Formation of Cyclized, including 3,5-Cyclosteroid, Alkenes from β,γ-Unsaturated Grignard Reagents induced by Elimination of a δ-Alkoxy Group

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Grignard reagents and lithium salts prepared from the epimers of 3β-chloro-7ξ-methoxycholest-5-ene, (**2**) and (**3**), were shown to undergo a stereoselective rearrangement/elimination process to give 3α,5α-cyclocholest-6-ene (**6**) as the major product. Similarly the Grignard reagent from a mixture of (*Z*)- and (*E*)-5-chloro-1-methoxy-2-phenylpent-2-ene, (**10**) and (**11**), gave 1-cyclopropyl-1-phenylethene (**9**). Reactions of the corresponding Grignard reagents lacking methoxy groups with water or carbon dioxide gave unrearranged products. It was concluded that cyclizations of this type can be brought about despite an unfavourable equilibrium between ring-opened and ring-closed Grignard intermediates, due to the possibility of conversion of an alkylmagnesium halide into a thermodynamically more stable alkoxymagnesium halide from proposed ring-closed Grignard intermediates.

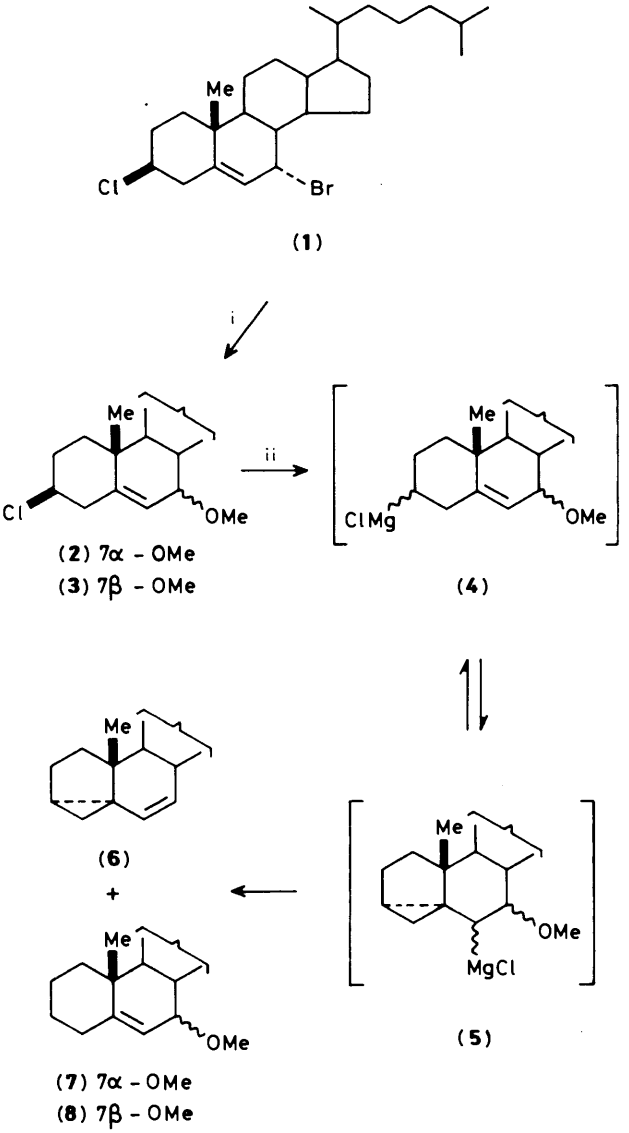
One of the most interesting organometallic rearrangements is intramolecular addition of a carbon–metal bond to a carbon–carbon double bond with formation of a three-membered ring. It has been argued that this reaction, as well as its reverse, *i.e.* β-cleavage with rupture of a strained ring, is an example of a general 'ring-chain tautomerism' between ring-opened and ring-closed organometallics.[1]

Whereas in most cases isolation or detection of the cyclic intermediate (or the products derived therefrom) is difficult, it appeared possible to take advantage of the above phenomenon in order to effect irreversible cyclization in a molecule by the following means: introduction of a δ-alkoxy group would lead to the possibility of 1,2-elimination of an alkoxymagnesium halide (in the Grignard case) from the rearranged, *i.e.* cyclized, intermediate, thus effectively trapping the three-membered-ring structure. The thermodynamically favourable conversion of an alkylmagnesium halide into an alkoxymagnesium halide in this process should serve to overcome the fact that an equilibrium between ring-opened and ring-closed Grignard intermediates would favour the former, due to ring-strain and entropic considerations. The only example of which we are aware of the usage of such an elimination to effect a rearrangement was in the ring cleavage of an alkoxybicyclo[3.2.0]heptanyl Grignard reagent.[2]

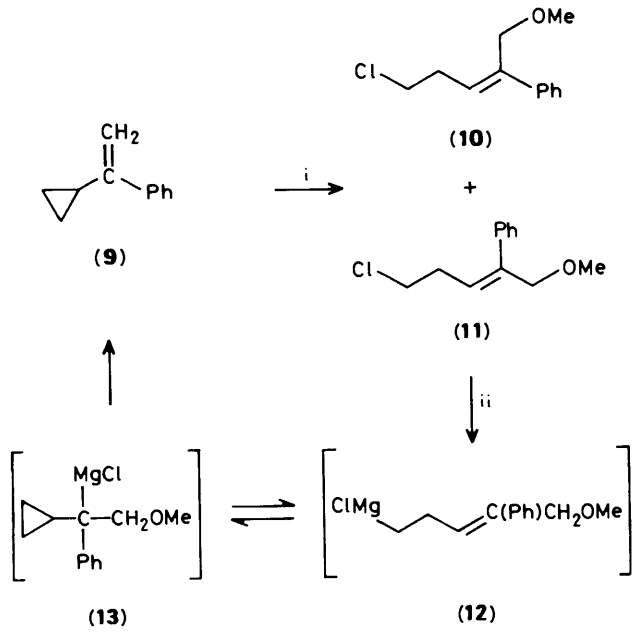
Whereas rearrangements of cholesteryl derivatives involving carbocation intermediates and formation of 3,5-cyclosteroid products are well known,[3] the reactions of Grignard reagents or alkali metal salts from cholesteryl halides afford only unrearranged products.[4] We decided to try to induce a 3,5-cyclosteroid rearrangement of a cholesteryl-type Grignard reagent by placement of a methoxy group at the δ- or 7-position. The success of this reaction (Scheme 1) encouraged us to apply a similar process to the case of the Grignard reagents from the open-chain methoxy halides (**10**) and (**11**) (Scheme 2). This system was chosen as it was expected, and found, that reactions of the Grignard reagents from the chlorides corresponding to (**10**) and (**11**), which lacked methoxy groups, would yield only unrearranged products.

Results and Discussion

The dihalide (**1**) was prepared from cholesterol as described by Bide *et al.*[5] Reaction of compound (**1**) with alkaline methanol yielded the epimers (**2**) and (**3**). These were separated and purified by open column chromatography or fractional crystal-



Scheme 1. *Reagents:* i, MeOH–KOH; ii, Mg–EtBr–Et_2O



Scheme 2. *Reagents and conditions:* i, MeOCl–u.v.–N_2–0 °C; then $ZnCl_2$; ii, Mg–EtBr–THF

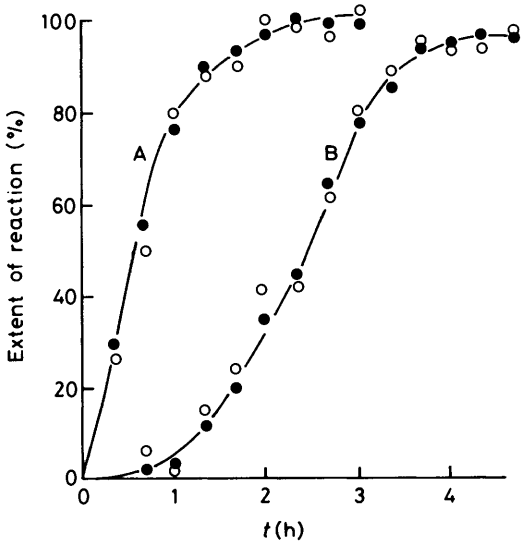


Figure. A, Rate of formation of Grignard reagent and B, elimination of C(7)–OMe from Grignard reagents of 3β-chloro-7ξ-methoxycholest-5-ene [(**2**), ●; (**3**), ○]

lization.* When treated with magnesium in refluxing diethyl ether, compound (**2**) or compound (**3**), or mixtures of them, afforded the 3,5-cycloalkene (**6**) in high yield, as well as small quantities of the by-products (**7**) and (**8**), respectively † (Scheme 1). The progress of the reactions was followed by n.m.r. analyses of samples withdrawn at various times. These revealed that formation of the Grignard reagents was complete after *ca.* 2 h. At that time only *ca.* 30% elimination of the C(7)-methoxy group had taken place. Completion of the elimination reaction required another 2 h. No significant difference between the rates of elimination from the Grignard reagents of halides (**2**) and (**3**) was detected (Figure).

Reaction of a mixture of halides (**2**) and (**3**) with lithium in diethyl ether and reflux of the resulting salt for 5 h also afforded compound (**6**) in good yield. Addition of anhydrous cobalt(II) chloride to a mixture of compounds (**2**) and (**3**) prior to formation of the Grignard reagents surprisingly did not alter the outcome of the reaction in any way. The presence of cobalt(II) chloride would be expected to promote free-radical-type processes during formation or reaction of the Grignard reagents.[6]

The alkene (**9**) was prepared according to the method of Sarel *et al.*[7] Addition of methyl hypochlorite under free-radical conditions[8] to the double bond of compound (**9**), followed by isomerization of the resulting adduct, gave the isomeric chloro ethers (**10**) and (**11**). Separation and purification of these was achieved by h.p.l.c.‡ Treatment of isomers (**10**) and (**11**) with magnesium in refluxing tetrahydrofuran (THF) gave the cyclic alkene (**9**) as the only detectable product (Scheme 2). When the Grignard reagent from 5-chloro-2-phenylpent-2-ene, *i.e.* the halide corresponding to (**10**) and (**11**) which lacks a methoxy group, was treated similarly and then hydrolysed with sulphuric acid, the product was 2-phenylpent-2-ene and no rearranged compounds were detected by n.m.r. spectroscopy.

As far as the mechanism of the rearrangement/elimination reaction is concerned, at least three possibilities may be considered. A concerted mechanism, in which the cyclization and elimination processes were synchronous, appears unlikely, since in this case the Grignard reagents from (**2**) and (**3**) would be expected to eliminate at different rates. On the other hand a stepwise mechanism, with equilibration between ring-opened [(**4**), (**12**)] and ring-closed [(**5**), (**13**)] Grignard reagents, followed by elimination, is consistent with the observations made. Here the cyclization step is probably rate-determining and the elimination step fast, *i.e.* the rate of formation of the cyclopropane (**6**) is independent of the C(7)-stereochemistry in intermediates (**4**) and (**5**), as observed. A further possibility is rearrangement/elimination during Grignard formation. It is known that free-radical intermediates may be involved in the formation of Grignard reagents.[9] If such an intermediate had sufficient lifetime, it might conceivably rearrange. This mechanism can be ruled out as the major pathway, since Grignard formation and elimination were separate events. Furthermore, the presence of cobalt(II) chloride, a reagent that promotes free-radical reactions, in the reaction mixture did not alter the outcome of the reaction. It should be pointed out that the foregoing arguments assume an identical mechanism for the two systems (Schemes 1 and 2) studied. In conclusion it would appear that the rearrangement/elimination reactions are best represented by the intermediates depicted in Schemes 1 and 2.

The finding that in Scheme 1 the rearrangement is stereoselective (in that none of the alternative 3β-5β-cyclocholest-6-ene was formed) is of interest. It is difficult to rationalize the reasons for this stereoselectivity, especially since the orientation of the initially formed C(3)–Mg bond is unknown. In any case formation of the new bond between C(3) and C(5) on the β-face

* The stereochemistry at C(7) in the epimers was assigned on the basis of their n.m.r. spectra and specific rotations (J. A. Mills, *J. Chem. Soc.*, 1952, 4976), in a manner analogous to that for other C(7)-alkoxy steroids (see, *e.g.*, T. Harano and K. Harano, *Kawasaki Med. J.*, 1976, **2**, 175).

† Carbonation (instead of hydrolysis) of Grignard mixtures which had reacted completely did not result in the isolation of the carboxylic acid derived from (**4**). This would have been the case if any Grignard reagent which had survived elimination was still present.

‡ The allylic and homoallylic coupling constants in the ^1H n.m.r. spectra were used to assign the geometric isomers. Generally these constants are larger when the protons in question are in a *cisoid* and *transoid* relationship, respectively. (L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' 2nd ed., Pergamon Press, Oxford, 1969, pp. 225, 316, 324). Specific examples for α-methylstyrenes are given by Davis and Roberts (D. R. Davis and J. D. Roberts, *J. Am. Chem. Soc.*, 1962, **84**, 2252).

of the molecule, whatever the transition states between species (**4**) and (**6**) may be, is probably energetically unfavourable because of severe steric congestion on the β-face in such states, mainly due to the axial C(19)-methyl group. Whereas in Scheme 1 the rearrangement goes from a secondary (**4**) to a secondary Grignard reagent (**5**), in Scheme 2 it goes from a relatively stable primary (**12**) to a presumably much less stable tertiary Grignard reagent (**13**). Furthermore the phenyl group probably destabilizes the cyclized intermediate (**13**), as has been shown in related systems.[10]

We conclude that rearrangements of the type described here can be induced, even in the face of unfavourable energetic factors in the cyclization step, simply by the presence of a δ-alkoxy group. The results of this study have led us to propose that the corresponding intermolecular reactions, additions of organometallic reagents to 3-alkoxyalkenes forming alkenes alkylated or arylated in an allylic position, and to alkynes with the production of allenes, may be feasible. These hypotheses are currently being tested.

Experimental

The starting materials cholesterol and cyclopropyl phenyl ketone were obtained commercially. Anhydrous diethyl ether was obtained from the technical solvent by drying with calcium chloride, then sodium wire and, finally distillation from lithium aluminium hydride under a stream of nitrogen just before use. Anhydrous THF was prepared by passing the technical solvent through a column of alumina, followed by refluxing over calcium hydride, and finally fractional distillation. Magnesium used was of Grignard grade (Ajax Chemicals, Sydney, N.S.W.). I.r. spectra were recorded on a Perkin-Elmer 197 spectrophotometer. ^{1}H N.m.r. spectra were recorded on a Varian XL200 instrument. The samples were made up in deuteriochloroform (containing $SiMe_4$ as the internal reference standard). ^{13}C N.m.r. spectra were recorded with full proton decoupling. A Kratos MS25 (70 eV electron impact) mass spectrometer was used. Microanalyses were carried out by AMDEL, Fishermen's Bend, Victoria. High-performance liquid chromatography (h.p.l.c.) was conducted using Waters Associates instrumentation with gradient elution and u.v. detector model 440 set at 254 nm (μBondapak C_{18} column, 78 mm × 30 cm). Specific rotations were measured using a Perkin-Elmer 141 polarimeter. The samples were made up as 1% w/v solutions in chloroform. M.p.s were measured on a Gallenkamp apparatus and are not corrected.

3β-Chloro-7ξ-methoxycholest-5-ene (**2**) *and* (**3**).—These compounds were prepared from cholesterol *via* 3β-chlorocholest-5-ene[11] and 7α-bromo-3β-chlorocholest-5-ene (**1**).[5] The latter (5.0 g, 10.3 mmol) as a solution in chloroform (60 cm^3) was added to a solution of potassium hydroxide (0.85 g, 15 mmol) in anhydrous methanol (60 cm^3). After 24 h the mixture was decanted from the precipitated potassium bromide, poured into water, and the organic layer was separated. This was combined with a chloroform extract (50 cm^3) of the aqueous layer, washed successively with 2M-sodium hydroxide and water, dried ($MgSO_4$), and evaporated. The residue was chromatographed on a column of alumina (neutral; activity II; 150 g). Six fractions (30 cm^3 each) were eluted with toluene–light petroleum (b.p. 70—90 °C) in ratios ranging from 1:0 to 0:1. Fractions 1—3 contained compound (**2**) and 5 and 6 contained its isomer (**3**). After evaporation and recrystallization of the residues from acetone, the following were obtained: 3β-*chloro-7α-methoxycholest-5-ene* (**2**) (2.06 g, 46.0%), granular prisms, m.p. 128—129 °C; $[\alpha]_D^{20}$ −111.3° (*c* 1.0 in $CHCl_3$); δ_H *inter alia* 0.67 (3 H, s, 18-H_3), 1.02 (3 H, s, 19-H_3), 1.48 (1 H, m, 8-H), 2.62 (2 H, m, 4-H_2), 3.29 (1 H, m, *J* 2.5 and 5.1 Hz, 7-H), 3.37 (3 H, s, OMe), 3.87 (1 H, m, 3-H), and 5.78 (1 H, d, *J* 5.1 Hz, 6-H); δ_C *inter alia* 19.0 (C-19), 24.2 (C-15), 33.6 (C-2), 37.6 (C-8), 42.2 (C-7), 43.6 (C-6), 49.2 (C-14), 57.2 (OMe), 59.6 (C-3), 122.4 (C-6), and 146.8 (C-5); and 3β-*chloro-7β-methoxycholest-5-ene* (**3**) (0.83 g, 18.5%), powdery white crystals, m.p. 104—105 °C; $[\alpha]_D^{20}$ +38.5° (*c* 1.0 in $CHCl_3$); δ_H *inter alia* 0.69 (3 H, s, 18-H_3), 1.07 (3 H, s, 19-H_3), 1.49 (1 H, m, 8-H), 2.60 (2 H, m, 4-H_2), 3.29 (3 H, s, OMe), 3.37 (1 H, d, *J* 9.3 Hz, 7-H), 3.79 (1 H, m, 3-H), and 5.51 (1 H, s, 6-H); δ_C *inter alia* 19.0 (C-19), 26.0 (C-15), 33.6 (C-2), 36.4 (C-8), 43.3 (C-4), 48.8 (C-14), 55.2 (OMe), 56.8 (C-7), 60.0 (C-3), 123.0 (C-6), and 144.6 (C-5). For both isomers (**2**) and (**3**) (Found: C, 77.0; H, 11.05; Cl, 18.4. $C_{28}H_{47}ClO$ requires C, 77.29; H, 10.89; Cl, 18.15%); $\nu_{max.}$(KBr) 2 925, 2 850, 2 800, 1 655, 1 460, 1 375, 1 320, 1 190, 1 110, 1 080, 995, 860, 820, and 755 cm^{-1}; *m/z* 434 (M^+), 366 (100%), 253, and 247. Compounds (**2**) and (**3**) were also separated and purified by fractional crystallization from acetone.

Grignard Reagents of Chlorides (**2**) *and* (**3**).—The reactions were conducted under strictly anhydrous conditions with slight positive pressure of dry, oxygen-free nitrogen and with both the epimers separately as well as with the epimeric mixture [3:1 (**2**):(**3**)]. Typically, a solution of the epimieric mixture (4.0 g, 9.2 mmol) in anhydrous diethyl ether (50 cm^3) was added to a mixture of magnesium turnings (0.5 g, 20 mmol) and bromoethane (0.40 cm^3, 10 mmol) in anhydrous diethyl ether (10 cm^3) during 1 h. The mixture was then refluxed for 4 h, cooled, hydrolysed with sulphuric acid (2M; 100 cm^3), and the layers were separated. The organic layer was combined with the diethyl ether extracts (2 × 25 cm^3) of the aqueous layer. This was washed successively with 2M-sodium hydroxide and water, dried ($MgSO_4$), and evaporated. Upon chromatography of the residue on a column of alumina (neutral; activity II; 150 g), the following were eluted: from the first 10 fractions (40 cm^3 each) in light petroleum (b.p. 40—60 °C) was obtained 3α,5α-cyclocholest-6-ene (**6**) (2.72 g, 80.0%), thick needles, m.p. 72 °C (from acetone) (lit.,[12] 73 °C); $[\alpha]_D^{20}$ −51.5° (*c* 1.0 in $CHCl_3$) (lit.,[12] −47.2°); $\nu_{max.}$(KBr) 3 060, 3 025, 2 950, 2 860, 1 640, 1 465, 1 380, 1 025, 940, and 920 cm^{-1}; δ_H *inter alia* 0.44 (1 H, dd, *J* 8.4 and 4.8 Hz, 4α-H), 0.72 (3 H, s, 18-H_3), 0.81 (1 H, dd, *J* 5.6 and 4.8 Hz, 4β-H), 0.90 (3 H, s, 19-H_3), 1.19 (1 H, m, 3-H), 5.20 (1 H, dd, *J* 10 and 3 Hz, 7-H), and 5.54 (1 H, d, *J* 10 Hz, 6-H); δ_C *inter alia* 14.6 (C-4), 17.8 (C-19), 25.2 (C-1), 25.7 (C-3), 31.5 (C-2), 36.5 (C-8), 36.6 (C-10), 43.3 (C-5), 46.1 (C-9), 127.5 (C-7), and 131.6 (C-6); *m/z* 368 (M^+), 253, and 247 (mixed-m.p. determination with an authentic sample* gave no depression; i.r., n.m.r., and mass spectra were also identical).

Fractions 11—14, eluted with 9:1 ⟶ 5:5 light petroleum–benzene, gave 7α-*methoxycholest-5-ene* (**7**) (175 mg, 4.75%), fine needles, m.p. 123—124 °C (from acetone–methanol) (Found: C, 83.7; H, 11.8. $C_{28}H_{48}O$ requires C, 83.93; H, 12.08%) $[\alpha]_D^{20}$ −100.2° (*c* 1.0 in $CHCl_3$); $\nu_{max.}$(KBr) 3 020, 2 830, 1 670, 1 100, and 1 090 cm^{-1}; δ_H *inter alia* 0.99 (3 H, s, 19-H_3), 3.29 (3 H, s, OMe), 3.55 (1 H, m, 7-H), and 5.75 (1 H, d, *J* 5.3 Hz, 6-H); *m/z* 400 (M^+), 368 (100%), 353, 253, and 247.

Fractions 15—18 were eluted with benzene and gave 7β-methoxycholest-5-ene (**8**) 64 mg, 1.74%), prisms, m.p. 92—94 °C (lit.,[13] 91 °C); $[\alpha]_D^{20}$ +14.2° (*c* 1.0 in $CHCl_3$) (lit.,[13] +14.38°); δ_H *inter alia* 1.02 (3 H, s, 19-H_3), 3.21 (3 H, s, OMe), 3.44 (1 H, d, *J* 8.5 Hz, 7-H), and 5.48 (1 H, s, 6-H); *m/z* 400 (M^+), 368 (100%), 353, 253, and 247.

In an experiment where previously dried cobalt(II) chloride (0.1 g g^{-1} steroid) was added to the magnesium before the

* Prepared from cholesterol by a method known to give the 3α,5α-cyclo-structure (E. S. Wallis, E. Fernholz, and T. Gephart, *J. Am. Chem. Soc.*, 1937, **59**, 137; A. Romeo and R. Villotti, *Ann. Chim. (Rome)*, 1957, **42**, 684).

addition of a 3:1 mixture of isomers (**2**) and (**3**), the yields of compounds (**6**), (**7**), and (**8**) after reaction and chromatography as above were similar, *viz.* 77.3, 4.2, and 1.5%. For semi-quantitative kinetic studies the reactions were conducted as described above, with the exception that the steroids were added to the reaction mixture all at once. Aliquots were then withdrawn at intervals of 20 min during a period of 4 h, hydrolysed immediately, worked up as above, and analysed by ^{1}H n.m.r. spectroscopy. The peaks due to the C(4) protons in (**2**) and (**3**), *i.e.* multiplets centred at δ 2.62 and 2.60 (the reaction products display no resonances with the same chemical shifts), and to the methoxy protons, singlets at δ 3.37 and 3.29, respectively, as well as the entire spectra, were integrated. Comparison of these integrals allowed analysis of the extent of Grignard reagent formation and elimination of the methoxy groups, respectively (see Figure).

Lithium Salts of Compounds (**2**) *and* (**3**).—Small slices of lithium (*ca.* 50 mg), previously cut from fresh lithium wire under mineral oil, were added to a 3:1 mixture of isomers (**2**) and (**3**) (2.0 g, 4.6 mmol) in anhydrous diethyl ether (120 cm^3). This mixture was refluxed for 5 h under dry nitrogen, then cooled, and hydrolysed carefully with water. The resulting layers were separated and the aqueous layer was extracted with diethyl ether. The combined ethereal fractions were washed successively with 2M-hydrochloric acid, 2M-sodium hydroxide, and water, dried ($MgSO_4$), and evaporated. Column chromatography (neutral alumina; activity II; 100 g) of the residue afforded the 3,5-cyclosteroid (**6**) (0.68 g, 39.8%) by elution with light petroleum (b.p. 40—60 °C; 70 cm^3). The physical constants and spectra were identical with those of an authentic sample. Unchanged starting material was eluted with benzene (200 cm^3).

(Z/E)-5-*Chloro*-1-*methoxy*-2-*phenylpent*-2-*ene* (**10**) *and* (**11**).—The reaction of cyclopropyl phenyl ketone with methylmagnesium iodide gave 1-cyclopropyl-1-phenylethanol,[7] which was dehydrated to 1-cyclopropyl-1-phenylethene (**9**).[7] Methyl hypochlorite (10 cm^3 of a freshly prepared 0.51M solution) in dichloromethane[8,14] was added dropwise to this alkene (0.6 g, 42 mmol; dissolved in 10 cm^3 CH_2Cl_2) at 0 °C and with u.v. irradiation (100 W GE mercury lamp) under dry, oxygen-free nitrogen. Evaporation of the solvent gave a residue containing 1-chloro-1-cyclopropyl-2-methoxy-1-phenylethane [δ_H (60 MHz) 0.4—0.7 (4 H, m, cyclopropyl CH_2s), 1.3—1.7 (1 H, m, cyclopropyl 1-H), 3.2 (3 H, s, OMe), 3.8 (2 H, s, CH_2), and 7.1—7.7 (5 H, m, Ph)].

This residue was redissolved in dry diethyl ether, and isomerization[8] involving ring-opening occurred when the solution was stirred at room temperature with anhydrous zinc chloride (0.5 g) for 1 h. Water was then added and the organic layer was separated, combined with the diethyl ether extracts (2 × 25 cm^3) of the aqueous layer, washed twice with water, dried ($MgSO_4$), and evaporated. The yield of the mixture of allyl ethers (**10**) and (**11**) so obtained was 0.75 g (86%, based on the alkene). Integration of the ^{1}H n.m.r. spectrum showed the isomers to be present in the ratio 3.5:1 [(**10**):(**11**)]. The crude product was purified by h.p.l.c. by elution with acetonitrile–water (6:4 ⟶ 8:2, linear gradient) during 20 min. The eluants corresponding to (Z)-5-*chloro*-1-*methoxy*-2-*phenylpent*-2-*ene* (**10**), and (E)-5-*chloro*-1-*methoxy*-2-*phenylpent*-2-*ene* (**11**) (analytical scale), or that corresponding to the isomeric mixture (preparative scale), were collected and the solvents were evaporated off. Water was removed azeotropically by adding dry acetonitrile at intervals. The title compounds were obtained as oils: (**10**), δ_H 2.75 (2 H, m, *J* 7.2 Hz, 4-H_2), 3.34 (3 H, s, OMe), 3.64 (2 H, t, *J* 7.2 Hz, 5-H_2), 4.35 (2 H, s, 1-H_2), 5.99 (1 H, t, *J* 7.2 Hz, 3-H), and 7.20—7.45 (5 H, m, Ph); δ_C 31.7 (C-5), 40.9 (C-4), 43.4 (C-1), 48.4 (OMe), 125.9 (C-3), 128.3 (C-2), 127.6, 128.0, 128.4, 129.0, 129.2, and 129.6 (aromatic); (**11**), δ_H 2.50 (2 H, m, *J* 1.15 and 7.2 Hz, 4-H_2), 3.34 (3 H, s, OMe), 3.50 (2 H, t, *J* 7.2 Hz, 5-H_2), 4.13 (2 H, m, *J* 1.15 Hz, 1-H_2), 5.77 (1 H, tt, *J* 1.15 and 7.2 Hz, 3-H), and 7.18—7.56 (5 H, m, Ph). For both (**10**) and (**11**) (Found: C, 68.2; H, 7.2; Cl, 16.6. $C_{12}H_{15}ClO$ requires C, 68.40; H, 7.17; Cl, 16.83%); $\nu_{max.}$(film) 3 060, 2 980, 2 850, 2 750, 1 940, 1 875, 1 795, 1 615, 1 590, 1 565, 1 435, 1 375, 1 250, 1 010, 880, 805, 760, and 690 cm^{-1}; *m/z* 210 (M^+), 178, 144 (100%), 129, 115, 103, 91, 77, and 51.

Grignard Reagents of Chlorides (**10**) *and* (**11**).—To magnesium turnings (0.13 g, 5.3 mmol) and bromoethane (1.0 cm^3, 2.4 mmol) in anhydrous THF (10 cm^3) was added the h.p.l.c.-purified mixture of chlorides (**10**) and (**11**) (0.5 g, 2.4 mmol) in anhydrous THF (10 cm^3). The mixture was refluxed for 5 h, cooled, hydrolysed by the addition of sulphuric acid (2M; 50 cm^3), and poured into tetrachloromethane. The layers were separated and the combined organic layer and the extracts (2 × 25 cm^3 CCl_4) of the aqueous layer were washed successively with 2M-sodium hydrogen carbonate and water, dried ($MgSO_4$), and evaporated. H.p.l.c. analysis of the residue showed that conversion of chlorides (**10**) and (**11**) into the cyclopropane (**9**) was complete and that no significant amounts of by-products had been formed. The residue was distilled from a Claisen–Vigreux flask to give pure 1-cyclopropyl-1-phenylethene (**9**) (214 mg, 62.5%), b.p. 96—98 °C/ 5 mmHg (lit.,[7] 92—94 °C/3 mmHg); $\nu_{max.}$ 3 100, 3 075, 3 025, 1 630, 1 000, and 710 cm^{-1}; δ_H 0.60 and 0.84 (4 H, m, cyclopropyl CH_2s), 1.65 (1 H, m, *J* 8.0 and 1.5 Hz, cyclopropyl 1-H), 4.94 (1 H, dd, *J* 1.0 and 1.5 Hz, C=C*H*H *cis* to cyclopropyl), 5.25 (1 H, d, *J* 1.0 Hz, C=CH*H cis* to phenyl), and 7.28—7.43 (5 H, m, Ph); δ_C 7.0 (cyclopropyl CH_2s), 16.0 (cyclopropyl C-1), 110 (C=*C*H_2), 127.4, 128.8, 129.6, 143.0, and 148.8 (aromatic and *C*=CH_2); *m/z* 144 (M^+), 129 (100%), 115, 103, and 91. The spectra were identical with those of authentic (**9**) prepared as above.

Grignard Reagent of 5-*Chloro*-2-*phenylpent*-2-*ene*.—Magnesium turnings (0.15 g, 6.1 mmol) were added to a solution of 5-chloro-2-phenylpent-2-ene[15] (1.0 g, 5.5 mmol) in anhydrous THF (25 cm^3). The mixture was refluxed under dry nitrogen for 5 h, then cooled, hydrolysed with sulphuric acid (2M; 50 cm^3), and poured into tetrachloromethane (100 cm^3). The separated aqueous layer was extracted with the same solvent (2 × 25 cm^3) and the combined organic fractions were washed with water, dried ($MgSO_4$), and evaporated. The residue was analysed by ^{1}H n.m.r. spectroscopy: no traces of products containing a cyclopropyl group were detected, *i.e.* no resonances with $\delta < 1.0$. The product of the reaction was the hydrolysate of the open-chain Grignard reagent, *i.e.* (*E*/*Z*)-2-phenylpent-2-ene. The n.m.r. spectrum observed for this mixture of isomers was consistent with the spectrum given for it by Zioudrou *et al.*[16]

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