $C_{32}H_{42}O$: C, 86.82; H, 9.56. Found: C, 86.51; H, 9.60.

(20(22)*E*),23*Z*,25*E*)-26-Phenyl-27-norcholesta-5,20(22),23,25-tetraen-3β-ol (7b, R^1 = H): MS, *m*/*z* 442 (M^+); ^1H NMR (500 MHz) δ 0.594 (s, 3 H, C-18 methyl), 0.997 (s, 3 H, C-19 methyl), 1.820 (s, 3 H, C-21 methyl), 3.530 (m, 1 H, H-3α), 5.361 (br d, 1 H, H-6), 6.101 (d of d, 1 H, *J* = 11.2, 11.1 Hz, H-24), 6.343 (d of d, 1 H, *J* = 11.6, 11.2 Hz, H-23), 6.468 (br d, 1 H, *J* = 11.6, H-22), 6.557 (d, 1 H, *J* = 15.1 Hz, H-26), 7.260 (d of d, 1 H, *J* = 11.1, 15.1 Hz, H-25). No C, H analysis due to instability.

(20(22)*E*,23*E*)-24-(2′-Naphthyl)chola-5,20(22),23-trien-3β-ol (8a, R^1 = H): mp 190.0–190.5 °C; MS, *m*/*z* 466 (M^+), 448 ($M^+ - H_2O$); $[\alpha]^{25}_D$ −25° (*c* 0.17, CH_2Cl_2); UV λ_{max}^{abs} (254, *271*, 280), (316, *331*) nm (MeOH), λ_{max}^{em} 407 nm (MeOH, λ_{ex} = 340 nm); ^1H NMR (500 MHz) δ 0.619 (s, 3 H, C-18 methyl), 1.014 (s, 3 H, C-19 methyl), 1.938 (s, 3 H, C-21 methyl), 3.524 (m, 1 H, H-3α), 5.363 (br d, 1 H, H-6), 6.129 (br d, 1 H, *J* = 10.9 Hz, H-22), 6.622 (d, 1 H, *J* = 15.4 Hz, H-24), 7.206 (d of d, 1 H, *J* = 15.4, 10.8 Hz, H-23), 7.394 (t, 1 H, *J* = 7.0 Hz, H-6′), 7.433 (t, 1 H, *J* = 7.2 Hz, H-8′), 7.638 (d, 1 H, *J* = 8.3 Hz, H-3′), 7.713 (s, 1 H, H-1′), 7.76 (m, 3 H, H-4′, H-5′ and H-8′). Anal. Calcd for $C_{34}H_{42}O$: C, 87.50; H, 9.07. Found: C, 87.29; H, 8.88.

(20(22)*E*,23*Z*)-24-(2′-Naphthyl)chola-5,20(22),23-trien-3β-ol (8b, R^1 = H): mp 180.0–181.0 °C; MS, *m*/*z* 466 (M^+), 448 ($M^+ - H_2O$); ^1H NMR (500 MHz) δ 0.649 (s, 3 H, C-18 methyl), 1.018 (s, 3 H, C-19 methyl), 1.899 (s, 3 H, C-21 methyl), 3.524 (m, 1 H, H-3α), 5.363 (br d, 1 H, H-6), 6.496 (d, 1 H, *J* = 11.2 Hz, H-24), 6.533 (br d, 1 H, *J* = 11.4 Hz, H-22), 6.593 (d of d, 1 H, *J* = 11.2, 11.4 Hz, H-23). Anal. Calcd for $C_{34}H_{42}O$: C, 87.50; H, 9.07. Found: C, 87.23; H, 8.99.

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Registry No. **3a**, 145-13-1; **3b**, 58701-45-4; **4a**, 99630-80-5; **4b**, 99602-17-2; **5** (cyclohexylimine), 109530-05-4; **5a**, 99602-18-3; **5b**, 99602-19-4; **6a** (R^1 = H), 109530-01-0; **6b** (R^1 = H), 109530-02-1; **7a** (R^1 = H), 99602-21-8; **7b** (R^1 = H), 99602-20-7; **8a** (R^1 = H), 109530-03-2; **8b** (R^1 = H), 109530-04-3; (*E*)-$(EtO)_2P(O)CH_2CH{=}CHPh$, 52378-69-5; (2*E*,4*E*)-$(EtO)_2P(O)CH_2(CH{=}CH)_2Ph$, 109529-99-9; (2*Z*,4*E*)-$(EtO)_2P(O)CH_2(CH{=}CH)_2Ph$, 109530-00-9; $(EtO)_2P(O)CH_2CH{=}NC_6H_{11}$, 54364-57-7; $(EtO)_2P(O)CH_2C_{10}H_7$-2, 57277-25-5; $Ph_3P^+CH_2Ph\ Br^-$, 1449-46-3; (*E*)-$Ph_3P^+CH_2CH{=}CHPh\ Br^-$, 38633-40-8; (*E*)-$BrCH_2CH{=}CHPh$, 26146-77-0; (*E*,*E*)-$HO_2C(CH{=}CH)_2Ph$, 28010-12-0; (*E*,*E*)-$MeO_2C(CH{=}CH)_2Ph$, 24196-39-2; (*E*,*E*)-$HOCH_2(CH{=}CH)_2Ph$, 58506-33-5; $BrCH_2(C{=}CH)_2Ph$, 109529-98-8.