Synthetic Studies on Aromatic Sesquiterpenoids: Synthesis of Curcumene Ether by Olefin Cyclisation

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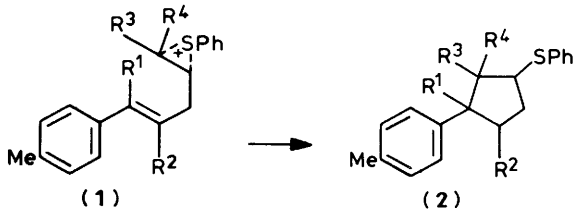
The acid-catalysed cyclisation of the olefinic β-hydroxy sulphides (**15a**) and (**15b**) gave 3-phenylthiocurcumene ether as a diastereoisomeric mixture [(**17**) and (**18**)] together with 5,5-dimethyl-4-phenylthio-1-*p*-tolylcyclohex-1-ene (**16**) and 2-methyl-3-(1-methyl-1-phenylthioethyl)-2-*p*-tolylcyclobutan-1-ol (**19**). The diastereoisomers (**17**) and (**18**) were converted into curcumene ether (**24**). Treatment of the silyl enol ether (**7**) with benzenesulphenyl chloride yielded 5-phenylthiomethyl-2-[phenylthio(*p*-tolyl)methylene]tetrahydrofuran (**8**) and 5-chloro-1,6-bis(phenylthio)-1-*p*-tolylhexan-2-one (**9**). 1-*p*-Tolylhexane-2,5-dione (**10**) was also synthesised from (**5**) employing a palladium-catalysed oxidation, and this result constitutes a formal total synthesis of cuparene (**11**).

Polyolefin cyclisations have been widely studied and are potentially useful for building polycyclic carbon frameworks.[1] We have already reported the syntheses of safranal[2] and caparrapi oxide[3] using the acid-catalysed cyclisation of olefinic β-hydroxy selenides, and we describe here an investigation of an olefin cyclisation mediated by a sulphur group instead of the selenide with a view to synthesising aromatic sesquiterpenes [*i.e.* (**1**) ⟶ (**2**), Scheme].



Scheme.

Results and Discussion

As a preliminary experiment, we investigated the synthesis of a cuparene derivative (**2**) *via* a carbon–carbon bond formation reaction by cyclisation of the olefinic ketone (**5**) using benzenesulphenyl chloride. The starting material (**5**) was easily prepared from the aldehyde (**3**)[4] *via* the alcohol (**4**) by a Grignard reaction with but-3-enylmagnesium bromide in tetrahydrofuran followed by oxidation with pyridinium chlorochromate in dichloromethane. Treatment of compound (**5**) with benzenesulphenyl chloride in dichloromethane afforded the β-chloro sulphide (**6**) [*m/z* 332 (M^+)]; however, this could not be converted into the desired cyclic product (**2**) under the various conditions used. We also prepared the silyl enol ether (**7**) by treatment of the ketone (**5**) with triethylamine and trimethylsilyl chloride in dimethylformamide and treated this benzenesulphenyl chloride as described above to give the monocyclic compound (**8**) [*m/z* 404 (M^+)] and the α-phenylthio ketone (**9**) [*m/z* 440 (M^+)] in 33 and 7% yields, respectively. Since the cyclisation of compounds (**6**) and (**7**) to give a cuparene derivative could not be achieved under the conditions described, the olefinic ketone (**5**) was treated with palladium chloride and cuprous chloride in aqueous dimethylformamide under oxygen to afford the diketone (**10**) in 55% yield; we have reported the conversion of compound (**10**) thus obtained into cuparene (**11**).[5] Therefore, this result constitutes a formal total synthesis of cuparene (**11**).

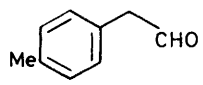
Secondly, the acid-catalysed cyclisation of the β-hydroxy sulphides was carried out as follows. The epoxide (**14**), derived from the alcohol (**12**)[6] *via* the diene (**13**) by treatment with mesyl chloride and triethylamine in dichloromethane followed by *m*-chloroperbenzoic acid in dichloromethane, was treated with sodium thiophenolate to give the β-hydroxy sulphides (**15a**) and (**15b**) in 24.3 and 48.7% yields, respectively. Compound (**15b**), the major product, was subjected to acid-catalysed cyclisation, as follows. A solution of (**15b**) in dichloromethane containing trifluoroacetic acid and trifluoroacetic anhydride was stirred for 7 h at room temperature to afford four cyclic products (**16**)—(**19**). This cyclisation was investigated under various reaction conditions and the results are summarised in the Table.

Table. Reaction of compounds (**15a**) and (**15b**) with trifluoroacetic acid[a]

Substrate	Time (h)	Products (% yield) (**16**)	(**17**) + (**18**)	(**19**)	(**15a**)[b]	(**15b**)[b]
(**15a**)	1	25.2	13	9.5	14.4	1.4
	7	7.1	25.7	28.6	14.3	7.1
	24	19.2	8.6	11.4	25.4	12.7
(**15b**)	1	25.2	5.7	3.3	28	14
	7	29.2	8.6	5.2	35.2	17.6
	24	20.7	6.2	7.6	26	13
(**15b**)[c]	7	37.5	3.1 + 15.4	10.8	22	10.8

[a] Substrate (210 mg, 0.64 mmol); trifluoroacetic acid (1 ml, 6 mmol); trifluoroacetic anhydride 2—3 drops); anhydrous dichloromethane (15 ml). [b] The yield of (**15a**) and (**15b**), obtained as a mixture, was measured by the ratio of peaks in the n.m.r. spectrum. [c] Listed in Experimental section.

Although the structure of compound (**16**) was deduced by the appearance of two vicinal methyl proton signals (δ 1.08 and 1.18, s) and an olefinic proton signal (δ 5.91, m) in the n.m.r. spectrum, it was confirmed by an oxidative elimination of the sulphide to yield the diene (**20**) [*m/z* 198 (M^+)], whose n.m.r. spectrum showed three olefinic proton signals [δ 5.64 (t), 5.98 (d), and 6.22 (d)]. The structures of the ethers (**17**) and (**18**) were determined by their transformations into compound (**24**), as follows. Oxidative elimination of the sulphides of (**17**) and (**18**) gave the same olefin, (**21**), which was hydrogenated over 10% palladium–carbon to yield curcumene ether (**24**), whose spectral data were identical with those reported.[7] Hydrogenolysis of the sulphide of compound (**17**) with Raney nickel also gave curcumene ether (**24**) directly, in 15% yield. The two products were assigned the stereochemistries (**17**) and (**18**) on the basis of



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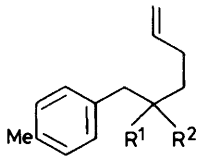
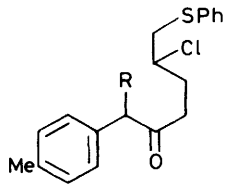
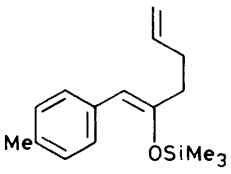


(4) R^1 = H, R^2 = OH
(5) R^1, R^2 = O



(6) R = H
(9) R = SPh



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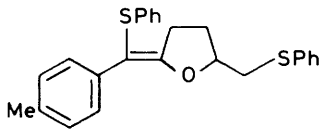

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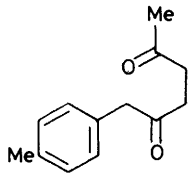

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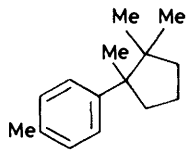

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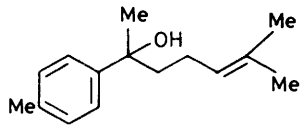

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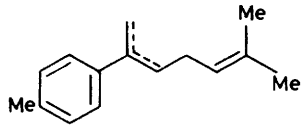
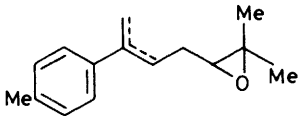
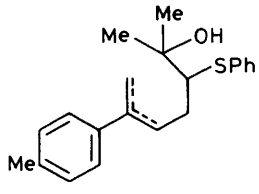


(13a,b)

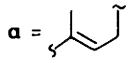


(14a,b)

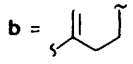


(15a,b)

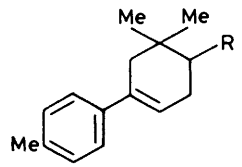
a =



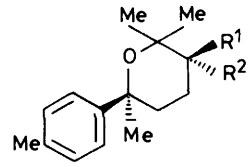
b =



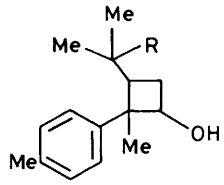
their n.m.r. spectra; one of the four methyl proton signals of (**18**) occurred at high field (δ 0.69) which suggests that it is located over the benzene ring and is shielded by the ring current. The structure of (**19**) was deduced from its transformation into the olefin (**22**) in the same way; in the n.m.r. spectrum, the signal due to the 1′-methyl group of compound (**19**) disappeared and additional olefinic proton signals were observed [δ 4.8 and 5.05 (each d, *J* 2 Hz)]. Moreover, catalytic hydrogenation of compound (**22**) with 10% palladium–carbon in methanol afforded compound (**23**) whose n.m.r. spectrum showed the



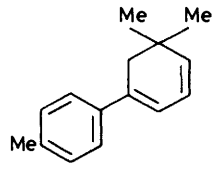
(16) R = SPh



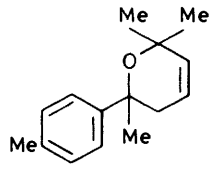
(17) R^1 = SPh, R^2 = H
(18) R^1 = H, R^2 = SPh



(19) R = SPh



(20)



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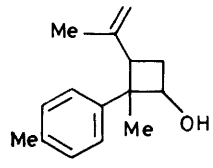

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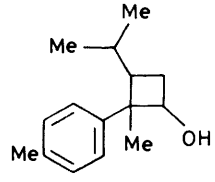

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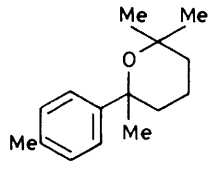

(24)

appearance of an isopropyl group. These facts strongly suggested the structures (**22**) and (**23**), and hence the cyclisation product was assigned the structure (**19**).

Thus, in the cyclisation of the β-hydroxy sulphides (**15a**) and (**15b**), the 3-phenylthiocurcumene ethers (**17**) and (**18**) were obtained and the formation of six- and four-membered rings was observed, but a cuparene-type product was not detected.

Experimental

I.r. spectra were obtained with a Hitachi 260-10 spectrometer, n.m.r. spectra with JEOL PMX-60 and JEOL JNM FX-100 instruments (tetramethylsilane as internal reference), and mass spectra with a JEOL JMS D-300 spectrometer. M.p.s were determined with a Yanagimoto micro apparatus. Ether refers to diethyl ether.

6-p-*Tolylhex*-1-*en*-5-*ol* (**4**).—To a stirred solution of but-3-enylmagnesium bromine [prepared from magnesium (4.36 g, 0.18 g-atom) and 4-bromobut-1-ene (24.18 g, 0.18 mol)] in anhydrous tetrahydrofuran (100 ml) was added dropwise a solution of *p*-tolylacetaldehyde (**3**)[4] (16 g, 10.12 mol) in

anhydrous tetrahydrofuran (30 ml) under nitrogen at 0 °C. After being stirred for 1 h at room temperature, the mixture was treated with solid ammonium chloride (10 g) and water (100 ml), and extracted with dichloromethane. The extract was washed with water and brine, and dried (Na_2SO_4). Evaporation of the solvent afforded a residue, which was chromatographed on silica gel (300 g) with benzene as eluant to give 6-p-*tolylhex*-1-*en*-5-*ol* (**4**) (19.8 g, 87%) as a colourless oil (Found: C, 82.3; H, 9.5. $C_{13}H_{18}O$ requires C, 82.05; H, 9.55%); $\nu_{max.}$($CHCl_3$) 3 600 (OH), 1 640 cm^{-1} (C=C); δ($CDCl_3$) 1.54—1.68 (2 H, m, 4-H_2), 2.08—2.22 (2 H, m, 3-H_2), 2.31 (3 H, s, ArMe), 2.72 (2 H, distorted dd, *J* 8 and 8 Hz, ArCH_2), 3.78 (1 H, m, 5-H), 4.89—5.14 (2 H, each m, C=CH_2), 5.63—5.97 (1 H, m, C=CH), and 7.09 (4 H, s, ArH); *m/z* 190 (M^+).

6-p-*Tolylhex*-1-*en*-5-*one* (**5**).—To a stirred mixture of pyridinium chlorochromate (13 g, 0.06 mol) in anhydrous dichloromethane (100 ml) was added in one portion a solution of (**4**) (7.6 g, 0.04 mol) in anhydrous dichloromethane (20 ml) under nitrogen at room temperature. The resultant mixture was further stirred for 1.5 h at the same temperature, then the solvent was removed under reduced pressure and the residue was treated with ether until the black solid became granular. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure to afford an oil, which was chromatographed on silica gel (200 g) with benzene as eluant to give 6-p-*tolylhex*-1-*en*-5-*one* (**5**) (6.5 g, 86.7%) as a colourless oil (Found: M^+, 188.1186. $C_{13}H_{16}O$ requires M^+, 188.1199); $\nu_{max.}$($CHCl_3$) 1 715 (C=O) and 1 640 cm^{-1} (C=C); δ($CDCl_3$) 2.31—2.45 (2 H, m, 3-H_2), 2.41 (3 H, s, ArMe), 2.59 (2 H, dt, *J* 3 and 6 Hz, 4-H_2), 3.72 (2 H, s, ArCH_2), 4.95—5.13 (2 H, each m, C=CH_2), 5.65—5.98 (1 H, m, C=CH), and 7.18 (4 H, s, ArH); *m/z* 188 (M^+).

5-*Chloro*-6-*phenylthio*-1-p-*tolylhexan*-2-*one* (**6**).—To a stirred solution of benzenesulphenyl chloride (1.15 g, 7.98 mmol) in anhydrous dichloromethane (100 ml) was added dropwise a solution of (**5**) (1 g, 5.32 mol) in anhydrous dichloromethane (50 ml) under nitrogen at −78 °C. The resultant mixture was gradually warmed to room temperature and stirred for 1 h. The reaction mixture was washed with water, saturated sodium hydrogen carbonate solution, and brine, and dried (Na_2SO_4). Then the solvent was evaporated off and the residue was chromatographed on silica gel (60 g) with benzene as eluant to give 5-*chloro*-6-*phenylthio*-1-p-*tolylhexan*-2-*one* (**6**) (1.7 g, 96%) as a yellow oil (Found: C, 68.7; H, 6.25. $C_{19}H_{21}ClOS$ requires C, 68.55; H, 6.35%); $\nu_{max.}$($CHCl_3$) 1 770 cm^{-1} (C=O); δ($CDCl_3$) 1.65—2.08 (2 H, m, 4-H_2), 2.30 (3 H, s, ArMe), 2.60 (2 H, t, *J* 5 Hz, 3-H_2), 3.60 (2 H, s, 1-H_2), 3.69—4.20 (1 H, m, 5-H), 7.05 (4 H, s, ArH), and 7.12—7.50 (5 H, m, SPh); *m/z* 332 (M^+) and 334 ($M^+ + 2$).

2-*Trimethylsilyloxy*-1-p-*tolylhexa*-1,5-*diene* (**7**).—To a stirred mixture of triethylamine (9.3 ml, 66.1 mmol), trimethylsilyl chloride (4.25 ml, 33.1 mmol), and anhydrous dimethylformamide (10 ml) was added a solution of (**5**) (3.11 g, 16.5 mmol) in anhydrous dimethylformamide (20 ml) under nitrogen at room temperature, and the resultant mixture was refluxed for 18 h. After being cooled to 0 °C, the reaction mixture was diluted with hexane and washed rapidly with saturated sodium hydrogen carbonate solution, 1.5M-hydrochloric acid, and saturated sodium hydrogen carbonate solution; the hexane layer was then dried (Na_2SO_4). Evaporation of the solvent afforded 2-trimethylsilyloxy-1-*p*-tolylhexa-1,5-diene (**7**) (3.7 g, 86%) as a brown oil, which was used for the next reaction without further purification; $\nu_{max.}$($CHCl_3$) 1 650 cm^{-1} (C=C); δ($CDCl_3$) 0.23 (9 H, s, SiMe_3), 2.33 (3 H, s, Ar*Me*), 2.20—2.50 (4 H, m, 3-H_2 and 4-H_2), 4.80—5.80 (3 H, m, olefinic H), 5.40 (1 H, s, ArC*H*=C), 6.96 (2 H, d, *J* 8 Hz, ArH), and 7.30 (2 H, d, *J* 8 Hz, ArH).

Treatment of the Silyl Ether (**7**) *with Benzenesulphenyl Chloride*.—To a stirred solution of (**7**) (0.5 g, 1.9 mmol) in anhydrous dichloromethane (200 ml) was added dropwise a solution of benzenesulphenyl chloride (0.56 g, 3.8 mmol) in anhydrous dichloromethane (10 ml) under nitrogen at −78 °C, and the resultant mixture was warmed to room temperature and stirred for 12 h. The solvent was then removed under reduced pressure, the residue was diluted with benzene, and the benzene layer was washed with water, saturated sodium hydrogen carbonate solution, and brine, and dried (Na_2SO_4). Evaporation of the solvent gave an oil, which was chromatographed on silica gel (50 g) with benzene as eluant to give 5-*phenylthiomethyl*-2-[*phenylthio*(p-*tolyl*)*methylene*]*tetrahydrofuran* (**8**) (251 mg, 33%) as an orange oil; elution with benzene–ethyl acetate (10:1 v/v) furnished 5-*chloro*-1,6-*bis*(*phenylthio*)-1-p-*tolylhexan*-2-*one* (**9**) (59 mg, 7.1%) as a yellow oil.

Compound (**8**) (Found: C, 73.85; H, 6.0. $C_{25}H_{24}OS_2$ requires C, 73.65; H, 6.05%), $\nu_{max.}$($CHCl_3$) 1 615 cm^{-1} (C=C); δ($CDCl_3$) 1.70—2.17 (2 H, m, 4-H_2), 2.19 (3 H, s, Ar*Me*), 2.70—3.03 (2 H, m, 3-H_2), 3.09 (2 H, d, *J* 5 Hz, SCH_2), 4.27—4.80 (1 H, m, 5-H), 7.02 and 7.22 (each 5 H, each s, 2 × SPh), 6.92 (2 H, d, *J* 8 Hz, ArH), and 7.55 (2 H, d, *J* 8 Hz, ArH); *m/z* 404 (M^+).

Compound (**9**) (Found: C, 67.9; H, 5.75. $C_{25}H_{25}ClOS_2$ requires C, 68.1; H, 5.7%), $\nu_{max.}$($CHCl_3$) 1 700 cm^{-1} (C=O); δ($CDCl_3$) 1.65—2.08 (2 H, m, 4-H_2), 2.26 (3 H, s, Ar*Me*), 2.65 (2 H, t, *J* 7 Hz, 3-H_2), 2.90—3.15 (2 H, m, 6-H_2), 3.8 (1 H, m, 5-H), 4.88 (1 H, s, 1-H), 7.12 (4 H, s, ArH), and 7.2 and 7.24 (each 5 H, each s, 2 × PhS); *m/z* 440 (M^+) and 442 ($M^+ + 2$).

1-p-*Tolylhexane*-2,5-*dione* (**10**).—A solution of the olefin (**5**) (200 mg, 1.06 mmol) in dimethylformamide (2 ml) and water (0.7 ml) in the presence of palladium chloride (40 mg, 0.23 mmol) and cuprous chloride (110 mg, 1.11 mmol) was stirred at ambient temperature for 20 h under oxygen, and worked up according to Tsuji's procedure[8] to give 1-*p*-tolylhexane-2,5-dione (**10**) (120 mg, 55%), which was identical with an authentic specimen.[5]

Dehydration of 6-*Hydroxy*-2-*methyl*-6-p-*tolylhept*-2-*ene* (**12**) *with Methanesulphonyl Chloride and Triethylamine*.—To a stirred solution of (**12**)[6] (34.67 g, 0.16 mol) and triethylamine (50 ml, 0.36 mol) in anhydrous dichloromethane (400 ml) was added dropwise methanesulphonyl chloride (14 ml, 0.18 mol) under nitrogen at 0 °C, and the resultant mixture was stirred for 1 h at the same temperature. Stirring was continued for 24 h at room temperature and then water was added (330 ml); the resulting mixture was extracted with dichloromethane, and the extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent afforded an oil, which was chromatographed on silica gel (500 g) with hexane as eluant to give a mixture (22.753 g, 72.3%) of 6-*methyl*-2-p-*tolylhepta*-2,5-*diene* (**13a**) and its isomer, the 1,5-*diene* (**13b**) as a colourless oil [(**13a**):(**13b**) = 1:2 w/w]. A small portion of the mixture was carefully rechromatographed on silica gel with hexane as eluant to separate the compounds.

Compound (**13a**): $\nu_{max.}$($CHCl_3$) 1 620 cm^{-1} (C=C); δ($CDCl_3$) 1.67 [3 H, s, C=C(*Me*)Me], 1.71 [3 H, d, *J* 1.5 Hz, C=C(Me)*Me*], 2.03 [3 H, d, *J* 1.5 Hz, C(Me)Ar], 2.32 (3 H, s, Ar*Me*), 2.87 (2 H, t, *J* 8 Hz, 4-H_2), 5.11—5.24 (1 H, m, CH=C), 5.71 (1 H, dt, *J* 1.5 and 8 Hz, ArC=C*H*), 7.08 (2 H, d, *J* 8 Hz, ArH), and 7.29 (2 H, d, *J* 8 Hz, ArH); *m/z* 200 (M^+).

Compound (**13b**): $\nu_{max.}$($CHCl_3$) 1 620 cm^{-1} (C=C); δ($CDCl_3$) 1.55 (3 H, s, C=C(*Me*)Me], 1.68 (3 H, d, *J* 1 Hz, C=C(Me)*Me*], 2.12 (2 H, q, *J* 8 Hz, 4-H_2), 2.24 (3 H, s, ArMe), 2.51 (2 H, t, *J* 8 Hz, 3-H_2), 5.01 and 5.24 (each 1 H, each d, *J* 1.5 Hz, C=CH_2),

5.06—5.20 (1 H, m, CH=C), 7.10 (2 H, d, *J* 8 Hz, ArH), and 7.32 (2 H, d, *J* 8 Hz, ArH); *m/z* 200 (M^+).

Epoxidation of Compound (**13**) *with* m-*Chloroperbenzoic Acid.*—To a stirred solution of (**13**) (24.12 g, 0.12 mol) in dichloromethane (500 ml) and saturated sodium hydrogen carbonate solution (200 ml) was added dropwise a solution of *m*-chloroperbenzoic acid (29.58 g, 0.12 mol) in dichloromethane (300 ml) at 0 °C, and the resultant mixture was stirred for 1.5 h at 0 °C. The organic layer was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure to afford an oil; this was chromatographed on silica gel (500 g), with benzene as eluant, giving a mixture (22.14 g, 85%) of 5,6-*epoxy*-6-*methyl*-2-p-*tolylhept*-2-*ene* (**14a**) and its isomer, the 1-*ene* (**14b**), as a colourless oil [(**14a**):(**14b**) = 1 : 2 w/w]. A small portion of the mixture was carefully rechromatographed on silica gel with benzene–hexane (4:1 v/v) as eluant, and the isomers thus separated.

Compound (**14a**) (Found: C, 82.8; H, 9.35. $C_{15}H_{20}O$ requires C, 83.3; H, 9.3%); $\nu_{max.}$($CHCl_3$) 1 620 (C=C) and 1 110 cm^{-1} (epoxide); δ($CDCl_3$) 1.23 (6 H, s, 6-Me × 2), 1.97 (3 H, s, C=CMe), 2.20—2.39 (2 H, m, 4-H_2), 2.27 (3 H, s, Ar*Me*), 2.60 (1 H, dd, *J* 5 and 6 Hz, 5-H), 5.60 (1 H, t, *J* 7 Hz, ArC=C*H*), 6.83 (2 H, d, *J* 8 Hz, ArH), and 7.09 (2 H, d, *J* 8 Hz, ArH); *m/z* 216 (M^+).

Compound (**14b**) (Found: C, 82.6; H, 9.35. $C_{15}H_{20}O$ requires C, 83.3; H, 9.3%); $\nu_{max.}$($CHCl_3$) 1 620 (C=C) and 1 110 cm^{-1} (epoxide); δ($CDCl_3$) 1.17 and 1.25 (each 3 H, each s, 6-Me × 2), 1.66 (2 H, q, *J* 7 Hz, 4-H_2), 2.32 (3 H, s, Ar*Me*), 2.61—2.76 (3 H, m, 3-H_2 and 5-H), 5.04 and 5.27 (each 1 H, each s, C=CH_2), 7.09 (2 H, d, *J* 8 Hz, ArH), and 7.28 (2 H, d, *J* 8 Hz, ArH); *m/z* 216 (M^+).

Cleavage of the Epoxide (**14**) *with Sodium Thiophenolate.*—A solution of sodium thiophenolate (18.58 g, 140.6 mmol) and (**14**) (15.2 g, 70.3 mmol) in ethanol (800 ml) was refluxed for 48 h. After removal of the solvent under reduced pressure, the residue was diluted with benzene and the benzene layer was washed with water and brine, and dried (Na_2SO_4). Removal of the solvent afforded a yellow oil, which was chromatographed on silica gel (300 g) with benzene–hexane (4:1 v/v) as eluant to give a mixture (16.73 g, 73%) of 6-*methyl*-5-*phenylthio*-2-p-*tolylhept*-2-*en*-6-*ol* (**15a**) and its isomer, the 1-*ene* (**15b**), as a yellow oil [(**15a**):(**15b**) = 1 : 2 w/w]. This mixture was separated carefully by chromatography on silica gel (400 g) with benzene–hexane (8:3 v/v) as eluant. The first elution afforded (**15b**) (10.7 g, 46.7%) and the second elution gave (**15a**) (5.7 g, 24.9%).

Compound (**15a**) (Found: C, 77.55; H, 7.85. $C_{21}H_{26}OS$ requires C, 77.25; H, 8.05%); $\nu_{max.}$($CHCl_3$) 3 500 (OH) and 1 620 cm^{-1} (C=C); δ($CDCl_3$) 1.28 and 1.35 (each 3 H, each s, 6-Me × 2), 2.0 (3 H, s, 2-Me), 2.27 (3 H, s, ArMe), 2.48—2.75 (2 H, m, 4-H_2), 3.16 (1 H, dd, *J* 4 and 10 Hz, 5-H), 5.84 (1 H, t, *J* 7 Hz, ArC=C*H*), and 7.05—7.47 (9 H, m, ArH); *m/z* 326 (M^+).

Compound (**15b**) (Found: C, 77.6; H, 7.9. $C_{21}H_{26}OS$ requires C, 77.25; H, 8.05%); $\nu_{max.}$($CHCl_3$) 3 500 cm^{-1} (OH); δ($CDCl_3$) 1.15 and 1.18 (each 3 H, each s, 6-Me × 2), 1.58—1.77 (2 H, m, 4-H_2), 2.33 (3 H, s, Ar*Me*), 2.59 (2 H, m, 3-H_2), 3.08 (1 H, dd, *J* 3 and 11 Hz, 5-H), 4.83 and 5.19 (each 1 H, each s, C=CH_2), and 7.05—7.54 (9 H, m, ArH); *m/z* 326 (M^+).

Reaction of Compound (**15**) *with Trifluoroacetic Acid.*—(*a*) To a stirred solution of (**15b**) (15 g, 39.9 mmol) in anhydrous dichloromethane (400 ml) was added dropwise a solution of trifluoroacetic acid (65 ml) and trifluoroacetic anhydride (1 ml) under nitrogen at 0 °C, and the resultant mixture was stirred for 7 h at room temperature. The reaction mixture was poured into saturated sodium hydrogen carbonate solution (400 ml), and extracted with dichloromethane. The extract was washed with water and brine, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (500 g) with benzene–hexane (1:3 v/v) as eluant. The first elution gave 5,5-*dimethyl*-4-*phenylthio*-1-p-*tolylcyclohex*-1-*ene* (**16**) (4.6 g, 37.5%) as a colourless oil; the second elution gave a mixture (2.41 g) of (3S)-2,2,6-*trimethyl*-3-*phenylthio*-6-p-*tolyltetrahydropyran* (**17**) and 2-*methyl*-3-(1-*methyl*-1-*phenylthioethyl*)-2-p-*tolylcyclobutan*-1-*ol* (**19**); the third elution gave (3R)-2,2,6-*trimethyl*-3-*phenylthio*-6-p-*tetrahydropyran* (**18**) (1.4 g, 10.8%) as a colourless oil; further elution with benzene afforded a mixture of isomers (**15a**) and (**15b**) (4.24 g) [(**15a**):(**15b**) = 2:1 w/w]. The crystalline compound (**17**) was separated from the oily compound (**19**) by filtration with hexane and then purified by recrystallisation from hexane. Thus products (**17**) (2 g, 15.4%) and (**19**) (0.4 g, 3.1%) were obtained.

Compound (**16**) (Found: M^+, 308.1580. $C_{21}H_{24}S$ requires M^+, 308.1597); $\nu_{max.}$($CHCl_3$) 1 640 cm^{-1} (C=C); δ($CDCl_3$) 1.08 and 1.18 (each 3 H, each s, 5-Me × 2), 1.25—2.34 (4 H, m, 3-H_2 and 6-H_2), 3.23 (1 H, dd, *J* 6 and 8 Hz, 4-H), 5.91 (1 H, m, ArC=C*H*), and 7.00—7.49 (9 H, m, ArH); *m/z* 308 (M^+).

Compound (**17**) (Found: C, 76.9; H, 8.1. $C_{21}H_{26}OS$ requires C, 77.25; H, 8.05%); δ($CDCl_3$) 1.32 and 1.44 (each 3 H, each s, Me × 2), 1.50 (3 H, s, Me), 1.90—2.20 (4 H, m, 4-H_2 and 5-H_2), 2.33 (3 H, s, Ar*Me*), 3.09 (1 H, m, 3-H), 7.03 (2 H, d, *J* 7 Hz, ArH), 7.34 (2 H, d, *J* 7 Hz, ArH), and 7.24 (5 H, s, SPh); *m/z* 326 (M^+).

Compound (**18**) (Found: M^+, 326.1694. $C_{21}H_{26}OS$ requires M^+, 326.1702); δ($CDCl_3$) 0.69 and 1.36 (each 3 H, each s, 2-Me × 2), 1.44 (3 H, s, 6-Me), 1.94—2.07 (4 H, m, 4-H_2 and 5-H_2), 2.33 (3 H, s, Ar*Me*), 3.09 (1 H, dd, *J* 7 and 8 Hz, 3-H), and 7.04—7.47 (9 H, m, ArH); *m/z* 326 (M^+).

Compound (**19**) (Found: M^+, 326.1683. $C_{21}H_{26}OS$ requires M^+, 326.1703); $\nu_{max.}$($CHCl_3$) 3400 cm^{-1} (OH); δ($CDCl_3$) 1.29 (6 H, s, isopropyl Me), 1.51 (3 H, s, 2-Me), 1.82—2.17 (3 H, m, 3-H and 4-H_2), 2.30 (3 H, s, Ar*Me*), 3.88 (1 H, t, *J* 6 Hz, 1-H), and 7.08—7.64 (9 H, m, ArH); *m/z* 326 (M^+).

(*b*) Treatment of (**15a**) and (**15b**) with trifluoroacetic acid and trifluoroacetic anhydride was carried out in a similar manner with different reaction times and the results are given in the Table.

5,5-*Dimethyl*-4-*phenylsulphinyl*-1-p-*tolylcyclohex*-1-*ene.*—To a stirred solution of compound (**16**) (100 mg, 0.33 mmol) in dichloromethane (10 ml) was added dropwise a solution of *m*-chloroperbenzoic acid (80 mg, 0.33 mmol) in dichloromethane (10 ml) at 0 °C, and the resultant mixture was stirred for 1 h at 0 °C. The organic layer was washed with saturated sodium hydrogen carbonate solution, water, and brine, and dried (Na_2SO_4). Evaporation of the solvent gave an oil, which was chromatographed on silica gel (40 g), with benzene–ethyl acetate (5:1 v/v) as eluant, to give 5,5-dimethyl-4-phenylsulphinyl-1-*p*-tolylcyclohex-1-ene (70 mg, 65.5%) as prisms, m.p. 117—119 °C (from hexane); δ($CDCl_3$) 1.25 and 1.49 (each 3 H, each s, 5-Me × 2), 1.72—2.63 (4 H, m, 3-H_2 and 6-H_2), 2.29 (3 H, s, Ar*Me*), 2.71—3.05 (1 H, m, 4-H), 5.67—5.87 (1 H, m, ArC=C*H*), 6.94 (4 H, s, ArH), and 7.34 (5 H, s, SPh); *m/z* 325 ($M^+ + 1$).

5,5-*Dimethyl*-1-p-*tolylcyclohexa*-1,3-*diene* (**20**).—A solution of 5,5-dimethyl-4-phenylsulphinyl-1-*p*-tolylcyclohex-1-ene (70 mg, 0.22 mmol) in toluene (20 ml) was refluxed for 2 h. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (30 g) with hexane as eluant to give 5,5-*dimethyl*-1-p-*tolylcyclohexa*-1,3-*diene* (**20**) (37 mg, 85%) as a colourless oil (Found: M^+, 198.1398. $C_{15}H_{18}$ requires M^+, 198.1406); $\nu_{max.}$($CHCl_3$) 1 640 cm^{-1} (C=C); δ($CDCl_3$) 1.05 (6 H, s, 5-Me × 2), 2.32 (3 H, s, Ar*Me*), 2.48 (2 H, d, *J* 2 Hz, 6-H_2), 5.64 (1 H, t, *J* 10 Hz, 3-H), 5.98 (1 H, d, *J* 10 Hz, 4-H), 6.22 (1

H, d, *J* 10 Hz, 2-H), 7.08 (2 H, d, *J* 8 Hz, ArH), and 7.33 (2 H, d, *J* 8 Hz, ArH); *m/z* 198 (M^+).

(3S)-2,2,6-*Trimethyl*-3-*phenylsulphinyl*-6-p-*tolyltetrahydropyran*.—To a stirred solution of (**17**) (300 mg, 0.92 mmol) in dichloromethane (30 ml) was added dropwise a solution of *m*-chloroperbenzoic acid (226.8 mg, 0.92 mmol) in dichloromethane (30 ml) at 0 °C. The dichloromethane layer was washed with saturated sodium hydrogen carbonate solution, water, and brine, and dried (Na_2SO_4). Removal of the solvent afforded an oil which was chromatographed on silica gel (40 g) with benzene–ethyl acetate (20:1 v/v) as eluant. The first elution gave (3S)-2,2,6-trimethyl-3-phenylsulphinyl-6-*p*-tolyltetrahydropyran (150 mg, 48%) as a colourless oil; $\nu_{max.}$($CHCl_3$) 1 070 cm^{-1} (sulphoxide); δ($CDCl_3$) 1.27—2.07 (4 H, m, 4-H_2 and 5-H_2), 1.48 and 1.60 (each 3 H, each s, 2-Me × 2), 1.65 (3 H, s, 6-Me), 2.13—2.4 (1 H, m, 3-H), 2.29 (3 H, s, Ar*Me*), 7.01 (2 H, d, *J* 8 Hz, ArH), 7.29 (2 H, d, *J* 8 Hz, ArH), and 7.45 (5 H, s, PhSO); *m/z* 343 ($M^+ + 1$). Further elution with benzene–ethyl acetate yielded (3S)-2,2,6-trimethyl-3-phenylsulphinyl-6-*p*-tolyltetrahydropyran (105 mg, 33%) as prisms (hexane), m.p. 110—112 °C; $\nu_{max.}$($CHCl_3$) 1 070 cm^{-1} (sulphoxide); δ($CDCl_3$) 1.08—1.95 (4 H, m, 4-H_2 and 5-H_2), 1.48 and 1.58 (each 3 H, each s, 2-Me × 2), 1.71 (3 H, s, 6-Me), 2.30 (3 H, s, Ar*Me*), 2.72 (1 H, dd, *J* 5 and 10 Hz, 3-H), 7.05 (2 H, d, *J* 8 Hz, ArH), 7.30 (2 H, d, *J* 8 Hz, ArH), and 7.42 × 7.80 (5 H, m, PhSO); *m/z* 343 ($M^+ + 1$).

(3R)-2,2,6-*Trimethyl*-3-*phenylsulphinyl*-6-p-*tolyltetrahydropyran*. —To a stirred solution of (**18**) (200 mg, 0.6 mmol) in dichloromethane (20 ml) was added dropwise a solution of *m*-chloroperbenzoic acid (150 mg, 0.6 mmol) in dichloromethane (20 ml) at 0 °C. The resulting mixture was washed with saturated sodium hydrogen carbonate solution, water, and brine, and dried (Na_2SO_4). After removal of the solvent, the residue was chromatographed on silica gel (40 g) with benzene–ethyl acetate (10:1 v/v) as eluant to give (3*R*)-2,2,6-trimethyl-3-phenylsulphinyl-6-*p*-tolyltetrahydropyran (95 mg, 45%) as prisms, m.p. 140—142 °C (from hexane); $\nu_{max.}$($CHCl_3$) 1 070 cm^{-1} (sulphoxide); δ($CDCl_3$) 0.89 and 1.30 (each 3 H, each s, 2-Me × 2), 1.12—2.08 (4 H, m, 4-H_2 and 5-H_2), 1.53 (3 H, s, 6-Me), 2.28 (3 H, s, Ar*Me*), 2.6 (1 H, dd, *J* 4 and 14 Hz, 3-H), 7.02 (2 H, d, *J* 8 Hz, ArH), 7.30 (2 H, d, *J* 8 Hz, ArH), and 7.51 (5 H, s, PhSO); *m/z* 343 ($M^+ + 1$).

3,4-*Dehydrocurcumene Ether* (**21**).—(*a*) A solution of (3*S*)-2,2,6-trimethyl-3-phenylsulphinyl-6-*p*-tolyltetrahydropyran (150 mg, 0.44 mmol) in toluene (30 ml) was refluxed for 6 h with stirring. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel (30 g) with benzene–hexane (7:3 v/v) as eluant to give 3,4-*dehydrocurcumene ether* (2,2,6-*trimethyl*-6-p-*tolyl*-5,6-*dihydro*-2H-*pyran*) (**21**) (70 mg, 74%) as a colourless oil (Found: C, 83.4; H, 9.2. $C_{15}H_{20}O$ requires C, 83.3; H, 9.3%); $\nu_{max.}$($CHCl_3$) 1 660 cm^{-1} (C=C); δ($CDCl_3$) 1.05 and 1.32 (each 3 H, each s, 2-Me × 2), 1.52 (3 H, s, 6-Me), 2.31 (3 H, s, Ar*Me*), 2.36 (2 H, d, *J* 9 Hz, 5-H_2), 5.58 (1 H, d, *J* 10 Hz, 3-H), 5.80 (1 H, dt, *J* 4 and 10 Hz, 4-H), 7.03 (2 H, d, *J* 8 Hz, ArH), and 7.33 (2 H, d, *J* 8 Hz, ArH); δ_C($CDCl_3$) 21.1 (q, Ar*Me*), 30.02, 30.26, and 30.46 (m, 3 × *Me*), 34.79 (t, CH_2), 72.46 and 73.68 (each s, C-2 and C-6), 120.85 (d, C-4), 125.87 and 128.55 (each d, C-2′ and C-3′ and C-5′ and C-6′), 134.78 (d, C-3), 136.0 (s, C-4′), and 145.16 p.p.m. (s, C-1′); *m/z* 216 (M^+).

(*b*) A solution of (3*S*)-2,2,6-trimethyl-3-phenylsulphinyl-6-*p*-tolyltetrahydropyran (100 mg, 0.3 mmol) in xylene (30 ml) was refluxed for 18 h with stirring. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel (20 g) with benzene–hexane (7:3 v/v) as eluant to give the product (**21**) (52 mg, 80%), which was identical with the authentic sample obtained above.

(*c*) A solution of (3*R*)-2,2,6-trimethyl-3-phenylsulphinyl-6-*p*-tolyltetrahydropyran (90 mg, 0.26 mmol) in toluene (20 ml) was refluxed for 10 h with stirring. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel (20 g) with benzene–hexane (3:7 v/v) as eluant to give the product (**21**) (50 mg, 88.4%), which was identical with the authentic sample.

Curcumene Ether (**24**).—(*a*) To a stirred solution of (**18**) (100 mg, 0.31 mmol) in ethanol (25 ml) was added Raney nickel (W-2; 6 g) at room temperature, and the resultant mixture was refluxed for 4 h with stirring. The mixture was filtered to remove insoluble material, and the solid was washed with ethanol. The combined filtrate was concentrated under reduced pressure affording an oil, which was chromatographed on silica gel (20 g) with benzene–hexane (1:3 v/v) as eluant to give curcumene ether (2,2,6-trimethyl-6-*p*-tolytetrahydropyran) (**24**) (10 mg, 15%) as a colourless oil (Found: C, 82.75; H, 9.8. Calc. for $C_{15}H_{22}O$: C, 82.5; H, 10.15%); δ(CCl_4) 0.70 and 1.15 (each 3 H, each s, 2-Me × 2), 1.10—1.69 (6 H, m, 3-H_2, 4-H_2, and 5-H_2), 1.27 (3 H, s, 6-Me), 2.26 (3 H, s, Ar*Me*), 7.03 (2 H, d, *J* 8 Hz, ArH), and 7.33 (2 H, d, *J* 8 Hz, ArH); *m/z* 218 (M^+), whose spectral data were identical with those reported.[7]

(*b*) A mixture of (**21**) (26 mg, 0.12 mmol), 10% palladium–carbon (7 mg), and methanol (10 ml) was stirred under hydrogen (1 atm) at room temperature for 12 h. The reaction mixture was filtered and the filtrate was evaporated to give an oil. The residue was chromatographed on silica gel (10 g) with benzene–hexane (3:7 v/v) as eluant to give the product (**21**) (23 mg, 87.7%) as a colourless oil, which was identical with the authentic sample.

2-*Methyl*-3-(1-*phenylsulphinyl*-1-*methylethyl*)-2-p-*tolylcyclobutan*-1-*ol*.—To a stirred solution of (**19**) (300 mg, 0.92 mmol) in dichloromethane (30 ml) was added dropwise a solution of *m*-chloroperbenzoic acid (226.8 mg, 0.92 mmol) in dichloromethane (30 ml) at 0 °C, and the resultant mixture was stirred for 1 h at 0 °C. The reaction mixture was washed with saturated sodium hydrogen carbonate solution, water, and brine, and dried (Na_2SO_4). Removal of the solvent afforded an oil, which was chromatographed on silica gel (50 g) with benzene–ethyl acetate (20:1 v/v) as eluant. The first elution gave 2-methyl-3-(1-phenylsulphinyl-1-methylethyl)-2-*p*-tolylcyclobutan-1-ol (170 mg, 54%) as a colourless oil; $\nu_{max.}$($CHCl_3$) 3 400 (OH), 1 070 cm^{-1} (sulphoxide); δ($CDCl_3$) 0.92 and 1.05 (each 3 H, each s, isopropyl Me), 1.50 (3 H, s, 2-Me), 1.82—2.17 (3 H, m, 3-H and 4-H_2), 2.26 (3 H, s, Ar*Me*), 4.23 (1 H, t, *J* 6 Hz, 1-H), and 6.88—7.40 (9 H, m, ArH); *m/z* 343 ($M^+ + 1$); further elution furnished 2-methyl-3-(1-phenylsulphinyl-1-methylethyl)-2-*p*-tolylcyclobutan-1-ol (134 mg, 42.6%) as a colourless oil; $\nu_{max.}$($CHCl_3$) 3 400 (OH), 1 070 cm^{-1} (sulphoxide); δ($CDCl_3$) 0.98 and 1.40 (each 3 H, each s, isopropyl Me), 1.58 (3 H, s, 2-Me), 1.80—2.21 (3 H, m, 3-H and 4-H_2), 2.31 (3 H, s, Ar*Me*), 3.70 (1 H, t, *J* 7 Hz, 1-H), and 7.00—7.62 (9 H, m, ArH); *m/z* 343 ($M^+ + 1$).

3-*Isopropenyl*-2-*methyl*-2-p-*tolylcyclobutan*-1-*ol* (**22**).—A solution of the sulphide obtained above (170 mg, 0.5 mmol) in toluene (30 ml) was refluxed for 6 h with stirring. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel (20 g) with benzene–hexane (3:7 v/v) as eluant to give 3-*isopropenyl*-2-*methyl*-2-p-*tolylcyclobutan*-1-*ol* (**22**) (70 mg, 65.2%) as a colourless oil. The other diastereoisomer 2-methyl-3-(1-phenylsulphinyl-1-methyl ethyl)-2-*p*-tolylcyclobutan-1-ol (134 mg, 0.39 mmol) was

treated similarly to give (**22**) (50 mg, 60%) as a colourless oil (Found: M^+, 216.1516. $C_{15}H_{20}O$ requires M^+, 216.1515); $\nu_{max.}(CHCl_3)$ 3 400 (OH), 1 650 cm^{-1} (C=C); $\delta(CDCl_3)$ 1.55 (3 H, s, 2-Me), 1.75 (3 H, s, C=CMe), 1.80—2.23 (3 H, m, 3-H and 4-H_2), 2.31 (3 H, s, Ar*Me*), 4.39 (1 H, t, *J* 6 Hz, 1-H), 4.80 and 5.05 (each 1 H, each d, each *J* 2 Hz, C=CH_2), 7.06 (2 H, d, *J* 8 Hz, ArH), and 7.27 (2 H, d, *J* 8 Hz, ArH); *m/z* 216 (M^+).

3-*Isopropyl*-2-*methyl*-2-p-*tolylcyclobutan*-1-*ol* (**23**).—A solution of (**22**) (20 mg, 0.093 mmol) in methanol (10 ml) was stirred for 6 h in the presence of hydrogen (1 atm) at room temperature. The catalyst was filtered through a Celite pad, and the filtrate was concentrated under reduced pressure to afford an oil, which was chromatographed on silica gel (10 g) with benzene–hexane (3 : 7 v/v) as eluant to give 3-*isopropyl*-2-*methyl*-2-p-*tolylcyclobutan*-1-*ol* (**23**) (16 mg, 80%) as a colourless oil (Found: C, 82.75; H, 10.0. $C_{15}H_{22}O$ requires C, 82.5; H, 10.15%); $\nu_{max.}(CHCl_3)$ 3 400 cm^{-1} (OH); $\delta(CDCl_3)$ 0.90 and 1.00 (each 3 H, each d, each *J* 6 Hz, isopropyl *Me*), 1.45—2.26 (4 H, m, 3-H and 4-H_2 and isopropyl C*H*), 1.49 (3 H, s, 2-Me), 2.32 (3 H, s, Ar*Me*), 3.65 (1 H, dd, *J* 7 and 13 Hz, 1-H), 7.08 (2 H, d, *J* 8 Hz, ArH), and 7.30 (2 H, d, *J* 8 Hz, ArH); *m/z* 218 (M^+).

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