Synthesis of Substituted Dibenzophospholes. Part 5.[1] Synthesis of Intermediates for 4- and 6-Aryl Substituents

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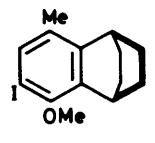
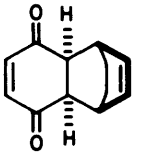
6-Iodo-5-methoxy-8-methyl-1,2,3,4-tetrahydro-1,4-ethanonaphthalene was prepared from the Diels–Alder adduct of benzoquinone and cyclohexadiene. Diels–Alder condensation of 2-acetamidobenzoquinone and 2-iodobenzoquinone (convenient, new syntheses of both quinones are described) with 2-methylcyclohexa-1,3-diene led to mixtures of adducts; the major adduct from the iodoquinone was isolated and found by *X*-ray analysis to have the methyl and iodo substituents at the 2- and 7-positions, respectively, of the 1,4-ethanonaphthalene skeleton. Addition of 2-acetamidobenzoquinone to mentha-2,6,8(9)-triene derived from (−)-carvone gave two regioisomers (structures determined by n.m.r. spectroscopy). In a smooth 4-step synthesis from 6,6-dimethylfulvene and benzoquinone, 6-iodo-9-*syn*-isopropyl-5,8-dimethoxy-1,2,3,4-tetrahydro-1,4-methanonaphthalene was prepared and its structure confirmed by *X*-ray analysis.

Parts 2 and 3 of this series[2,3] report syntheses of 4,6-diaryl-5-hydroxydibenzophosphole 5-oxides as part of a project[4] for designing enzyme-like catalysts for the hydration of alkenes in aqueous solution. In this project, substituents on the 4- and 6-aryl groups are seen as important in defining a hydrophobic cleft for reception of the alkene. Substituents which can freely adopt a number of conformations may notionally be able to provide a better fit between catalyst and substrate; but this is achieved at the cost of a larger entropy of complex formation. On the whole it seems best to choose a hydrophobic envelope which, though not rigid, is of limited mobility. The aryl groups themselves have this quality and previous *X*-ray studies[3] have shown them adapting to complex formation. Rigid substituents on the aryl group share its limited mobility and—provided that their geometry is near the optimum—may be expected to promote efficient substrate binding at minimal entropy cost.

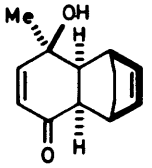
Since the aryl groups enter the synthesis as aryl iodides, we have examined preparative routes to iodobenzenes in which the benzene ring forms a bridge across a cyclopentane or cyclohexane ring. Some observations incidental to this work have already been reported.[4] The Diels–Alder synthesis, with benzoquinones as philodiene precursors of the aromatic rings, offered a simple entry to the desired structures. Sometimes, both oxygen atoms of the quinone could be allowed to remain as alkoxy groups in the final product, but this was not always desirable and one of our first syntheses was aimed at an iodide (**1**) in which one oxygen had been replaced by methyl.



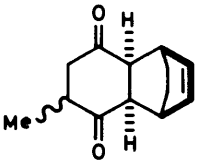
(**1**)



(**2**)

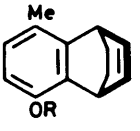


(**3**)

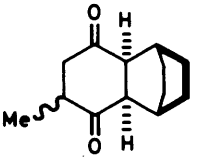


(**4**)

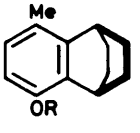
Conditions were found for the addition of methyl-lithium to the adduct (**2**) from benzoquinone and cyclohexa-1,3-diene so that the major product was the alcohol (**3**) with minor amounts of the ketone (**4**). The total reaction product was boiled with formic acid in chloroform, affording the phenol (**5**). This could not be crystallized, though it was characterized as the crystalline acetate (**6**), and it was more convenient to hydrogenate the total product at this stage and to separate the crystalline phenol (**7**) from the saturated dione (**8**). Iodination of the phenol with potassium tri-iodide in aqueous ethylamine, followed by methylation, then gave the desired product (**1**) in satisfactory overall yield. A minor by-product was the ether (**9**).



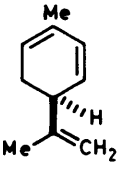
(**5**) R = H
(**6**) R = Ac



(**8**)



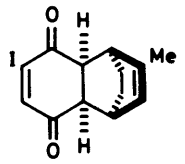
(**7**) R = H
(**9**) R = Me



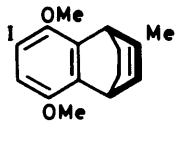
(**10**)

Some exploration of adducts from substituted benzoquinones and non-symmetrical dienes was also made to find out whether regioselective addition or easy separation of isomers would lead to shorter syntheses of more highly substituted products. 2-Acetamidobenzoquinone and especially 2-iodobenzoquinone were obvious choices as philodienes and since a satisfactory laboratory preparation was known for neither of these, procedures were devised and are reported in the Experimental section. The two non-symmetrical dienes were 2-methylcyclohexa-1,3-diene and the menthatriene (**10**), prepared respectively from 2-methylcyclohex-2-enone and (−)-(*R*)-carvone by the tosylhydrazone–methyl-lithium method.[5]

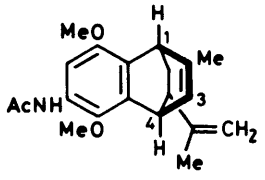
The addition of iodobenzoquinone to methylcyclohexadiene proceeded easily, and recrystallization of the adduct gave a homogeneous substance identified by *X*-ray analysis (see the Experimental section) as the dione (**11**). This was the unwanted regioisomer, and although the crude adduct and its product [largely (**12**)] of aromatization and methylation showed signs of



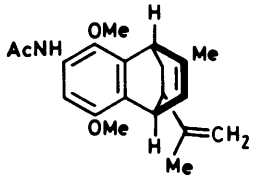
(**11**)



(**12**)



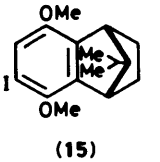
(**13**)



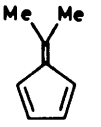
(**14**)

the presence of the desired 6-iodo-2-methyl-1,4-ethanonaphthalene derivatives there was no indication that their isolation would be easy or profitable. Addition of acetamidobenzoquinone to methylcyclohexadiene also gave a mixture of regioisomers; the adduct and its aromatization product were crystalline and the presence of two components could be detected only by n.m.r. spectroscopy at high resolution or by high-performance liquid chromatography (h.p.l.c.).

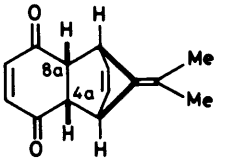
Reaction of iodobenzoquinone with the menthatriene (**10**) gave no adduct, and the isolation of iodohydroquinone (as the diacetate) from the reaction mixture indicated that dehydrogenation of the triene had occurred. With acetamidobenzoquinone, the triene gave a crystalline optically active adduct in high yield. This was not homogeneous and the product of aromatization and methylation was shown by h.p.l.c. to be a mixture of comparable amounts of two isomers, along with traces of a third. The two isomers were separated by preparative h.p.l.c. and were assigned the structures (**13**) and (**14**) by n.m.r. spectroscopic techniques. The bridgehead protons at positions 1 and 4 gave discrete signals in both isomers and were easily distinguished by the coupling (*J* 6 Hz) between 4-H and the alkenic proton 3-H, demonstrated by double resonance. The methoxy groups also gave discrete signals. In experiments using the nuclear Overhauser effect, irradiation at the upfield methoxy frequency in the isomer (**13**) caused enhancement of the signal for 4-H. When the downfield methoxy frequency was irradiated there was little enhancement of the 1-H signal but a very marked enhancement of the aromatic proton signal. With the isomer (**14**), exactly complementary behaviour was observed, irradiation of the upfield methoxy frequency affecting the signal due to 1-H and irradiation of the downfield methoxy frequency affecting the aromatic proton signal. It seems that the acetamido group forces the adjacent methoxy group into a conformation in which its methyl hydrogens are close to the bridgehead; the other methoxy group, not having this constraint, adopts a conformation in which its methyl hydrogens are close to the aromatic hydrogen. This experiment permits assignment of all structural details except the stereochemistry of the isopropenyl group. The chemical shifts for the protons of this group are similar in both isomers and do not show the shielding that would be expected were these groups *syn* to the aromatic ring. They are therefore assigned to the *anti* positions, as would also be inferred from a probable preference in the diene synthesis for the benzoquinone to be attached *anti* to the isopropenyl group. The difficulty of separating the two isomers discouraged further work on this approach.



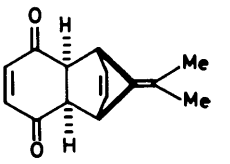
(**15**)



(**16**)



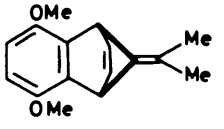
(**17**)



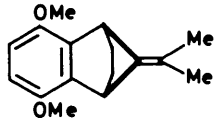
(**18**)

Another objective for synthesis was the iodomethanonaphthalene (**15**), a molecule with two different faces which could complement one another in defining the hydrophobic cleft of a 4,6-diaryl-5-hydroxydibenzophosphole 5-oxide in which it supplied both aryl substituents. An obvious starting point for the synthesis was 6,6-dimethylfulvene (**16**), easily obtainable from cyclopentadiene and acetone. The diene condensation of this with benzoquinone was already known[6] to yield a mixture of the *endo* (**17**) and *exo* (**18**) adducts (separated as their 6,7-epoxides) and treatment of a similar mixture with methyl sulphate and aqueous sodium hydroxide had given a 7% overall yield of the dimethoxy compound (**19**).[7] We found this sequence to be much cleaner than its reputation. When a mixture of dimethylfulvene and benzoquinone was kept in ether for a week and the ether then replaced by methanol, the *exo* adduct (**18**)—presumably the more stable isomer—was obtained in almost quantitative yield. Slow conversion into the *endo* isomer (**17**) (not isolated) was observed in chloroform solution: in the n.m.r. spectrum the singlet at δ 2.58 attributed to the 4a- and 8a-H in (**18**) became accompanied by a multiplet at δ 3.21 assigned to the corresponding hydrogens in the *endo* isomer. The difference in multiplicity of the two signals is a natural consequence of the difference in dihedral angle with the bridgehead hydrogens, and the upfield location of the signal from (**18**), due to shielding by the 2,3-double bond, was also predictable. The poor yield reported by Paquette *et al.*[7] in the aromatization–methylation could be reproduced in their conditions, but addition of methyl sulphate to a solution of the adduct (**18**) in methanolic sodium methoxide gave the desired product (**19**) in 80% yield. Probably, the stronger base was effective in promoting the double enolization which is essential to aromatization. In any case, the arene (**19**) and its derivatives are now easily accessible in quantity.

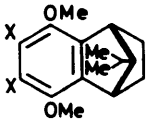
Selective hydrogenation of the arene (**19**), using either Wilkinson's catalyst or a small amount of palladized carbon, gave the dihydro derivative (**20**). This has previously been made[7] by a longer synthesis. When either of the arenes (**19**) or (**20**) was hydrogenated over a normal amount of palladized carbon or platinum, the desired *syn*-isopropyl compound (**21**) was formed exclusively. On iodination, the iodo compound (**15**) was formed, but the di-iodo compound (**22**) was produced with unexpected ease in the same conditions. *syn*-Stereochemistry in the iodo compound (**15**), already indicated by n.m.r. spectra,



(19)



(20)



(21) X = H
(22) X = I

was confirmed by *X*-ray analysis (see the Experimental section). Applications of the iodides (**1**) and (**15**) will be reported in later papers of this series.

Experimental

Except where otherwise stated, n.m.r. spectra were run in $CDCl_3$ with tetramethylsilane as the standard; i.r. spectra refer to paraffin pastes, light petroleum or hexanes means a fraction of mean b.p. *ca.* 70 °C, ether refers to diethyl ether, $NaHCO_3$ to saturated aqueous sodium hydrogen carbonate, and brine to saturated aqueous sodium chloride. M.p.s are uncorrected and solvents were evaporated under reduced pressure.

Preparation of 1,4-*Dihydro*-8-*methyl*-1,4-*ethanonaphthalen*-5-*ol and Intermediates*.—Dry toluene (400 ml) in a 1-litre flask with 3 vertical necks was stirred and cooled in solid CO_2–isopropyl alcohol during the simultaneous addition (50 min) of the cyclohexadiene–benzoquinone adduct[8] (**2**) (30.8 g) in toluene (150 ml) and of methyl-lithium (1.36M in ether; 120.5 ml). Addition was regulated so that methyl-lithium was never in excess. After 15 min acetic acid (20 ml) in water (180 ml) was added at a fast drop-rate. The resulting pale yellow liquid was warmed to dissolve some solid and filtered through Celite; the toluene layer was filtered through cotton and evaporated under reduced pressure to leave a partly crystalline residue (A).

In other runs the residue (A) was recrystallized several times from carbon tetrachloride to yield colourless blades, m.p. 128—129 °C, of (1SR,4RS,4aSR,8SR,8aRS)-4,4a,8,8a-*tetrahydro*-8-*hydroxy*-8-*methyl*-1,4-*ethanonaphthalen*-5(1a*H*)-*one* (**3**) (Found: C, 76.2; H, 7.6. $C_{13}H_{16}O_2$ requires C, 76.5; H, 7.8%); $\nu_{max.}$ 3 459, 3 276, 3 051, 1 667, 1 647, and 1 627 cm^{-1}; δ_H (60 MHz) 1.30—1.80 (8 H, m), 2.20—2.30 (4 H, m), 5.85 (1 H, d, *J* 11 Hz), 6.10 (1 H, d, *J* 7 Hz), 6.26 (1 H, d, *J* 7 Hz), and 6.60 (1 H, d, *J* 11 Hz).

To continue the synthesis the product (A) was boiled under reflux in chloroform (500 ml) containing formic acid (90%; 30 ml). After 26 h the acid was removed ($NaHCO_3$) and the chloroform was removed completely, finally by 3 evaporations under reduced pressure after addition of ethanol, to leave an oil (B).

In other runs, 1,4-dihydro-8-methyl-1,4-ethanonaphthalen-5-ol (**5**) was separated at this point as its crystalline acetate. The oil (B) (15 g) in pyridine (30 ml) and acetic anhydride (15 ml) was warmed at 60 °C for 2.5 h and at 80 °C for 0.5 h. The neutral product, recovered in the usual manner, crystallized from methanol at −20 °C to afford a poor recovery (4.12 g) of almost pure acetate which was recrystallized from ether, first at −78 °C and then twice at room temperature, to yield colourless plates, m.p. 73.5—74 °C, of 1,4-*dihydro*-8-*methyl*-1,4-*ethanonaphthalen*-5-*yl acetate* (**6**) (Found: C, 79.1; H, 7.0. $C_{15}H_{16}O_2$ requires C, 78.9; H, 7.1%); δ_H (60 MHz) 1.5 (br s), 2.35 (br s), 4.1 (br m), 6.45 (apparent t), 6.63 (d, *J* 8 Hz), and 6.90 (d, *J* 8 Hz). The other major component of oil (B), the product of 1,4-addition of methyl-lithium, was isolated in another experiment by the removal of phenolic material as described below for the dihydro derivative. The residual oil crystallized partially and the solid material was separated by spinning the mixture at 3 500 r.p.m. for many hours in a centrifuge tube divided horizontally by a sintered filter. Three recrystallizations from light petroleum gave 1,4,4a,6,7,8a-*hexahydro*-6-*methyl*-1,4-*ethanonaphthalene*-5,8-*dione* (**4**) as prisms, m.p. 71—71.5 °C (Found: C, 76.5; H, 8.1. $C_{13}H_{16}O_2$ requires C, 76.4; H, 7.9%); $\nu_{max.}$ 3 032m, 3 022s, and 1 700vs cm^{-1}.

To continue the synthesis the oil (B) (30.1 g) in ethanol (300 ml) was stirred under hydrogen with palladium-on-calcium carbonate (3 g of 10%) until the hydrogen uptake had ceased (24 h). Catalyst and solvent were removed and the residual oil in toluene (5 ml) and light petroleum (100 ml) was extracted with aqueous sodium hydroxide (2M; 10 × 50 ml), each extract being acidified immediately after separation. The crude phenol (24 g) was recovered by means of ether. The unextracted material (10.6 g) became partly crystalline and was purified by centrifugation as for the dehydro analogue (above) and was recrystallized from ether to yield 1,2,3,4,4a,6,7,8a-*octahydro*-6-*methyl*-1,4-*ethanonaphthalene*-5,8-*dione* (**8**) as prisms, m.p. 72—74 °C (Found: C, 75.8; H, 8.7. $C_{13}H_{18}O_2$ requires C, 75.7; H, 8.8%). The crude phenol contained neutral material entrained in the initial extractions; it was redissolved in toluene–light petroleum and extraction was repeated using 0.5M-aqueous alkali for the first 4 extractions, 1M for the fifth and 2M for the last four. This gave a crystalline phenol (14.2 g) which was recrystallized from dichloromethane at −78 °C to yield 1,2,3,4-*tetrahydro*-8-*methyl*-1,4-*ethanonaphthalen*-5-*ol* (**7**) (10.7 g) in several crops as chunky prisms, m.p. 117—120 °C (Found: C, 82.7; H, 8.7. $C_{13}H_{16}O$ requires C, 82.9; H, 8.6%); δ_H (60 MHz) 1.23, 1.36, 1.63, and 1.75 (8 H, br q), 2.20 (3 H, s), 3.21 (2 H, m), 4.57 (2 H, s), 6.43 (d, *J* 8 Hz), and 6.77 (d, *J* 8 Hz).

1,2,3,4-*Tetrahydro*-6-*iodo*-5-*methoxy*-8-*methyl*-1,4-*ethanonaphthalene* (**1**).—The phenol (**7**) (9 g) in aqueous ethylamine (70%; 90 ml) containing a little sodium dithionite was cooled quickly in ice and treated rapidly with swirling and cooling with an ice cold, nitrogen-purged aqueous solution (110 ml) of iodine (12.9 g) in potassium iodide. The purple solution was added to a mixture of ice and sulphuric acid (2M; 300 ml). Extraction with ether (3 ×) gave a red oil (14.7 g) which was dissolved in dry dimethylformamide (90 ml) and iodomethane (9.05 ml). Sodium hydride (1.44 g free from mineral oil) suspended in dimethylformamide was added during 40 min with stirring and ice cooling. Next day dilution with water and extraction with light petroleum (3 ×) gave a red oil which was put on a column of alumina (70 × 100 mm) and eluted with chloroform–light petroleum (1:4 v/v). Distillation then gave a lower fraction (0.14 g), b.p. 70 °C/0.1 mmHg (see later), and the required product (13.8 g), b.p. 112—114 °C/0.11 mmHg, which crystallized. Recrystallization from pentane gave the *iodo ether* (**1**) as plates, m.p. 50—51 °C (Found: C, 51.4; H, 5.4. $C_{14}H_{17}IO$ requires C, 51.2; H, 5.2%); δ_H (80 MHz) 1.25—1.82 (8 H, m), 2.25 (3 H, d, *J* 0.5 Hz), 3.17 (1 H, br s), 3.41 (1 H, br s), 3.75 (3 H, s), and 7.46 (1 H, d, *J* 0.5 Hz). The lower-boiling fraction (above) crystallized;

recrystallization from methanol gave chunky prisms, m.p. 68—69 °C, of 1,2,3,4-*tetrahydro*-5-*methoxy*-8-*methyl*-1,4-*ethanonaphthalene* (**9**) (Found: C, 83.2; H, 9.2. $C_{14}H_{18}O$ requires C, 83.1; H, 9.0%); δ_H (60 MHz) 1.25—1.82 (8 H, m), 2.28 (3 H, s), 3.20 (1 H, br s), 3.50 (1 H, br s), 3.80 (3 H, s), 6.65 (1 H, d, *J* 8 Hz), and 6.98 (1 H, d, *J* 8 Hz). The same compound was obtained by methylating the crude phenol (**5**) and hydrogenating the product.

2-*Iodo*-1,4-*benzoquinone*.—2-Iodophenol (30.8 g) in aqueous sodium hydroxide (2M; 110 ml) was treated with a suspension (*ca.* 400 ml) of diazosulphanilic acid prepared as usual from 4-aminobenzenesulphonic acid dihydrate (33 g), hydrochloric acid (*d* 1.16; 31 ml), sodium nitrite (12 g), and sodium carbonate decahydrate (21.4 g). The mixture was warmed and mixed thoroughly with an aqueous slurry of sodium dithionite (62 g). When the reduction seemed complete the mixture was cooled in ice and the yellow precipitate was collected and dried (25.7 g). Some of it (2.1 g) was recrystallized from chloroform and then sublimed at 110—120 °C/10 mmHg to yield white crystals of 4-*amino*-2-*iodophenol* which sublimed in an evacuated tube without melting (Found: C, 30.4; H, 2.8; N, 6.0. C_6H_6INO requires C, 30.7; H, 2.6; N, 6.0%). A sample acetylated at 100 °C with acetic anhydride and pyridine gave, after crystallization from dichloromethane, 4-acetamido-2-iodophenyl acetate, m.p. 186 °C (lit.,[9] m.p. 186 °C). The remainder of the crude product, dissolved in sulphuric acid (2M; 250 ml), was stirred with manganese dioxide (10 g, then 5 g after 15 min) for 2 h, then filtered (Celite). Filtrate and solid were both extracted with ether until the extracts (total *ca.* 500 ml) were faintly yellow. Evaporation left a black residue which was extracted repeatedly with hot light petroleum. The extracts when cooled below 0 °C deposited tan crystals, m.p. 59—61 °C (lit.,[10] m.p. 62 °C), of the 2-iodoquinone (13 g, 2 crops).

2-*Acetamido*-1,4-*benzoquinone*.—(*a*) Potassium nitrosodisulphonate (8 g) was dissolved in aqueous sodium dihydrogen phosphate (10.2 g in 750 ml) and disodium hydrogen phosphate (3.33 g). To the stirred solution, 2-acetamidophenol (3 g) in acetone (100 ml) was added all at once. After 15 min more potassium nitrosodisulphonate (7 g) was added and after a further 15 min the mixture was extracted with chloroform. The washed (water), dried ($MgSO_4$) extract deposited a brown solid when concentrated. This was passed in chloroform through a column of silica to yield pale yellow crystals, m.p. 146—148 °C (lit.,[11] m.p. 142 °C) of the quinone.

(*b*) A cheaper preparation for larger scale work started from 2,4-dinitrophenol. To this (25.5 g) in hydrochloric acid (*d* 1.16; 258 ml) granulated tin (96 g) was added. The mixture needed to be cooled in ice after 15—20 min to prevent boiling; larger quantities were prepared in batches of this size and united after the reduction had ceased. The solution, when cool, was filtered from a little residual tin, cooled in ice, and saturated with dry hydrogen chloride. The diaminophenol dihydrochloride (28.83 g) which crystallized was collected, washed with ice cold concentrated hydrochloric acid, dried, dissolved in water (130 ml), and treated with acetic anhydride (30 ml) followed at once by sodium acetate (30 g) in water (36 ml). The resulting white solid was collected from the ice-cooled mixture, washed with ice–water and dried. This crude 2,4-bis(acetamido)phenol (22 g) was oxidized as required. The phenol (16.43 g) was ground with 0.5M-sulphuric acid and stirred with further acid (940 ml in all). Manganese dioxide (20.6 g) was added and after 30 min, the mixture was filtered (Celite) and the dark red filtrate was extracted six times with dichloromethane which was then dried ($MgSO_4$) and evaporated. The crystalline quinone (11.5 g), m.p. 141—142.5 °C, could be purified as above or by sublimation at low pressure, but was satisfactory for diene addition.

(4R)-4-*Isopropenyl*-1-*methylcyclohexa*-1,5-*diene*.—This improves an earlier synthesis[5] from carvone of unspecified chirality. (−)-(*R*)carvone (7.51 g) and *p*-tolylsulphonylhydrazine (9.31 g) in benzene (50 ml) were boiled under a Dean–Stark trap for 1.5 h. The product (14.5 g) was recovered in 3 crops, m.p. 157—158 °C (decomp.). A sample recrystallized from benzene formed stout prisms, m.p. 158—160 °C, of (**R**)-*carvone p-tolylsulphonylhydrazone* (Found: C, 64.4; H, 6.9; N, 8.9. $C_{17}H_{22}N_2O_2S$ requires C, 64.1; H, 7.0; N, 8.8%). The hydrazone (50 g) was powdered finely, suspended in ether, and stirred with ice-cooling during the addition (3.5 h) of methyl-lithium (1.5M in ether; 45 ml). After 1 h (no cooling) water was added to dissolve the solids. The ether layer was washed (water and brine), dried ($MgSO_4$), and the ether removed through an efficient fractionating column. The residue was distilled, b.p. 63—63.5 °C/15 mmHg, to afford the menthatriene (**10**) (19.2 g); d_{20}^{20} 0.856; $\alpha_D^{14.5}$ +161° (neat) (lit.,[12] d_4^{20} 0.8578; $[\alpha]_D^{20}$ +163.5°, for a product containing some cymene).

2-Methylcyclohexa-1,3-diene, b.p. 106—108 °C (lit.,[13] b.p. 108—110 °C) was similarly prepared in 40—45% yield from 2-methylcyclohex-2-enone *p*-tolylsulphonylhydrazone (m.p. 162—163 °C) except that addition of methyl-lithium was at −10 °C and that cooling was maintained for 1 h before work-up after a further 2 h.

1SR,4SR,4aRS,8aSR-1,4,4a,8a-*Tetrahydro*-7-*iodo*-2-*methyl*-1,4-*ethanonaphthalene*-5,8-*dione*.—A solution of 2-iodobenzoquinone (1.3 g) and 2-methylcyclohexa-1,3-diene (0.8 g) in ether (20 ml) was left for 5 days and then concentrated. The yellow solid was recrystallized from ether–light petroleum yielding the *dione* (**11**) (1.6 g), m.p. 118—119 °C. The sample for analysis and *X*-ray crystallography was recrystallized from ether (Found: C, 47.7; H, 3.9. $C_{13}H_{13}IO_2$ requires C, 47.6; H, 4.0%); $\nu_{max.}$ 1 680 and 1 650 cm^{-1}.

1,4-*Dihydro*-5,8-*dimethoxy*-7(and-6)-*iodo*-2-*methyl*-1,4-*ethanonaphthalene*.—A mixture of the dione (**11**) (150 mg), potassium carbonate (200 mg) and iodomethane (0.5 ml) in dry dimethylformamide (15 ml) was stirred for 24 h. After the addition of water, the product was recovered by means of ether and was purified by passing it in light petroleum through a column of alumina. The *iodo ether* (**12**) (145 mg) was analysed after evaporative distillation under reduced pressure (Found: C, 50.9; H, 5.0. $C_{15}H_{17}IO_2$ requires C, 50.6; H, 4.8%); *m/z* 356 (M^+), 328 and 313; δ_H 0.8—1.62 (4 H, m), 1.85 (3 H, br s), 3.8 (6 H, s), 4.0—4.37 (2 H, m), 6.0 (1 H, m), and 7.0 (1 H, s).

(1S,4R,10R)-6-*Acetamido*-1,4-*dihydro*-10-*isopropenyl*-5,8-*dimethoxy*-2-*methyl*-1,4-*ethanonaphthalene and* (1S,4R,10R)-1,4-*Dihydro*-7-*acetamido*-10-*isopropenyl*-5,8-*dimethoxy*-2-*methyl*-1,4-*ethanonaphthalene*.—A mixture of 2-acetamidobenzoquinone (24 g) and the menthatriene (**10**) (22 g) in chloroform (75 ml) was left under nitrogen for 14 days. The filtrate from a small amount of black precipitate was concentrated under reduced pressure and treated with ether to yield a crystalline mixture (39 g) of adducts. A sample for analysis was recrystallized from ether, m.p. 144—146 °C (decomp.). (Found: C, 72.4; H, 7.45; N, 4.6. Calc. for $C_{18}H_{21}NO_3$: C, 72.2; H, 7.1; N, 4.7%). A mixture of the product (1 g), dimethylformamide (10 ml), potassium carbonate (1 g), iodomethane (1 ml), methanol (2.5 ml), and lithium hydroxide (175 mg) was heated under nitrogen at 100 °C for 1.5 h when zinc powder (0.5 g) was added, followed after a short time by more iodomethane (0.5 ml), and heating was continued for 1.5 h. Water (100 ml) was added to the cooled mixture and the product, recovered by means of ether, was passed in ether–light petroleum through a column of alumina. The product (0.86 g), m.p. 131—133 °C, was essentially a mixture of the 6- and 7-acetamido compounds (**13**) and (**14**).

These were separated by h.p.l.c. at 2 000 psig on a column (300 × 3.9 mm) of Hypersil (5 μm) in ether–hexanes (3:2 v/v) containing 0.4% isopropyl alcohol; the mixture (0.1 mg) in solvent (10 μl) was injected at 5 min intervals (flow rate 2 ml min^{-1}). The two major peaks and a small intermediate peak were well resolved and three fractions were collected accordingly.

The least polar fraction on evaporation and crystallization of the residue from ether yielded the *6-acetamido isomer* (**13**) named above, m.p. 135.5—136.5 °C (Found: C, 73.7; H, 7.7; N, 4.3. $C_{20}H_{25}NO_3$ requires C, 73.4; H, 7.6; N, 4.3%); δ_H (360 MHz) 1.70 (3 H, s), 1.68—1.75 (1 H, m), 1.86 (3 H, d, *J* 1.6 Hz), 2.17 (3 H, s), 2.1—2.2 (1 H, m), 3.73 (3 H, s), 3.78 (3 H, s), 4.04 (1 H, m), 4.11 (1 H, dd, *J* 6, 2 Hz), 4.69 (2 H, d, *J* 12 Hz), 5.88 (1 H, d, *J* 6 Hz), 7.68 (1 H, br s, NH), and 7.75 (1 H, s). The most polar fraction, similarly treated, afforded the *7-acetamido isomer* (**14**) named above, m.p. 121.5—123 °C (Found: C, 73.4; H, 7.7; N, 4.3%); δ_H (360 MHz) 1.36—1.42 (1 H, m), 1.72 (3 H, s), 1.70—1.73 (1 H, m), 1.89 (3 H, d, *J* 1.6 Hz), 2.19 (3 H, s), 2.21—2.25 (1 H, m), 3.76 (3 H, s), 3.80 (3 H, s), 3.95 (1 H, m), 4.28 (1 H, dd, *J* 6, 2 Hz), 4.71 (2 H, d, *J* 12 Hz), 5.75 (1 H, d, *J* 6 Hz), 7.71 (1 H, br s, NH), and 7.76 (1 H, s). The ratio of 6-isomer to 7-isomer was *ca.* 5:4.

6,6-*Dimethylfulvene*.—A mixture of cyclopentadiene (freshly distilled; 39.6 g) and acetone (53 ml) was added under nitrogen with stirring and ice cooling to sodium ethoxide [from sodium (13.8 g) in ethanol (300 ml)]. After 1 h at room temperature the mixture was diluted with water (600 ml) and extracted with ether (3 × 150 ml). The ether layers were washed (water and brine) and dried ($MgSO_4$). The ether was removed through a fractionating column and the residue was distilled, to yield the fulvene (**16**) (45.6 g, 71.5%) as a yellow oil, b.p. 46—48 °C/10 mmHg.

(1RS,4SR,4aSR,8aRS)-1,4,4a,8a-*Tetrahydro*-9-*isopropylidene*-1,4-*methanonaphthalene*-5,8-*dione*.—Benzoquinone (2.5 g) and 6,6-dimethylfulvene (4.4 g) in dry ether (20 ml) were left for one week under nitrogen. Methanol (10 ml) was added and the ether was boiled off. Next day the pale yellow plates were collected and two smaller crops were obtained by concentration. The *exo adduct* (**18**) (4.89 g) had m.p. 127.5—128 °C (Found: C, 78.5; H, 6.5. $C_{14}H_{14}O_2$ requires C, 78.5; H, 6.5%); $\nu_{max.}$ 1 660 cm^{-1}; δ_H (60 MHz) 1.44 (6 H, s), 2.58 (2 H, s), 3.69 (2 H, apparent t, *J* 2 Hz), 6.45 (2 H, apparent t, *J* 2 Hz), and 6.67 (2 H, s).

1,4-*Dihydro*-9-*isopropylidene*-5,8-*dimethoxy*-1,4-*methanonaphthalene*.—The *exo*-adduct (**18**) (8 g) was added under nitrogen to a stirred solution of sodium methoxide [from sodium (3.4 g) in dry methanol (100 ml)]. The dropwise addition of methyl sulphate (14 ml) was started immediately; when it was complete the mixture was warmed at 70 °C for 2 h, cooled, diluted with water (350 ml), and extracted with dichloromethane. The extract was washed (water and brine), dried ($MgSO_4$) and evaporated and the residue in ether–light petroleum (1:1 v/v) was passed through alumina, recovered, and recrystallized from methanol, to yield the product (**19**) (7.2 g), m.p. 138.5—139 °C (lit.,[7] m.p. 137—137.5 °C) (Found: C, 79.2; H, 7.6. Calc. for $C_{16}H_{18}O_2$: C, 79.3; H, 7.4%); δ_H (60 MHz) 1.54 (6 H, s), 3.79 (6 H, s), 4.62 (2 H, m), 6.36 (2 H, m), and 6.46 (2 H, s).

1,2,3,4-*Tetrahydro*-9-*isopropylidene*-5,8-*dimethoxy*-1,4-*methanonaphthalene*.—The dihydronaphthalene (**19**) (300 mg) and tris(triphenylphosphine)rhodium chloride (100 mg) in benzene (50 ml) were stirred under hydrogen until absorption had ceased. The product recovered by evaporation was purified by passage in ether–light petroleum (1:19 v/v) through alumina.

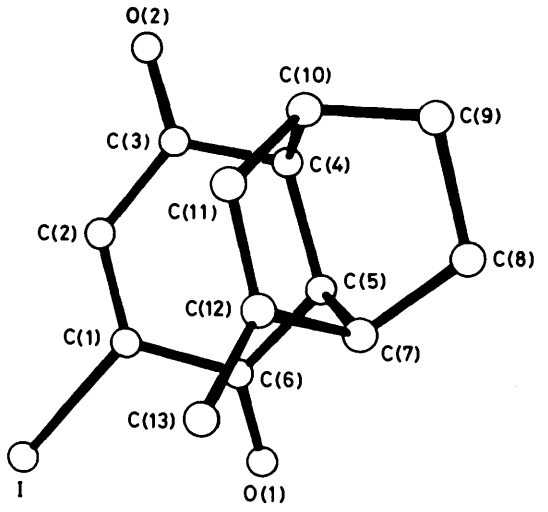


Figure 1. Molecular structure of compound (**11**).

Table 1. Compound (**11**); fractional atomic co-ordinates (× 10^4) with estimated standard deviations in parentheses

	x	*y*	*z*
I	3 758.0(19)	4 042.8(7)	1 911.7(7)
O(1)	2 340(19)	5 544(9)	1 029(5)
O(2)	6 234(16)	7 027(7)	2 738(5)
C(1)	4 309(19)	5 363(10)	1 849(8)
C(2)	5 210(22)	5 771(10)	2 298(8)
C(3)	5 598(19)	6 701(10)	2 280(7)
C(4)	5 213(20)	7 240(10)	1 714(6)
C(5)	4 091(23)	6 804(11)	1 208(7)
C(6)	3 490(19)	5 878(11)	1 330(7)
C(7)	5 192(22)	6 772(12)	586(8)
C(8)	5 514(26)	7 689(14)	390(8)
C(9)	6 577(31)	8 158(13)	900(10)
C(10)	6 961(23)	7 523(11)	1 421(8)
C(11)	7 919(21)	6 750(12)	1 163(8)
C(12)	6 920(24)	6 335(11)	730(8)
C(13)	7 448(32)	5 543(14)	379(10)

Crystallization from methanol afforded the tetrahydronaphthalene (**20**) (300 mg), m.p. 130—131 °C (lit.,[7] m.p. 129—130 °C) (Found: C, 78.7; H, 8.1. Calc. for $C_{16}H_{20}O_2$: C, 78.7; H, 8.2%); δ_H (60 MHz) 1.15—1.4 (2 H, m), 1.62 (6 H, s), 1.75—2.0 (2 H, m), 3.78 (6 H, s), 4.0 (2 H, m), and 6.56 (2 H, s). The same product was obtained in somewhat lower (84%) yield by hydrogenation in ether–ethanol over a small amount (4% wt) of 10% palladium-on-carbon.

1,2,3,4-*Tetrahydro*-9-syn-*isopropyl*-5,8-*dimethoxy*-1,4-*methanonaphthalene*.—A suspension of palladium-on-carbon (150 mg of 10%) in ethanol (30 ml) was saturated with hydrogen; the isopropylidene compound (**20**) (500 mg) was added and the mixture was stirred under hydrogen until absorption had ceased. Removal of the catalyst and solvent left an oil (500 mg) which solidified. Recrystallization from methanol gave the syn-*isopropyl compound* (**21**), m.p. 57.5—58.5 °C (Found: C, 78.1; H, 9.0. $C_{16}H_{22}O_2$ requires C, 78.0; H, 8.9%); δ_H (60 MHz) 0.81 (6 H, d, *J* 6 Hz), 1.0 (1 H, m), 1.13—1.18 (2 H, m), 1.52 (1 H, d), 1.91 (2 H, m), 3.45 (2 H, m), 3.76 (6 H, s), and 6.59 (2 H, s). The same product was obtained by hydrogenation of the dihydronaphthalene (**19**) over palladium-on-carbon or platinum.

Table 2. Compound (**11**); intramolecular distances (Å) and angles (°) with estimated standard deviations in parentheses

(*a*) Bonds

I–C(1)	2.076(9)	O(1)–C(6)	1.203(10)
O(2)–C(3)	1.205(11)	C(1)–C(2)	1.338(13)
C(1)–C(6)	1.500(13)	C(2)–C(3)	1.459(13)
C(3)–C(4)	1.497(13)	C(4)–C(5)	1.533(12)
C(4)–C(10)	1.532(13)	C(5)–C(6)	1.517(14)
C(5)–C(7)	1.574(14)	C(7)–C(8)	1.49(2)
C(7)–C(12)	1.508(14)	C(8)–C(9)	1.54(2)
C(9)–C(10)	1.511(15)	C(10)–C(11)	1.499(14)
C(11)–C(12)	1.358(15)	C(12)–C(13)	1.49(2)

(*b*) Angles

C(2)–C(1)–C(6)	119.9(9)	C(1)–C(2)–C(3)	122.9(9)
O(2)–C(3)–C(2)	118(1)	O(2)–C(3)–C(4)	120.7(9)
C(2)–C(3)–C(4)	121.6(9)	C(3)–C(4)–C(5)	116.1(8)
C(3)–C(4)–C(10)	108.6(8)	C(5)–C(4)–C(10)	108.5(7)
C(4)–C(5)–C(6)	117.0(8)	C(4)–C(5)–C(7)	108.5(8)
C(6)–C(5)–C(7)	106.1(8)	O(1)–C(6)–C(1)	118(1)
O(1)–C(6)–C(5)	122(1)	C(1)–C(6)–C(5)	119.9(8)
C(5)–C(7)–C(8)	107.3(9)	C(5)–C(7)–C(12)	107.7(8)
C(8)–C(7)–C(12)	109.6(9)	C(7)–C(8)–C(9)	109.2(9)
C(8)–C(9)–C(10)	109(1)	C(4)–C(10)–C(9)	109(1)
C(4)–C(10)–C(11)	110.3(8)	C(9)–C(10)–C(11)	109.5(9)
C(10)–C(11)–C(12)–	110.6(9)	C(7)–C(12)–C(11)	115(1)
C(7)–C(12)–C(13)	120(1)	C(11)–C(12)–C(13)	125(1)

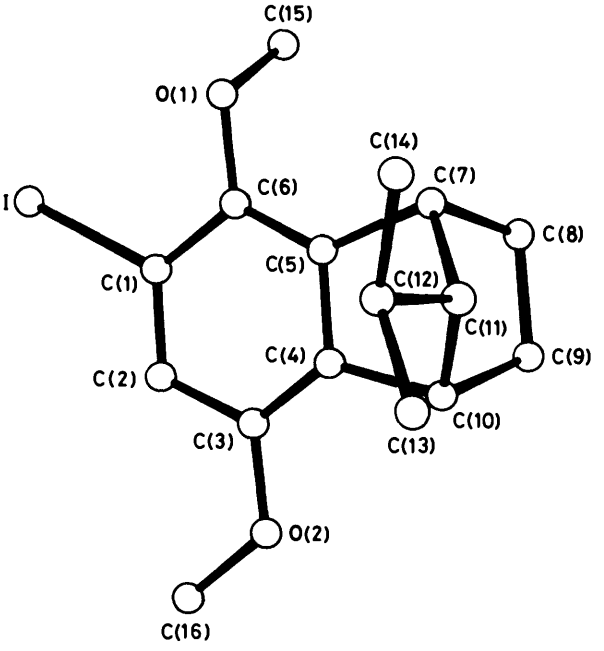


Figure 2. Molecular structure of compound (**15**).

1,2,3,4-*Tetrahydro*-6-*iodo*-9-syn-*isopropyl*-5,8-*dimethoxy*-1,4-*methanonaphthalene*.—A mixture of the *syn*-isopropyl compound (**21**) (4.92 g), iodine (2.05 g), periodic acid (0.92 g dihydrate), acetic acid (25 ml), water (5 ml), and sulphuric acid (4 drops) was heated at 70—75 °C until the iodine colour faded (1 h), then diluted with cold water and extracted with ether. The ether was washed (water and aqueous $NaHCO_3$), dried ($MgSO_4$), and evaporated. The residue, after passage in ether–light petroleum through an alumina column, was recrystallized from methanol, to afford the 6-*iodo compound* (**15**) (5.64 g), m.p. 67.5—68.5 °C (Found: C, 51.5; H, 5.7. $C_{16}H_{21}IO_2$ requires C, 51.6; H, 5.6%); δ_H (60 MHz) 0.80 (6 H, d, *J* 6 Hz), 0.95—1.15 (3 H, m), 1.51 (1 H, m), 1.92 (2 H, m), 3.4 (2 H, m), 3.72 (6 H, s), and 7.2 (1 H, s); *m/z* 372 (M^+, 100%).

1,2,3,4-*Tetrahydro*-6,7-*di*-*iodo*-9-syn-*isopropyl*-5,8-*dimethoxy*-1,4-*methanonaphthalene*.—When doubled proportions of iodine and periodic acid were used in the iodination procedure described above, the product (in 89% yield) was the 6,7-*di*-*iodo compound* (**22**), m.p. 88—89 °C (Found: C, 38.3; H, 4.1. $C_{16}H_{20}I_2O_2$ requires C, 38.6; H, 4.0%); δ_H (60 MHz) 0.84 (6 H, d, *J* 6 Hz), 0.92—1.35 (3 H, m), 1.54 (1 H, m), 2.0 (2 H, m), 3.43 (2 H, m), and 3.77 (6 H, s).

Crystal Structures of 1,4,4a,8a-*Tetrahydro*-7-*iodo*-2-*methyl*-1,4-*ethanonaphthalene*-5,8-*dione* (**11**) *and* 1,2,3,4-*Tetrahydro*-6-*iodo*-9-syn-*isopropyl*-5,8-*dimethoxy*-1,4-*methanonaphthalene* (**15**).—Data for both determinations were obtained with an Enraf–Nonius CAD4 diffractometer in the θ/2θ mode, Δθ = (0.80 + 0.35 tan θ)°, maximum scan time 60 s, using monochromated Mo-K_α radiation, λ = 0.710 69 Å. Unit cell dimensions were calculated from the setting angles for 25 reflections with θ *ca.* 15°.

Compound (**11**). $C_{13}H_{11}IO_2$, *M* = 326.1, orthorhombic, space group *Pbca*, *a* = 15.368(4), *b* = 7.604(3), *c* = 21.435(4) Å, *U* = 2 504.9 Å^3, *Z* = 8, D_c = 1.72 g cm^{-3}, μ(Mo-K_α) 25.6 cm^{-1}. Crystal size *ca.* 0.45 × 0.15 × 0.10 mm. Data measured for *h*, *k*, *l*, 2 < θ < 25°. 1 165 Reflections with $|F^2| > \sigma(F^2)$, with $\sigma(F^2) = [\sigma^2(I) + (0.02I)^2]^{1/2}/\text{Lp}$. No crystal decay. No correction for absorption. The structure determination used the Enraf–Nonius SDP program package on a PDP 11/34 computer. Routine heavy atom methods. Full matrix least squares refinement with I, O, and C atoms anisotropic. Hydrogen atoms included at fixed calculated positions (C–H 1.08 Å and B_{iso} = 8.0 Å^2). Weighting scheme $w = 1/\sigma^2(F)$. Final residuals *R* = 0.081, *R'* = 0.090. A final difference map

Table 3. Compound (**15**); intramolecular distances (Å) and angles (°) with estimated standard deviations in parentheses

(*a*) Bonds

I–C(1)	2.090(10)	O(1)–C(6)	1.396(10)
O(1)–C(15)	1.427(15)	O(2)–C(3)	1.387(12)
O(2)–C(16)	1.408(13)	C(1)–C(2)	1.401(13)
C(1)–C(6)	1.379(13)	C(2)–C(3)	1.393(13)
C(3)–C(4)	1.365(13)	C(4)–C(5)	1.379(13)
C(4)–C(10)	1.506(14)	C(5)–C(6)	1.386(13)
C(5)–C(7)	1.528(14)	C(7)–C(8)	1.60(2)
C(7)–C(11)	1.570(14)	C(8)–C(9)	1.507(15)
C(9)–C(10)	1.563(14)	C(10)–C(11)	1.52(2)
C(11)–C(12)	1.544(14)	C(12)–C(13)	1.52(2)
C(12)–C(14)	1.53(2)		

(*b*) Angles

I–C(1)–C(2)	118.5(7)	I–C(1)–C(6)	119.2(7)
C(2)–C(1)–C(6)	122.3(9)	C(6)–O(1)–C(15)	115.6(9)
C(3)–O(2)–C(16)	119.8(8)	C(1)–C(2)–C(3)	117.0(9)
O(2)–C(3)–C(2)	121.8(9)	O(2)–C(3)–C(4)	116.6(9)
C(2)–C(3)–C(4)	121(1)	C(3)–C(4)–C(5)	120(1)
C(3)–C(4)–C(10)	133(1)	C(5)–C(4)–C(10)	107.2(9)
C(4)–C(5)–C(6)	121(1)	C(4)–C(5)–C(7)	106.7(9)
C(6)–C(5)–C(7)	132.5(9)	O(1)–C(6)–C(1)	120.5(9)
O(1)–C(6)–C(5)	121.1(9)	C(1)–C(6)–C(5)	118.2(9)
C(5)–C(7)–C(8)	105.5(8)	C(5)–C(7)–C(11)	99.6(8)
C(8)–C(7)–C(11)	98.9(8)	C(7)–C(8)–C(9)	103.2(9)
C(8)–C(9)–C(10)	104(1)	C(4)–C(10)–C(9)	106.6(9)
C(4)–C(10)–C(11)	101.3(9)	C(9)–C(10)–C(11)	100.2(8)
C(7)–C(11)–C(10)	94.0(8)	C(7)–C(11)–C(12)	115.9(9)
C(10)–C(11)–C(12)	117.3(9)	C(11)–C(12)–C(13)	110(1)
C(11)–C(12)–C(14)	109(1)	C(13)–C(12)–C(14)	111(1)

Table 4. Compound (**15**); fractional atomic co-ordinates (× 10^4) with estimated standard deviations in parentheses

	x	*y*	*z*
I	−928.8(15)	−337.1(9)	−1 088.5(5)
O(1)	879(14)	−1 809(7)	154(4)
O(2)	−52(11)	2 978(7)	1 041(4)
C(1)	−157(15)	224(11)	−75(6)
C(2)	−433(14)	1 441(10)	123(6)
C(3)	156(17)	1 796(11)	791(6)
C(4)	1 016(16)	1 006(10)	1 225(5)
C(5)	1 220(13)	−196(10)	1 024(6)
C(6)	606(15)	−609(10)	375(6)
C(7)	2 089(16)	−844(11)	1 648(6)
C(8)	686(19)	−893(12)	2 264(7)
C(9)	477(16)	427(12)	2 471(7)
C(10)	1 728(16)	1 129(11)	1 966(6)
C(11)	3 212(16)	232(12)	1 941(6)
C(12)	4 779(16)	587(12)	1 485(7)
C(13)	5 664(21)	1 707(14)	1 795(8)
C(14)	6 016(21)	−494(14)	1 446(7)
C(15)	−233(21)	−2 700(14)	458(8)
C(16)	−799(22)	3 869(13)	600(7)

was featureless. Since the space group is centrosymmetric it contains both the molecule as shown (Figure 1) and its enantiomer. The fractional atomic co-ordinates are shown in Table 1 and the bond lengths and angles in Table 2.

Compound (**15**). $C_{16}H_{21}IO_2$, M = 372.3, orthorhombic, space group $P_{2_12_12_1}$, a = 7.811(1), b = 10.958(1), c = 18.785(1) Å, U = 1 607.9 Å^3, Z = 4, D_c = 1.54 g cm^{-1}, μ(Mo-K_α) 20.1 cm^{-1}. Crystal size *ca.* 0.13 × 0.10 × 0.10 mm. Data measured for +h+k+l, $2 < \theta < 20°$. 721 Unique reflections with $|F^2| > \sigma(F^2)$, $\sigma(F^2) = [\sigma^2(I) + (0.02I)^2]^{1/2}/\mathrm{Lp}$. No crystal decay. Empirical absorption correction based on psi scans.

The structure determination, made as with (**11**), used routine heavy atom methods. Full matrix least squares refinement with *I* anisotropic. The two opposite absolute configurations gave R = 0.0470 (0.0476) and R' = 0.0560 (0.0566) and results are given for the lower residuals. Hydrogen atoms included at fixed positions (C–H 1.08 Å and B_{iso} = 6.0 Å^2). Weighting scheme $w = 1/\sigma^2(F)$. Final residuals R = 0.038, R' = 0.041. A final difference map was featureless. The structure of one enantiomer is shown in Figure 2, the fractional atomic co-ordinates in Table 3, and the bond lengths and angles in Table 4. Hydrogen atom co-ordinates and thermal parameters for both structures are available on request from the Cambridge Crystallographic Data Centre.*

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* See 'Instructions for Authors (1987),' paragraph 5.6.3 in *J. Chem. Soc., Perkin Trans. 1*, 1987, Issue 1.

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