Arene Oxides of Quinoline: Epoxidation, *N*-Oxidation and *N*-Methylation Reactions

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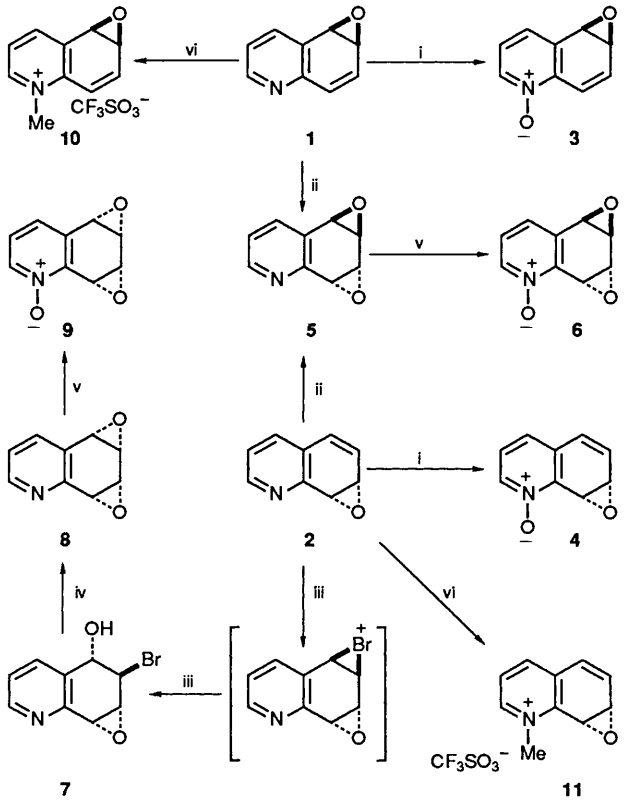
trans-5,6,7,8-Diepoxy-5,6,7,8-tetrahydroquinoline **5**, 5,6-epoxy-5,6-dihydroquinoline 1-oxide **3**, 7,8-epoxy-7,8-dihydroquinoline 1-oxide **4** and *trans*-5,6,7,8-diepoxy-5,6,7,8-tetrahydroquinoline 1-oxide **6** have been formed by oxidation of the corresponding arene oxides of quinoline, 5,6-epoxy-5,6-dihydroquinoline **1** and 7,8-epoxy-7,8-dihydroquinoline **2**. The *cis*-diepoxides, *cis*-5,6,7,8-diepoxy-5,6,7,8-tetrahydroquinoline **8** and *cis*-5,6,7,8-diepoxy-5,6,7,8-tetrahydroquinoline 1-oxide **9** were both obtained by a stepwise synthesis from 7,8-epoxy-7,8-dihydroquinoline **2** *via* the bromohydrin **7**. *N*-Methylation of 5,6-epoxy-5,6-dihydroquinoline **1** and 7,8-epoxy-7,8-dihydroquinoline **2** with methyl trifluoromethanesulphonate yielded the corresponding *N*-methylquinolinium arene oxide salts **10** and **11**.

The ubiquitous nature of quinoline in the environment,[1-3] allied to its established role as both a mutagen[4,5] and a carcinogen,[6,7] has prompted an intensive study of its metabolism by animal enzyme systems both at these[8] and other[6] laboratories. Quinoline differs from the majority of carcinogenic polycyclic arenes and azaarenes[9] by being devoid of a bay-region. As part of a programme to determine the origin of the mutagenic/carcinogenic properties of quinoline, chemical synthetic routes to both arene oxide and *trans*-dihydro diol metabolites of quinoline (at the 5,6- and 7,8-bonds) have previously been reported.[8] The present work (and the preliminary communication[10]) is concerned with the synthesis of a range of oxidation products of the arene oxides which are potential minor metabolites of quinoline and could contribute to its carcinogenicity.

Results and Discussion

Naphthalene and 1,2-epoxy-1,2-dihydronaphthalene have been oxidized to the corresponding arene dioxide (*trans*-1,2,3,4-diepoxy-1,2,3,4-tetrahydronaphthalene) chemically[11] and by liver microsomal enzymes.[12] In view of the structural similarity between naphthalene and quinoline the chemical synthesis of both *cis*-**8** and *trans*-5,6,7,8-diepoxy-5,6,7,8-tetrahydroquinoline **5** has been undertaken in the present study. The ability of animal enzymes to effect both *N*-oxidation[6] and *N*-methylation[13] of quinoline has now led to the chemical synthesis of a new range of *N*-oxide (**3**, **4**, **6**, **9**) and *N*-methyl (**10**, **11**) derivatives of quinoline arene oxides **1** and **2**. These products of epoxidation, *N*-oxidation and *N*-methylation of quinoline arene oxides may thus be considered as potential minor metabolites of quinoline and possible mutagens.

Both heteroatom oxidation (to yield quinoline *N*-oxide[6]) and arene epoxidation (to yield 5,6-epoxy-5,6-dihydro- **1** and 7,8-epoxy-7,8-dihydroquinoline **2**)[8] have been found in the metabolism of quinoline by animal enzymes. While heteroatom oxidation to yield quinoline *N*-oxide is the major chemical oxidation (peroxyacid) pathway for quinoline, aromatic hydroxylation (to yield 3-hydroxyquinoline) has also been observed as a minor contributor.[14] The chemical oxidation of the arene oxides of quinoline has been briefly discussed in a preliminary report of the present study.[10]



Scheme 1 The formulae shown indicate relative and not absolute configurations. *Reagents and conditions:* i, MCPBA/$CHCl_3$/H_2O/Na_2CO_3; ii, NaOCl/CH_2Cl_2/Bu_4NHSO_4; iii, NBA/H_2O/THF; iv, NaOMe/H_2O/THF; v, DMD/acetone; vi, CF_3SO_3Me/CH_2Cl_2.

Attempted peroxyacid epoxidation of arene oxides (*e.g.* 1,2-epoxy-1,2-dihydronaphthalene) normally results in aromatization due to their sensitivity toward acidic conditions. Earlier studies have shown that the arene oxides of quinoline are generally more stable than arene oxides of polycyclic aromatic hydrocarbons[8] and should thus be more resistant to aromatization during both chemical and enzyme-catalysed reactions and may yield a new range of products and

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metabolites. This has been verified by oxidation of the 5,6- **1** and 7,8-arene oxide **2** of quinoline using *meta*-chloroperoxybenzoic acid (MCPBA) in a two phase (chloroform–aqueous sodium carbonate) system where the corresponding *N*-oxides were isolated in acceptable (82, 57%) yield. The *N*-oxide arene oxide compounds **3** and **4** proved to be less stable (particularly compound **4**) and thus more difficult to purify than the parent arene oxides **1** and **2**. *N*-Oxidation of arene oxides **1** and **2** replaces the basic nitrogen lone pair by an electron-donating oxide substituent, which, through resonance of the formal negative charge, diminishes the electron-withdrawing character of the heterocyclic ring. Thus, a decreased stability of the *N*-oxide arene oxide products **3** and **4** relative to the quinoline oxides **1** and **2** should result.

Epoxidation of quinoline arene oxides **1** and **2** to give *ca.* 45% yields of *trans*-5,6,7,8-diepoxy-5,6,7,8-tetrahydroquinoline **5** (without evidence of *N*-oxidation) was achieved using a non-acidic two phase oxidizing system *i.e.* buffered aqueous sodium hypochlorite (pH 8.6)–dichloromethane in the presence of a phase transfer reagent, Bu_4NHSO_4. Isolation of a pure sample of the *trans*-diepoxide **5** was complicated by its instability during purification (rapid discoloration in air) and by the formation of a minor halogenated product whose spectral (IR, NMR, MS) characteristics were consistent with addition of chlorine at the olefinic bonds of arene oxides **1** and **2**. The *trans*-configuration for arene dioxide **5** was deduced from the ^1H NMR spectrum and from chromatographic characteristics relative to those of the corresponding *cis*-isomer **8**.

The *cis*-arene dioxide **8** could not be synthesised directly by oxidation of the arene oxides **1** and **2** and an alternative stepwise route *via* bromohydrin **7** was therefore employed. Treatment of 7,8-epoxy-7,8-dihydroquinoline **2** with an aqueous solution of tetrahydrofuran (THF) containing *N*-bromoacetamide was assumed to proceed *via* formation of a *trans* cyclic bromonium ion intermediate (Scheme 1) to yield the bromohydrin **7** as the only identified isomer. Treatment of bromohydrin **7** with sodium methoxide in anhydrous THF yielded the *cis*-arene dioxide **8** exclusively. The stereochemical assignments to the *trans* **5** and *cis* **8**-arene dioxides were made on the basis of (*a*) R_f values from TLC analysis, (*b*) ^1H NMR coupling constants and δ values for the 6-H and 7-H protons and (*c*) comparison with the corresponding *cis* and *trans* naphthalene dioxides.[15]

The more polar *cis*-arene dioxide **8** had a lower R_f (0.3) than the corresponding *trans* isomer **5** [R_f 0.6, silica gel, methanol–chloroform (4:96)]. The coupling constant $J_{6,7}$ was larger (3.02 Hz) for the *cis* arene dioxide **8** than for the *trans* isomer **5** (1.85 Hz). An inspection of the corresponding molecular models showed that the dihedral angle between the 6-H and 7-H protons was close to 90° for the *trans* isomer **5** but much smaller for the *cis* isomer **8**. Furthermore, the non-benzylic 6-H and 7-H protons were found to be downfield (at δ *ca.* 4.1) of the benzylic 5-H and 8-H protons (δ 3.73, 3.91) in the *trans* isomer **5** only, presumably due to the proximate deshielding zones of the neighbouring oxirane ring. By contrast, the 6-H and 7-H protons appeared in their normal position (δ *ca.* 3.97) relative to the benzylic 5-H and 8-H protons (δ 4.05, 4.18) in the ^1H NMR spectrum of the *cis* isomer. A similar smaller coupling constant and downfield shift for the non-benzylic protons was found for *trans*-1,2,3,4-diepoxy-1,2,3,4-tetrahydronaphthalene.[15]

Oxidation of both *trans* **5** and *cis* **8** arene dioxides by MCPBA yielded the corresponding *N*-oxides **6** and **9**; however, partial decomposition of the products during the synthesis and purification of these water-soluble compounds gave considerably reduced yields. Dimethyldioxirane (DMD) in acetone is a very powerful neutral oxidant which has previously been used in *N*-oxidation.[16,17] This reagent was found to give the required *N*-oxides **6** and **9** in quantitative yields from the corresponding arene dioxides **5** and **8**. A major advantage of this procedure was that product isolation required no extraction, simply evaporation of solvent and excess of oxidant.

As part of a kinetic investigation into the solvolysis and aromatization of the arene oxides **1** and **2**[18] the effect of protonation of the nitrogen atom was considered. For these studies the *N*-methyl cation of 5,6-epoxy-5,6-dihydroquinoline **10** was previously synthesised[18] as a model compound using dimethyl sulphate. An improved method of synthesis for compound **10** has now been found. Thus, the action of methyl trifluoromethanesulphonate (one of the most powerful methylating reagents available) on the quinoline arene oxides **1** and **2** gives the corresponding *N*-methyl cations **10** and **11** as crystalline trifluoromethanesulphonate salts under mild conditions (−5 to −10 °C) and in high yield (83–87%). In contrast with many of the other products derived from the arene oxides **1** and **2** which are relatively unstable, the *N*-methyl quarternary salts **10** and **11** proved to be remarkably stable compounds which were unchanged after a 4 week period at ambient temperature in either the crystalline state or in $CDCl_3$ solution.

The *N*-methyl cation of 5,6-epoxy-5,6-dihydroquinoline **10** has previously[18] been found to be much more susceptible to nucleophilic attack by hydroxide ion than the parent arene oxide **1** (rate difference 5×10^4). More detailed studies of the attack of nucleophiles on both arene oxides **1** and **2** and the *N*-methyl cations **10** and **11** will be reported elsewhere.

The arene oxides **1** and **2**, *N*-oxide arene oxides **3** and **4**, arene dioxides **5** and **8**, and 5,6-epoxy-*N*-methyl-5,6-dihydroquinolinium ion **10** have all been tested for mutagenicity using the Ames method.[19] Of these compounds only arene oxide **2**, the *N*-methyl arene oxide **10**, and the *trans* dioxide **5** were appreciably mutagenic; however, their specific mutagenic activities were not as high as that of quinoline itself. Thus, in the event that any of the compounds shown in Scheme 1 are detected as minor metabolites of quinoline in mammals, it is unlikely that they will make a significant contribution to the mutagenic/carcinogenic character of this azaarene.

Experimental

^1H NMR spectra were recorded using 250 MHz (Bruker WH250), 300 MHz (General Electric QE300), and 400 MHz (Bruker WP400) instruments. *J* Values are in Hz. Mass spectra were recorded at 70 eV using an AEI-MS902 instrument updated by VG instruments. Accurate molecular masses were determined by the peak matching method using perfluorokerosene as reference.

5,6-Epoxy-5,6-dihydroquinoline **1** and 7,8-epoxy-7,8-dihydroquinoline **2** were synthesised by the previously reported methods.[8]

5,6-Epoxy-5,6-dihydroquinoline 1-Oxide **3**.—5,6-Epoxy-5,6-dihydroquinoline **1** (0.046 g, 0.32 mmol) and *m*-chloroperoxybenzoic acid (0.072 g, 0.42 mmol) in chloroform (5 ml) were stirred with $NaHCO_3$ (0.1 g) in water (4 ml) for 0.5 h at 5 °C and for 7 h at 18 °C. The chloroform solution was diluted (30 ml, $CHCl_3$), washed with $NaHSO_3$, Na_2CO_3, dried (K_2CO_3) and concentrated to yield *5,6-epoxy-5,6-dihydroquinoline 1-oxide* **3**. Purification by column chromatography (basic alumina, using $CHCl_3$ as eluent) yielded the *N*-oxide **3** (0.042 g, 82%), m.p. 127–130 °C (ethyl acetate–hexane) (Found: M^+, 161.0475. $C_9H_7NO_2$ requires *M*, 161.0477); δ_H(250 MHz; $CDCl_3$) 4.17 (1 H, m, 6-H), 4.50 (1 H, d, $J_{5,6}$ 3.65, 5-H), 6.82 (1 H, dd, $J_{7,8}$ 10.15, $J_{6,7}$ 3.65, 7-H), 7.21 (1 H, dd, $J_{2,3}$ 6.75, $J_{3,4}$ 7.60, 3-H), 7.50 (1 H, d, $J_{3,4}$ 7.60, 4-H), 7.73 (1 H, dd, $J_{7,8}$ 10.22, $J_{6,8}$ 1.20, 8-H) and 8.27 (1 H, dd, $J_{2,3}$ 6.50, $J_{2,4}$ 1.05, 2-H).

7,8-Epoxy-7,8-dihydroquinoline 1-Oxide **4**.—*N*-Oxidation of

7,8-epoxy-7,8-dihydroquinoline **2** (0.128 g, 0.90 mmol) using *m*-chloroperoxybenzoic acid (0.18 g, 1.04 mmol) was carried out in a similar manner to that for compound **3**. Yield 0.081 g (57%), m.p. 115–130 °C (decomp.) (Found: M^+, 161.0478. $C_9H_7NO_2$ requires *M*, 161.0477); δ_H(250 MHz; $CDCl_3$) 4.17 (1 H, m, 7-H), 5.43 (1 H, d, $J_{7,8}$ 3.9, 8-H), 6.66 (2 H, m, 5-H and 6-H), 7.25 (2 H, m, 3-H and 4-H) and 8.24 (1 H, dd, $J_{2,3}$ 6.2, $J_{2,4}$ 1.1, 2-H).

trans-5,6,7,8-*Diepoxy*-5,6,7,8-*tetrahydroquinoline* **5**.—To a solution of 7,8-epoxy-7,8-dihydroquinoline **2** (0.2 g, 1.4 mmol) in dichloromethane (30 ml) was added aqueous sodium hypochlorite (14%; 15 ml) buffered to pH 8.6 with 0.6 mol dm^{-3} potassium phosphate (10 ml) and a phase transfer catalyst, tetrabutyl ammonium hydrogensulphate (0.06 g). The solution was stirred at room temperature for 18 h, the organic layer was separated, and the aqueous phase was extracted with dichloromethane (3 × 20 ml). The combined organic extracts were washed with sodium thiosulphate (0.1 mol dm^{-3}; 20 ml), dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified by preparative TLC on silica gel using diethyl ether as eluent to yield trans-5,6,7,8-*diepoxy*-5,6,7,8-*tetrahydroquinoline* **5** (0.098 g, 44%, R_f 0.35), m.p. 44–46 °C (diethyl ether–pentane) (Found: M^+, 161.0475. $C_9H_7NO_2$ requires *M*, 161.0477); δ_H(300 MHz, $CDCl_3$) 3.73 (1 H, d, $J_{5,6}$ 3.9, 5-H), 3.91 (1 H, d, $J_{7,8}$ 3.9, 8-H), 4.04–4.10 (2 H, m, 6-H and 7-H), 7.28 (1 H, dd, $J_{3,4}$ 7.7, $J_{2,3}$ 4.9, 3-H), 7.73 (1 H, dd, $J_{3,4}$ 7.7, $J_{2,4}$ 1.5, 4-H) and 8.55 (1 H, dd, $J_{2,3}$ 4.9, $J_{2,4}$ 1.5, 2-H).

Treatment of 5,6-epoxy-5,6-dihydroquinoline **1** (0.2 g, 1.4 mmol) with aqueous sodium hypochlorite (14%; 15 ml) in a similar manner to arene oxide **2**, again yielded *trans*-5,6,7,8-diepoxy-5,6,7,8-tetrahydroquinoline **5** (0.108 g, 48%) after TLC purification. This purification step was required in order to separate the major *trans* diepoxide product **5** from a minor component which appeared to be 7,8-dichloro-5,6-epoxy-5,6,7,8-tetrahydroquinoline on the basis of ^1H NMR and MS data.

6-*Bromo*-5-*hydroxy*-7,8-*epoxy*-5,6,7,8-*tetrahydroquinoline* **7**.—*N*-Bromoacetamide (0.26 g, 1.9 mmol) was added to a solution of 7,8-epoxy-7,8-dihydroquinoline **2** (0.25 g, 1.7 mmol) in THF (3 ml) and water (1.5 ml) and was stirred at room temperature for 4 h. The THF was removed under reduced pressure, water (5 ml) was added to the residue and the product was extracted with dichloromethane. The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to yield 6-*bromo*-5-*hydroxy*-7,8-*epoxy*-5,6,7,8-*tetrahydroquinoline* **7** (0.38 g, 91%), m.p. 142–156 °C (decomp.) (dichloromethane–diethyl ether) (Found: C, 44.6; H, 3.15; N, 5.5. $C_9H_8BrNO_2$ requires C, 44.6; H, 3.3; N, 5.5%); δ_H(300 MHz, $CDCl_3$) 2.93 (1 H, br s, OH), 4.21 (1 H, m, 7-H), 4.41 (1 H, d, $J_{7,8}$ 3.8, 8-H), 4.78 (2 H, m, 5-H and 6-H), 7.41 (1 H, m, 3-H), 7.73 (1 H, d, $J_{3,4}$ 7.5, 4-H) and 8.63 (1 H, d, $J_{2,3}$ 4.8, 2-H).

cis-5,6,7,8-*Diepoxy*-5,6,7,8-*tetrahydroquinoline* **8**.—Sodium methoxide (0.5 g) was added to a solution of 6-bromo-5-hydroxy-7,8-epoxy-5,6,7,8-tetrahydroquinoline **7** (0.36 g, 1.5 mmol) in THF (50 ml) and stirred at 0 °C for 1 h and at room temperature for 4 h. The solvent was removed under reduced pressure and the residue was treated with water (10 ml) and extracted with dichloromethane. The latter extract was dried ($MgSO_4$) and the solvent was removed under reduced pressure. Preparative TLC purification of the residue on silica gel using diethyl ether as eluent (4 elutions) yielded pure cis-5,6,7,8-*diepoxy*-5,6,7,8-*tetrahydroquinoline* **8** (0.16 g, 67%, R_f 0.3), m.p. 138–152 °C (decomp.) (dichloromethane–diethyl ether) (Found: M^+, 161.0473. $C_9H_7NO_2$ requires *M*, 161.0477); δ_H(300 MHz, $CDCl_3$) 3.97 (2 H, m, 6-H and 7-H), 4.05 (1 H, d, $J_{5,6}$ 3.2, 5-H), 4.18 (1 H, d, $J_{7,8}$ 3.1, 8-H), 7.38 (1 H, m, 3-H), 7.95 (1 H, dd, $J_{3,4}$ 7.6, $J_{2,4}$ 1.6, 4-H) and 8.65 (1 H, dd, $J_{2,3}$ 4.9, $J_{2,4}$ 1.6, 2-H).

trans-5,6,7,8-*Diepoxy*-5,6,7,8-*tetrahydroquinoline* 1-*Oxide* **6**.—*trans*-5,6,7,8-Diepoxy-5,6,7,8-tetrahydroquinoline **5** (0.059 g, 0.37 mmol) in acetone (10 ml) was cooled to *ca.* 10 °C and was mixed with an acetone solution of dimethyldioxirane (0.06 mol dm^{-3}; 13 ml) prepared by the literature method.[16] The acetone solution was stirred for 3 h at *ca.* 10 °C and the product **6** was isolated after removal of solvent under reduced pressure (0.06 g, 93%). Recrystallization from ethyl acetate–hexane gave trans-5,6,7,8-*diepoxy*-5,6,7,8-*tetrahydroquinoline* 1-*oxide* **6**, m.p. 130–135 °C (decomp.) (Found: M^+, 177.0421. $C_9H_7NO_3$ requires *M*, 177.0426); δ_H(400 MHz, $CDCl_3$) 3.69 (1 H, d, $J_{5,6}$ 3.8, 5-H), 3.99 (1 H, dd, $J_{5,6}$ 3.8, $J_{6,7}$ 1.4, 6-H), 4.07 (1 H, dd, $J_{6,7}$ 1.4, $J_{7,8}$ 4.1, 7-H), 4.63 (1 H, d, $J_{7,8}$ 4.1, 8-H), 7.30 (1 H, m, 3-H), 7.39 (1 H, m, 4-H) and 8.24 (1 H, dd, $J_{2,3}$ 6.40, $J_{2,4}$ 1.12, 2-H).

cis-5,6,7,8-*Diepoxy*-5,6,7,8-*tetrahydroquinoline* 1-*Oxide* **9**.—Treatment of *cis*-5,6,7,8-diepoxy-5,6,7,8-tetrahydroquinoline **8** (0.019 g, 0.12 mmol) with dimethyldioxirane (0.06 mol dm^{-3} solution in acetone; 12 ml) in a similar manner to the *trans* diepoxide **5**, yielded cis-5,6,7,8-*diepoxy*-5,6,7,8-*tetrahydroquinoline* 1-*oxide* **9** (0.21 g, 99%) as a crystalline solid, m.p. 135–150 °C (decomp.) (ethyl acetate–hexane) (Found: M^+, 177.0426. $C_9H_7NO_3$ requires *M*, 177.0426); δ_H(400 MHz, $CDCl_3$) 3.96 (2 H, m, 6-H and 7-H), 4.03 (1 H, d, $J_{5,6}$ 3.57, 5-H), 4.86 (1 H, d, $J_{7,8}$ 3.33, 8-H), 7.26 (1 H, dd, $J_{2,3}$ 6.6, $J_{3,4}$ 7.8, 3-H), 7.50 (1 H, d, $J_{3,4}$ 7.8, 4-H) and 8.29 (1 H, dd, $J_{2,4}$ 1.2, $J_{2,3}$ 6.6, 2-H).

5,6-*Epoxy*-5,6-*dihydro*-N-*methylquinolinium Trifluoromethanesulphonate* **10**.—To a solution of 5,6-epoxy-5,6-dihydroquinoline **1** (0.33 g, 2.28 mmol) in dichloromethane (10 ml), methyl trifluoromethanesulphonate (0.26 ml, 2.3 mmol) in dichloromethane (5 ml) was added dropwise over 0.5 h at −10 °C. Stirring was continued for 0.25 h at −10 °C and 0.5 h at room temperature. The solvent was removed under reduced pressure to yield a crude product which was recrystallised from dichloromethane to yield 5,6-*epoxy*-5,6-*dihydro*-N-*methylquinolinium trifluoromethanesulphonate* **10** (0.58 g, 83%), m.p. 79–83 °C (dichloromethane) (Found: C, 42.5; H, 3.3; N, 4.5. $C_{11}H_{10}F_3NO_4S$ requires C, 42.7; H, 3.2; N, 4.5%); δ_H(300 MHz; [$^2H_6$]acetone) 4.54 (1 H, m, 6-H), 4.66 (3 H, s, Me), 5.08 (1 H, d, $J_{5,6}$ 3.4, 5-H), 7.58 (2 H, m, 7-H and 8-H), 8.13 (1 H, m, 3-H), 9.06 (1 H, d, $J_{3,4}$ 7.8, 4-H) and 9.15 (1 H, d, $J_{2,3}$ 6.2, 2-H).

7,8-*Epoxy*-7,8-*dihydro*-N-*methylquinolinium Trifluoromethanesulphonate* **11**.—Methyl trifluoromethanesulphonate (0.26 ml, 2.3 mmol) in dichloromethane (5 ml) was added to a solution of 7,8-epoxy-7,8-dihydroquinoline **2** (0.33 g, 2.28 mmol) and worked up in a similar manner to that described for the arene oxide **1**. The crude product was recrystallized from dichloromethane to yield 7,8-*epoxy*-7,8-*dihydro*-N-*methylquinolinium trifluoromethanesulphonate* **11** (0.61 g, 87%), m.p. 108–110 °C (Found: C, 42.3; H, 3.1; N, 4.8. $C_{11}H_{10}F_3NO_4S$ requires C, 42.7; H, 3.2; N, 4.5%); δ_H(300 MHz; [$^2H_6$]acetone) 4.54 (1 H, m, 7-H), 4.89 (3 H, s, Me), 5.34 (1 H, d, $J_{7,8}$ 3.9, 8-H), 7.01 (1 H, dd, $J_{5,6}$ 9.6, $J_{6,7}$ 3.6, 6-H), 7.19 (1 H, dd, $J_{5,6}$ 9.6, $J_{5,7}$ 1.7, 5-H), 8.24 (1 H, m, 3-H), 8.73 (1 H, d, $J_{3,4}$ 8.1, 4-H) and 9.15 (1 H, d, $J_{2,3}$ 6.0, 2-H).

Acknowledgements

We gratefully acknowledge financial support from the Cancer Research Campaign (J. J. M°C), DENI (L. H.), and The Queen's University of Belfast (H. P. P.). We wish to thank Dr.

O. W. Howarth at the SERC Centre for Nuclear Magnetic Resonance, University of Warwick, for providing 400 MHz NMR spectra.

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Paper 1/02064A
Received 1*st May* 1991
Accepted 28*th May* 1991