A Novel Probe for Free Radicals featuring Epoxide Cleavage

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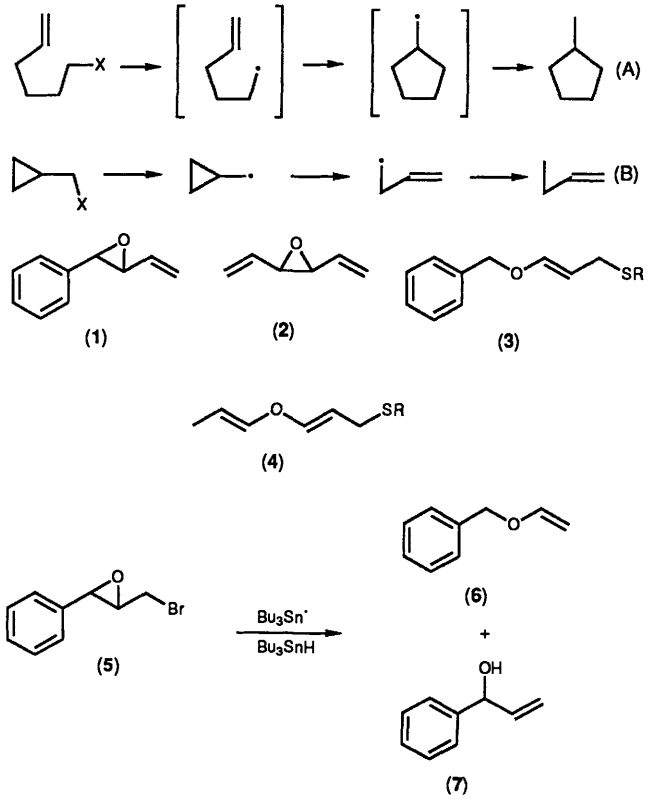
This paper describes the identification of carbon–carbon bond cleavage within a defined range of epoxides as being a reaction type which is specifically diagnostic of free radicals adjacent to the epoxide. The speed of the epoxide cleavage is greater than that of hex-5-enyl radical cyclisation, and hence the reaction is kinetically competent to act as a new and discriminating type of probe for free radicals in solution.

A recent surge in interest is evident in detecting radical intermediates in chemical reactions.[1] Whereas spectroscopic methods such as ESR[2] and CIDNP are very useful for indicating the presence of radicals, these methods have inherent drawbacks: *e.g.* (*a*) the difficulty in estimating quantitatively the extent of radical reaction and (*b*) the necessity of a reasonable flux of radicals to allow detection. Chemical reporter groups have been used to detect free radicals either by spin trapping[2] (by reaction of the radical with a nitroso compound or nitrone to form a stabilised product radical) or by other chemical reactions. Two reactions have principally been used in this context, *viz.* cyclisation of hex-5-enyl systems[3] as in equation (A) or the ring cleavage of cyclopropylmethyl systems[4] as in equation (B) (Scheme 1).



Scheme 1.

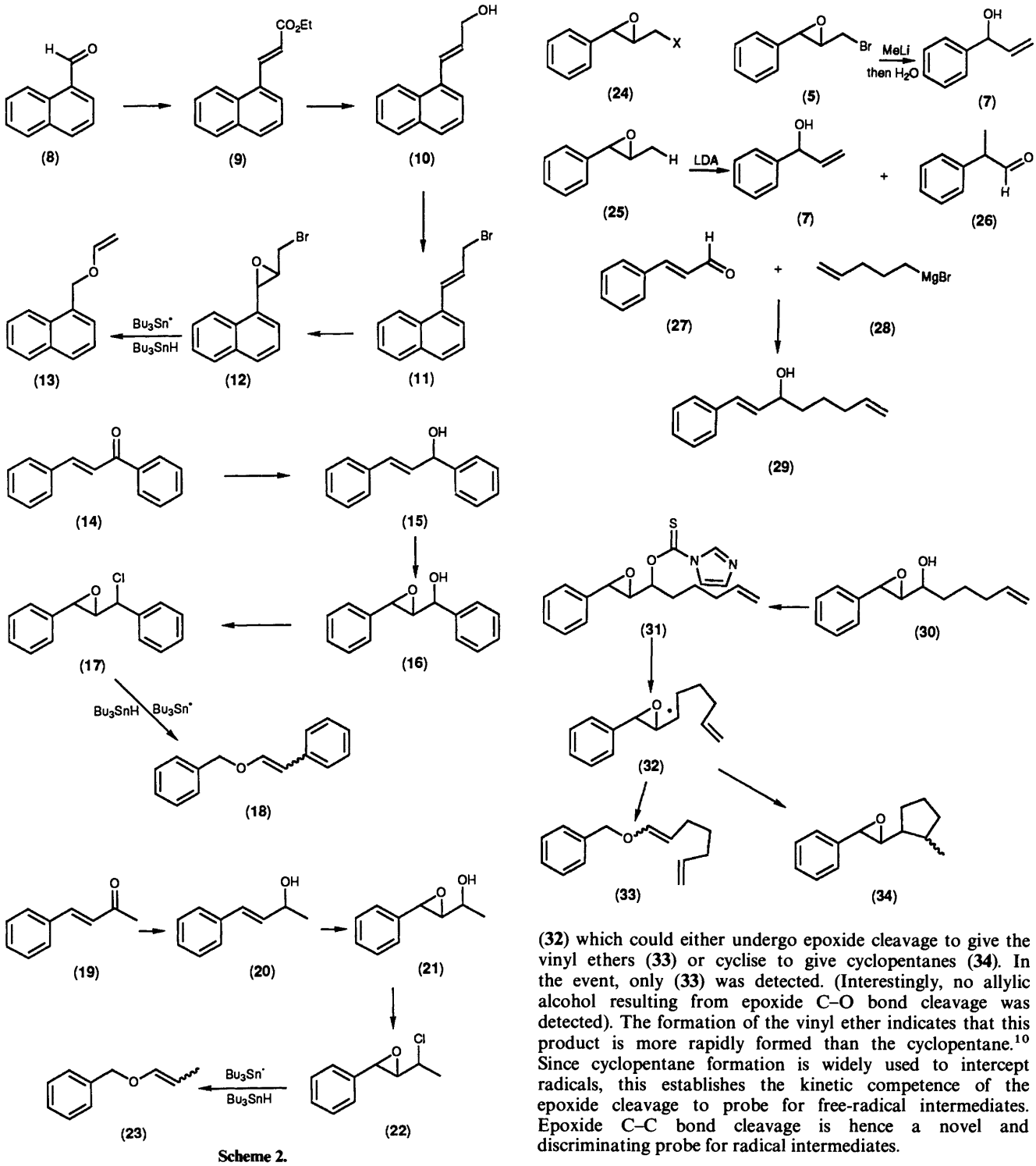
In the case of the hex-5-enyl cyclisation, problems arise because the detection of cyclised product may or may not indicate homolysis of the C–X bond; the corresponding hex-5-enylsodium also undergoes cyclisation[5] even though such species are best regarded as anions. Garst[5] has suggested that a substituted version of this reporter group might be used to differentiate between radicals and anions, but it remains to be seen if this approach is uniformly useful.

For cyclopropylmethyl systems, the corresponding radical formed on homolysis of the C–X bond undergoes rapid ring opening with butenyl products ultimately being isolated. However the detection of ring-opened products of this sort does not necessarily imply the intermediacy of radicals, as the corresponding anions give the same products albeit at different rates.[6]

With this as background we began to look for a system which could unambiguously report radicals and which would react rapidly enough to be useful.[7] Our work deals with C–C bond cleavage within epoxides. In 1970, Stogryn and Gianni reported[8] that thiyl radical addition to (**1**) and (**2**) led exclusively to the vinyl ethers (**3**) and (**4**) resulting from epoxide C–C bond cleavage. Many of the reactions we wished to test for radical intermediates feature displacement of a halide. So we investigated whether a molecule such as (**5**), the epoxide formed from cinnamyl bromide, would behave under radical cleavage conditions in a similar manner. We found two products, benzyl vinyl ether (**6**), which was always the major product, and the allylic alcohol (**7**). These products were identified by comparison with authentic samples synthesised by alternative literature routes.[9] The observation of allylic alcohol (**7**) was a surprise to us, and so we investigated a series of related compounds (**12**), (**17**), and (**22**) to see if these also gave a mixture of vinyl ether and allylic alcohol. The synthetic routes to these molecules and the products of their reactions with tributyltin radicals are shown in Scheme 2.

We observed only the vinyl ethers (**13**), (**18**), and (**23**) resulting from epoxide C–C bond cleavage. In all subsequent work the epoxide (**5**) remains unique in giving two product types. Accordingly C–C bond cleavage leads to the *sole* product, or in the case of (**5**), the *major* product of these radical reactions.

We next sought to ensure that treatment of molecules such as (**24**) for X = halide or other groups, under conditions of heterolysis of the C–X bond, would not lead to epoxide C–C bond cleavage. Precedent suggests of course that we would be justified in our hope, but we nevertheless performed the following two experiments for security. In the first, (**5**; X = Br) was treated with methyl-lithium. This led solely and cleanly to the allylic alcohol (**7**). Similarly, in the second experiment, reaction of (**25**; X = H) with lithium di-isopropylamide (LDA) led predominantly to (**7**). A second product (**26**) was formed in low yield. The heterolytic rearrangement leading to (**26**) is well precedented. In neither of these experiments was epoxide C–C bond cleavage observed. Therefore in systems like (**24**) where



Scheme 2.

epoxide C–C bond cleavage is observed and where the only pathways open for reaction involve initial homolysis or anion-induced heterolysis of the C–X bond, this C–C cleavage indicates the presence of radicals.

For this reaction to be useful as a radical probe, it was necessary also to establish that it proceeds at a sufficiently rapid rate to intercept free radicals before alternative reactions cause their destruction. Rather than perform a lengthy kinetic analysis, we synthesised the thiocarbonyl derivative (**31**). Treatment with tributyltin radicals would liberate radical (**32**) which could either undergo epoxide cleavage to give the vinyl ethers (**33**) or cyclise to give cyclopentanes (**34**). In the event, only (**33**) was detected. (Interestingly, no allylic alcohol resulting from epoxide C–O bond cleavage was detected). The formation of the vinyl ether indicates that this product is more rapidly formed than the cyclopentane.[10] Since cyclopentane formation is widely used to intercept radicals, this establishes the kinetic competence of the epoxide cleavage to probe for free-radical intermediates. Epoxide C–C bond cleavage is hence a novel and discriminating probe for radical intermediates.

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 machine. ^{13}C NMR spectra were recorded at 22.5 MHz on a Jeol FXC 90Q, at 63 MHz on a Bruker WM 250, and at 100 MHz on a Bruker AM 400 machine. All NMR experiments were carried out in $CDCl_3$ with tetramethylsilane as internal reference. UV spectra were recorded on a Philips PU 8700 series instrument. Mass spectra

were recorded on a VG micromass 70E or an AEI MS 902 instrument.

Where necessary, solvents were distilled before use. Tetrahydrofuran (THF) was distilled from potassium–benzophenone.

1-Bromo-2,3-epoxy-3-phenylpropane (**5**).—Cinnamyl bromide (3.94 g, 20 mmol) in dichloromethane (30 ml) was added dropwise to a stirred slurry of *m*-chloroperbenzoic acid (4.31 g, 25 mmol) in dichloromethane (10 ml). The resulting solution was stirred at 0 °C for 12 h; the precipitate was filtered off and the filtrate washed with aqueous sodium sulphite (5% w/v; *ca.* 3 × 30 ml) until a negative reaction with starch–KI paper was observed. The separated organic phase was then sequentially washed with aqueous sodium hydrogen carbonate (10% w/v; 3 × 50 ml), water (2 × 30 ml), and saturated brine (20 ml), dried (Na_2SO_4), filtered, and evaporated to dryness under reduced pressure. Recrystallisation afforded the desired *oxirane* (**5**) as colourless crystals (3.81 g, 88.6%), m.p. 46 °C (from light petroleum) (Found: C, 50.9; H, 4.25; Br, 39.3. C_9H_9BrO requires C, 50.7; H, 4.2; Br, 39.5%); ν_{max} 2 920 (C–H), 1 463, and 1 380 cm^{-1} (CH_2); δ_H(250 MHz) 3.31 (1 H, dt, *J* 1.9 and 5.8 Hz, 2-H), 3.50–3.52 (2 H, m, CH_2Br), 3.82 (1 H, d, *J* 1.9 Hz, 1-H), and 7.25–7.38 (5 H, m, Ph); δ_C(22.5 MHz) 31.96, 60.34, 60.94, 125.78, 128.65, and 136.13; *m/z* 214.988 and 212.990 ($M + H^+$, 5.9 and 5.8%), and 133.066 ($M^+ - Br$, 100%).

Radical Cleavage of the Oxirane (**5**).—The halogeno-oxirane (**5**) (2.13 g, 10 mmol) was added to solvent (benzene, tetrahydrofuran, or diethyl ether) (100 ml) held in a 2-necked flask equipped with a rubber septum, magnetic stirring bar, and reflux condenser. The resulting solution was thoroughly degassed and held at reflux under a nitrogen atmosphere. Tributyltin hydride (3.06 g, 10.5 mmol) and azoisobutyronitrile (AIBN; 0.05 g) were dissolved in the solvent (5 ml) and added gradually *via* syringe during 4 h. The resulting solution was refluxed for a further 12 h. Solvent removal at water pump pressure followed by preparative TLC (hexane–dichloromethane; 4:1) yielded two products as colourless oils: benzyl vinyl ether (**6**) (0.402 g, 33%); $\nu_{max.}$ 3 045 and 2 906 cm^{-1}; δ_H(250 MHz) 4.08 (1 H, dd, *J* 6.8 and 2.1 Hz, O–CH=C*H*H), 4.30 (1 H, dd, *J* 14.3 and 2.1 Hz, O–CH=CH*H*), 4.74 (2 H, s, $PhCH_2O$), 6.54 (1 H, dd, *J* 6.8 and 14.3 Hz, $OCH=CH_2$), and 7.32 (5 H, m, Ph); δ_C(22.5 MHz) 70.18, 87.46, 127.54, 127.91, 128.58, 137.04, and 151.72; *m/z* 134 (M^+ 5%) and 91 (100); and 1-phenylprop-2-en-1-ol (**7**), (0.15 g, 12%); ν_{max} 3 480 and 3 098 cm^{-1}; δ_H(250 MHz) 2.22 (1 H, br s, OH), 5.14–5.40 (3 H, m), 6.02 (1 H, m, $CH=CH_2$), and 7.34 (5 H, m, Ph); δ_C(22.5 MHz) 75.42, 115.43, 126.43, 127.79, 128.64, 140.41, and 142.75; *m/z* 134 (M^+ 80%) and 77 (100).

Ethyl 3-(*1-Naphthyl*)*propenoate* (**9**).—(Ethoxycarbonylmethylene)triphenylphosphorane (36.0 g, 0.10 mol) and 1-naphthaldehyde (15.4 g, 0.10 mol) were heated under reflux in dichloromethane (250 ml) for 1 h. The reaction mixture was cooled and evaporated to dryness. Chromatography on silica gel with dichloromethane removed triphenylphosphine oxide. The mixture of desired product and unchanged aldehyde was dissolved in diethyl ether (50 ml) and stirred vigorously with saturated aqueous sodium metabisulphite (75 ml) for 2 h. The solution was filtered. The organic layer was separated, dried, and evaporated to dryness to afford the ester (**9**) as a yellow oil (15.6 g, 69%); ν_{max} 1 705 (CO, α,β-unsaturated ester), 1 630 (C=C), and 985 (HC=CH) cm^{-1}; δ_H(90 MHz) 1.34 (3 H, t, *J* 6 Hz, OCH_2CH_3), 4.26 (2 H, q, *J* 6 Hz, OCH_2), 6.56 (1 H, d, *J* 10 Hz, $=CHCO_2Et$), 7.30–8.20 (7 H, m, ArH), and 8.50 (1 H, d, *J* 10 Hz, $CH=CHCO_2Et$); δ_C(22.5 MHz) 14.3, 60.4, 120.9, 123.3, 124.9, 125.3, 126.1, 126.7, 128.6, 130.3, 131.4, 131.8, 133.7, 141.5, and 166.7; *m/z* 226 (M^+, 54%), 181 (29), 153 (100), and 152 (51) (Found: M^+, 226.0993. $C_{15}H_{14}O_2$ requires *M*, 226.0994).

3-(1-Naphthyl)prop-2-enol (**10**).—To a stirred solution of the ester (**9**) (3.5 g, 15 mmol) in dry diethyl ether (150 ml) at −78 °C, di-isobutylaluminium hydride (35 ml; 1.5M in hexanes; 52 mmol) was added. The mixture was stirred at −78 °C for 3 h then slowly warmed to room temperature. The product was cautiously added to diethyl ether (20 ml)–water (40 ml). The white gelatinous precipitate formed was dissolved by vigorously stirring with aqueous sodium hydroxide (2M). The aqueous layer was extracted with diethyl ether (3 × 20 ml) and the combined organic extracts were dried and evaporated to dryness. Chromatography on silica gel with dichloromethane–hexane (2:1) as eluant yielded the *alcohol* (**10**) as a viscous, colourless oil (2.0 g, 71%) (Found: C, 84.5; H, 6.8. $C_{13}H_{12}O$ requires C, 84.75; H, 6.6%); ν_{max} 3 400 (OH), 1 600 (C=C), and 970 (HC=C) cm^{-1}; δ_H(90 MHz) 2.63 (1 H, br s, OH), 4.36 (2 H, dd, *J* 6 and 1 Hz, CH_2OH), 6.35 (1 H, dt, *J* 16 and 6 Hz, $=CHCH_2$), and 7.17–8.25 (8 H, m, ArH and $CH=CHCH_2$); δ_C(63 MHz), 63.7, 123.8, 123.9, 125.6, 125.7, 126.0, 127.9, 128.5, 131.2, 131.9, 133.7, and 134.5; *m/z* 184 (M^+ 93%), 165 (68), 153 (73), 141 (100), and 128 (58) (Found: M^+, 184.0884. $C_{13}H_{12}O$ requires *M* 184.0888).

1-Bromo-2,3-epoxy-3-(1-naphthyl)propane (**12**).—To a solution of *N*-bromosuccinimide (1.94 g, 0.010 mol) in dry dichloromethane (5 ml) at −8 °C under nitrogen dimethyl sulphide (0.9 ml), 0.012 mol) was added dropwise and the resulting bright yellow solution was stirred for 5 min. The allylic alcohol (**10**) (2.46 g, 0.013 mol) was added. The mixture was stirred for 1 h at −8 °C and for 1 h at room temperature. The solution was poured into ice-cold brine (40 ml) and extracted with diethyl ether (3 × 40 ml). The combined extracts were washed with cold brine, dried, and evaporated to dryness to yield the allylic bromide (**11**) as a yellow oil. The bromide (**11**) was dissolved in dichloromethane (30 ml) and a solution of *m*-chloroperbenzoic acid (2.66 g, 0.015 mol) in dichloromethane (30 ml) was added dropwise with stirring. The solution was stirred for 2 h, and washed successively with aqueous sodium sulphite (3 × 15 ml), sodium hydrogen carbonate (3 × 15 ml), and brine (15 ml). The organic material was dried and evaporated to dryness. Chromatography on silica gel with hexane–ethyl acetate (1:1) as eluant afforded the *epoxide* (**12**) as a colourless oil (1.22 g, 47%) (Found: C, 59.0; H, 4.4; Br, 29.6. $C_{13}H_{11}BrO$ requires C, 59.3; H, 4.2; Br, 30.49%); ν_{max} 1 600 (ArH), 1 220 (epoxide), and 780 (CBr) cm^{-1}; δ_H(400 MHz) 3.31 [1 H, ddd, *J* 6.3, 5.6, and 2.0 Hz, (O)C*H*CH_2], 3.56 (1 H, dd, *J* 10.6 and 6.3 Hz, HC*H*Br), 3.72 (1 H, dd, *J* 10.6 and 5.6 Hz, *H*CHBr), 4.43 [1 H, d, *J* 2.0 Hz, ArCH(O)], and 7.10–8.20 (7 H, m, ArH); δ_H(23 MHz) 31.8, 58.7, 60.1, 122.6, 123.0, 125.5, 126.1, 126.6, 128.8, 131.3, 132.1, and 133.3; *m/z* 264 (M^+, 9%), 262 (M^+, 10), 184 (15), 183 (100), and 128 (18) (Found: M^+, 263.9969 and 261.9987. $C_{13}H_{11}BrO$ requires *M*, 263.9973 and 261.9993).

(*1-Naphthylmethoxy*)*ethene* (**13**).—Epoxide (**12**) (0.65 g, 2.5 mmol) was heated under reflux with Bu_3SnH (0.87 g, 3.0 mmol) in dry, degassed toluene (30 ml). A solution of AIBN (0.01 g) in dry, degassed toluene (2 ml) was added dropwise over 1 h. After refluxing for a further 14 h the reaction mixture was cooled then evaporated to dryness. Chromatography using hexane then dichloromethane–hexane (1:3) as eluants afforded the *ether* (**13**) as a pale yellow oil (0.31 g, 67%); ν_{max} 1 620 (C=C), 1 210 (CO, ether), and 990 ($HC=CH_2$) cm^{-1}; δ_H(250 MHz) 4.16 (1 H, dd, *J* 6.7 and 2.2 Hz, =CH*H*), 4.43 (1 H, dd, *J* 14.3 and 2.1 Hz, =C*H*H), 5.20 (2 H, s, OCH_2), 6.65 (1 H, dd, *J* 14.3 and 7.0 Hz, OCH=), 7.53 (4 H, m, ArH), 7.87 (1 H, m, ArH), and 8.01 (2 H,

m, ArH); δ_C(100 MHz) 68.9, 87.7, 123.8, 125.4, 126.0, 126.5, 128.8, 129.1, 131.8, 132.0, and 151.8; *m/z* 184 (M^+, 9%) and 141 (100) (Found: M^+, 184.0880. $C_{13}H_{12}O$ requires *M*, 184.0881).

1,3-*Diphenylprop*-2-*enol* (**15**).—Sodium borohydride (2.27 g, 0.06 mol) was added in small portions to a stirred solution of 1,3-diphenylprop-2-en-1-one (6.25 g, 0.03 mol) in methanol (375 ml). The solution was stirred for 1 h and evaporated to dryness, and the residue taken up in ethyl acetate (150 ml). The organic solution was washed with water (2 × 50 ml), dried, and evaporated to dryness to afford the *alcohol* (**15**) as a white solid (6.0 g, 96%), m.p. 50–52 °C (Found: C, 85.65; H, 6.85. $C_{15}H_{14}O$ requires C, 85.7; H, 6.7%); ν_{max} 3 330 (OH), 1 640 (C=C), and 970 (HC=CH) cm^{-1}; δ_H(90 MHz) 2.44 (1 H, br s, OH), 5.27 [1 H, d, *J* 6 Hz, C*H*(OH)], 6.26 [1 H, dd, *J* 16 and 6 Hz, =C*H*C(OH)], 6.60 (1 H, d, *J* 16 Hz, ArCH=), and 7.25 (10 H, m, ArH); δ_C(22.5 MHz) 75.0, 126.4, 126.7, 127.8, 128.6, 130.6, 131.7, and 142.9; *m/z* 210 (M^+, 92%), 192 (22), 105 (100), and 91 (38) (Found: M^+, 210.1043. $C_{15}H_{14}O$ requires *M*, 210.1045).

2,3-*Epoxy*-1,3-*diphenylpropanol* (**16**).—To a stirred solution of the alcohol (**15**) (5.6 g, 0.027 mol) in dichloromethane (50 ml), a solution of *m*-chloroperbenzoic acid (5.5 g, 0.032 mol) in dichloromethane (50 ml) was added dropwise. The solution was stirred for 3 h, and washed successively with aqueous sodium sulphite (3 × 20 ml), sodium hydrogen carbonate (3 × 20 ml), and brine (20 ml). The organic material was dried and evaporated to dryness. Chromatography on silica gel with dichloromethane as eluant afforded the α,β-*epoxy alcohol* (**16**) as two diastereoisomers, D1 and D2, in the form of white crystalline solids (total yield 4.8 g, 71%).

Diastereoisomer D1 had m.p. 70–71 °C (Found: C, 79.4; H, 6.4. $C_{15}H_{14}O_2$ requires C, 79.6; H, 6.25%); ν_{max} 3 440 (OH) and 900 (CO, epoxide) cm^{-1}; δ_H(90 MHz) 2.85 (1 H, d, *J* 5 Hz, OH), 3.26 [1 H, dd, *J* 5 and 3 Hz, C*H*OCH(OH)], 3.97 (1 H, d, *J* 3 Hz, ArCHO), 4.78 [1 H, t, *J* 5 Hz, C*H*(OH)], and 7.32 (10 H, m, ArH); δ_C(22.5 MHz) 56.9, 65.8, 73.5, 125.7, 126.3, 128.1, 128.3, 128.5, 128.7, 136.4, and 140.3.

Diastereoisomer D2 had m.p. 69–70 °C (Found: C, 79.85; H, 6.45); ν_{max} 3 400 (OH) and 907 (CO, epoxide) cm^{-1}; δ_H(90 MHz) 2.56 (1 H, br s, OH), 3.25 [1 H, t, *J* 3 Hz, C*H*OCH(OH)], 4.08 (1 H, d, *J* 3 Hz, ArCHO), 4.96 [1 H, d, *J* 3 Hz, C*H*(OH)], and 7.32 (10 H, m, ArH); δ_C(23 MHz) 55.2, 65.0, 71.5, 125.8, 126.6, 128.4, 128.7, 136.7, and 139.5.

1-*Chloro*-2,3-*epoxy*-1,3-*diphenylpropane* (**17**).—The α,β-epoxy alcohol (**16**) (1.44 g, 6.4 mmol), triphenylphosphine (1.67 g, 6.4 mmol), and acetonitrile (1.0 ml) were heated under reflux in carbon tetrachloride (50 ml) for 15 min. A further portion of triphenylphosphine (1.0 g, 4.4 mmol) was added and the mixture was heated under reflux for a further 30 min. The mixture was cooled and then filtered. The solvent was removed *in vacuo* to afford a solid. Chromatography on silica gel with diethyl ether–hexane (1:3) as eluant afforded the desired chloride (**17**) as a mixture of two diastereoisomers in the form of a white crystalline solid (70 mg, 45%), m.p. 47–49 °C (Found: C, 73.75; H, 5.55. $C_{15}H_{13}ClO$ requires C, 73.6; H, 5.35%); ν_{max} 1 310 (CO, epoxide) cm^{-1}; δ_H(250 MHz) 3.46 [1 H, dd, *J* 6.2 and 1.8 Hz, (O)C*H*CHCl], 3.90 [1 H, d, *J* 1.8 Hz, ArCH(O)], 4.78 and 4.82 (1 H, 2 × d, *J* 7.3 and 6.2 Hz, C*H*Cl), and 7.16–7.50 (10 H, m, ArH); δ_C(22.5 MHz) 58.7, 58.9, 61.7, 63.2, 64.4, 65.1, 125.7, 126.4, 127.4, 127.7, 128.5, 128.7, 128.9, 136.0, and 137.5; *m/z* 209 (M^+ − Cl, 25%), 140 (37), 138 (100), 125 (41), and 103 (48).

Treatment of the Oxirane (**17**) *with Tributyltin Hydride and AIBN*.—The oxirane (**17**) (140 mg, 0.5 mmol) and Bu_3SnH (0.13 ml, 0.5 mmol) were heated under reflux in dry, degassed toluene (25 ml). A solution of AIBN (10 mg) in toluene (2 ml) was added dropwise over 1 h and the reaction mixture was then refluxed for a further 3 h. After cooling the solution was evaporated to dryness. Chromatography on preparative silica gel plates with carbon tetrachloride as eluant resulted in removal of all the tin residues. Further chromatography on plates with light petroleum–dichloromethane (9:1) afforded (*Z*)- and (*E*)-1-*phenyl*-2-(*phenylmethoxy*)*ethene* (**18**) separately as colourless oils (89 mg, 85%, *Z*:*E* 1:1.3). The (*E*)-vinyl ether (**18**) had ν_{max} 1 640 (C=C) and 1 080 (CO, ether) cm^{-1}; δ_H(250 MHz), 4.89 (2 H, s, CH_2O), 5.96 (1 H, d, *J* 12.9 Hz, ArCH=), 7.08 (1 H, d, *J* 12.9 Hz, OCH=), and 7.11–7.39 (10 H, br m, ArH); δ_C(23 MHz), 72.1, 107.2, 125.3, 125.9, 127.7, 128.2, 128.7, 136.4, 137.0, and 147.9; *m/z* 210 (M^+, 16%), 118 (7), and 91 (100) (Found: M^+ 210.1056. $C_{15}H_{14}O$ requires *M*, 210.1045). The (*Z*)-vinyl ether (**18**) had ν_{max} 1 645 (C=C) and 1 090 (CO, epoxide) cm^{-1}; δ_H(250 MHz) 4.94 (2 H, s, CH_2O), 5.25 (1 H, d, *J* 7.1 Hz, ArCH=), 6.24 (1 H, d, *J* 7.1 Hz, OCH=), and 7.13–7.64 (10 H, br m, ArH); δ_C(100 MHz) 74.9, 106.3, 125.8, 127.2, 128.0, 128.2, 128.3, 128.6, 135.9, 137.2, and 146.3; *m/z* 210 (M^+, 15%), 118 (2), and 91 (100) (Found: M^+, 210. 1019).

(*E*)-4-*Phenylbut*-3-*en*-2-*ol* (**20**).—Sodium borohydride (6.1 g, 0.16 mol) was added in small portions to a stirred solution of (*E*)-4-phenylbut-3-en-2-one (**19**) (11.7 g, 0.08 mol) in methanol (400 ml). The solution was stirred for 1 h and evaporated to dryness, and the residue taken up in ethyl acetate (200 ml). The organic solution was washed with water (2 × 50 ml), dried, and evaporated to dryness to afford the *alcohol* (**20**) as a white solid (10.2 g, 86%), m.p. 34–35 °C (Found: C, 80.9; H, 8.3. $C_{10}H_{12}O$ requires C, 81.0; H, 8.2%); ν_{max} 3 450 (OH) and 970 (C=C) cm^{-1}; δ_H(90 MHz) 1.25 (3 H, d, *J* 6 Hz, Me), 2.04 (1 H, br s, OH), 4.25 (1 H, dq, *J* 6 and 6 Hz, C*H*OH), 6.24 [1 H, dd, *J* 17 and 6 Hz, =C*H*CH(OH)], 6.62 (1 H, d, *J* 17 Hz, ArCH=), and 7.35 (5 H, m, ArH); δ_C(22.5 MHz) 23.5, 68.8, 126.5, 127.6, 128.6, 129.4, 133.8, and 136.9; *m/z* 148 (M^+, 100%), 130 (19), and 105 (100) (Found: M^+, 148.0917. $C_{10}H_{12}O$ requires *M*, 148.0889).

3,4-*Epoxy*-4-*phenylbutan*-2-*ol* (**21**).—To a stirred solution of the alcohol (**20**) (8.0 g, 54 mmol) in dichloromethane (75 ml) a solution of *m*-chloroperbenzoic acid (14.0 g, 81 mmol) in dichloromethane (100 ml) was added dropwise. The mixture was stirred for 2.5 h and evaporated to dryness. The residue was taken up in diethyl ether (150 ml) and washed successively with aqueous sodium sulphite (3 × 30 ml), sodium hydrogen carbonate (3 × 20 ml), and brine (30 ml). The organic material was dried and evaporated to dryness. Chromatography on silica gel with diethyl ether–hexane (1:1) as eluant afforded the desired epoxide (**21**) as a mixture of two diastereoisomers in the form of a colourless oil (7.7 g, 87%); ν_{max} 3 450 (OH) and 900 (CO, epoxide) cm^{-1}; δ_H(400 MHz) 1.31 (minor) and (1.34 (major) (3 H, 2 × d, *J* 6.5 Hz, Me), 2.70 (1 H, br s, OH), 3.05 [1 H, m, (O)C*H*COH], 3.80 (1 H, dq, *J* 6.5 and 1.4 Hz C*H*OH, major), 3.85 [1 H, d, *J* 2.1 Hz, ArCH(O), minor], 396 [1 H, d, *J* 2.1 Hz, ArCH(O) major], 4.08 (1 H, dq, 6.5 and 2.9 Hz, C*H*OH, minor), and 7.30 (5 H, m, ArH); δ_C 18.9, 19.9, 55.0, 56.6, 65.2, 65.6, 66.4, 67.3, 125.7, 128.3, 128.5, 136.9, and 137.1; *m/z* 164 (M^+, 1%), 107 (100) and 91 (85) (Found: M^+, 164.0803, $C_{10}H_{12}O_2$ requires *M*, 164.0837).

2-*Chloro*-3,4-*epoxy*-4-*phenylbutane* (**22**).—The α,β-epoxy alcohol (**21**) (2.00 g, 13 mmol), triphenylphosphine (3.36 g, 13 mmol), and acetonitrile (2 ml) were heated under reflux in carbon tetrachloride (75 ml) for 4 h. The reaction mixture was cooled and the solvent was removed *in vacuo*. Diethyl ether (50 ml) was added and the precipitated triphenylphosphine oxide was removed by filtration. The diethyl ether was removed

in vacuo and the residue taken up in dichloromethane (50 ml). A solution of *m*-chloroperbenzoic acid (3.00 g, 17 mmol) in dichloromethane (50 ml) was added dropwise. The solution was stirred for 15 h, and washed successively with aqueous sodium sulphite (2 × 30 ml), sodium hydrogen carbonate (2 × 30 ml), and brine (30 ml). The organic material was dried and evaporated to dryness. Chromatography on silica gel with diethyl ether–hexane (2:3) as eluant afforded the α,β-epoxy chloride (**22**) as a mixture of two diastereoisomers in the form of a colourless oil (1.23 g, 52%); ν_{max} 1 230 (CO, epoxide) and 800 cm^{-1}; δ_H(400 MHz) 1.57 and 1.63 (3 H, 2 × d, *J* 6.8 Hz, Me), 3.13 and 3.16 [1 H, 2 × dd, *J* 6.9, 6.8, and 2.0, 1.9 Hz, (O)C*H*CCl], 3.79–3.93 (2 H, br m, ArCH and C*H*Me), and 7.23–7.37 (5 H, br m, ArH); δ_C(22.5 MHz) 21.0, 21.6, 56.2, 57.1, 58.1, 58.6, 65.1, 65.5, 125.7, 128.5, and 136.3; *m/z* 147 (M^+ − Cl, 43%), 107 (100), and 91 (46).

Treatment of the α,β-Epoxy Chloride (**22**) *with Tributyltin Hydride and AIBN.*—The α,β-epoxy chloride (**22**) (1.87 g, 10 mmol) and Bu_3SnH (3.60 ml, 13 mmol) were heated under reflux in dry, degassed THF (100 ml). A solution of AIBN (20 mg) in THF (5 ml) was added dropwise over 1 h and the mixture was then refluxed for a further 3 h. After cooling the solution was evaporated to dryness. Chromatography on silica gel with dichloromethane–hexane (1:1) as eluant afforded a 2:1 mixture of (*Z*)- and (*E*)-1-benzyloxypropene (**23**) as a colourless oil (1.22 g, 83%); ν_{max} 1 670, 1 660 (C=C), and 1 080 (CO, ether) cm^{-1}; δ_H(400 MHz) 1.56 (*E*) and 1.63 (*Z*) (3 H, 2 × dd, *J* 6.7, 6.9, and 1.5, 1.7 Hz, =CH*Me*), 4.44 (*Z*) and 4.89 (*E*) (1 H, 2 × dq, *J* 6.7, 12.6, and 6.7, 6.7 Hz, =C*H*Me), 4.70 (*E*) and 4.80 (*Z*) (2 H, 2 × s, CH_2O), 6.02 (*Z*) and 6.32 (*E*) (1 H, 2 × dq, *J* 6.7, 1.7, and 12.6, 1.5 Hz, OC*H*=CHMe), and 7.20–7.38 (5 H, br m, ArH); δ_C (22.5 MHz) 9.3, 12.4, 71.1, 73.5, 99.4, 101.7, 127.2, 127.4, 127.7, 128.3, 137.6, 137.9, 145.3, and 146.4; *m/z* 148 (M^+, 12%), 92 (42), 91 (100), and 41 (6) (Found: M^+, 148.0872. $C_{10}H_{12}O$ requires *M*, 148.0888).

1,2-*Epoxy*-1-*phenylpropane* (**25**).—A thoroughly dried flask equipped with a calcium chloride guard tube was charged with *m*-chloroperbenzoic acid (9.13 g, 53 mmol) and dichloromethane (30 ml). A solution of 1-phenylpropene (5.0 g, 42.3 mmol) in dichloromethane (50 ml) was added dropwise to the stirred slurry of peracid during 1 h. The resulting mixture was stirred at room temperature for a further 3 h. The mixture was filtered and the white precipitate washed with dichloromethane (3 × 5 ml). The combined filtrate and washings were treated with aqueous sodium sulphite (10% w/v, *ca.* 3 × 30 ml) until the organic phase gave a negative reaction with starch–KI paper. The separated organic phase was then washed with aqueous sodium hydrogen carbonate (10% w/v; 4 × 30 ml), water (30 ml), and finally saturated brine (20 ml). The organic phase was then dried ($MgSO_4$), filtered, and evaporated to low volume. Column chromatography using flash silica with dichloromethane as eluant gave the desired epoxide (**25**) as a colourless oil (2.96 g, 51%), as a 1:1 mixture of *cis*- and *trans*-isomers; ν_{max} 3 024, 2 918, 1 600, 1 580, and 1 500 cm^{-1}; δ_H(90 MHz) 1.04 (3 H, d, *J* 5.25 Hz, *cis*-Me), 1.39 (3 H, d, *J* 5.03 Hz, *trans*-Me), 2.95 (1 H, dq, *J* 2.19 and 5.0 Hz, *trans*-2-H), 3.25 (1 H, m, *cis*-2-H), 3.52 (1 H, d, *J* 2.19 Hz, *trans*-1-H), 3.97 (1 H, d, *J* 4.37 Hz, *cis*-1-H), and 7.25 (5 H, m, *cis* + 5 H, m, *trans*, Ph); δ_C(22.5 MHz) 12.41, 17.72, 54.83, 57.32, 58.73, 59.33, 125.47, 126.50, 127.86, 128.29, 129.92, 131.43, and 137.75; *m/z* 134.07 (M^+, 71%) and 105.06 (M^+ − 29) (100).

Heterolytic Cleavage of 1,2-*Epoxy*-1-*phenylpropane* (**25**).—To a stirred solution of LDA (8 mmol) in tetrahydrofuran (50 ml) at −78 °C, a solution of the epoxide (**25**) (1.0 g, 7.6 mmol) in dry diethyl ether (5 ml) was added dropwise under nitrogen *via* a syringe. The mixture was allowed to warm to room temperature and was stirred for 24 h, when it became red. The solution was poured onto water (50 ml) and extracted with diethyl ether (100 ml). The separated organic phase was dried ($MgSO_4$), filtered, and evaporated to dryness. Column chromatography on silica gel (hexane–chloroform as eluant) afforded two products as colourless oils: 1-phenylprop-2-enol (**7**) (0.93 g, 92%) (spectra as for previous sample); and 2-phenylpropanal (**26**) (0.06 g, 6%), ν_{max} 3 120, 2 950, 2 740, and 1 742 cm^{-1}; δ_H(90 MHz) 1.46 (3 H, d, *J* 7.5 Hz, Me), 3.67 (1 H, q, *J* 7.5 Hz, PhC*H*), 7.45 (5 H, m, Ph), and 9.75 (1 H, br s, CHO); *m/z* 134.07 (M^+, 32%) and 105.07 (M^+ − 29) (100).

1-*Phenylocta*-1,7-*dien*-3-*ol* (**29**).—A solution of cinnamaldehyde (**27**) (1.92 g, 16.0 mmol) in dry ether (30 ml) was added dropwise to a stirred solution of pent-4-enylmagnesium bromide (**28**) prepared from 5-bromopent-1-ene (3.04 g, 20.4 mmol) and magnesium (1.02 g, 42 mmol) in ether (20 ml). The mixture was heated under reflux for 15 min and cooled to 0 °C, and saturated aqueous ammonium chloride added. The aqueous phase was extracted with ether (× 3) and the combined extracts were washed with water (× 2), dried (Na_2SO_4), and evaporated *in vacuo*.

Chromatography [HF_{254}; 45 g; chloroform–light petroleum (4:1) as eluant] afforded 1-*phenylocta*-1,7-*dien*-3-*ol* (**29**) (2.73 g, 85%) as an oil; ν_{max} 3 353 (O–H), 1 670, 1 642, and 1 600 cm^{-1}; δ_H(90 MHz) 1.4–2.1 (7 H, m, 4-H, 5-H, 6-H, and 3-OH), 4.2 (1 H, q, *J* 6 Hz, 3-H), 4.8–5.1 (2 H, m, 8-H), 5.5–6.0 (1 H, m, 7-H), 6.15 (1 H, dd, *J* 16 and 6 Hz, 2-H), and 6.5 (1 H, d, *J* 16 Hz, 1-H); δ_C (22.5 MHz) 24.86, 33.69, 36.94, 72.75, 114.73, 126.54, 127.57, 128.60, 130.12, 132.83, 137.00, and 138.68; *m/z* 202 (M^+, 14%), 184 (19), and 133 (100) (Found: M^+, 202.1358. $C_{14}H_{18}O$ requires *M*, 202.1357).

1,2-*Epoxy*-1-*phenyloct*-7-*en*-3-*ol* (**30**).—The dienol (**29**) (400 mg, 1.98 mmol), acetylacetonato(oxo)vanadium (20 mg), and t-butyl hydroperoxide (80%; 1.5 ml, 15 mmol) were heated together in toluene (20 ml) at 60 °C for 30 min, the mixture poured into aqueous sodium thiosulphate (50 ml), and the aqueous phase extracted with ether (× 3). The combined organic fractions were washed successively with aqueous sodium thiosulphate (× 2) and water (× 2), dried (Na_2SO_4), and evaporated *in vacuo*.

Chromatography [HF_{254}; 30 g; chloroform–hexane (4:1) as eluant] gave the *epoxide* (**30**) (370 mg, 86%) as an oil; ν_{max} 3 432 (br), 1 642, and 1 605 cm^{-1}; δ_H(90 MHz) 1.4–2.2 (6 H, m, 4-H, 5-H, and 6-H), 2.4 (1 H, s, 3-OH), 3.0 (1 H, t, *J* 3 Hz, 2-H), 3.8–4.0 (2 H, m, 3-H and 1-H), 4.8–5.1 (2 H, m, 8-H), 5.5–6.0 (1 H, m, 7-H), and 7.1–7.4 (5 H, m, Ph); δ_C (22.5 MHz) 24.70, 33.64, 33.85, 55.09, 56.71, 65.06, 65.82, 68.90, 71.18, 114.90, 125.79, 128.33, 128.55, 136.95, and 138.41; *m/z* 218 (M^+, 2%), 200 (5), and 107 (100) (Found: M^+, 218.1309. $C_{14}H_{18}O_2$ requires *M*, 218.1306).

O-(1,2-*Epoxy*-1-*phenyloct*-7-*en*-3-*yl*) *Imidazol*-1-*thiocarboxylate* (**31**) *and its Reaction with Tributyltin Hydride.*—1,2-Epoxy-1-phenyloct-7-en-3-ol (**30**) (223 mg, 1.02 mmol) and *N*,*N*-thiocarbonyldi-imidazole (368 mg, 2.06 mmol) were heated under reflux in dichloromethane (50 ml) for 1 h and the mixture evaporated *in vacuo* to afford the crude thiocarboxylate (**31**) as an oil; δ_H(90 MHz) 1.4–2.2 (6 H, m, 4-H, 5-H, and 6-H), 3.15 (1 H, dd, *J* 5 and 2 Hz, 2-H), 3.9 (1 H, d, *J* 2 Hz, 1-H), 4.9–5.1 (2 H, m, 8-H), 5.5–6.0 (2 H, m, 3-H and 7-H), and 7.3 (5 H, m, Ph).

The residue was dissolved in toluene (30 ml) and AIBN (10 mg) was added. The solution was heated to reflux under nitrogen and a solution of tributyltin hydride (0.55 ml, 2.05 mmol) in toluene (10 ml) was added during 10 min. A solution of AIBN (5 mg) in toluene (10 ml) was added and the solution was heated under reflux overnight and evaporated *in vacuo*.

Chromatography on preparative chromatography plates doped with potassium carbonate gave 1-benzyloxyhepta-1,6-diene (**33**) (112 mg, 54%) as a mixture of *Z*- and *E*-isomers, δ(90 MHz) 1.2–2.3 (6 H, m, 3-H, 4-H, and 5-H), 4.45 (0.5 H, q, *J* 7 Hz, 2-H of *Z*-isomer), 4.75 and 4.85 (2 × 1 H, s, $PhCH_2$), 4.9–5.2 (2.5 H, m, 7-H and 2-H, *E*), 5.7–6.0 (1 H, m, 6-H), 6.1 (0.5 H, d, *J* 6 Hz, 1-H, *Z*), and 7.3–7.5 (5 H, m, Ph); *m/z* 202 (M^+) and 91 ($PhCH_2$, 100%); ν_{max} 1 725, 1 650, 1 640, 740, and 700 cm^{-1}; δ_C(22.5 MHz) 23.5, 27.0, 29.0, 29.7, 32.9, 33.2, 70.9, 73.4, 104.5, 107.2, 114.0, 114.2, 126.9, 129.1, 137.1, 137.6, 138.3, 138.5, 144.4, and 145.8.

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