Regioselectivity of Radical-induced Bond Cleavages in Epoxides

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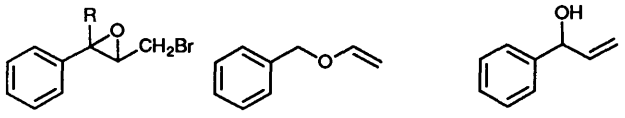
Radical-induced carbon–carbon and carbon–oxygen bond cleavage reactions in a highly substituted epoxide, and in epoxides fused to other rings are reported. Substitution at the site of the developing radical assists C–C bond cleavage. In ring-fused epoxides, C–C bond cleavage was not seen where stereoelectronic factors oppose it.

The cleavage of small rings by adjacent radicals has become a major field of study in recent years. The early mechanistic studies of Davies[1] and Norman[2] and early synthetic studies by Barton[3] have been complemented by mechanistic and synthetic studies by many groups.[4,5] Most of the epoxide cleavages have involved C–O bond cleavage, but from the report of Stogryn and Gianni[6] it was apparent that C–C bond cleavage could be observed with certain substrates. Thus we[7] and others[8] have reported examples of C–C bond cleavage in epoxides adjacent to aromatic rings. In this paper, we have sought evidence for C–C bond cleavage in more complex epoxides.



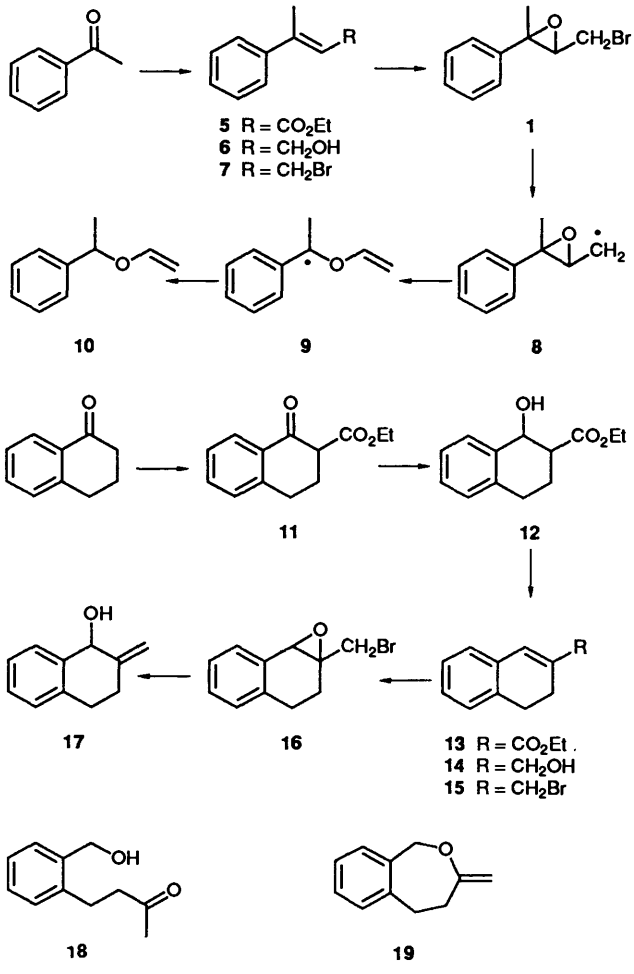
1 R = Me
2 R = H

3

4

Initial studies were performed on the bromo epoxide **1**. In earlier studies,[7] it had been found that two products resulted from reaction of the bromo epoxide **2**. These were the vinyl ether **3** and the allylic alcohol **4**, the products of C–C and C–O bond cleavages respectively. For **1**, it was assumed that a radical resulting from C–C bond scission would be more stabilised than for **2**. It is not yet known if vinyl ether formation occurs as the result of kinetic or thermodynamic control of epoxide cleavage. If the reaction is irreversible, then it is possible that the stability of the ultimate radical is reflected in the transition state leading to the cleavage. If the reaction is reversible,[9] then the C–C bond cleavage should lead to the more stable radical anyway. Hence we wished to investigate if the cleavage of **1** would be regiospecific.

A Reformatsky reaction[10] between acetophenone and ethyl bromoacetate followed by acidic dehydration of the resulting β-hydroxy ester afforded the desired ethyl 3-phenylbut-2-enoate **5**. The α,β-unsaturated ester was cleanly reduced with 2 equiv. of diisobutylaluminium hydride to yield 3-phenylbut-2-en-1-ol **6**. Transformation of this allylic alcohol into the bromide **7** was achieved[11] by treatment with dimethyl sulfide and *N*-bromosuccinimide at −10 °C. No evidence of allylic transposition was found. Epoxidation of **7** with *m*CPBA proceeded rapidly affording the desired 2-bromomethyl-3-phenyloxirane **1**. It was not possible to distil this epoxide without decomposition. Treatment of the bromo epoxide with tributyltin hydride and AIBN under reflux in diethyl ether for 32 h led to C–C bond rupture giving the radical **9** which abstracted hydrogen from tributyltin hydride to afford the vinyl ether **10**. No allylic alcohol analogous to **4** was isolated or observed in the NMR spectra of the crude reaction mixture. Hence the incorporation of the C-3 methyl group has a marked effect on product distribution on comparison with **2**.



5 R = CO_2Et
6 R = CH_2OH
7 R = CH_2Br

1

10 **9** **8**

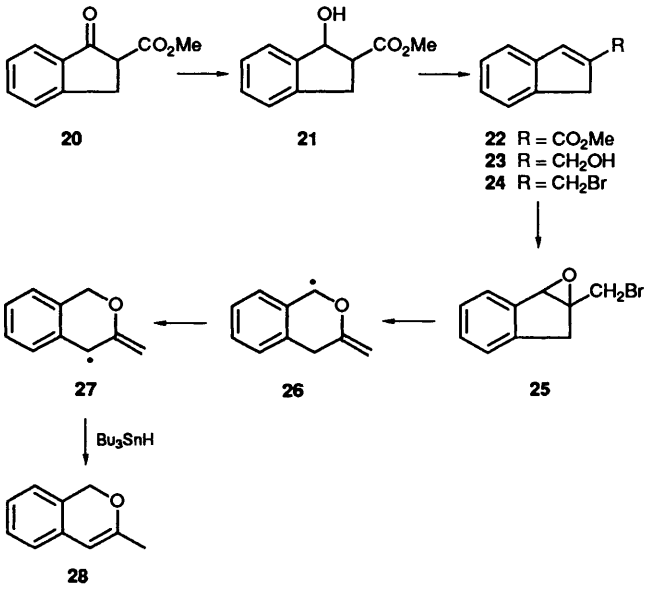
11 **12**

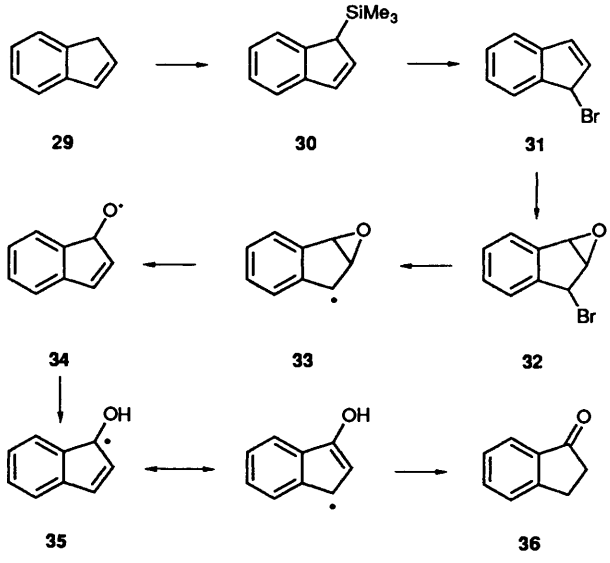
17 **16**

13 R = CO_2Et
14 R = CH_2OH
15 R = CH_2Br

18 **19**

None of the examples of C–C bond cleavage so far has featured a ring-fused epoxide.[12] To explore the chemistry of these systems, three epoxides were prepared, **16**, **25** and **32**. The tetrahydronaphthalene **16** was synthesised from tetralone as shown. Treatment with tributyltin hydride afforded two products. Spectroscopic data were consistent with 4-[2-(hydroxymethyl)phenyl]butan-2-one **18** and 1-hydroxy-2-methylene-1,2,3,4-tetrahydronaphthalene **17**. The hydroxy ketone can only arise from C–C bond scission of the oxirane and presumably involved the oxepane **19** as an intermediate, which underwent facile hydration on silica to yield a hemiketal which tautomerised to its acyclic isomer.[13] (Attempts to trap the oxepane with tetracyclone[14] or tetracyanoethylene[15] were unsuccessful.) This substrate **16** therefore undergoes both C–C and C–O bond cleavage similar to molecule **2**.





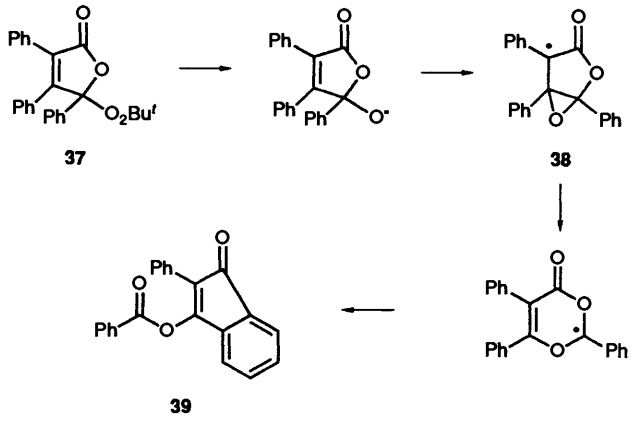
The indanone, **20**, was similarly converted into the bromo epoxide **25**. Indanone **20** was best obtained by treatment of the lithium salt of indanone with dry carbon dioxide gas, careful acidification and reaction with diazomethane.

The reaction of **25** with tributyltin hydride and AIBN surprisingly gave the chromene **28** as the sole isolated product. This is an isomer of one of the expected products and necessarily arises from C–C bond homolysis. Its formation requires the benzyl radical **26** formed after initial C–C bond scission to undergo an inter- or intra-molecular hydrogen atom abstraction yielding an isomeric radical **27**. Hydrogen atom abstraction from tributyltin hydride then gives the chromene.

The final epoxide studied was 1-bromo-2,3-epoxy-2,3-dihydroindene **32**. This was prepared to probe the stereoelectronic requirements of the homolytic cleavage.[5,16] Synthesis of the required halogeno epoxide **32** necessitated the preparation of 1-bromoindene **31**. Attempts to generate this allylic bromide from *N*-bromosuccinimide and indene were made[17] as early as 1944; however yields were found to be poor or variable in our hands. Therefore we chose to use an alternative route *via* the silylindene. Treatment of indene with butyllithium at 30 °C and quenching of the intermediate indenyllithium with chlorotrimethylsilane afforded 1-trimethylsilylindene **30**. Reaction of this silylindene[18] with dioxane dibromide in chloroform gave a deep red oil. Purification of this oil on alumina afforded 1-bromoindene as a pale yellow liquid, and epoxidation gave the bromo epoxide **32**.

Reaction of this compound with tributyltin hydride and AIBN in tetrahydrofuran (THF) surprisingly generated indanone as the sole isolated product. This compound results from expected C–O bond cleavage to yield the radical **34**. Being an oxyl radical this must be more unstable than the isomeric radical **35**, and so hydrogen atom abstraction either directly by the oxyl radical or possibly *via* an indirect route using tributyltin radicals gives the more stable **35**, which is easily converted into indanone. Since this sole isolated product results from kinetically favoured C–O bond cleavage, this reaction is subject to the same stereoelectronic requirements as the corresponding cyclopropane cleavage[16] and cleavage of alkyl-substituted epoxides. This is very interesting since homolysis of the peroxide **37** at 115–120 °C has been shown[12] to lead to the indanone **39**, and it has been suggested that this results from the pathway shown. Here, the constrained radical **38** causes C–C bond cleavage contrary to the stereoelectronic bias but giving the thermodynamically more stable radical. It is not known if initial reversible C–O bond cleavage has occurred and if the absence of a suitable hydrogen atom source to quench the reaction has permitted the isolation of the indanone **39**.

It is seen that in these more complicated examples, products resulting from C–C bond cleavage are observed, but not in the case of **33**, where stereoelectronic factors[5] direct C–O bond cleavage. The isolation of the vinyl ether **10** as the sole isolated product from cleavage of the epoxide in radical **8** indicates that the extent of substitution of the developing radical centre plays a role in determining the regioselectivity of cleavage.



Experimental

IR spectra were obtained on a Pye-Unicam SP3-100 spectrometer. ^{1}H NMR spectra were recorded at 90 MHz on a Perkin-Elmer R32, at 250 MHz on a Bruker WM 250, and at 400 MHz on a Bruker AM 400 instrument. ^{13}C NMR spectra were recorded at 22.5 MHz on a JEOL FXC90Q, at 63 MHz on a Bruker WM 250 and at 100 MHz on a Bruker AM 400 instrument. All NMR experiments were carried out in $CDCl_3$ with tetramethylsilane as internal reference; *J* values are given in Hz. UV spectra were recorded on a Philips PU8700 series instrument. Mass spectra were recorded on a VG micromas 70E or an AEI MS902 instrument. All solvents were distilled before use. Tetrahydrofuran (THF) was distilled from potassium–benzophenone. Chromatography was performed on Kieselgel 60 (Fluka).

Ethyl 3-Phenylbut-2-enoate[19] **5**.—An aliquot (10 cm^3) of a solution of ethyl bromoacetate (20.57 g, 0.125 mol) and

acetophenone (18.38 g, 0.153 mol) in diethyl ether (15 cm^3) and benzene (40 cm^3) was added to activated zinc dust (10.2 g, 0.152 mol). When reaction started, the rest of the solution was added at such a rate to allow a rapid but controlled reflux. After complete addition, the reaction mixture was heated under reflux for a further hour, cooled and poured onto a mixture of crushed ice (25 g) and sulfuric acid (2 mol dm^{-3}, 50 cm^3). Extraction into diethyl ether and evaporation yielded a crude brown oil which was added to toluene (300 cm^3) and toluene-*p*-sulfonic acid (50 mg). Water was removed as an azeotrope by using a Dean–Stark apparatus, and the residue was chromatographed (95:5 hexane–diethyl ether) to afford ethyl 3-phenylbut-2-enoate **5** as a pale yellow oil (16.46 g, 55%); ν_{max}/cm^{-1} 3070, 2993, 1714, 1635 and 1178; δ_H(80 MHz; $CDCl_3$) 1.30 (3 H, t, *J* 7.15, $CO_2CH_2CH_3$), 2.56 [3 H, d, *J* 1.3, $PhC(CH_3)$=CR], 4.20 (2 H, q, *J* 7.15, $CO_2CH_2CH_3$), 6.12 (1 H, q, *J* 1.3, 2-H) and 7.25–7.54 (5 H, m, Ph); *m*/*z* 190 (M^+, 100%), 161 (45) and 145 (78).

3-*Phenylbut*-2-*enol* **6**.—Diisobutylaluminium hydride (100 mmol) in hexanes was added dropwise to a solution of the α,β-unsaturated ester (9.04 g, 47.5 mmol) in dry ether (50 cm^3) at −30 °C. The mixture was then stirred at room temp for 12 h before being cautiously added to moist diethyl ether (100 cm^3) and then vigorously stirred with sodium hydroxide (2 mol dm^{-3}, 75 cm^3). The separated ethereal phase was washed with brine, dried over sodium sulfate, filtered and evaporated to yield the allylic alcohol **6** as a colourless oil[20] (6.28 g, 89.5%); ν_{max}/cm^{-1} 3360, 3031, 2929 and 1445; δ_H(90 MHz; $CDCl_3$) 1.99 (3 H, s, Me), 2.93 (1 H, br s, OH), 4.28 (2 H, d, *J* 6.5, CH_2OH), 5.92 [1 H, dt, *J* 1.3, 6.5, $PhC(CH_3)$=C*H*CH_2OH] and 7.18–7.34 (5 H, m, Ph); *m*/*z* 148 (M^+, 85%), 133 (32) and 130 (100).

1-*Bromo*-3-*phenylbut*-2-*ene* **7**.—A solution of dimethyl sulfide (2.62 g, 42.2 mmol) in dichloromethane (15 cm^3) was added dropwise over 10 min to a stirred suspension of *N*-bromosuccinimide (7.62 g, 42.8 mmol) in dry dichloromethane at −10 °C. The yellow suspension was stirred at −10 °C for 5 min and then the allylic alcohol (7.01 g, 42.6 mmol) was added. After stirring at −10 °C for 2 h and at room temp for 1 h, the solvent was evaporated and diethyl ether was added. After washing with brine, the ethereal solution was dried, filtered and evaporated to yield the allylic bromide[20] **7** (6.98 g, 78.1%); δ_H(80 MHz; $CDCl_3$) 2.03 (3 H, d, *J* 1.3, CH_3), 4.52 (2 H, d, *J* 8.55, CH_2Br), 6.01 (1 H, tq, *J* 1.3 and 8.55, MeC=C*H*) and 7.25 (5 H, m, Ph); *m*/*z* 131 (M^+ − Br, 100%), 130 (98) and 115 (63).

2-*Bromomethyl*-3-*methyl*-3-*phenyloxirane* **1**.—A solution of the allylic bromide **7** (7.0 g, 33.3 mmol) in dichloromethane (65 cm^3) was added dropwise over 30 min to a suspension of *m*-chloroperbenzoic acid (6.0 g, 34.7 mmol) in dichloromethane (15 cm^3). The mixture was stirred for 3 h, and then washed with sodium sulfite (10% w/v, 100 cm^3) until a negative reaction with starch–iodide paper was obtained, and then with sodium hydrogen carbonate, brine and finally water. The solution was dried, filtered and evaporated to leave a residue which was chromatographed (2:1 hexane–dichloromethane) to yield 2-*bromomethyl*-3-*methyl*-3-*phenyloxirane* **1** as a colourless oil (7.05 g, 93%); ν_{max}/cm^{-1} 3051, 3020, 2982 and 1219; δ_H(400 MHz; $CDCl_3$) 1.71 (3 H, s, CH_3), 3.21 (1 H, dd, *J* 6.2 and 7.3, OC*H*CH_2Br), 3.42–3.63 (2 H, 2 × dd, *J* 6.2, 7.3 and 10.5, CH_2Br) and 7.34 (5 H, m, Ph); δ_C(22.5 MHz; $CDCl_3$) 17.54, 20.37, 62.86, 64.04, 125.09, 127.59, 128.34 and 141.51; *m*/*z* 227 (M^+, 1%), 225 (M^+, 1%), 147 (100) (Found: M^+, 227.0095. $C_{10}H_{11}BrO$ requires *M*, 227.0030).

Homolytic Cleavage of 2-*Bromomethyl*-3-*methyl*-3-*phenyloxirane*.—Tributyltin hydride (0.644 g, 2.21 mmol) and azoisobutyronitrile (10 mg) were dissolved in diethyl ether (10 cm^3) and added over 24 h to a refluxing solution of bromo epoxide **1** (0.5 g, 2.21 mmol). After 8 h, the solvent was evaporated and the residue chromatographed (using silica impregnated with 2% w/w sodium hydrogen carbonate) to yield the vinyl ether **10** as a colourless oil (0.134 g, 41%); ν_{max}/cm^{-1} 3040, 3020, 2980, 1630 and 1195; δ_H(90 MHz; $CDCl_3$) 1.50 (3 H, d, *J* 6.5, CH_3), 3.97 (1 H, dd, *J* 1.5 and 6.5, CH=CH_2, *cis*), 4.26 (1 H, dd, *J* 1.5 and 14.2, CH=CH_2, *trans*), 4.87 (1 H, q, *J* 6.5, CH_3CH), 6.30 (1 H, dd, *J* 6.5 and 14.2, O–C*H*=CH_2) and 7.29 (5 H, s, Ph); δ_C(22.5 MHz; $CDCl_3$) 23.63, 77.53, 89.34, 125.91, 127.64, 128.61, 143.08 and 150.72; *m*/*z* 148 (M^+, 10%), 144 (10), 105 (100) (Found: M^+, 148.0872. $C_{10}H_{12}O$ requires *M*, 148.0882).

Ethyl 1-*Oxo*-1,2,3,4-*tetrahydronaphthalene*-2-*carboxylate*[21] **11**.—1-Tetralone (20.0 g, 137 mmol) in dry toluene (50 cm^3) was added dropwise under nitrogen to a stirred suspension of toluene-washed sodium hydride (6.6 g, 274 mmol). The resulting dark blue solution was heated under reflux for 30 min, and diethyl carbonate (24.0 g, 137 mmol) was then added. A vigorous exothermic reaction ensued. The resulting suspension was refluxed for 1 h, cooled and quenched with 4 mol dm^{-3} hydrochloric acid (100 cm^3). The solution was diluted with water and extracted with diethyl ether. The extracts were dried, filtered and evaporated and distilled to yield ethyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate **11** as a straw coloured liquid (20.2 g, 61.3%) (b.p. 162 °C at 13 mmHg). ν_{max}/cm^{-1} 3330, 3025, 1733, 1642 and 1272; δ_H(90 MHz; $CDCl_3$) shows mixture of keto and enol forms: 1.34 (3 H, t, *J* 7.0, $CO_2CH_2CH_3$, keto form), 1.38 (3 H, t, *J* 7.0, $CO_2CH_2CH_3$, enol form), 2.20–3.10 (4 H, m, $ArCH_2CH_2R$), 3.59 (1 H, dd, *J* 7.0 and 10.0, R_2CHCO_2, keto form), 4.24 (1 H, q, *J* 7.0, $CO_2CH_2CH_3$, keto form), 4.28 (1 H, q, *J* 7.0, $CO_2CH_2CH_3$, enol form), 7.29 (3 H, m, ArH), 7.78 (1 H, m, Ar-H, enol form), 8.01 (1 H, m, Ar-H, keto form) and 12.5 (1 H, s, enol OH); δ_C(22.5 MHz; $CDCl_3$) 14.12, 14.24, 20.53, 26.36, 27.58, 27.74, 54.55, 60.44, 61.13, 96.96, 124.26, 126.50, 126.79, 127.36, 127.65, 128.76, 130.05, 130.40, 131.80, 133.76, 139.31, 143.63, 165.00, 170.13, 172.69 and 193.07; *m*/*z* 218 (M^+, 100%), 172 (74) and 14 (84) (Found: M^+, 218.0988. $C_{13}H_{14}O_3$ requires *M*, 218.0942).

Ethyl 1-*Hydroxy*-1,2,3,4-*tetrahydronaphthalene*-2-*carboxylate* **12**.—A suspension of sodium borohydride (0.45 g, 10.7 mmol) in absolute ethanol (20 cm^3) was added dropwise to a solution of β-keto ester **11** (9.35 g, 43 mmol) in absolute ethanol (100 cm^3) at −10 °C with stirring. After 6 h, the reaction was quenched with 1 mol dm^{-3} hydrochloric acid (10 cm^3) and water (40 cm^3). The ethanol was removed under reduced pressure and the residues were extracted into diethyl ether (2 × 50 cm^3). The ether extracts were dried, filtered and evaporated to give a yellow oil which was chromatographed (90:10 hexane–ethyl acetate) to give *ethyl* 1-*hydroxy*-1,2,3,4-*tetrahydronaphthalene*-2-*carboxylate* **12** as a pale yellow oil (4.85 g, 51.4%); ν_{max}/cm^{-1} 3461, 3062, 2940 and 1721; δ_H(90 MHz; $CDCl_3$) 1.27 (3 H, t, *J* 7.0 $CO_2CH_2CH_3$), 2.11 (2 H, m, $ArCH_2CH_2$), 2.80 [3 H, m, $ArCH_2CH_2CH(CO_2Et)$], 3.04 (1 H, br s, OH), 4.19 (2 H, q, *J* 7.0, $CO_2CH_2CH_3$), 5.01 (1 H, 2 × d, *J* 3.0, ArC*H*[OH]) and 7.15 (4 H, m, ArH); δ_C(22.5 MHz; $CDCl_3$) 13.93, 19.51, 24.06, 28.12, 45.46, 48.49, 60.46, 67.56, 69.40, 125.96, 126.8, 126.99, 127.75, 127.96, 128.64, 129.64, 135.28, 135.82, 136.80, 137.89, 173.90 and 174.51; *m*/*z* (FAB) 220 (M^+, 3%) and 203 (100).

Ethyl 3,4-*Dihydronaphthalene*-2-*carboxylate*[22] **13**.—Ethyl 1-hydroxy-1,2,3,4-tetrahydronaphthalene-2-carboxylate **12** (4.05 g, 18 mmol) was added to a solution of toluene-*p*-sulfonic acid (0.2 g) in toluene (75 cm^3). The resulting solution was refluxed using a Dean–Stark apparatus until no further water was collected. The solvent was evaporated and the residue distilled

to yield ethyl 3,4-dihydronaphthalene-2-carboxylate **13** (3.48 g, 94%) (121 °C at 2.5 mmHg); ν_{max}/cm^{-1} 3060, 2980, 1701 and 1211; δ_H(90 MHz; $CDCl_3$) 1.35 (3 H, t, *J* 7.0, $CO_2CH_2CH_3$), 2.74 (4 H, m, $ArCH_2CH_2$), 4.27 (2 H, q, *J* 7.0, $CO_2CH_2CH_3$), 7.20 (4 H, s, ArH) and 7.51 (1 H, t, *J* 1.4, ArCH=C); δ_C(22.5 MHz; $CDCl_3$) 14.42, 22.38, 27.69, 60.63, 126.77, 128.45, 129.43, 129.70, 132.73, 136.31, 137.01 and 167.46; *m/z* 202 (M^+, 38%), 173 (20), 157 (21) and 129 (100) (Found: M^+, 202.0964. $C_{13}H_{14}O_2$ requires *M*, 202.0998).

1,2-*Dihydro*-3-*hydroxymethylnaphthalene*[22] **14**.—A solution of the unsaturated ester **13** (4.0 g, 20.1 mmol) in dry diethyl ether (100 cm^3) was cooled to −40 °C. An excess of diisobutylaluminium hydride in hexanes (40 cm^3, 60 mmol) was added over 30 min. The resulting solution was allowed to warm to room temperature and to stir for 12 h and was then quenched with water (2 cm^3) and then sodium hydroxide (2 mol dm^{-3}) was added. The mixture was extracted with diethyl ether, the ether extracts were washed with brine, dried over magnesium sulfate, filtered and evaporated. The residue was chromatographed (hexane–ethyl acetate) affording the alcohol **14** as a colourless oil (2.87 g, 91%); ν_{max}/cm^{-1} 3355, 3020 and 2863; δ_H(90 MHz; $CDCl_3$) 2.24 (2 H, t, *J* 8.5, $ArCH_2CH_2$), 2.30 (1 H, br s, OH), 2.81 (2 H, t, *J* 8.5, $ArCH_2CH_2$), 4.17 (2 H, s, CH_2OH), 6.41 (1 H, t, *J* 1.3, $ArCH{=}CR_2$) and 7.08 (4 H, m, ArH); δ_C(22.5 MHz; $CDCl_3$) 24.38, 27.85, 66.04, 122.44, 126.07, 126.52, 126.83, 127.31, 134.03, 134.95 and 140.42; *m/z* 160 (M^+, 81%), 142 (54) and 129 (100) (Found: M^+, 160.0901. $C_{11}H_{12}O$ requires *M*, 160.0908).

3-*Bromomethyl*-1,2-*dihydronaphthalene* **15**.—A stirred suspension of *N*-bromosuccinimide (2.54 g, 14.2 mmol) in dry dichloromethane (3 cm^3) was cooled to −30 °C. A solution of dimethyl sulfide (0.93 g, 14.1 mmol) in dichloromethane (10 cm^3) was added over a period of 5 min. The unsaturated alcohol **14** (2.21 g, 14.1 mmol) dissolved in dry dichloromethane (10 cm^3) was added dropwise and the mixture was stirred for 5 h. The solvent was removed and ether (50 cm^3) was added. The ether solution was washed with brine, dried, filtered and evaporated to yield the 3-bromomethyl-1,2-dihydronaphthalene **15** (3.1 g, 87%). This unstable allylic bromide was used immediately without further purification; ν_{max}/cm^{-1} 3020 and 1238; δ_H(90 MHz; $CDCl_3$) 2.41 (2 H, t, *J* 8.7, $ArCH_2CH_2$), 2.84 (2 H, t, *J* 8.7, $ArCH_2CH_2$), 4.13 (2 H, s, CH_2Br), 6.54 (1 H, s, ArCH=C) and 7.12 (4 H, m, ArH).

2-*Bromomethyl*-1,2,3,4-*tetrahydronaphthalene* 1,2-*Oxide* **16**.—A solution of the allylic bromide **14** (3.1 g, 13.7 mmol) in dry dichloromethane (25 cm^3) was cooled to −10 °C. *m*-Chloroperbenzoic acid (3.6 g, 21 mmol) in dichloromethane was added. This solution was stirred for 12 h at 0 °C, filtered and then washed with sodium sulfite solution until a negative reaction with starch–iodide paper was obtained. The organic layer was then washed with sodium hydrogen carbonate solution, with brine and with water, dried, filtered and evaporated to yield crude product. Column chromatography (hexane) afforded 2-*bromomethyl*-1,2,3,4-*tetrahydronaphthalene* 1,2-*oxide* **16** as a white solid (3.06 g, 92%) (m.p. 38 °C) (Found: C, 55.2; H, 4.6; Br, 33.4. Calc. for $C_{11}H_{11}BrO$. C, 55.4; H, 4.8; Br, 33.8%); ν_{max}/cm^{-1} 2942, 1221 and 771; δ_H(90 MHz; $CDCl_3$) 1.8–2.1 (1 H, m, 3-H), 2.35–3.10 (3 H, m, 3-H and CH_2CH_2), 3.84 [1 H, s, $ArCH(O)CR_2$] and 7.32 (4 H, m, Ar); δ_C(22.5 MHz; $CDCl_3$) 23.84, 25.58, 36.85, 60.84, 62.52, 126.34, 128.40, 128.94, 129.43, 131.87 and 136.80; *m/z* (FAB) 237 (M^+, 9%) and 159 (100).

Homolytic Cleavage of Bromo Epoxide **16**.—A solution of tributyltin hydride (0.61 g, 2.15 mmol), AIBN (30 mg), in dry benzene (5 cm^3) was slowly added by motorised syringe to a refluxing solution of the bromo epoxide **16** (0.50 g, 2.1 mmol) in dry benzene. After 24 h, the solvent was removed and the residue chromatographed (hexane–dichloromethane) to afford two products:

4-[2-(Hydroxymethyl)phenyl]butan-2-one[13] **18** (0.133 g, 34.7%); ν_{max}/cm^{-1} 3448, 3064, 2936, 1720 and 756; δ_H(400 MHz; $CDCl_3$) 2.03 (3 H, s, CH_3), 2.73 (4 H, m, 3-H and 4-H), 4.60 (1 H, s, OH), 5.23 (2 H, s, CH_2OH) and 7.03–7.26 (4 H, m, ArH); δ_C(100 MHz; CD_2Cl_2) 24.81, 29.03, 43.77, 62.37, 125.56, 127.23, 128.02, 128.14, 138.02, 138.78 and 207.39; *m/z* 178 (M^+, 2%), 160 (42), 117 (100) (Found: M^+, 178.0969. $C_{11}H_{14}O_2$ requires *M*, 178.1001).

1-Hydroxy-2-methylene-1,2,3,4-tetrahydronaphthalene **17** (0.071 g, 21%); ν_{max}/cm^{-1} 3365, 3070, 2929 and 1655; δ_H(90 MHz; $CDCl_3$) 1.90 (1 H, br s, OH), 2.44–2.75 (2 H, m, $ArCH_2CH_2$), 2.83–3.08 (2 H, m, $ArCH_2CH_2$), 5.18 (3 H, m, $C{=}CH_2$ and 1-H), 7.09–7.41 (3 H, m, Ar-H) and 7.48–7.67 (1 H, m, Ar-H); δ_C(22.5 MHz; $CDCl_3$) 29.15, 31.10, 71.81, 109.71, 126.66, 127.80, 128.51, 137.12, 138.85 and 148.39; *m/z* 160 (M^+, 100%), 145 (33) and 116 (27) (Found: M^+, 160.0887. $C_{11}H_{12}O$ requires *M*, 160.0908).

Methyl 1-*Oxoindan*-2-*carboxylate* **20**.—Indan-1-one (4.05 g, 30.2 mmol) was dissolved in dry THF (30 cm^3) and cooled to −78 °C. Lithium diisopropylamide (32.5 mmol) in THF was then added. The mixture was stirred for 15 min, and carbon dioxide was bubbled through the solution. After warming to room temp., the addition of carbon dioxide was continued for a further hour, and then the reaction solvent was evaporated. The colourless solid was dissolved in water, carefully acidified and extracted with diethyl ether, and the resulting acid was esterified with diazomethane and purified by chromatography (1:1 hexane–chloroform) to yield the title compound **20** as a pale yellow oil. (3.16 g, 54%). ν_{max}/cm^{-1} 3418, 2954, 1742, 1714 and 1654; δ_H(90 MHz; $CDCl_3$) 3.21–3.80 (3 H, m, aliphatic 2-H, 3-H, 3'-H), 3.78 (3 H, s, OMe), 6.98–7.74 (4 H, m, Ph) and 10.4 (0.1 H, enolic OH); δ_C(22.5 MHz; $CDCl_3$) 25.76, 30.27, 32.44, 36.07, 52.43, 53.08, 120.58, 123.51, 124.10, 124.43, 124.64, 126.49, 126.59, 127.14, 127.68, 129.30, 134.45, 135.26, 153.46, 169.45, 198.86 and 199.19; *m/z* 190 (M^+, 44%), 159 (22), 130 (100), 103 (65) and 77 (40) (Found: M^+, 190.0662; $C_{11}H_{10}O_3$ requires *M*, 190.0670).

Methyl Indene-2-*carboxylate* **22**.—Sodium borohydride (0.94 g, 24.8 mmol), was added cautiously to methanol (30 cm^3). To this suspension was slowly added a solution of the keto ester **20** (4.27 g, 24.7 mmol) in methanol (15 cm^3). The resulting solution was stirred at room temp. and monitored by TLC. When iron(III) chloride no longer showed the presence of the keto ester, the excess of methanol was evaporated and the residue dissolved in 1 mol dm^{-3} hydrochloric acid, and extracted with diethyl ether. The extracts were combined, dried, filtered and evaporated, and then heated under reflux in toluene (150 cm^3) with toluene-*p*-sulfonic acid (0.5 g) for 4 h. The residue obtained after evaporation of the solvent was chromatographed in 3:1 hexane–chloroform to give the α,β-unsaturated ester **22** as a pale yellow solid. (1.61 g, 44.1%) (m.p. 36–38 °C) (Found: C, 75.9; H, 5.9. $C_{11}H_{10}O_2$ requires C, 75.8; H, 5.7%); ν_{max}(KBr disk)/cm^{-1} 3060, 1690 and 1236; δ_H(90 MHz; $CDCl_3$) 3.66 (2 H, d, *J* 1.75, $ArCH_2R$), 3.83 (3 H, s, CO_2Me) 7.35 (4 H, m, ArH), 7.71 (1 H, t *J* 1.5, $ArCH{=}C[CO_2Me]$); δ_C(22.5 MHz; $CDCl_3$) 38.42, 51.52, 123.36, 124.23, 126.88, 127.59, 137.12, 141.13, 142.75, 144.81 and 165.35; *m/z* 174 (M^+, 53%), 143 (20), 115 (100) (Found: M^+, 174.0682. $C_{11}H_{10}O_2$ requires *M*, 174.0710).

2-*Hydroxymethylindene* **23**.—A hexane solution of diisobutylaluminium hydride (15.5 cm^3, 15.5 mmol) was added dropwise

over 20 min to a stirred solution of the unsaturated ester **22** (1.26 g, 7.7 mmol) in dry diethyl ether (40 cm^3) at −78 °C. The resulting mixture was allowed to warm up to room temperature and was stirred for a further 8 h, before being pipetted onto 2 mol dm^{-3} sodium hydroxide. The mixture was extracted with diethyl ether (2 × 50 cm^3), the aqueous residues were neutralised with 2 mol dm^{-3} hydrochloric acid and re-extracted with ethyl acetate. The combined organic phases were washed with brine (2 × 50 cm^3) dried over magnesium sulfate, filtered and evaporated and the residue chromatographed [3:1 hexane–chloroform] to give *2-hydroxymethylindene* **23** as a straw coloured oil (1.06 g, 96%); ν_{max}/cm^{-1} 3352, 3081, 2916 and 1416; δ_H(90 MHz; $CDCl_3$) 3.66 [2 H, s, $ArCH_2C(CH_2OH)$], 4.22 (1 H, br s, OH), 4.33 (2 H, s, CH_2OH), 6.54 [1 H, s, $ArCH{=}C(CH_2OH)$] and 7.05–7.31 (4 H, m, ArH); δ_C(22.5 MHz; $CDCl_3$) 38.58, 61.19, 120.49, 123.47, 124.17, 126.12, 127.15, 143.13, 144.43 and 148.55; *m/z* 146 (M^+, 67%), 128 (83) and 116 (100) (Found: M^+, 146.0728. $C_{10}H_{10}O$ requires *M*, 146.0731).

2-Bromomethylindene **24**.—A stirred suspension of *N*-bromosuccinimide (1.48 g, 8.35 mmol) in dry dichloromethane (3 cm^3) was cooled to −30 °C. A solution of dimethyl sulfide (0.495 g, 7.97 mmol) in dichloromethane (5 cm^3) was added dropwise over 10 min. The yellow suspension was stirred for 5 min at −30 °C before adding a solution of the alcohol (1.02 g, 7.59 mmol) in dichloromethane (10 cm^3). The mixture was stirred for 3 h, and then allowed to come to room temp. and allowed to stir for a further hour. After evaporation of the solvent, the residue was extracted with diethyl ether and these extracts were washed with ice-cold brine. The organic extracts were dried, filtered and evaporated to give a dark oil which was chromatographed (alumina; 40–60 light petroleum) yielding *2-bromomethylindene* **24** as a yellow oil (1.53 g, 91.3%); ν_{max}/cm^{-1} 3069, 2931 and 1241; δ_H(90 MHz; $CDCl_3$) 3.15 [2 H, s, $ArCH_2C(CH_2Br)$], 4.40 (2 H, s, CH_2Br), 6.83 [1 H, br s, $ArCH{=}C(CH_2Br)$] and 7.05–7.63 (4 H, m, ArH); δ_C(22.5 MHz; $CDCl_3$) 30.45, 39.82, 121.41, 123.90, 125.47, 126.66, 131.76, 143.78, 144.16 and 144.38; *m/z* 210 (M^+, 14%), 208 (M^+, 15%) and 129 (100) (Found: M^+, 209.9856. $C_{10}H_9Br$ requires *M*, 209.9831) (Found: M^+, 207.9885. $C_{10}H_9Br$ requires *M*, 207.9871).

2-Bromomethylindene 1,2-Oxide **25**.—A suspension of *m*-chloroperbenzoic acid (1.28 g, 7.5 mmol) in dichloromethane (15 cm^3) was slowly added to a solution of the allylic bromide **24** (1.05 g, 5.07 mmol) cooled to 0 °C. The resulting solution was stirred for 1 h at 0 °C and for 12 h at room temp. The precipitate was filtered and the filtrate was washed with a solution of sodium sulfite (20% w/v), until a negative reaction to starch–iodide paper was obtained, and then with sodium hydrogen carbonate solution, water and brine successively. The dichloromethane solution was dried, filtered and evaporated and then chromatographed (4:1 hexane–dichloromethane) to give the *2-bromomethylindene 1,2-oxide* **25** as a pale yellow oil (0.519 g, 44.7%), ν_{max}/cm^{-1} 3020, 2909, 1222; δ_H(90 MHz; $CDCl_3$) 3.13 (2 H, 2 × d, *J* 18.1, $ArCH_2C$), 3.78 (2 H, q, *J* 10.9, CH_2Br), 4.19 (1 H, s, ArCHO) and 7.02–7.48 (4 H, m, ArH); δ_C(22.5 MHz; $CDCl_3$) 33.38, 35.92, 66.04, 67.07, 124.93, 125.85, 126.18, 128.61, 140.32 and 143.62; *m/z* 226 (M^+, 2%), 224 (M^+, 2%), 145 (100) (Found: M^+, 225.9831. $C_{10}H_9BrO$ requires *M*, 225.9871); (Found: M^+, 223.9840. $C_{10}H_9BrO$ requires *M*, 223.9859).

Homolytic Cleavage of 2-Bromomethylindene 1,2-Oxide.—Bromo epoxide **25** (0.238 g, 1.06 mmol) was added to de-gassed dry benzene (75 cm^3) and heated under reflux. A solution of tributyltin hydride (0.321 g, 1.1 mmol) and AIBN (25 mg) in dry benzene (4 cm^3) was added to the refluxing solution over 5 h. After heating for a further 15 h, the solvent was removed and the residue chromatographed twice on flash silica with (a) 40–60 light petroleum and (b) 95:5 hexane–dichloromethane as eluents, affording 3-methyl-1*H*-2-benzopyran **28** as the sole product (0.051 g, 33%); ν_{max}/cm^{-1} 1635 and 1049; δ_H(90 MHz; $CDCl_3$) 1.92 (3 H, s, Me), 5.07, (2 H, s, $ArCH_2O$), 5.65 (1 H, s, ArCH=C–) and 6.83–7.45 (4 H, m, ArH); δ_C(22.5 MHz; $CDCl_3$) 19.51, 68.75, 101.53, 122.22, 123.69, 125.69, 128.13, 128.40, 128.72 and 132.19; *m/z* 146 (M^+, 81%) and 145 (100) (Found: M^+, 146.0741. $C_{10}H_{10}O$ requires *M*, 146.0740).

1-Trimethylsilylindene **30**.—A solution of indene (5.55 g, 48 mmol) in sodium-dried toluene (30 cm^3), was stirred under nitrogen at 0 °C. Butyllithium (33.2 cm^3, 50 mmol) was added slowly. The pale yellow solution was allowed to warm to room temp. and was stirred for 24 h to ensure complete lithiation. During this time the solution became dark brown in colour. Trimethylchlorosilane (6.51 g, 50 mmol) was added to the cooled solution of indenyllithium at −10 °C. The flask was fitted with a reflux condenser and refluxed under nitrogen for 12 h. The crude material was poured onto iced water and extracted. The organic phase was separated, dried over magnesium sulfate, filtered and evaporated to low volume. Distillation at reduced pressure afforded 1-trimethylsilylindene as a pale yellow liquid (5.18 g, 55.2%) (b.p. 106 °C/12 mmHg); ν_{max}/cm^{-1} 2970, 1450 and 850; δ_H(90 MHz; $CDCl_3$) 0.01 (9 H, s, $SiMe_3$), 3.63 [1 H, m, $ArCH(SiMe_3)CH{=}CH–$], 6.77 [1 H, dd, *J* 1.9 and 5.4, $ArCH(SiMe_3)CH{=}CH$], 7.03 [1 H, dd, *J* 1.9 and 5.4, $ArCH(SiMe_3)CH{=}CH$] and 7.29–7.55 (4-H, m, Ar); δ_C(22.5 MHz; $CDCl_3$) −2.42, 46.60, 121.08, 122.76, 123.74, 124.88, 128.99, 135.71, 144.27 and 145.46; *m/z* 188 (M^+, 93%), 173 (18), 116 (48), 75 (100) (Found: M^+, 188.1017. $C_{12}H_{16}Si$ requires *M*, 188.1208).

Generation of Dioxane Dibromide.—Bromine (32.0 g, 0.2 mol) was cautiously added dropwise with vigorous stirring to dry, freshly distilled dioxane (16.0 g, 0.181 mol). After the addition was complete, the reaction mixture was allowed to cool and was then poured onto freshly distilled 40–60 light petroleum. The yellow precipitate was filtered off and dried, and stored under nitrogen at −5 °C prior to use.

1-Bromoindene **31**.—Trimethylsilylindene **30** (2.0 g, 10.7 mmol) was dissolved in dry THF (265 cm^3) in a foil-covered flask and cooled to −78 °C. Dioxane dibromide (2.92 g, 11.8 mmol) in dry THF (15 cm^3) was slowly added. The reaction was allowed to warm to room temperature and then evaporated to leave an oil which was chromatographed with pentane as eluent to give pure 1-bromoindene **31** as a pale yellow liquid (1.79 g, 86%). ν_{max}/cm^{-1} 3082, 1620 and 665; δ_H(90 MHz; $CDCl_3$) 5.56 [1 H, br s, $ArCH(Br)CH{=}$], 6.35 (1 H, d, *J* 2.0 and 5.6, 3-H), 6.69 (1 H, d, *J* 5.6, 3-H), 7.20 (3 H, s, Ar-H) and 7.46–7.51 (1 H, m, 7-H); δ_C(22.5 MHz; $CDCl_3$) 46.87, 121.84, 124.82, 126.45, 128.56, 132.62, 136.47, 141.51 and 144.60; *m/z* 196 (M^+, 11%), 194 (M^+, 10%) and 115 (100) (Found: M^+, 195.9760. C_9H_7Br requires *M*, 195.9713).

3-Bromoindene 1,2-Oxide **32**.—A solution of 1-bromoindene (1.43 g, 7.37 mmol) in dichloromethane (15 cm^3) was added dropwise over 15 min to a suspension of *m*-chloroperbenzoic acid (1.52 g, 8.85 mmol) in dichloromethane (10 cm^3) at −10 °C and stirred at 5 °C for 24 h. The precipitate was filtered and the residue evaporated, washed with 10% aqueous sodium sulfite (4 × 25 cm^3), saturated sodium hydrogen carbonate (3 × 30 cm^3), water and saturated brine (each 30 cm^3). The organic phase was dried over magnesium sulfate, filtered and evaporated to yield an oil which was chromatographed with diethyl ether as eluent to give *3-bromoindene 1,2-oxide* as a yellow oil (1.03 g, 67%); ν_{max}/cm^{-1} 3065, 1220 and 847; δ_H(90

MHz; $CDCl_3$), 4.34 (2 H, m, 2,3-H), 5.25 [1 H, br s, ArC*H*(Br)] and 7.18–7.37 (4 H, m, Ar); δ_C(22.5 MHz; $CDCl_3$) 46.65, 58.03, 62.14, 125.15, 127.48, 128.56, 129.43, 140.27 and 144.43; *m/z* 211, (M^+, 2%), 209, (M^+, 2%) and 131 (100) (Found: M^+, 209.968. C_9H_7BrO requires *M*, 209.969).

Homolytic Cleavage of 3-*Bromoindene* 1,2-*Oxide*.—Tributyltin hydride (337 mg, 1.16 mmol) and epoxy bromide **32** (203 mg, 0.996 mmol) were dissolved in THF under nitrogen and heated under reflux. A solution of AIBN (30 mg) in THF (3 cm^3) was added over 5 h. Reflux was continued for a further 10 h. The reaction was allowed to cool, the solvent evaporated and the residue chromatographed using hexane–dichloromethane as eluent, to yield indan-1-one (68 mg, 52%) (m.p. 39–40 °C); ν_{max}/cm^{-1} 1710; δ_H(90 MHz; $CDCl_3$) 2.49–2.66 (2 H, m, PhCOCH_2), 2.95–3.11 (2 H, m, PhCH_2CH_2CO) and 7.19–7.70 (4 H, m, Ph); δ_C(22.5 MHz; $CDCl_3$) 25.30, 35.72, 123.03, 126.29, 126.72, 133.98, 136.63, 154.46 and 205.92; *m/z* 132 (M^+, 9%) and 131 (13) (Found: M^+, 132.0613. C_9H_8O requires *M*, 132.0651).

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