An Approach to the Construction of Aromatic Steroids Using Electrocyclic Ring Closure

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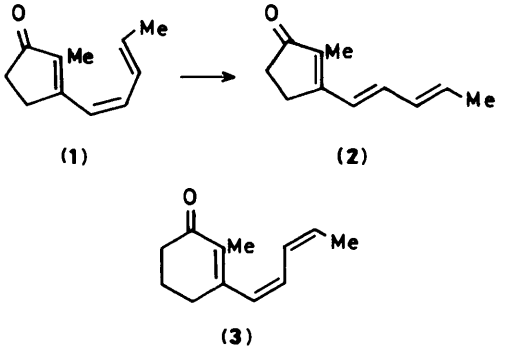
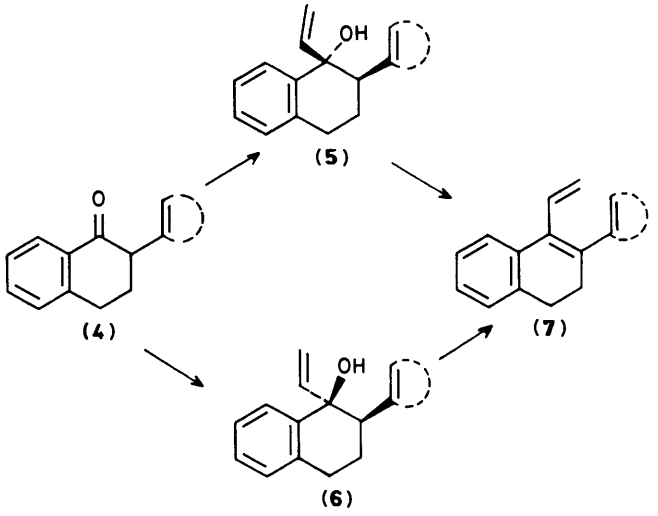
Methods for the construction of conjugated trienes in which the central double bond is part of a ring system have been investigated. 2-Chloro-3,4-dihydronaphthalen-1(2*H*)-one is treated with vinyl-lithium reagents to give the alcohols (**10**) which, when heated with ethylmagnesium bromide, rearrange with loss of chloride anions to the α-vinyl ketones (**4**). The 2-substituted naphthalenone (**4f**), prepared in this way, is converted into the conjugated triene (**7c**) by reaction with vinylmagnesium bromide followed by acid-catalysed dehydration. This is cyclised thermally or by irradiation to the cyclohexadienes (**13**) and (**14**). By an analogous series of reactions, 5,6,11,12-tetrahydrochrysene (**16**) is prepared from 2-phenyltetralone.

Investigations of the electrocyclic ring closure of conjugated trienes, and particularly the observations of the different stereochemical outcome of thermal and photochemical cyclisation, provided some of the most important experimental work on which the principles of conservation of orbital symmetry were based. Although the formulation of the Woodward–Hoffmann rules sparked off a great deal of mechanistic investigation, the thermal reaction has found relatively little use as a synthetic method.[1] The photocyclisation of stilbenes and related compounds has proved to be the major synthetic application of the electrocyclic reaction.[2] The thermal cyclisation of highly functionalised trienes is often in competition with other reactions which limit its usefulness as a synthetic procedure: for example, the trienone (**1**) failed to cyclise because of preferential conversion into the (*E*)-isomer (**2**)[3] and the trienone (**3**) underwent a [1,7] hydrogen shift in preference to disrotatory ring closure.[4]



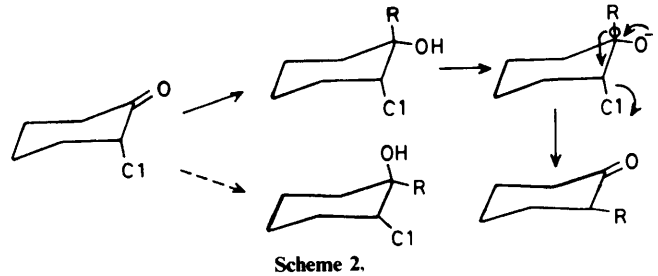
Problems associated with (*Z*)- to (*E*)-isomerisation of the central double bond of a triene can be avoided if this bond is part of a ring system. There are no good general methods for the synthesis of trienes of this type available at present, however. We have investigated several new approaches to such compounds and in this paper report on one route in which the triene is generated from a cyclic ketone. We chose to use 3,4-dihydronaphthalen-1(2*H*)-one (α-tetralone) as the starting material since successful cyclisations of trienes derived from tetralones could ultimately provide routes to aromatic steroids.

The route is outlined in Scheme 1. 2-Vinyltetralones (**4**) were converted into the diastereoisomeric alcohols (**5**) and (**6**) by reaction with vinylmagnesium bromide, and the alcohols were then dehydrated to the trienes (**7**). There are several methods available for the preparation of α-vinyl ketones from the



Scheme 1.

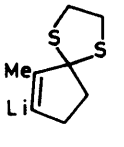
corresponding ketones.[5,6] The method which we used to prepare the 2-vinyltetralones (**4**) is based on one previously described for the preparation of 2-vinylcyclohexanones from 2-chlorocyclohexanone.[6] The first step is the nucleophilic addition of a vinylmagnesium halide or a vinyl-lithium reagent to the carbonyl group of the chloro-ketone. This results in predominant or exclusive formation of the *cis* chlorohydrin because nucleophilic attack takes place mainly on the face opposite to that bearing the (axial) chloro substituent (Scheme 2). Base-induced 1,2-migration of the vinyl group, with elimination of chloride anion, takes place exclusively in the *cis* chlorohydrin, as shown in Scheme 2.



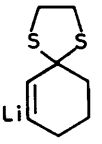
Scheme 2.

A reaction sequence of this type has previously been used to prepare 2-phenyltetralone from 2-chlorotetralone.[7] We set out to investigate extensions of the reaction, in particular by using

cyclic vinyl anions with protected carbonyl functionality which could ultimately be used as components in the synthesis of aromatic steroids. The known[8] vinyl-lithium species (**8**) and (**9**) were prepared essentially by the literature methods. We also investigated the reaction of 2-chlorotetralone with vinylmagnesium bromide, phenylmagnesium bromide, 2-furyllithium, and 2-thienyl-lithium.

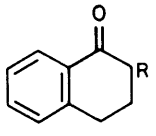


(**8**)

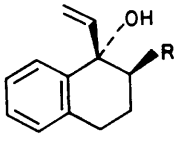


(**9**)

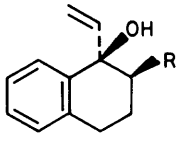
Addition of these organometallic reagents to the carbonyl group of 2-chlorotetralone resulted in almost exclusive formation of the *cis* chlorohydrins (**10**): only with vinylmagnesium bromide was the *trans* isomer detected as a minor component. The yields of the isolated chlorohydrins were only moderate, probably because of competing deprotonation of the chloro ketone by the organometallic reagents. When heated with ethylmagnesium bromide in benzene the chlorohydrins gave the corresponding α-vinyl ketones (**4**). In most cases the products were isolated by chromatography in excellent yield, but the vinyl ketones (**4a**) and (**4e**) were not obtained pure. From the n.m.r. spectra of the crude products it appeared that they had partly isomerised to the conjugated ketones (**11**) and (**12**), respectively.



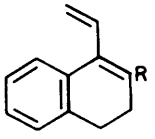
(**4**)



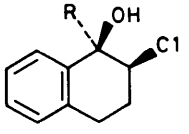
(**5**)



(**6**)



(**7**)



(**10**)

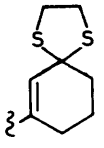
(**4a**), (**10a**) R = $CH{=}CH_2$

(**4b**), (**5a**), (**6a**), (**7a**), (**10b**) R = Ph

(**4c**), (**10c**), R = 2-furyl

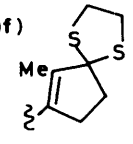
(**4d**), (**5b**), (**6b**), (**7b**), (**10d**), R = 2-thienyl

(**4e**), (**10e**) R =

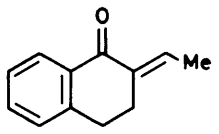


(**4f**), (**6c**), (**7c**), (**10f**)

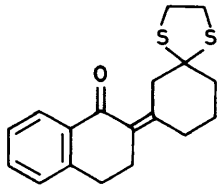
R =



The reactions of the ketones (**4b**), (**4d**), and (**4f**) with vinylmagnesium bromide were then investigated. 2-Phenyltetralone (**4b**) gave a mixture of the diastereoisomeric alcohols (**5a**) and (**6a**), which were separated by column chromatography,



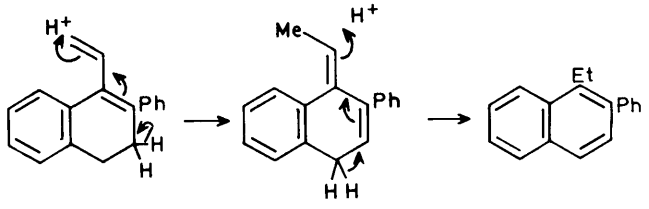
(**11**)



(**12**)

the isomer (**6a**) being isolated first as the major component. This is consistent with predominant attack by the nucleophile on the less hindered face of the ketone. The isomers were distinguishable from their n.m.r. spectra, the signal for 2-H in the isomer (**5a**) being downfield of that in (**6a**) because of its proximity to the hydroxy group. The combined yield of the two isomers was moderate (65%), possibly because of competing deprotonation of the ketone by vinylmagnesium bromide. 2-Thienyltetralone similarly gave alcohols (**5b**) (25%) and (**6b**) (31%). The vinyl ketone (**4f**) gave the alcohol (**6c**) as the only isolated product in 40% yield: in this case the greater size of the 2-substituent results in greater selectivity of attack on the carbonyl group.

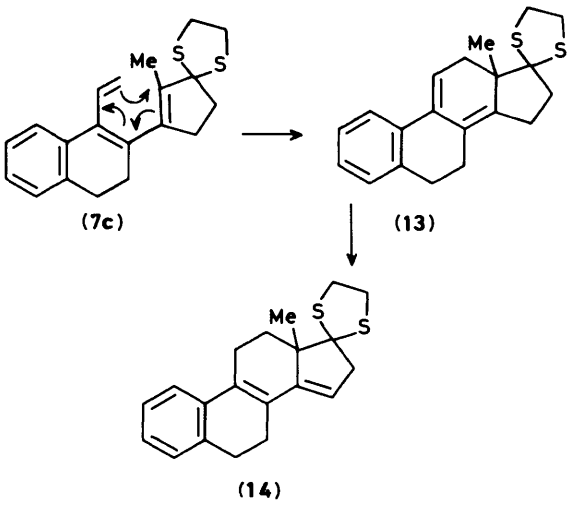
Dehydration of the tertiary allylic alcohols to conjugated trienes (**7**) was easily achieved by heating the alcohols in the presence of toluene-*p*-sulphonic acid (PTSA) for a few minutes. As expected, the diastereoisomeric alcohols (**5a**) and (**6a**) gave the same product (**7a**) under these conditions and in subsequent experiments the mixture was not separated before dehydration. By this means the compounds (**7a**—**c**) were isolated in moderate yield. Excessive heating with PTSA has to be avoided, otherwise the dehydration products can aromatise by proton transfer. For example, the major product of heating the alcohols (**5a**) and (**6a**) with PTSA for 3.5 h is 1-ethyl-2-phenylnaphthalene, which is probably derived from the dihydronaphthalene (**7a**) by prototropic rearrangement (Scheme 3).



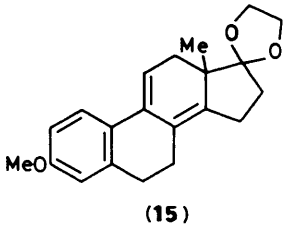
Scheme 3.

The triene (**7c**) was cyclised by heating in xylene at 140 °C for 34 h to give, as major product, the cyclohexadiene (**13**), which was isolated (39%) by preparative layer chromatography (p.l.c.). Irradiation of the triene at 300 nm was less efficient and gave the same product (10%) accompanied by products of decomposition. An attempt to accelerate the cyclisation by carrying out the reaction in bromobenzene at 156 °C gave the conjugated isomer (**14**) (33%) (Scheme 4). An estrapentaene (**15**) with 1,3,5(10),8(14),9(11)-unsaturation has recently been prepared by Sternberg and Vollhardt, who used cobalt-mediated intramolecular [2 + 2 + 2] cycloaddition to create the steroid skeleton.[9] The n.m.r. spectrum of compound (**13**) supports the proposed structure and also shows close similarities to that reported for the analogous compound (**15**). For example, the signal for the vinylic 11-H appears as a double doublet (*J* 6.6 and 2.9 Hz) at δ 6.15 for compound (**13**) and as a double doublet (*J* 6.8 and 3.0 Hz) at δ 6.11 for compound (**15**). In the n.m.r. spectrum of the conjugated isomer (**14**) the vinylic hydrogen at C-15 appears as a weakly split multiplet at δ 5.78, again in accord with literature analogies.[9]

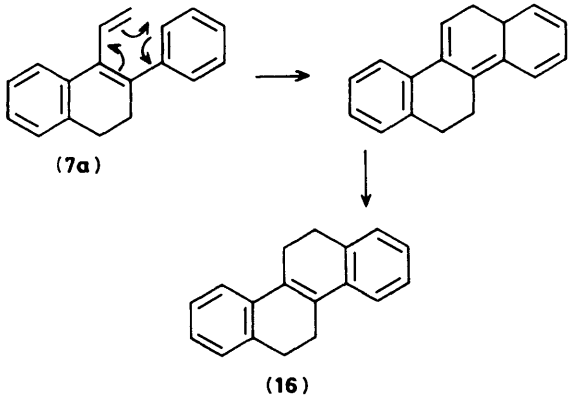
1,2-Dihydro-3-phenyl-4-vinylnaphthalene (**7a**) required a higher temperature to effect cyclisation: it was heated in degassed 1,2-dichlorobenzene at 180 °C and some starting material remained after 4 days. The components of the reaction



Scheme 4.



mixture were separated by p.l.c. and the major product was identified as the known[10] 5,6,11,12-tetrahydrochrysene (**16**) (Scheme 5). The same product was obtained, and in better yield, when the vinylnaphthalene (**7a**) was subjected to flash vacuum pyrolysis at 730 °C and 0.1 mmHg pressure. The same pyrolysis technique failed to give recognisable products from the corresponding 2-thienylnaphthalene (**7b**): a mixture of products was obtained, the components of which could not be separated by p.l.c.



Scheme 5.

We have thus established that the cyclisation of the triene (**7c**) is potentially a viable method of constructing the C ring of aromatic steroids. In particular, the methyl substituent on the cyclopentenyl group does not apparently inhibit the cyclisation process, and there is no evidence for side-reactions such as [1,7] hydrogen shifts which might have been anticipated. The method may also provide a route to other fused phenanthrenes since we have shown that a phenyl substituent can participate as a component in the triene cyclisation. The major disadvantages of the route are the poor overall yields of the trienes and the limitations in its scope which are imposed by the method of constructing the vinyl ketones. The low yields are mainly a result of the inefficient addition of organometallic reagents to readily enolisable ketones. Various attempts have been reported in the literature to overcome this problem, notably the recent use of organotitanium and organozirconium reagents.[11] Our preliminary attempts to improve the route by using such alternative techniques have been unsuccessful. We are currently investigating alternative methods of synthesis of trienes of this type based on the Vilsmaier–Haack–Arnold formylation of ketones.[12]

Experimental

^{1}H N.m.r. spectra were recorded on a Perkin-Elmer R34 instrument, operating at 220 MHz, or on a Bruker WM250 instrument, operating at 250 MHz; $CDCl_3$ was used as solvent. Flash chromatography[13] was carried out using Kieselgel 60 (Merck) and p.l.c. was performed on plates coated with a 1 mm layer of Kieselgel 60 PF254 (Merck). Medium-pressure column chromatography was carried out as described by Taber.[14] Commercial butyl-lithium was estimated before use by the acid–base titration method of Whitesides *et al.*[15] Reactions of organolithium reagents were performed under dry nitrogen; tetrahydrofuran (THF) was freshly distilled from sodium before use. Light petroleum refers to the fraction b.p. 40—60 °C. Extracts were dried over magnesium sulphate. Ether refers to diethyl ether.

2-*Chloro*-3,4-*dihydronaphthalen*-1(2H)-*one* (**4**; R = Cl).—To a solution of α-tetralone (10.0 g, 68 mmol) in dichloromethane (200 cm^3) at 0 °C was added a solution of chlorine (4.83 g, 68 mmol) in dichloromethane (100 cm^3) during 1.5 h. The solution was allowed to attain room temperature, and was then washed successively with water, aqueous sodium hydrogen carbonate, and brine, and then dried, and the solvent was removed to leave a yellow oil. Crystallisation gave the title compound (7.6 g, 61%), m.p. 35—39 °C (from ether–light petroleum) (lit.,[16] 44—45.5 °C). Material of this purity was found to be satisfactory for subsequent reactions.

3-*Bromocyclohex*-2-*en*-1-*one*.—3-Methylsulphonylcyclohex-2-enone[17] (6.61 g, 34.8 mmol), benzyltriethylammonium bromide (23.6 g), and boron trifluoride–ether (4.93 g, 34.7 mmol) were stirred in dichloromethane (180 cm^3) at room temperature for 1.5 h. The organic phase was washed successively with water and brine, then dried, and the solvent was removed. Flash chromatography gave (with ether) the title bromo-enone[18] (4.37 g, 57% from cyclohexane-1,3-dione); δ 1.50—3.00 (6 H, m) and 6.49 (1 H, t, *J* 2.0 Hz).

3-*Bromocyclohex*-2-*enone Ethylene Dithioacetal*.—The above bromo-enone (4.37 g, 19.5 mmol), boron trifluoride–ether (0.8 cm^3), ethane-1,2-dithiol (2.58 g, 27.4 mmol), and 5 Å molecular sieves (4 g) were stirred together in chloroform for 4 h under nitrogen. The reaction mixture was then washed successively with sodium hydrogen carbonate and brine. The solution was dried and the solvent was removed to leave an oil. Flash chromatography gave [with ether–light petroleum (1:25)] the title dithioacetal[8] (4.60 g, 73%); δ 1.50—3.00 (6 H, m), 3.34 (4 H, br s), and 6.25 (1 H, t, *J* 1.0 Hz).

3-*Bromo*-2-*methylcyclopent*-2-*enone Ethylene Dithioacetal*.—3-Bromo-2-methylcyclopent-2-enone[8] (6.55 g, 37.1 mmol), ethanedithiol (4.45 g, 46.8 mmol), boron trifluoride–ether (0.89 cm^3), and 4 Å molecular sieves (10 g) were stirred in

chloroform (125 cm^3) under nitrogen for 64 h. The product was isolated, as in the preceding experiment, to give the title dithioacetal[8] (6.07 g, 65%); δ 1.87 (3 H), 2.55—2.80 (4 H, m), and 3.30 (4 H). The bromo enone (1.64 g, 25%) was also recovered from the chromatography column.

c-2-*Chloro*-1,2,3,4-*tetrahydro*-1-*vinylnaphthalen*-r-1-*ol* (**10a**) *and Its* trans-*Isomer*.—A solution of 2-chlorotetralone (1.23 g, 6.5 mmol) in THF (10 cm^3) was added dropwise during 0.5 h to a solution of vinylmagnesium bromide (18.2 mmol) in THF (25 cm^3) at 0 °C. After 3 h the reaction mixture was poured into aqueous ammonium chloride. The product was isolated by extraction with ether. The solution was dried and evaporated to leave an oil (1.16 g). This was subjected to medium-pressure column chromatography to give [with ether–light petroleum (1:4)] the alcohol (**10a**) (0.66 g, 49%) as an oil, b.p. 100 °C at 0.5 mmHg; $\nu_{max.}$ 3 500 and 1 690 cm^{-1}; δ 2.15—2.60 (2 H, m), 2.80 (1 H, OH), 2.80—3.25 (2 H, m), 4.44 (1 H, t, *J* 5 Hz, 2-H), 5.32 (1 H, dd, A*B*X), 5.37 (1 H, dd, *A*BX), 6.10 (1 H, dd, AB*X*), and 7.20—7.80 (4 H, m); J_{AB} 1.5, J_{AX} 10.0, and J_{BX} 16.7 Hz; *m/z* 210 and 208 (M^+).

Further elution gave the *trans*-alcohol (0.195 g, 14%) as an oil; $\nu_{max.}$ 3 430 and 1 680 cm^{-1}; δ 208—2.48 (2 H, m), 2.54 (1 H, OH), 2.85—3.23 (2 H, m), 4.34 (1 H, dd, *J* 10.1 and 2.1 Hz, 2-H), 5.15 (1 H, dd), 5.26 (1 H, dd), 6.28 (1 H, dd), and 7.05—7.52 (4 H, m); the vinylic signals when analysed as an ABX system gave J_{AB} 1.3, J_{AX} 10.6, and J_{BX} 16.7 Hz.

c-2-*Chloro*1,2,3,4-*tetrahydro*-1-*phenylnaphthalen*-r-1-*ol* (**10b**).—This was isolated (40%) from the reaction of 2-chlorotetralone (13.2 mmol) and phenylmagnesium bromide (30 mmol) and had m.p. 92—94 °C (from ether–light petroleum) (lit.,[7] 98—99 °C).

c-2-*Chloro*-1-(2-*furyl*)-1,2,3,4-*tetrahydronaphthalen*-r-1-*ol* (**10c**).—A solution of 2-chlorotetralone (1.80 g, 10 mmol) in ether (10 cm^3) was added dropwise during 15 min to a solution of 2-furyl-lithium[19] [prepared from furan (3.0 g, 40 mmol) in ether (15 cm^3)] cooled to −78 °C. After 0.5 h the solution was allowed to warm to room temperature. Hydrolysis and flash chromatography of the product mixture gave [with ether–light petroleum (1:8)] the title compound (1.21 g, 49%) as an air-sensitive oil; $\nu_{max.}$ 3 550, 1 614, 1 505, and 1 464 cm^{-1}; δ 2.00—2.40 (2 H, m), 2.80—3.00 (3 H, m), 4.99 (1 H, dd, *J* 6.5 and 4.0 Hz, 2-H), 6.15 (1 H, m), 6.34 (1 H, m), and 7.00—7.60 (5 H, m). This was used directly for the preparation of the ketone (**4c**).

c-2-*Chloro*-1,2,3,4-*tetrahydro*-1-(2-*thienyl*)*naphthalen*-r-1-*ol* (**10d**).—A solution of chlorotetralone (1.34 g, 7.4 mmol) in ether (5 cm^3) was added dropwise during 45 min to a solution of 2-thienyl-lithium[19] [prepared from thiophene (1.5 g, 20 mmol) in ether (8 cm^3)] cooled to −78 °C. After 1 h the solution was allowed to attain room temperature. Flash chromatography of the product obtained after hydrolysis gave [with ether–light petroleum (1:9)] the *naphthalenol* (**10d**) (747 mg, 38%) as a yellow oil; b.p. 140 °C at 0.1 mmHg (Found: C, 63.3; H, 4.9. $C_{14}H_{13}ClOS$ requires C, 63.5; H, 4.95%); $\nu_{max.}$ 3 550 and 1 609 cm^{-1}; δ 2.16 (2 H, m), 2.87 (1 H, dt, *J* 17.1 and 2.9 Hz), 3.05—3.25 (1 H, m), 3.27 (1 H, OH), 4.66 (1 H, dd, *J* 5.4 and 3.4 Hz, 2-H), 6.44 (1 H, m), 6.77 (1 H, m), 7.00—7.30 (4 H, m), and 7.48 (1 H, m); *m/z* 266 and 264 (M^+).

3-(t-2′-*Chloro*-1′,2′,3′,4′-*tetrahydro*-1′-*hydroxynaphthalen*-r-1′-*yl*)*cyclohex*-2-*enone Ethylene Dithioacetal* (**10e**).—The lithiocyclohexene (**9**) was prepared[8] from 3-bromocyclohex-2-enone dithioethylene acetal (1.62 g, 6.45 mmol) and butyl-lithium (7.70 mmol) in THF (20 cm^3) at −78 °C. After 1 h a solution of 2-chlorotetralone (1.75 g, 9.67 mmol) in THF (15 cm^3) was added dropwise. The reaction mixture was maintained at −78 °C for 3 h and then allowed to warm to 0 °C. After hydrolysis the product mixture was subjected to medium-pressure chromatography, which gave [with ether–light petroleum (1:1)] the *dithioacetal* (**10e**) (1.16 g, 51%) as a gum (Found: M^+, 352.0724. $C_{18}H_{21}ClOS_2$ requires *M*, 352.0721); $\nu_{max.}$ 3 495, 1 613, and 1 460 cm^{-1}; δ 1.20 (1 H, m), 1.70 (3 H, m), 2.04 (1 H, m), 2.24 (3 H, m), 2.47 (1 H, m), 2.67 (1 H, OH), 2.80—3.15 (2 H, m), 3.15—3.60 (4 H, m), 4.54 (1 H, dd, *J* 10.2 and 3.2 Hz, 2′-H), 6.14 (1 H, 2-H), and 7.07—7.60 (4 H, m).

3-(t-2′-*Chloro*-1′,2′,3′,4′-*tetrahydro*-1′-*hydroxynaphthalen*-r-1′-*yl*)-2-*methylcyclopent*-2-*enone Ethylene Dithioacetal* (**10f**).—The lithiocyclopentene (**8**) was prepared[8] from the corresponding bromo ketone (4.0 g, 15.9 mmol) and butyl-lithium (17.5 mmol) in THF (80 cm^3) at −78 °C. After 1.5 h a solution of 2-chlorotetralone (3.3 g, 18.3 mmol) in THF (30 cm^3) was added dropwise. The reaction mixture was stirred for 3 h at −78 °C and then allowed to warm to 0 °C. Flash chromatography of the product mixture obtained after hydrolysis gave [with ether–light petroleum (1:19)] the *dithioacetal* (**10f**) (2.30 g, 41%), m.p. 105—106 °C (from light petroleum) (Found: C, 61.2; H, 6.1. $C_{18}H_{21}ClOS_2$ requires C, 61.3; H, 6.0%); $\nu_{max.}$(KBr) 3 515 and 1 598 cm^{-1}; δ 1.66 (3 H), 2.11—2.65 (6 H, m), 2.71 (1 H, OH), 2.80—3.16 (2 H, m), 3.28 (4 H, br s), 4.55 (1 H, dd, *J* 9.3 and 2.9 Hz), and 7.05—7.45 (4 H, m). 2-Chlorotetralone (1.00 g) was also recovered from the column.

Conversion of Chlorohydrins (**10**) *into Ketones* (**4**). *General Procedure*.—The chlorohydrin (2—5 mmol) was added, as a benzene solution, dropwise to a solution of ethylmagnesium bromide (1 equiv.) in benzene at 0 °C. The reaction mixture was stirred at 0 °C for 15 min, during which time the magnesium alkoxide precipitated out. The reaction mixture was then heated under reflux for the period indicated, t.l.c. being used to determine completion of the reaction. After hydrolysis with aqueous ammonium chloride, the product was purified by chromatography as indicated.

(*a*) Chlorohydrin (**10a**) (450 mg, 2.15 mmol) gave, after heating for 10 min and medium-pressure chromatography, the ketone (**4a**) (65 mg, 17%) as an oil which was not completely pure (n.m.r.); $\nu_{max.}$ 1 685 and 1 600 cm^{-1}; δ (ABXM system) 3.20 (1 H, m, ABX*M*), 5.18 (2 H, m, *AB*XM), and 6.12 (1 H, ddd, AB*X*M); J_{AX} 10.7, J_{BX} 16.9, and J_{XM} 6.0 Hz.

Alternatively, chromatography was not attempted, and the yield of ketone (**4a**) was estimated as 35% from the n.m.r. spectrum of the crude product. The ketone was characterised as its 2,4-*dinitrophenylhydrazone*, m.p. 200—202 °C (from ethyl acetate–light petroleum) (Found: C, 61.3; H, 4.6; N, 15.8. $C_{18}H_{16}N_4O_4$ requires C, 61.4; H, 4.6; N, 15.9); δ 1.90—2.28 (2 H, m), 2.67—3.10 (2 H, m), 3.90 (1 H, m), 5.30 (2 H, m), 6.00 (1 H, ddd), 7.15—7.50 (4 H, m), 8.33 (2 H, m), and 9.15 (1 H, d).

(*b*) Chlorohydrin (**10b**) (1.44 g, 5.36 mmol) gave, after 5.5 h, 3,4-dihydro-2-phenylnaphthalen-1(2*H*)-one (**4b**) (1.23 g, 100%), which was essentially pure by n.m.r. and t.l.c. Recrystallisation of a small portion gave crystals, m.p. 70—74 °C (from ethanol) (lit.,[7] 71—74 °C).

(*c*) Chlorohydrin (**10c**) (1.21 g, 4.86 mmol) gave, after heating for 6 h and flash chromatography, the ketone (**4c**) (0.90 g, 87%) as an oil; $\nu_{max.}$ 1 685 and 1 600 cm^{-1}; δ 2.39 (2 H, m), 2.99 (2 H, t, *J* 5.9 Hz), 3.88 (1 H, dd, *J* 7.3 and 5.4 Hz), 6.12 (1 H, d, *J* 3.9 Hz), 6.29 (1 H, m), 7.05—7.55 (4 H, m), and 8.04 (1 H, d, *J* 7.8 Hz); 2,4-*dinitrophenylhydrazone*, m.p. 191—194 °C (from ethyl acetate) (Found: C, 61.0; H, 4.2; N, 14.35. $C_{20}H_{16}N_4O_5$ requires C, 61.2; H, 4.1; N, 14.3%).

(*d*) Chlorohydrin (**10d**) (1.89 g, 7.14 mmol) gave, after heating for 6 h and flash chromatography, 3,4-*dihydro*-2-(2-*thienyl*)-*naphthalen*-1(2H)-*one* (**4d**) (1.41 g, 87%), m.p. 90—90.5 °C from

ether–hexane) (Found: C, 73.7; H, 5.4. $C_{14}H_{12}OS$ requires C, 73.65; H, 5.3%); $\nu_{max.}$ 1 703 and 1 610 cm^{-1}; δ 2.10—2.50 (2 H, m), 2.92 (2 H, t, *J* 5.6 Hz), 3.89 (1 H, ddd, *J* 9.4, 4.6, and 1.1 Hz), 6.72 (1 H, m), 6.80 (1 H, m), 7.00—7.37 (4 H, m), and 7.93 (1 H, d, *J* 8.8 Hz); *m/z* 228 (M^+).

(*e*) Chlorohydrin (**10e**) (706 mg, 2.00 mmol) gave, after heating for 2.5 h and medium-pressure chromatography, the ketone (**4e**) (318 mg, 50%) as a gum (Found: M^+, 316.0914. $C_{18}H_{20}OS_2$ requires M^+, 316.0954); $\nu_{max.}$ 1 690 and 1 608 cm^{-1}; δ 1.60—2.50 (9 H, m), 2.85—3.20 (2 H, m), 3.30 (4 H, br), 5.70 (1 H, br), 7.07—7.70 (3 H, m), and 8.06 (1 H, m).

(*f*) Chlorohydrin (**10f**) (2.30 g, 6.50 mmol) gave, after 15 min, *the ketone* (**4f**) (2.00 g, 97%), m.p. 99—101 °C (from ether–light petroleum) (Found: C, 68.6; H, 6.6. $C_{18}H_{20}OS_2$ requires C, 68.3; H, 6.4%); $\nu_{max.}$(KBr) 1 678 and 1 593 cm^{-1}; δ 1.81 (3 H, d, *J* 2 Hz), 2.02—2.45 (4 H, m), 2.48—2.70 (2 H, m), 2.93—3.20 (2 H, m), 3.31 (4 H, m), 3.50 (1 H, dd, *J* 10.8 and 6.9 Hz), 7.20—7.62 (3 H, m), and 8.05 (1 H, d, *J* 7.8 Hz); *m/z* 316 (M^+), 256 and 255.

Alcohols (**5a**) *and* (**6a**) *From the Ketone* (**4b**).—A solution of the ketone (**4b**) (1.24 g, 5.34 mmol) and vinylmagnesium bromide (100 mmol) in THF (100 cm^3) was heated under reflux for 10 h. After quenching, the products were separated by flash chromatography [ether–light petroleum (1:9)]. First eluted was the *alcohol* (**6a**) (620 mg, 46%), m.p. 88—90 °C (from ethanol) (Found: C, 86.25; H, 7.2. $C_{18}H_{18}O$ requires C, 86.4; H, 7.25%); $\nu_{max.}$ 3 450 and 1 600 cm^{-1}; δ 1.67 (1 H, OH), 1.89—2.05 (1 H, m), 2.35—2.60 (1 H, m), 2.90—3.10 (3 H, m), 5.10 (2 H, m, *AB*X), 5.95 (1 H, m, AB*X*), and 7.10—7.50 (9 H, m); J_{AX} 10.1, J_{BX} 17.3, and J_{AB} 1.1 Hz; *m/z* 250 (M^+) and 146; *m** (250→146) 85.3

Next eluted was the alcohol (**5a**) (260 mg, 19%) as an oil; δ 1.85—2.35 (3 H, m, reduces to 2 H after D_2O shake), 2.80—3.40 (3 H, m), 4.73 (1 H, dd, A*B*X), 5.02 (1 H, dd, *A*BX), 5.95 (1 H, dd, AB*X*), and 7.10—7.70 (9 H, m).

Alcohols (**5b**) *and* (**6b**) *From the Ketone* (**4d**).—A solution of the ketone (**4d**) (434 mg, 1.9 mmol) and vinylmagnesium bromide (10 mmol) in THF (27 cm^3) was heated under reflux for 24 h. P.l.c. of the product mixture obtained after quenching gave [with ether–light petroleum (1:19)] as the major component the *alcohol* (**6b**) as an oil (Found: M^+, 256.0905. $C_{16}H_{16}OS$ requires *M*, 256.0919); $\nu_{max.}$ 3 540 and 1 615 cm^{-1}; δ 1.79 (1 H, OH), 1.80—2.40 (2 H, m), 2.75 (2 H, m), 3.18 (1 H, dd, *J* 12.2 and 3.9 Hz), 5.01 (2 H, m, *AB*X), 5.76 (1 H, dd, AB*X*), 6.65—6.85 (2 H, m), 6.90—7.35 (4 H, m), and 7.27 (1 H, m); J_{AX} 10.8, J_{BX} 18.6, and J_{AB} 1.1 Hz.

A second component, an oil, was identified as the alcohol (**5b**) (121 mg, 25%) on the basis of its i.r. and n.m.r. spectra; $\nu_{max.}$ 3 540 and 1 610 cm^{-1}; δ 2.10—2.28 (2 H, m), 2.28 (1 H, OH), 2.90—3.05 (2 H, m), 3.40 (1 H, dd, *J* 9.8 and 7.4 Hz), 4.80 (1 H, d, A*B*X), 5.03 (1 H, d, *A*BX), 5.92 (1 H, dd, AB*X*), 6.90 (1 H, m), 6.97 (1 H, m), 7.05—7.30 (4 H, m), and 7.48 (1 H, m); J_{AX} 10.8 and J_{BX} 18.6 Hz (J_{AB} not resolved).

Alcohol (**6c**) *From the Ketone* (**4f**).—A solution of the ketone (**4f**) (2.00 g, 6.3 mmol) and vinylmagnesium bromide (40 mmol) in THF (60 cm^3) was heated under reflux for 1.5 h. Medium-pressure chromatography of the product mixture obtained after quenching gave [with ether–light petroleum (1:19)] the *alcohol* (**6c**) (898 mg, 40%) as an oil (Found: M^+, 344.1248. $C_{20}H_{24}OS_2$ requires *M*, 344.1268); $\nu_{max.}$ 3 400 and 1 640 cm^{-1}; δ 1.62 (1 H, OH), 1.77 (3 H), 2.10—2.68 (6 H, m), 2.78 (1 H, dd, *J* 13.2 and 2.5 Hz), 2.88—3.05 (2 H, m), 3.30 (4 H, br), 5.28 (1 H, dd, *A*BX), 5.44 (1 H, dd, A*B*X), 5.90 (1 H, dd, AB*X*), and 7.10—7.44 (4 H, m).

1,2-*Dihydro*-3-*phenyl*-4-*vinylnaphthalene* (**7a**).—A solution containing a mixture of the alcohols (**5a**) and (**6a**) (100 mg, 0.40 mmol), hydroquinone (2 mg), and PTSA (2 mg) in degassed benzene (75 cm^3) was heated for 5 min under reflux under nitrogen with a Dean–Stark water separator. The solution was washed successively with aqueous sodium hydrogen carbonate and brine, and was then dried, and concentrated to leave an oil. This was purified by passage of a solution in light petroleum through a short column of alumina. The *title compound* (**7a**) was obtained as an oil (70 mg, 75%), b.p. 150 °C at 0.2 mmHg (Found: C, 92.8; H, 7.45. $C_{18}H_{16}$ requires C, 93.1; H, 6.95%); $\lambda_{max.}$(EtOH) 298 nm; δ 2.55 (2 H, m, ABX*M*), 2.77 (2 H, m), 5.26 (2 H, m, *AB*XM), 6.48 (1 H, tdd, AB*X*M), and 7.10—7.60 (9 H, m); J_{AX} 11.1, J_{BX} 17.8, J_{AB} 2.0, and J_{XM} 1.0 Hz.

In the presence of oxygen and with extended reaction times two other major products were detected. One was identified as 2-phenyltetralone (**4b**) by comparison with an authentic specimen; the other had signals in the n.m.r. spectrum at δ 1.25 (t, *J* 7.7 Hz) and 3.01 (q, *J* 7.7 Hz), and it was tentatively identified as 1-ethyl-2-phenylnaphthalene.

1,2-*Dihydro*-3-(2-*thienyl*)-4-*vinylnaphthalene* (**7b**).—By using the same procedure as in the preceding preparation the alcohols (**5b**) and (**6b**) (325 mg, 1.26 mmol) were converted into the *title compound* (**7b**), an oil (120 mg, 40%) (Found: M^+, 238.0771. $C_{16}H_{14}S$ requires *M*, 238.0794); δ 2.60—3.10 (4 H, m), 5.51 (2 H, m, *AB*X), 6.89 (1 H, dd, AB*X*), 7.00—7.50 (6 H, m),, and 7.60 (1 H, m); J_{AX} 10.8, J_{BX} 19.1, and J_{AB} 1.5 Hz. The dd at δ 6.89 is broadened by homoallylic coupling.

3-(3′,4-*Dihydro*-1′-*vinylnaphthalen*-2′-*yl*)-2-*methylcyclopent*-2-*enone EthyleneDithioacetal* (**7c**).—The alcohol (**6c**) (285 mg, 0.83 mmol) was dehydrated as in the preceding preparations to give the *title compound* (**7c**) (175 mg, 65%) as a yellow oil (Found: M^+, 326.1199. $C_{20}H_{22}S_2$ requires *M*, 326.1161); $\lambda_{max.}$(EtOH) 289 nm (ε 28 000); δ 1.73 (3 H), 2.22—2.38 (2 H, t, *J* 7.8 Hz), 2.40—2.55 (2 H, m), 2.54—2.67 (2 H, m), 2.74 (2 H, t, *J* 7.1 Hz), 3.34 (4 H, m), 5.35 (2 H, m, *AB*X), 6.42 (1 H, dd, AB*X*), and 7.00—7.70 (4 H, m); J_{AX} 10.8, J_{BX} 18.6, and J_{AB} 2 Hz; *m/z* 326, 265, and 251.

Cyclisation of the Naphthalene (**7a**).—(a) *In solution.* Compound (**7a**) (69 mg) was heated at 180 °C under nitrogen in dry degassed 1,2-dichlorobenzene (15 cm^3) containing quinoline (5 mg). After 4 days the solvent was removed and the residue was subjected to p.l.c. This gave 5,6,11,12-tetrahydrochrysene (**16**) (20 mg, 29%), m.p. 105—106 °C (lit.,[10] 101—103 °C); $\lambda_{max.}$(EtOH) 230 (ε 17 400), 237 (19 500), 245 (13 200), 310 (21 400), 324 (27 500), and 340 nm (18 600); δ 2.66 (4 H, m), 2.88 (4 H, m), and 7.05—7.42 (8 H, m); *m/z* (chemical ionisation with isobutane) 233 and 232 (M^+).

(b) *By flash vacuum pyrolysis.* Compound (**7a**) (110 mg) was distilled slowly through a quartz tube at 730 °C and 0.01 mmHg pressure. P.l.c. of the pyrolysate gave unchanged vinylnaphthalene (**7a**) (30 mg) and 5,6,11,12-tetrahydrochrysene (**16**) (49 mg, 61% based on starting material consumed).

Cyclisation of the Triene (**7c**).—(a) *In* p-*xylene* (139 °C). A solution of the triene (**7c**) (44 mg) in degassed *p*-xylene (20 cm^3) containing hydroquinone (5 mg) was heated under reflux for 34 h. The solvent was removed, and p.l.c. of the residue [ether–light petroleum (1:99)] gave estra-1,3,5(10),8(14),9(11)-pentaen-17-one ethylene dithioacetal (**13**) (17 mg, 39%) as an unstable yellow oil; $\lambda_{max.}$ 280 nm; δ 1.20 (3 H), 2.20—2.62 (6 H, m), 2.72 (2 H, t, *J* 6.3 Hz), 3.13 (1 H, d, *J* 16.8 Hz, showing further splitting, 12-H), 3.20—3.40 (5 H, m, 12-H and SCH_2CH_2S), 6.15 (1 H, dd, *J* 6.6 and 2.9 Hz, 11-H), 7.08—7.36 (3 H, m, 2-, 3-, and 4-H), and 7.56 (1 H, d, *J* 6.3 Hz, 1-H).

(b) *In bromobenzene* (156 °C). A solution of the triene (**7c**) (383 mg) in dry degassed bromobenzene (50 cm^3) containing

hydroquinone (5 mg) was heated under reflux for 16 h. The solvent was removed, and the residue was subjected to p.l.c. This gave *estra*-1,3,5(10),8,14-*pentaen*-17-*one ethylene dithioacetal* (**14**) as a yellow oil (137 mg, 33%) (Found: M^+, 326.1199. $C_{20}H_{22}S_2$ requires M, 326.1161); $\lambda_{max.}$(EtOH) 236 (ε 14 000), 244 (11 500), 297 (17 800), 310 (22 000), and 324 nm (20 700); δ 1.12 (3 H), 1.66 (1 H, m, 12-H), 2.22—2.75 (5 H, m, 6-H_2, 11-H_2, and 12-H), 2.79 (2 H, t, *J* 7.1 Hz, 7-H_2), 3.05 (1 H, dd, *J* 17.6 and 3.6 Hz, 16-H), 3.15—3.50 (5 H, m, 16-H and SCH_2CH_2S), 5.78 (1 H, m, 15-H), 7.10—7.33 (3 H, m), and 7.38 (1 H, d, *J* 7.3 Hz); δ(C_6D_6) 1.17 (3 H), 1.71 (1 H, m), 1.95—3.00 (11 H, m), 3.08 (1 H, dd, *J* 17.8 and 3.4 Hz, 16-H), 3.40 (1 H, d, *J* 17.8 Hz, broadened by further small coupling, 16-H), 5.54 (1 H, m, 15-H), and 6.90—7.40 (4 H, m). Irradiation at δ 5.54 caused the dd at δ 3.08 to collapse to a d (*J* 17.8 Hz) and the d at δ 3.40 to become less broad.

(c) *By irradiation.* The triene (**7c**) (114 mg) was dissolved in a degassed mixture of ether and pentane (1:10; 15 cm^3) and the solution was irradiated under nitrogen at 300 nm in a Rayonet reactor. After 3 h the n.m.r. spectrum of the reaction mixture showed it to consist of the starting triene (**7c**) and the estrapentaene (**13**) (3:7). The mixture was subjected to irradiation for a further 12 h, during which period a yellow precipitate appeared. P.l.c. of the product mixture gave the estrapentaene (**13**) (15 mg, 10%).

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References

1 E. N. Marvell, 'Thermal Electrocyclic Reactions,' Academic Press, New York, 1980.
2 F. B. Mallory and C. W. Mallory, *Org. React.*, 1984, **30**, 1.
3 R. H. Bradbury, T. L. Gilchrist, and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1981, 3234.
4 R. Ramage and A. Sattar, *Chem. Commun.*, 1970, 173.
5 J. K. Crandall, J. P. Arrington, and J. Hen, *J. Am. Chem. Soc.*, 1967, **89**, 6208; D. L. J. Clive and C. G. Russell, *J. Chem. Soc., Chem. Commun.*, 1981, 434.
6 A. Marcou, W. Chodkiewicz, and P. Cadiot, *Bull. Soc. Chim. Fr.*, 1967, 2429; M. Nishino, H. Kondo, and A. Miyake, *Chem. Lett.*, 1973, 667; D. A. Holt, *Tetrahedron Lett.*, 1981, **22**, 2243.
7 A. S. Hussey and R. R. Herr, *J. Org. Chem.*, 1959, **24**, 843.
8 C. Shih and J. S. Swenton, *J. Org. Chem.*, 1982, **47**, 2825.
9 E. D. Sternberg and K. P. C. Vollhardt, *J. Org. Chem.*, 1982, **47**, 3447; 1984, **49**, 1574.
10 T. A. Lyle and G. H. Daub, *J. Org. Chem.*, 1979, **44**, 4933.
11 B. Weidmann and D. Seebach, *Angew. Chem., Int. Ed. Engl.*, 1983, **22**, 31.
12 Z. Arnold and A. Holý, *Collect. Czech. Chem. Commun.*, 1961, **26**, 3059; I. R. Robertson and J. T. Sharp, *Tetrahedron*, 1984, **40**, 3095.
13 W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.
14 D. F. Taber, *J. Org. Chem.*, 1982, **47**, 1351.
15 G. M. Whitesides, C. P. Casey, and J. K. Krieger, *J. Am. Chem. Soc.*, 1971, **93**, 1379.
16 C. L. Stevens, J. T. Beerebroon, and K. G. Rutherford, *J. Am. Chem. Soc.*, 1955, **77**, 4590.
17 C. J. Kowalski and K. W. Fields, *J. Org. Chem.*, 1981, **46**, 197.
18 C. Shih and J. S. Swenton, *Tetrahedron Lett.*, 1981, **22**, 4217.
19 D. J. Chadwick and C. Willbe, *J. Chem. Soc., Perkin Trans. 1*, 1977, 887.

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