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THE ARENE OXIDE–OXEPINE VALENCE ISOMERIZATION; A DYNAMIC NMR INVESTIGATION USING A PROCHIRAL SUBSTITUENT

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Dedicated to Professor Michael J.S. Dewar on the occasion of his 70th birthday.

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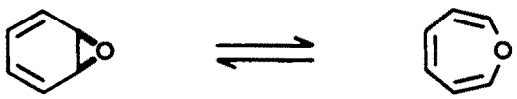
Abstract. - The geminal α-methylene protons in 3-ethylnaphthalene-1,2-oxide show chemical shift nonequivalence in ^{1}H NMR spectra recorded at ambient temperature consistent with a high barrier to enantiomerization via the oxepine tautomer. The methylene protons in α-benzoyloxytoluene-2,3-oxide which are a singlet at ambient temperature split into an AB system at -135 °C and there is evidence of *ca.* 5% of the oxepine isomer. Lineshape analysis of the coalescing arene oxide AB signals provides the activation parameters for the valence isomerization/degenerate racemization process: $\Delta G^{\ddagger}$ = 7.6 kcal mol^{-1}, $\Delta H^{\ddagger}$ = 8.6 kcal mol^{-1}, $\Delta S^{\ddagger}$ = 5.8 cal K^{-1} mol^{-1}.

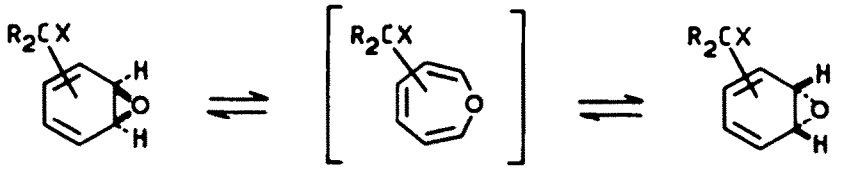
Benzene oxide (1) was first prepared by Vogel and coworkers about twenty five years ago.[1] It was shown to interconvert rapidly with its valence isomer oxepine (2) by a thermally allowed disrotatory electrocyclic process.[2]



(1) (2)

The rate constants for the isomerization were determined by Günther using low temperature ^{1}H NMR spectroscopy.[3] The equilibrium position was found to favour the lower enthalpy oxide form at low temperatures whereas the higher entropy oxepine predominated at, or above, ambient temperature.[2,3]

Although numerous substituted benzene oxides/oxepines have since been synthesised,[4] there have been few measurements of the rate of valence isomerization. This is probably due to the fact that although the valence equilibrium is reasonably balanced in the parent compound, steric or electronic effects from substituents often shift the position of equilibrium so that it strongly favours a single valence isomer. In this situation, ordinary low temperature NMR investigations may not provide any information on the isomerization process. However, in compounds where the equilibrium constant is very small, leading to complete predominance of the arene oxide valence tautomer, a prochiral substituent[5] could render the isomerization process observable by NMR spectroscopy. Thus in the frozen benzene oxide tautomer (3), the paired ligands (R) in the prochiral substituent are diastereotopic and potentially anisochronous. Rapid enantiomerization (3) ⇌ (3') via the higher energy oxepine valence isomer (4) should render the diastereotopic R groups effectively enantiotopic and



(3) (4) (3')

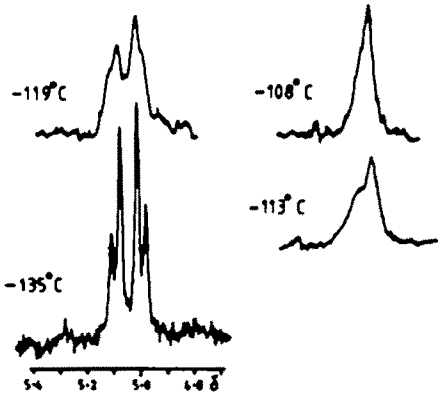
isochronous on the NMR time-scale[5] and hence enable the rate constants for (3) ⇌ (3') and (3) ⇌ (4) to be determined. This approach is illustrated in the present account by incorporating a prochiral methylene substituent on the arene oxide.

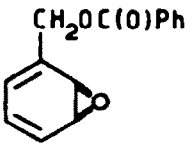
RESULTS AND DISCUSSION

In principle a prochiral substituent should function at any position in an arene oxide as a probe for the presence or absence of net molecular symmetry planes on the NMR time-scale. However, substitution at the 3-position appeared the most attractive since in benzene oxide systems literature data suggest that substitution at the 3-position tends to move the valence equilibrium strongly in favour of the oxide form.[4,6] Additionally, a prochiral group at the 3-position is sufficiently close to the anisotropic epoxide moiety to offer a reasonable expectation of a measurable chemical shift nonequivalence of the diastereotopic paired ligands in the substituent. In the case of polycyclic arene oxides, for example, naphthalene-1,2-oxide, synthetic considerations concerned with the reactivity of tertiary alkyl bromide intermediates also favour the incorporation of a prochiral alkyl group at the 3-position.

In order to test this proposal, α-Benzoyloxytoluene-2,3-oxide (5) appeared to be a good candidate for study as it contains an uncoupled prochiral methylene group at the 3-position. It was prepared from benzoic acid using the elegant seven step synthetic route devised by Ganem and coworkers.[7]

The chemical shifts of the epoxide ring carbons C-2 and C-3 (δ 84.2 and 85.3 in $CDCl_3$) and their attached protons (δ 4.60 and 4.55 in $CDCl_3$) at ambient temperature establish that the benzene oxide form of (5) predominates in the dynamic valence isomerization. Previous work has established that the HC-O and ^{13}C-O chemical shifts in the oxide form are in the range δ 4.0-4.7 and δ 56-75 respectively whereas these nuclei resonate at much higher frequency in the oxepine tautomer, viz. δ 5.6-5.9 and δ 120-161 respectively.[2,8-10] The α-methylene protons gave a sharp singlet signal at δ 4.97 as expected for a rapidly tautomerizing and enantiomerizing system at ambient temperature. On cooling a solution of (5) in dimethyl ether below -100 °C, the α-methylene signal first broadened selectively, then collapsed and reappeared at -135 °C as an AB quartet (δ_A 5.07, δ_B 4.98, J_{AB} 13.1 Hz) at 400 MHz (Figure 1).





(5)

Figure 1. 400 MHz ^1H NMR spectra of compound (5) in dimethyl ether at various temperatures.

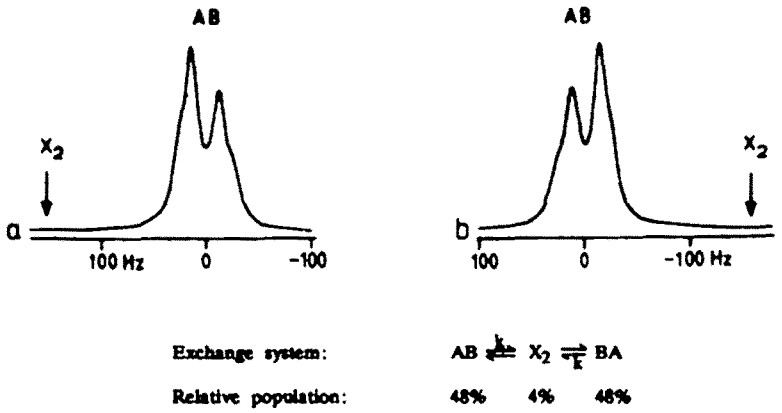


Figure 2. Calculated ^{1}H NMR spectra for the above exchange system with $k = 50\ s^{-1}$ and the X_2 site situated at higher (a) or lower (b) frequency of the AB system.

Clearly at -135 °C enantiomerization of (5) via the oxepine tautomer is slow on the NMR time-scale, leading to chemical shift nonequivalence of the diastereotopic geminal methylene protons. Normally for the coalescence of an AB system to a singlet, the rate constant can be estimated at the coalescence temperature using a simple analytical equation.[11] Alternatively the coalescing AB bandshape can be calculated using a relatively simple computer program.[12] However in the case of compound (5) a close inspection of the coalescing AB system over the temperature range -135 to -108 °C revealed that the high frequency side of the quartet broadened more than the low frequency component (Figure 1). Such behaviour is not consistent with a simple collapse of an AB quartet to a singlet where (as in the present case) the natural linewidths of the H_A and H_B signals are equal.

An asymmetrical AB coalescence of the type observed for compound (5) can be simulated using the Binsch DNMR/3 program[13] by including a small proportion of a third site (X) in the exchange process. This third site, which is assigned to the α-methylene protons in the intermediate oxepine tautomer, is predicted to lie on the low frequency (upfield) side of the arene oxide AB quartet in order to reproduce the more rapid collapse in the higher frequency component of the AB system (Figure 2).

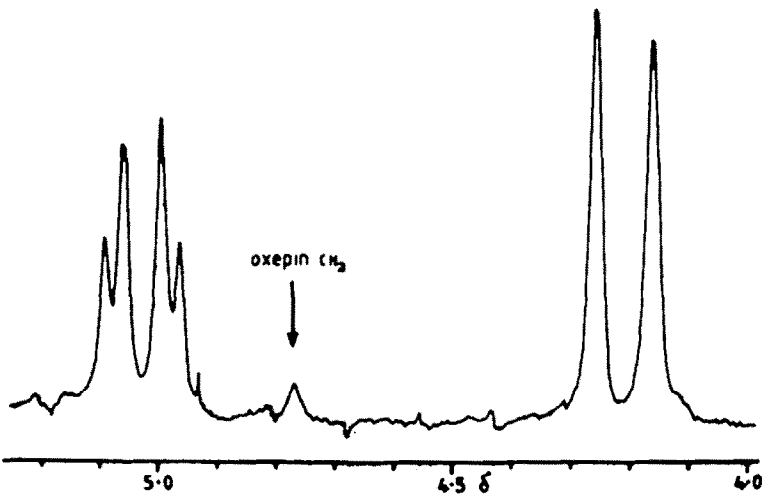
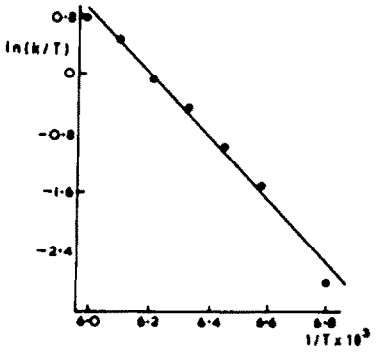


Figure 3. 400 MHz ^{1}H NMR spectrum of compound (5) in dimethyl ether at -142 °C

Table 1. Dynamic ^1H NMR data for compound (5)

Exchange system:			AB $\underset{k}{\rightleftharpoons}$ X_2 $\underset{k}{\rightleftharpoons}$ BA			
Relative population:			47.25%	5.5%	47.25%	
Temperature, °C:	−126	−121	−118	−115	−112	−109	−106
k, s^{-1}:	9	34	58	100	150	260	360



$\Delta H^{\ddagger}$ = 8.6 ± 0.5 kcal mol^{-1}
$\Delta S^{\ddagger}$ = 5.8 ± 3.0 cal K^{-1} mol^{-1}
$\Delta G^{\ddagger}$ = 7.6 ± 0.1 kcal mol^{-1} at −108 °C

Figure 4. Plot of ln(k/T) vs. 1/T for compound (5) together with the activation parameters for isomerization/racemization.

In the light of this prediction, the spectrum of (5) was reinvestigated at slightly lower temperature (−142 °C) using a longer accumulation to improve the signal to noise ratio. A small signal with a relative integrated intensity of 5% was detected at δ 4.76 (Figure 3). Irradiation of this signal produced a reduction in the intensity of the AB quartet by saturation transfer, thereby establishing that this minor component was indeed involved in the exchange process. Knowing the position of the oxepine signal (δ 4.76) relative to the arene oxide AB system, the relative proportion of the oxepine signal was adjusted to provide an optimum fit between calculated and experimental spectra in the exchange broadened region. The optimized population of the oxepine site was determined to be 5.5% which agrees well with the value of 5% measured by direct integration of the X_2 signal at −142 °C.

Careful matching of expanded scale experimental NMR spectra recorded over the temperature range −126 to −106 °C with bandshapes calculated using the DNMR3 program gave the rate constants shown in Table 1. A plot of ln(k/T) vs. 1/T gave a correlation coefficient of 0.994 and the enthalpy and entropy of activation as listed in Figure 4.

The measured rate constants k and derived activation parameters (Table 1) correspond to the arene oxide to oxepine process. Since there is a 50% chance of the intermediate oxepine (X_2) returning to the original arene oxide (AB) rather than converting to the enantiomeric arene oxide (BA), the rate constants for enantiomerization are one half those given in Table 1, and $\Delta S^{\ddagger}$ and $\Delta G^{\ddagger}$ should be adjusted accordingly. However the rate constants and activation parameters for degenerate racemization of chiral (5) are equivalent to the data given in Table 1.

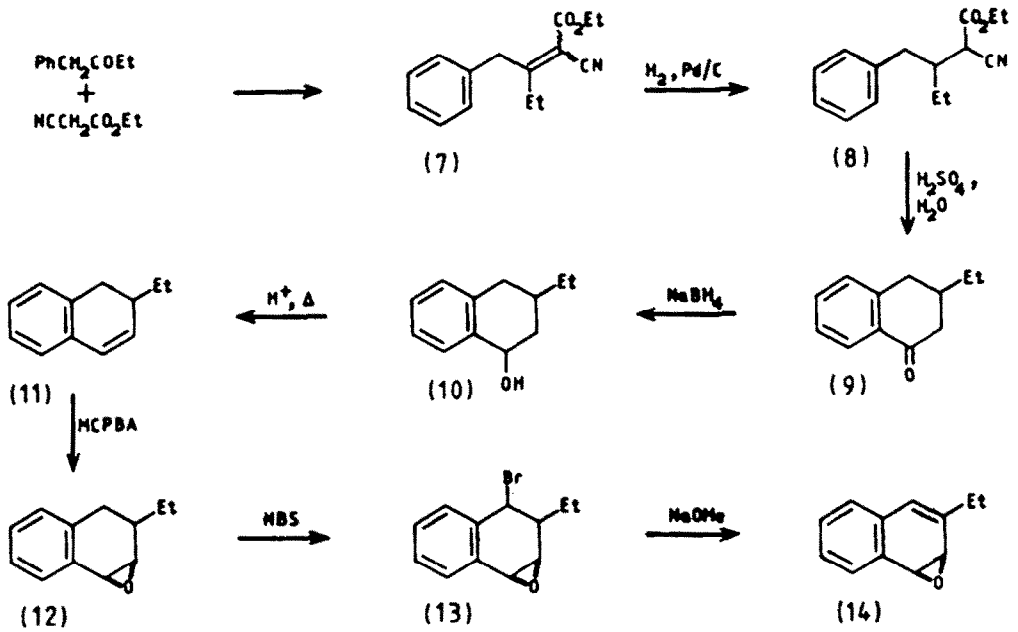
The activation parameters given in Table 1 are identical within experimental errors to those derived from the data listed by Vogel and Günther[2] for the isomerization of benzene oxide to oxepine ($\Delta H^{\ddagger}$ 8.8 kcal mol^{-1}, $\Delta S^{\ddagger}$ 6.6 cal mol^{-1} K^{-1}, $\Delta G^{\ddagger}$ 7.7 kcal mol^{-1} at −113 °C) and toluene-1,2-oxide to 2-methyloxepine ($\Delta H^{\ddagger}$ 8.9 kcal mol^{-1}, $\Delta S^{\ddagger}$ 5.7 cal mol^{-1} K^{-1}, $\Delta G^{\ddagger}$ 8.0 kcal mol^{-1} at −113 °C). Clearly the introduction of the CH_2OCOPh substituent at the 3-position in benzene oxide has little effect on the barrier to isomerization to the 3-substituted oxepine. However the CH_2OCOPh substituent does appreciably perturb the equilibrium so that it is heavily biased towards the arene oxide at low temperatures. The 3-CH_2OCOPh group is situated at the terminus of a homoannular 1,3-diene moiety in the arene oxide form of (5) and may selectively stabilize this valence tautomer by hyperconjugation.[6]

A tacit assumption in equating the rate of racemization of a substituted benzene oxide with the rate of isomerization to the oxepine is that the rate of enantiomerization of the nonplanar oxepine intermediate by ring inversion (6 ⇌ 6') is comparatively rapid.

(6) (6′)

In the case of compound (5) the observation that the methylene resonance in the minor oxepine component was a singlet at −142 °C (Figure 3) rather than an AB quartet strongly suggests that the ring inversion process in the oxepine is fast even at −142 °C, though an accidental chemical shift equivalence of diastereotopic geminal methylene protons cannot be excluded. This view is supported by the recent report[14] that the barrier to ring inversion in a simple oxepine (2-cyano-7-ethyloxepine), determined by low-temperature NMR spectroscopy, is $\Delta G^{\ddagger}$ 6.5 kcal mol^{-1}. This barrier is indeed significantly lower than the measured barrier to valence isomerization in arene oxide (5) given in Table 1, though the difference is not particularly large.

In an attempt to extend this study to polycyclic arene oxides, 3-ethylnaphthalene-1,2-oxide (14) was synthesised. The route started from 1-phenyl-2-butanone and involved eight steps (Scheme I).



Scheme I

The synthesis was complicated by the fact that intermediates (7), (8), (10), (12) and (13) were stereoisomeric mixtures. In particular, the four diastereoisomers of the bromo-epoxide (13) could not be separated due to the lability of this compound. Two isomers (presumably having the ethyl group *trans* to bromine) failed to eliminate HBr to form the desired arene oxide (14). This resulted in (14) being obtained only in admixture with these isomers of (13), and attempts to purify (14) were thwarted by the instability of this arene oxide. A variant in the synthetic route involving the reaction of alkene (11) with N-bromoacetamide/LiOAc/AcOH to form the bromoacetate, followed by bromination with N-bromosuccinimide at the benzylic methylene position and elimination, gave a less pure sample of the arene oxide (14). Stereochemical problems with the elimination in these stereoisomeric intermediates were again evident. Nevertheless (14) was unambiguously characterized by its ^{1}H NMR spectrum and by precise mass measurement (Experimental Section). In particular the CH_2 group of (14), which is connected to an alkene moiety, occurred in a characteristic position in the ^{1}H NMR spectrum,

and the assignments of the other signals of (14) were confirmed by decoupling experiments. Additionally the addition of a trace of hydrochloric acid to the NMR sample of (14) brought about immediate disappearance of the various signals attributed to the arene oxide. Acid catalysed aromatization is a characteristic reaction of arene oxides.

In the 400 MHz ^{1}H NMR spectrum of (14) the methylene protons showed a complex multiplet characteristic of the AB region of an ethyl group ABX_3 system with a small additional allylic coupling (*ca.* 1.5 Hz) to the vinyl proton. Irradiation of the methyl triplet signal at δ 1.24 in deuteriochloroform produced essentially an AB quartet for the methylene protons (δ_A 2.48, δ_B 2.53, J_{AB} 15.7 Hz).

The observation of diastereotopic geminal methylene protons is indicative of the maintenance of chiral integrity of (14) on the NMR time-scale. The thermal instability of (14) limited high temperature NMR studies, but in 1,1,2,2-tetrachloroethane solution (containing a trace of deuteriopyridine as stabilizer) the ethyl group ABX_3 pattern persisted up to 100 °C at which temperature (14) decomposed. This indicates that the barrier to enantiomerization in (14) is greater than 21 kcal mol^{-1} (based on a maximum line broadening of 1 Hz at 100 °C). Naphthalene-1,2-oxide has been isolated in optically active form at ambient temperature.[15] Racemization is unusually slow due to the loss in resonance energy on converting naphthalene-1,2-oxides to the corresponding oxepines.[16] Nevertheless, the observation of geminal chemical shift nonequivalence in (14) established that a prochiral methylene substituent at the 3-position could provide information on the rate of enantiomerization/valence isomerization in polycyclic arene oxides.

This approach might be extended to arene oxides of other polycyclic aromatic hydrocarbons, some of which (e.g. benzo[e]pyrene 1,2-oxide) are predicted[16] to have much lower barriers to enantiomerization. However the incorporation of a 3-substituent by an analogous route to that shown in Scheme 1 may be expected to cause similar synthetic complications which could prevent the isolation of a pure sample of the arene oxide.

Acknowledgements. – We thank the S.E.R.C. for supporting this work with a research grant and for providing a studentship to M.R. We are also grateful to Dr. O.W. Howarth for 400 MHz spectra run under the auspices of the S.E.R.C. High Field NMR Service at Warwick, and to the S.E.R.C. NMR Program Library (Daresbury) for providing copies of their version (DNMRS and DNMRL) of the DNMR3 program.

EXPERIMENTAL

NMR spectra were obtained using Bruker WH-400, Bruker WM-250, Varian XL-100 or Jeol FX-60 instruments in deuteriochloroform unless specified otherwise with tetramethylsilane as reference. Accurate relative molecular masses were determined by the peak-matching method using perfluorokerosene as reference on an AEI-MS902 mass spectrometer (updated by V.G. Instruments).

Dynamic NMR Studies. Low temperature ^{1}H NMR experiments were performed in dimethyl ether at 400 MHz on the Bruker WH-400 instrument. Probe temperatures were calibrated with a digital copper constantan thermocouple inserted in a dummy sample of the same volume. Exchange-broadened spectra were calculated using the S.E.R.C. NMR Program Library (Daresbury) version (DNMRS) of the Binsch DNMR3 program.[13]

1-(Hydroxymethyl)-2,5-cyclohexadiene-1-carboxylic acid. This compound was prepared in 45% yield by the reaction of the dianion of 1,4-dihydrobenzoic acid[7] (5.5 g) with formaldehyde according to the procedure of Ganem *et al.*,[7] m.p. 95–96 °C (lit.[7] 97–99 °C), δ_H ($CDCl_3$) 2.70 (2H, broad s, allylic H), 3.71 (2H, s, CH_2O) and 5.7–6.2 (4H, m, vinyl H).

5-Bromo-1-(hydroxymethyl)-7-oxabicyclo[4.2.0]oct-2-en-8-one. Bromolactonization of the above acid (2.8 g) using the method of Ganem *et al.*[7] gave the bromolactone (1.9 g, 44%), m.p. 48–49 °C (lit.[7] 50–55 °C), δ_H ($CDCl_3$) 2.72 (2H, m, allylic H), 3.09 (1H, broad s, OH), 3.77 and 4.08 (2H, AB quartet, J 11 Hz, CH_2O), 4.57 (1H, m, CHBr), 5.07 (1H, d, J 3 Hz, CHO), 5.62 (1H, d, J 10 Hz, vinyl H) and 5.9–6.2 (1H, m, vinyl H).

1-[(Benzoyloxy)methyl]-5-bromo-7-oxabicyclo[4.2.0]oct-2-en-8-one. Treatment of the above bromolactone (1.7 g) with benzoyl chloride (1.5 g) and pyridine (1.7 g) in dichloromethane gave the benzoate (2.2 g, 92%), m.p. 96–97 °C (lit.[7] 103–104 °C), δ_H ($CDCl_3$) 2.75 (2H, broad s, allylic H), 4.60 (3H, m, CHBr and CH_2O), 5.04 (1H, d, J 3 Hz, CHO), 5.78 (1H, d, J 3 Hz, vinyl H), 6.0–6.2 (1H, m, vinyl H), 7.51 (3H, m, aromatic) and 8.10 (2H, m, aromatic).

1-[(Benzoyloxy)methyl]-6-bromo-3,8-dioxatricyclo[5.2.0.0^{2,4}]nonan-9-one. Epoxidation of the above benzoyloxy bromolactone (2.2 g) with peroxytrifluoroacetic acid in dichloromethane in the presence of Na_2HPO_4 as described by Ganem[7] gave a yellow oil (2.0 g). [CAUTION Adequate protection against explosion should be adopted when using high-test H_2O_2; efficient stirring of the reaction mixture must be maintained]. Column chromatography on silica gel using hexane–ethyl acetate (10:1) as eluant gave first the minor isomer (0.4 g, 18%), m.p. 92–93 °C (lit.[7] 94.5–96 °C), δ_H ($CDCl_3$) 2.80 (2H, m, CH_2), 3.3–3.6 (2H, m, epoxide H), 4.40 (1H, m, CHBr), 4.78 (2H, s, CH_2O), 4.95 (1H, d, J 3 Hz, CHO), 7.54 (3H, m, aromatic) and 8.10 (2H, m, aromatic). Continued elution afforded the major isomer (1.2 g, 53%), m.p. 121–123 °C (lit.[7] 122–124 °C), δ_H ($CDCl_3$), 2.53 (2H, m, CH_2), 3.49 (2H, m, epoxide H), 4.41 (1H, m, CHBr), 4.70 (2H, s, CH_2O), 4.89 (1H, d, J 3 Hz, CHO), 7.54 (3H, m, aromatic) and 8.15 (2H, m, aromatic).

7-Oxabicyclo[4.1.0]hepta-2,4-diene-2-methanol benzoate (α-benzoyloxytoluene-2,3-oxide) (5). Reaction of the above epoxylactone (0.23 g) with DBU in dry benzene under nitrogen[7] followed by chromatography on alumina (Woelm, activity IV) with benzene as eluant gave the pure arene oxide 5 (0.07 g, 48%) as a yellow oil, δ_H (C_6D_6), 4.37 (1H, m, epoxide H), 4.53 (1H, m, epoxide H), 4.72 (1H, s, CH_2O), 5.62–6.15 (3H, complex m, alkene), 7.16 (3H, m, aromatic) and 8.07 (2H, m, aromatic). [All glassware used in preparing or handling 5 was previously rinsed in 30% ammonium hydroxide and dried at 120 °C].

Ethyl(2-cyano-3-ethyl-4-phenyl)but-2-enoate (7). 1-Phenyl-butan-2-one (14.8 g, 0.1 mol), cyanoethylacetate (22.6 g, 0.2 mol), acetic acid (20 cm^3) and ammonium acetate (8 g) were heated at reflux in anhydrous benzene (100 cm^3) for 24 h. The product mixture was cooled, washed with water, dried (Na_2SO_4) and concentrated under vacuum. Distillation under reduced pressure yielded the product 7 (24 g, 99%) as an oil which was a 1:1 mixture of E/Z-isomers, b.p. 140–150 °C/0.5 mm. (Found: C, 74.1; H, 7.0; N, 6.35. $C_{15}H_{17}O_2N$ requires C, 74.1; H, 7.0; N, 6.2%), IR (film) 2220 (CN), 1722 cm^{-1} (CO), δ_H 7.18–7.35 (10H, m, aromatic), 4.31 (2H, q, J 7.2 Hz, OCH_2), 4.29 (2H, q, J 7.0 Hz, OCH_2'), 4.21 (2H, s, Ph$\underline{CH_2}$), 3.90 (2H, s, Ph$\underline{CH_2}'$), 2.69 (2H, q, J 7.5 Hz, C–CH_2), 2.49 (2H, q, J 7.5 Hz, C–CH_2'), 1.35 (3H, t, J 7.5 Hz, OCMe), 1.20 (3H, t, J 7.0 Hz, OCMe'), 1.13 (3H, t, J 7.5 Hz, CCMe), 1.05 (3H, t, J 7.5 Hz, CCMe').

Ethyl(2-cyano-3-ethyl-4-phenyl)butanoate (8). Olefin 7 (24.0 g, 0.1 mol) was catalytically reduced in ethanol solution (300 cm^3) using palladium on charcoal (1.0 g, 5%). The mixture was stirred for 16 h under normal pressure of hydrogen when the reaction was complete (2.2 litres H_2 absorbed). The catalyst was filtered off and filtrate was concentrated under vacuum. The product was distilled under reduced pressure to yield the desired ester 8 (22.0 g, 91%) as a colourless oil which appeared to be a mixture of diastereoisomers, b.p. 120–124 °C/0.05 mm. (Found: C, 73.6; H, 7.7; N, 6.2. $C_{15}H_{19}O_2N$ requires C, 73.5; H, 7.8; N, 6.2%), IR (film) 2240 (CN), 1740 cm^{-1} (CO), δ_H ($CDCl_3$) 7.18–7.36 (10H, m, aromatic), 4.20 (2H, q, J 7.2 Hz, OCH_2), 4.10 (2H, q, J 7.2 Hz, OCH_2'), 3.65 (1H, d, J 3.8 Hz, C$\underline{H}$'–CN), 3.39 (1H, d, J 3.8 Hz, C$\underline{H}$–CN), 3.04 (1H, dd, Ph$\underline{CH}$), 2.75 (2H, m, Ph$\underline{CH_2}'$), 2.50 (1H, m, Ph$\underline{CH}$), 2.37 (2H, m, $\underline{H}$–C–Et, $\underline{H}'$–C–Et), 1.58 (4H, m, $\underline{CH_2}$Me, $\underline{CH_2}'$Me), 1.28 (3H, t, J 7.2 Hz, OC$\underline{Me}$), 1.27 (3H, t, J 7.2 Hz, OC$\underline{Me}'$), 1.03 (3H, J 7.5 Hz, CC$\underline{Me}'$), 0.96 (3H, J 7.5 Hz, CC$\underline{Me}$).

3-Ethyl-1-oxo-1,2,3,4-tetrahydronaphthalene (9). A solution of cyanoester 8 (20 g, 0.08 mol) in acetic acid (120 cm^3) water (60 cm^3) and conc. sulphuric acid (60 cm^3) was heated at reflux for 20 h. The mixture was cooled and a further portion of acetic acid (60 cm ^{3}) and sulphuric acid (30 cm^3) was added before continuing the reflux for an additional 6 h. The product mixture was cooled and ether was added. The ether solution was washed with water, sodium carbonate solution (10%), water and dried (Na_2SO_4) before concentration. An oil was obtained which was distilled under reduced pressure to yield the ketone (13.0 g, 91%), b.p. 116–118 °C/0.8 mm. (Found: C, 82.7, H, 8.2. $C_{12}H_{14}O$ requires C, 82.8, H, 8.1%), IR (film) 1680 cm^{-1} (CO), δ_H ($CDCl_3$) 8.01 (1H, d, J 7.7 Hz, H_8), 7.48–7.21 (3H, m, H_5, H_6, H_7), 2.97 (1H, dd, J 16.0, 3.7 Hz, H_4), 2.75 (1H, dd, J 16.0, 3.7 Hz, H_2), 2.67 (1H, dd, J 16.0, 10.6 Hz, H_4), 2.28 (1H, dd, J 16.0, J 10.6 Hz, H_2), 2.05 (1H, m, H_3), 1.46 (2H, m, $\underline{CH_2}$Me), 0.97 (3H, t, J 7.4 Hz, Me).

3-Ethyl-1-hydroxy-1,2,3,4-tetrahydronaphthalene (10). Excess sodium borohydride (3 g) was added in portions to a stirred solution of ketone 9 (5.2 g, 0.03 mol) in methanol (50 cm^3) at 0 °C. Stirring was continued for 4 h at room temperature and the product mixture was concentrated under vacuum. The concentrate was dissolved in diethyl ether and this solution was washed with water, dried ($MgSO_4$) and concentrated to yield a solid (5.0 g, 95%). Recrystallization from pentane yielded a single isomer of alcohol 10, m.p. 68–69 °C. (Found: C, 81.8; H, 9.0. $C_{12}H_{16}O$ requires C, 81.8; H, 9.1%), IR (film) 3310 cm^{-1} (OH), δ_H ($CDCl_3$) 7.58–7.00 (4H, m, aromatic), 4.82 (1H, dd, J 10.7, 5.6 Hz, C$\underline{H}$OH), 2.84 (1H, dd, J 17.0, 3.3 Hz, H_4), 2.45 (1H, dd, J 16.3, 11.4 Hz, H_4), 2.31 (1H, m, H_3), 1.53 (2H, m, H_2), 1.43 (2H, m, $\underline{CH_2}$Me), 0.98 (3H, t, J 7.4 Hz, Me).

1,2-Dihydro-2-ethyl-naphthalene (11). A solution of alcohol 10 (1.76 g, 0.01 mol) was dissolved in benzene (50 cm^3) and a small quantity of p-toluenesulphonic acid (0.1 g) was added. The solution was heated under reflux in a Dean–Stark apparatus for 1 h. The solution was cooled, washed with water, dried (Na_2SO_4) and concentrated to yield a viscous oil. Distillation under reduced pressure gave the desired olefin 11 (1.3 g, 82%), b.p. 84–86 °C/22 mm. (Found: C, 91.2; H, 8.8. $C_{12}H_{14}$ requires C, 91.1; H, 8.9%), δ_H ($CDCl_3$) 7.25–7.00 (4H, m, aromatic), 6.41 (1H, d, J 9.6 Hz, H_4), 5.92 (1H, dd, J 9.6, 3.5 Hz, H_3), 2.85 (1H, dd, J 15.3, 6.7 Hz, H_1), 2.59 (1H, dd, J 15.3, 10.6 Hz, H_1), 2.34 (1H, m, H_2), 1.40 (2H, m, $\underline{CH_2}$Me), 0.95 (3H, t, Me).

1,2-Epoxy-3-ethyl-1,2,3,4-tetrahydronaphthalene (12). A solution of olefin 11 (0.22 g, 1.39 mmol) in dichloromethane (30 cm^3) was stirred with phosphate buffer (pH 8.00, 30 cm^3) at 0 °C. Metachloroperoxybenzoic acid (0.29 g, 1.68 mmol) was added to the stirred mixture in small portions over a ten minute period. The mixture was stirred at room temperature for 3.5 h prior to addition of a further portion of peroxy acid (0.29 g) at 0 °C. The mixture was stirred at room temperature overnight. The organic layer was separated, washed successively with solutions of sodium sulphite, sodium bicarbonate and water, then dried (Na_2SO_4) and concentrated. The tetrahydroepoxide 12 was obtained as an oil consisting of two isomers (38:62) which was purified by distillation (0.22 g, 90%), b.p. 48–50 °C/0.1 mm. (Found: C, 83.0; H, 8.3. $C_{12}H_{14}O$ requires C, 82.8; H, 8.1%), δ_H ($CDCl_3$) 7.04–7.42 (8H, m, aromatic), 3.86 (1H, d, J 4.3 Hz, H_1), 3.81 (1H,

d, J 4.2 Hz, H_1'), 3.61 (1H, d, J 4.2 Hz, H_2), 3.56 (1H, m, H_2'), 2.91 (1H, dd, J 9.2, 15.5 Hz, H_4'), 2.46–2.59 (3H, m, $2H_4$ + H_4'), 2.38 (1H, m, H_3'), 1.84 (1H, m, H_3), 1.79 (1H, m, CHMe), 1.69 (1H, m, CHMe), 1.30 (1H, m, CH'Me), 1.12 (3H, t, J 7.4 Hz, Me), 1.02 (1H, m, CH'Me), 0.95 (3H, t, J 7.2 Hz, Me').

4-Bromo-1,2-epoxy-3-ethyl-1,2,3,4-tetrahydronaphthalene (13). A stirred mixture of the tetrahydroepoxide 12 (0.21 g, 1.21 mmol), N-bromosuccinimide (0.22 g, 1.24 mmol) and α,α'-azoisobutyrodinitrile (0.001 g) in carbon tetrachloride (10 cm^3) was irradiated using a sunlamp under an atmosphere of nitrogen at 60 °C. The reaction was found to be complete after 0.75 h. The succinimide was filtered off and the filtrate was concentrated to yield a viscous oil which was too unstable for further purification. The product was a mixture of four bromoepoxide isomers 13 (0.3 g, 98%) which were characterized by n.m.r. analysis and used immediately in the final stage. (Found: m/z 252.0146. $C_{12}H_{13}OBr$ requires 252.0150), δ_H ($CDCl_3$) 7.19–7.80 (16H, m, aromatic), 5.27 (1H, d, J 4.3 Hz, H_4), 5.27 (1H, d, J 4.3 Hz, H_4'), 5.20 (1H, bs, H_4''), 4.96 (1H, d, J 10.8 Hz, H_4'''), 3.92–3.95 (4H, m, H_1, H_1', H_1'', H_1'''), 3.67–3.76 (4H, m, H_2, H_2', H_2'', H_2'''), 3.00–2.16 (4H, m, H_3, H_3', H_3'', H_3'''), 2.16–1.70 (8H, m, CH_2Me), 0.97–1.20 (12H, m, Me).

3-Ethyl-naphthalene-1,2-oxide (14). A mixture of bromoepoxide stereoisomers 13 (0.25 g, 0.98 mmol) sodium methoxide (0.5 g) and dry tetrahydrofuran (5 cm^3) was stirred at 0 °C for 20 h. The reaction mixture was diluted with cold diethyl ether (50 cm^3), washed with water (2 x 15 cm^3), dried (K_2CO_3) and concentrated to yield a pale yellow residue of the crude arene oxide (14). N.m.r. analysis of this unstable sample showed the presence of arene oxide (33%) and unreacted bromoepoxide isomers (67%). Estimated yield of the arene oxide 14 was 0.05 g (29%). (Found: m/z 172.0887. $C_{12}H_{12}O$ requires 172.0888), δ_H ($CDCl_3$) 6.97–7.48 (4H, m, aromatic), 6.46 (1H, d, J 1.4 Hz, H_4), 4.45 (1H, d, J 4.0 Hz, H_1), 3.98 (1H, dd, J 2.0, 4.0 Hz, H_2), 2.48–2.53 (2H, m, CH_2Me), 1.24 (3H, t, J 7.5 Hz, Me). The arene oxide peaks were found to disappear upon addition of acid, and a phenolic product, RMM 172, was formed.

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