Intramolecular Cyclisation of Phenolic Oximes. Part II.[1] Cyclisations with Brominating Agents

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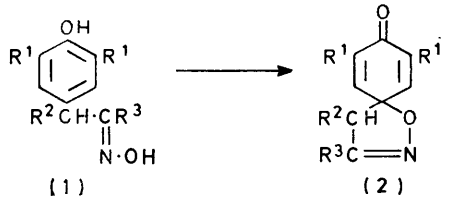
Intramolecular cyclisation of *p*-hydroxyarylpropan-2-one oximes to 2,5-dienonespiroisoxazolines can be achieved by using bromine, *N*-bromosuccinimide, or tetrabromocyclohexa-2,5-dienone. With an analogous *ortho*-phenolic oxime only the last of these was effective, the structure of the 2,4-dienonespiroisoxazoline formed being confirmed by an independent synthesis.

In Part I [1] we reported that manganese(III) trisacetylacetonate (MTA) was an effective reagent for the conversion of *para*-phenolic oximes (1) into spirodienones (2) but not for the corresponding conversion of the *ortho*-isomers, *i.e.* (3) ⟶ (4). Since the latter cyclisation is closely related to a possible biogenetic route to aerothionin [1,2] we have sought other reagents with which to effect this change. Consideration of the

[1] Part I, A. R. Forrester, R. H. Thomson, and S. O. Woo, preceding paper.

[2] E. Fattorusso, L. Minale, G. Sodano, K. Moody, and R. H. Thomson, *J.C.S. Perkin I*, 1972, 18.

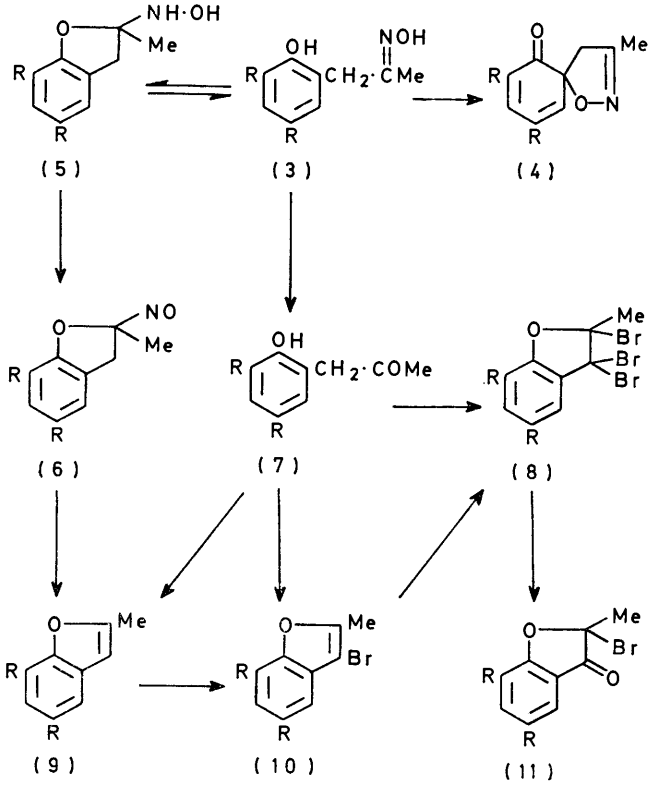
several which have been used previously to convert phenolic derivatives into spirodienones led us to examine bromine and positive brominating agents,[3,4] since these



(1) (2)

usually give high yields of cyclised products and in this instance could serve the dual purpose of brominating and oxidatively cyclising an aerothionin precursor.

Cyclisations with Molecular Bromine.—It was first established that molecular bromine, like MTA, would intramolecularly cyclise *para*-phenolic oximes to spirodienones. Thus, oxidation of the pyruvate oxime (1; $R^1 = R^2 = H$, $R^3 = CO_2Me$) with bromine water gave the corresponding dibromospiroisoxazoline (2; $R^1 = Br$, $R^2 = H$, $R^3 = CO_2Me$) in 65% yield. This oxidation is closely analogous to previously reported [3,4] cyclisations of phenolic amides and acids with bromine.



(5) (3) (4)

(6) (7) (8)

(9) (10) (11)

SCHEME 1

Similar treatment of the *ortho*-phenolic oximes gave no spirodienones. Instead, the phenolic oxime (3; R = H) with an excess (5.5 mol. equiv.) of bromine water gave the tribromobenzofuran (10; R = Br) (9%) and the tribromobenzofuranone (11; R = Br) (6%). Use of less bromine (2 mol. equiv.) and avoiding aqueous solvents offered no advantage: only the tribromobenzofuran (10; R = Br) (17%), the dibromophenolic oxime (3; R = Br), and the dibromo-ketone (7; R = Br) (8%) were isolated. With the di-t-butyl phenolic oxime (3; R = Bu^t) and an equimolar amount of bromine in chloroform only the bromobenzofuran (10; R = Bu^t) (49%) and starting material were obtained. The benzofuranone (11; R = Br) showed characteristic carbonyl i.r. absorption at 1 730 cm^{-1} and n.m.r. signals due to a methyl group at δ 2.23 and to two *meta*-coupled aromatic protons.

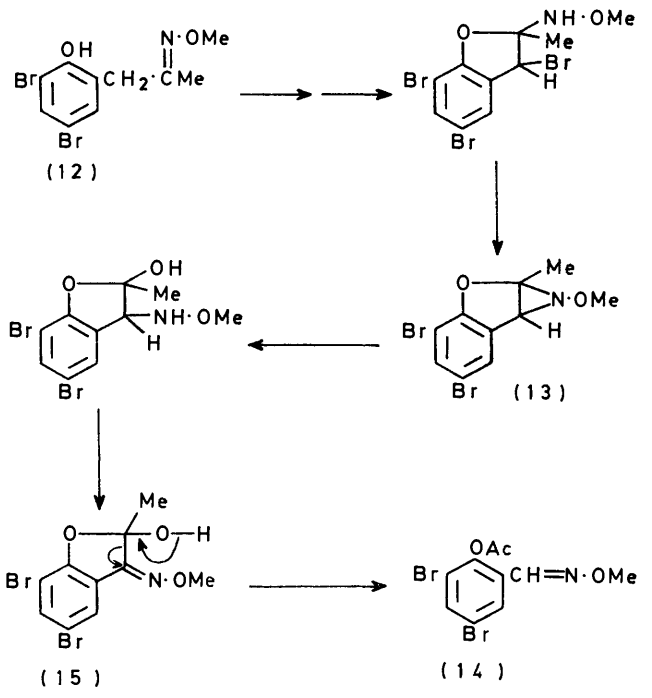
The dibromophenolic ketone (7; R = Br) is most probably formed by hydrolysis of the oxime, catalysed by the hydrobromic acid formed during nuclear bromination, the dibromobenzofuran (9; R = Br) being a cyclodehydration product of the ketone in the acidic medium (Scheme 1). Addition of solid sodium hydrogen carbonate to the bromination mixture in chloroform did not alter the course of these reactions. Oxidation of the ring tautomer (5; R = Br) of the phenolic oxime followed by loss of nitroxyl (NHO) from the ensuing nitrosodihydrobenzofuran (6; R = Br) would also give the dibromobenzofuran (9; R = Br) but the spectroscopic evidence (n.m.r. only) indicates that the phenolic oxime (3; R = Br) exists entirely in the chain form in chloroform solution. Further bromination of the dibromobenzofuran would yield the tribromobenzofuran (10; R = Br). We assume that the immediate precursor of the benzofuranone (11; R = Br) is the pentabromobenzofuran (8; R = Br), which is hydrolysed during work-up. There are two obvious ways in which the pentabromobenzofuran could arise from the ketone (7; R = Br). In one [(10; R = Br) ⟶ (8; R = Br)] the additional bromine atoms are introduced after benzofuran formation, and in the other the ketone is dibrominated at the α-position before cyclodehydration occurs.

Bromination of the phenolic oxime ether (12) in aqueous ethyl acetate also failed to give a spiroisoxazoline. With 2 mol. equiv. of bromine only nuclear bromination occurred, and with an excess of bromine a complex mixture was obtained from which only one product was isolated. We have identified this product as the acetoxydibromobenzaldehyde *O*-methyloxime (14) on the basis of its elemental analysis and i.r. (1 760 cm^{-1}), n.m.r. (Ac and MeO signals at δ 2.37 and 3.98, respectively, and CH=N singlet at δ 7.94), and mass spectra. This was confirmed by a conventional synthesis from 4,6-dibromosalicylaldehyde. We have not attempted to elucidate the individual steps in this rearrangement since they are not relevant to our main objective. However, a likely immediate precursor of the *O*-methyloxime (14) is the benzofuranone oxime (15), which could undergo ring opening as indicated. Since it is unlikely that both de(methoxyimin)ation and

[3] E. J. Corey and L. F. Haefele, *J. Amer. Chem. Soc.*, 1959, **81**, 2225; G. L. Schmir, L. A. Cohen, and B. Witkop, *J. Amer. Chem. Soc.*, 1959, **81**, 2228.

[4] G. W. Perold, A. J. Hodgkinson, and A. S. Howard, *J.C.S. Perkin I*, 1972, 2450.

re(methoxyimin)ation at an adjacent carbonyl group would occur under the reaction conditions employed, an

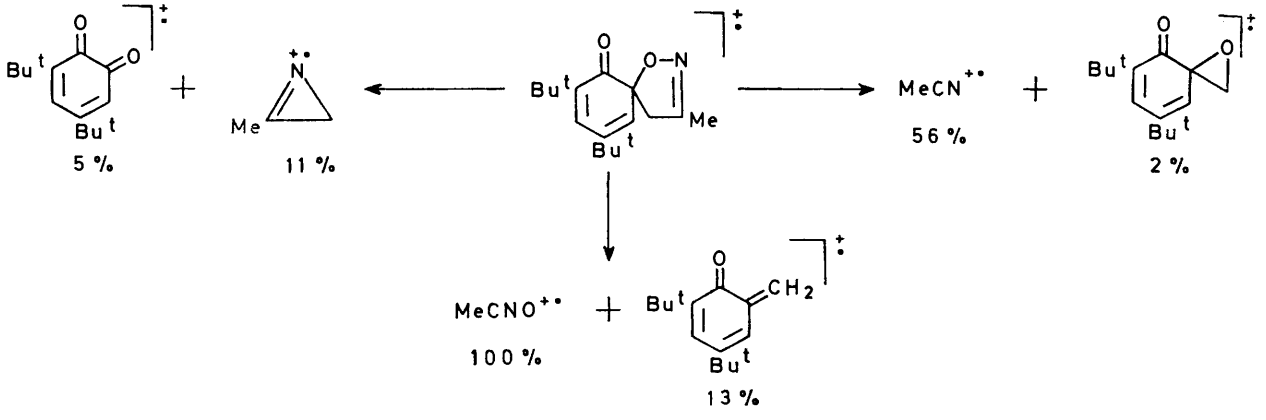


SCHEME 2

intramolecular shift of the methoxyamino-group by way of aziridine intermediate (13) (formed as shown in Scheme 2) may well be implicated.

Cyclisation with Positive Brominating Reagents.—In order to avoid the production of hydrogen bromide, which can catalyse both hydrolysis of the oxime and cyclodehydration of the resulting ketone to a benzofuran, we turned our attention to other electrophilic brominating agents. Accordingly, reaction of the phenolic oxime (1; $R^1 = Bu^t$, $R^2 = H$, $R^3 = Me$) with *N*-bromosuccinimide gave the corresponding spiroisoxazoline (2; $R^1 = Bu^t$, $R^2 = H$, $R^3 = Me$) in 72% yield, and the phenolic alcohol (16) gave the spiro-oxolan (17) (25%) with 2,4,4,6-tetrabromocyclohexa-2,5-dienone. The latter reagent was particularly promising since reaction proceeds under mild conditions, *i.e.* at room temperature in an organic solvent.[5] When this reagent was used to brominate the *o*-phenolic oxime (3; R = Bu^t) only small amounts of the benzofuran (9; R = Bu^t) and 3-bromobenzofuran (10; R = Bu^t) were formed; the major product, apart from 2,4,6-tribromophenol, was a pale yellow crystalline solid, $C_{17}H_{25}NO_2$ which we consider to be the desired spiroisoxazoline (4; R = Bu^t) on the following evidence. Its n.m.r. spectrum showed signals from two weakly coupled dienone protons at δ 5.95 and 6.35 and from two strongly coupled (J = 18 Hz) methylene protons at δ 2.82 and 3.28. In this respect the spectrum differs significantly from those of the spirocyclohexa-2,5-dienones (2) in which the methylene protons resonate as a singlet, but is very similar to those of aerothionin [2] and homoaerothionin which show strongly coupled (J 18 Hz) methylene signals at δ *ca.* 3.14 and 3.84. Molecular models indicate that the magnetic non-equivalence is due to the anisotropy of the carbonyl group, which in conformation (18) deshields H_b relative to H_a. The i.r. spectrum showed characteristic 2,4-dienone absorption at 1 674 cm^{-1} and no hydroxy-absorption. Fragmentation of the isoxazoline ring in the mass spectrometer occurred in a similar way (Scheme 3) to that described [1] for the analogous cyclohexa-2,5-dienonespiroisoxazolines (2).

Formation of the spiroisoxazoline (4; R = Bu^t) most probably proceeds *via* the bromo-dienone (19a) by intramolecular nucleophilic displacement, but an intramolecular S_N1 (with allylic rearrangement) or S_N2' reaction of the isomeric bromodienones (19b and c), with which (19a) is probably in equilibrium, would yield the same product.



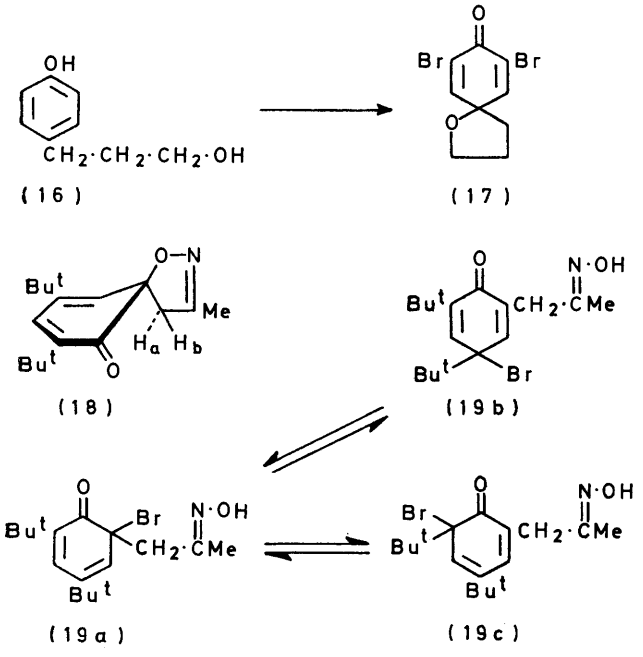
SCHEME 3

In order to confirm the structure of the spiroisoxazoline (18) its synthesis by an independent route was undertaken, beginning with the oxime (20; R = H), the

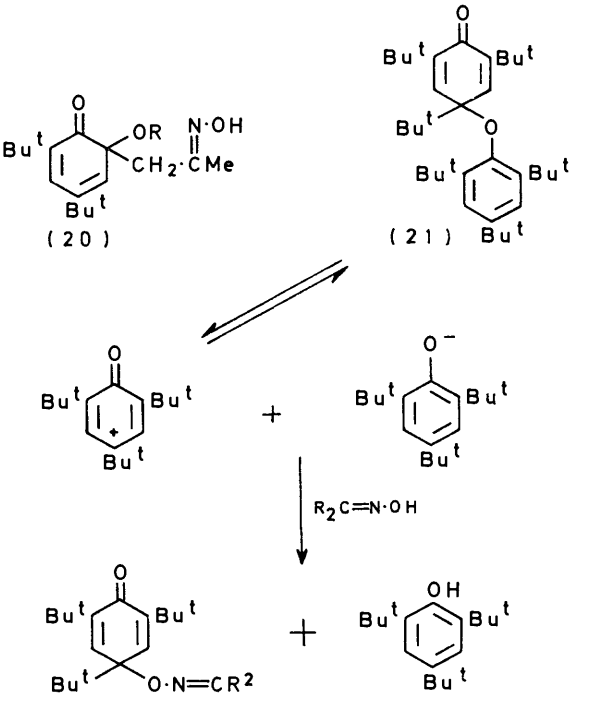
[5] V. Calo, F. Ciminale, L. Lopez, G. Pesce, and P. E. Todesco, *Synthesis*, 1972, 432.

parent ketone being of known structure.[6] Cyclodehydration of this dienone oxime to the spiroisoxazoline (18) could not be achieved by reaction with hydrogen chloride, acetic anhydride, or dicyclohexylcarbodi-imide (DCC). With hydrogen chloride in ethanol the ethyl ether (20; R = Et) was formed, and acetic anhydride in pyridine yielded the diacetate of (20; R = H); DCC had little effect on the oxime and gave only a trace of the *o*-benzoquinone. In benzene saturated or 0.28M with respect to hydrogen chloride the oxime did cyclise but only after rearrangement, and yielded not a spiroisoxazoline but an oxazine derivative. The chemistry of this novel transformation will be reported subsequently. A product identical with that obtained from the reaction of the *ortho*-phenolic oxime (3; R = Bu^t) with the tetrabromodienone was finally obtained by heating the oxime monoacetate (20; R = Ac) with an organic base. Of the several bases examined as solvents for this intramolecular nucleophilic substitution, most efficient conversion was achieved with boiling pyridine. Refluxing in 3-methylpyridine or simply short-path distillation of the acetate (20; R = Ac) at 125—130 °C *in vacuo* also resulted in some cyclodehydration to the spiroisoxazoline, but much intractable material was also produced.

We conclude that the oxidative intramolecular cyclisations of phenolic oximes to spiroisoxazolines described in this and the preceding paper did not proceed by way of



phenoxyl–iminoxyl diradical intermediates. Indeed the reactions which most probably did yield phenoxyl and/or iminoxyl radicals, the ferricyanide oxidations,[1] gave no spiroisoxazolines. In view of the above mechanistic conclusion we are sceptical of the intermolecular phenoxyl–iminoxyl coupling proposed by



SCHEME 4

Müller *et al.*[7] for the reaction of hindered phenoxyls with oximes, especially since it has been shown recently [8] that the O–H bond strength of 2,4,6-tri-t-butylphenol (81.2 kcal mol^{-1}) is lower than that of simple oximes (*ca.* 86 kcal mol^{-1}). By analogy with our previous mechanistic proposals for the intramolecular cyclisations we suggest that nucleophilic substitution (S_N1) by the oxime hydroxy-group on a low steady-state concentration of the dienone dimer (21) is a more likely event. This may be regarded as a disproportionation of the phenoxyl *via* a dienone intermediate followed by capture of the resulting phenoxonium ion by the oxime (*cf.* ref. 9) (Scheme 4). Such a process would account more readily for the high yield of hydroxyiminodienones obtained in the intermolecular reaction and the apparent absence of products derived entirely from iminoxyl radicals notionally formed by hydrogen abstraction or electron transfer.

EXPERIMENTAL

For general methods, see Part I.[1]

Reactions of Phenolic Oximes with Bromine.—(i) Methyl *p*-hydroxyphenylpyruvate oxime (120 mg) in ethyl acetate (5 ml) was shaken with bromine (415 mg) in water (5 ml) for 2 h. The organic layer was washed with water, dried ($MgSO_4$), and evaporated to give methyl 7,9-dibromo-8-oxo-1-oxa-2-azaspiro[4.5]deca-2,6,9-triene-3-carboxylate (2;

[6] R. Magnusson, *Acta Chem. Scand.*, 1960, **14**, 1643; 1964, **18**, 421.

[7] E. Müller, R. Mayer, B. Narr, A. Schick, and K. Scheffler, *Annalen*, 1961, **645**, 1.

[8] L. R. Mahoney, G. D. Mendenhall, and K. U. Ingold, *J. Amer. Chem. Soc.*, 1973, **95**, 8611.

[9] V. V. Ershov, A. A. Volodkin, A. I. Prohofev, and S. P. Solodovnekov, *Russ. Chem. Rev.*, 1973, **42**, 740.

R^1 = Br, R^2 = H, R^3 = CO_2Me) (75 mg, 65%), m.p. 198—200° (from ethyl acetate).

(ii) (*a*) *o*-Hydroxyphenylpropan-2-one oxime (990 mg) in ethyl acetate (25 ml) was shaken with bromine (5.28 g, 1.8 ml) in water (30 ml) for 2 h. The organic layer was washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated. The residual red oil was chromatographed in petrol–chloroform (1 : 9) to give (a) 3,5,7-*tribromo*-2-*methylbenzofuran* * (200 mg, 9%), m.p. 127—128.5° (from petrol) (Found: Br, 65.3%; M^+, 365.7888. $C_9H_5{}^{79}Br_3O$ requires Br, 65.0%; *M*, 365.7892), $\lambda_{max.}$ 223, 264, 290, and 298 nm (log ε 4.02, 4.01, 3.46, and 3.37), δ 2.52 (3 H, s, Me), 7.51 (1 H, d, *J* 2 Hz, ArH), and 7.58 (1 H, d, *J* 2 Hz, ArH); and (b) 2,5,7-*tribromo*-2-*methylbenzofuran*-3(2H)-*one* * (145 mg, 6%), m.p. 112—113.5° (from petrol) (Found: Br, 63.0%; M^+, 381.7832. $C_9H_5{}^{79}Br_3O$ requires Br, 62.8%; *M*, 381.7841), $\nu_{max.}$ 1 730 cm^{-1}, $\lambda_{max.}$ 227, 268, and 259 nm (log ε 4.44, 3.83, and 3.63), δ 2.21 (3 H, s, Me), 7.85 (1 H, d, *J* 2 Hz, ArH), and 7.99 (1 H, d, *J* 2 Hz, ArH).

(*b*) *o*-Hydroxyphenylpropan-2-one oxime (495 mg) in chloroform (25 ml) was treated dropwise with bromine (1.28 g, 0.44 ml) in chloroform (15 ml) at 0 °C. The mixture was stirred at room temperature for 2 h, was washed with aqueous sodium hydrogen carbonate and water, and dried. The oil remaining after removal of solvent was chromatographed in chloroform to give (a) 5,7-*dibromo*-2-*methylbenzofuran* (146 mg, 17%), m.p. 92° (from petrol) (Found: C, 37.2; H, 2.4; Br, 55.0. $C_9H_6Br_2O$ requires C, 37.3; H, 2.1; Br, 55.1%), $\lambda_{max.}$ 219, 257, 287, and 295 nm (log ε 4.36, 3.90, 3.21, and 3.21), δ 2.49 (3 H, s, Me), 6.38 (2 H, s, CH=), and 7.5 (2 H, s, ArH); (b) 3,5-*dibromo*-2-*hydroxyphenylpropan*-2-*one* * (70 mg, 8%), m.p. 80° (from petrol–benzene) (Found: Br, 51.6%; M^+, 305.8893. $C_9H_8{}^{79}Br_2O_2$ requires Br, 51.9%; *M*, 305.8890), $\nu_{max.}$ 3 180 and 1 700 cm^{-1}, $\lambda_{max.}$ 212, 226sh, and 294 nm (log ε 4.40, 3.98, and 3.41), δ 2.4 (3 H, s, Me), 3.72 (2 H, s, CH_2), 6.2 (1 H, s, OH), 7.19 (1 H, d, *J* 2 Hz, ArH), and 7.53 (1 H, d, *J* 2 Hz, ArH); and (c) 3,5-*dibromo*-2-*hydroxyphenylpropan*-2-*one oxime* * (100 mg, 10%), m.p. 87.5—88.5° (from benzene) (Found: C, 34.3; H, 3.1; Br, 47.8; N, 4.4%; M^+, 320.9003. $C_9H_8{}^{79}Br_2NO_2$ requires C, 33.4; H, 2.8; Br, 49.5; N, 4.6%; *M*, 320.8999), $\nu_{max.}$ 3 410 and 3 240 cm^{-1}, $\lambda_{max.}$ 210 and 294 nm (log ε 4.45 and 3.29), δ (*syn*- and *anti*-forms, respectively) 1.92 and 1.91 (3 H, s, Me), 3.52 and 3.70 (2 H, s, CH_2), 7.22 (1 H, d, *J* 4 Hz, ArH), 7.37 (1 H, s, OH), and 7.55 (1 H, d, *J* 4 Hz, ArH).

When this oxidation was repeated with sodium hydrogen carbonate (3 g) dispersed in the chloroform solution during addition of the bromine, 3,5-dibromo-2-hydroxyphenylpropan-2-one (250 mg, 26%), 5,7-dibromo-2-methylbenzofuran (70 mg, 8%), and 3,5-dibromo-2-hydroxyphenylpropan-2-one (trace) were obtained.

(iii) 1-(2-Hydroxy-3,5-di-t-butylphenyl)propan-2-one oxime (554 mg) in chloroform (9 ml) was treated with bromine (320 mg, 0.11 ml) in chloroform (6 ml) at 0 °C. After 2 h at room temperature the mixture was worked up as in (ii) to give, after chromatography in benzene–chloroform (1 : 1), 3-*bromo*-2-*methyl*-5,7-*di*-t-*butylbenzofuran* * (318 mg, 49%), b.p. 95—98° at 0.15 mmHg (Found: Br, 24.7%; M^+, 322.0957. $C_{17}H_{23}{}^{79}BrO$ requires Br, 24.7%; *M*, 322.0931), $\nu_{max.}$ (film) 1 612 cm^{-1}, $\lambda_{max.}$ 230, 253, 278, and 288 nm (log ε 3.67, 4.09, 3.42, and 3.38), δ (CCl_4) 1.40 (9 H, s, Bu^t), 1.51 (9 H, s, Bu^t), 2.53 (3 H, s, Me), and 7.25 (2 H, s, ArH), and starting material (230 mg).

(iv) (*a*) *o*-Hydroxyphenylpropan-2-one *O*-methyloxime (1.074 g) in ethyl acetate (25 ml) was shaken with bromine (5.28 g, 1.8 ml) in water (30 ml) for 2 h. The organic layer was washed with saturated sodium hydrogen carbonate, dried, and evaporated. The residual red oil was chromatographed in benzene–chloroform (1 : 1) to give 2-*acetoxy*-3,5-*dibromobenzaldehyde O*-*methyloxime* (14) (75 mg, 35%), m.p. 101° (from petrol–benzene) (Found: Br, 45.0; N, 3.7%; M^+, 348.8951. $C_{10}H_9Br_2NO_3$ requires Br, 45.0; N, 3.9%; *M*, 348.8950), $\nu_{max.}$ 1 760 cm^{-1}, $\lambda_{max.}$ 225 and 281 nm (log ε 4.45 and 4.13), δ 2.37 (3 H, s, Me), 3.98 (3 H, s, OMe), 7.73 (1 H, d, *J* 3 Hz, ArH), 7.89 (1 H, d, *J* 3 Hz, ArH), and 7.96 (1 H, s, CH=N). An authentic specimen of this product was prepared from 3,5-dibromo-2-hydroxybenzaldehyde by methoxyimination followed by acetylation (standard procedures).

(*b*) The propanone *O*-methyloxime (537 mg) in chloroform (25 ml) was treated at 0 °C with bromine (960 mg, 0.33 ml) in chloroform (15 ml). After stirring for 2 h the mixture was washed with saturated aqueous sodium hydrogen carbonate and water, dried, and evaporated. The residue was chromatographed on a silica column with benzene to give 1-(3,5-*dibromo*-2-*hydroxyphenyl*)*propan*-2-*one* O-*methyloxime* * (600 mg, 59%) as a viscous oil (Found: Br, 46.2; N, 3.2%; M^+, 334.9158. $C_{10}H_{11}{}^{79}Br_2NO_2$ requires Br, 47.4; N, 4.1%; *M*, 334.9155), $\nu_{max.}$ (film) 3 500 (COH) and 3 250 cm^{-1} (NOH), $\lambda_{max.}$ 238 and 292 nm (log ε 3.75 and 3.48), δ (*syn*- and *anti*-forms, respectively) 1.88 (3 H, s, Me), 3.48 and 3.61 (2 H, s, CH_2), 3.88 and 3.94 (3 H, s, OMe), 7.23 (1 H, d, *J* 3 Hz, ArH), 7.27 (1 H, s, OH), and 7.53 (1 H, d, *J* 3 Hz, ArH).

Oxidation of Phenolic Oximes with Positive Halogen Compounds.—(i) 1-(4-Hydroxy-3,5-di-t-butylphenyl) propan-2-one oxime (70 mg) in chloroform (10 ml) was added to *N*-bromosuccinimide (49.5 mg) in chloroform (20 ml). The mixture was stirred for 1 h and then washed with saturated aqueous sodium hydrogen carbonate and water, dried, and evaporated. Chromatography of the residual oil in petrol–ethyl acetate (6 : 1) gave 3-methyl-7,9-di-t-butyl-1-oxa-2-azaspiro[4.5]deca-2,6,9-trien-8-one [1] (2; R^1 = Bu^t, R^2 = R^3 = H) (60 mg, 72%).

(ii) 1-(3,5-Dibromo-2-hydroxyphenyl)propan-2-one oxime (646 mg) and 2,4,4,6-tetrabromocyclohexa-2,5-dienone [5] (902 mg) were dissolved in acetonitrile (50 ml) and left at room temperature for 24 h. The oil obtained on removal of the solvent was chromatographed in chloroform to give 5,7-dibromo-2-methylbenzofuran (325 mg, 56%), m.p. 92°, and 2,4,6-tribromophenol (510 mg, 70%).

(iii) 1-(2-Hydroxy-3,5-di-t-butylphenyl)propan-2-one oxime (554 mg) and 2,4,4,6-tetrabromocyclohexa-2,5-dienone (902 mg) were dissolved in acetonitrile (40 ml) and left for 24 h. Chromatography of the oil obtained on removal of the solvent in benzene–chloroform (1 : 1) gave (a) 3-*methyl*-7,9-*di*-t-*butyl*-1-*oxa*-2-*azaspiro*[4.5]*deca*-2,7,9-*trien*-6-*one* (4; R = Bu^t) (110 mg, 20%) as yellow needles, m.p. 106° (from hexane) (Found: C, 74.3; H, 9.3; N, 5.4%; M^+, 275.1883. $C_{17}H_{25}NO_2$ requires C, 74.2; H, 9.1; N, 5.1%; *M*, 275.1885), $\nu_{max.}$ 1 674 cm^{-1}, $\lambda_{max.}$ 214 and 325 nm (log ε 3.92 and 3.09), δ 1.12 (9 H, s, 7-Bu^t), 1.22 (9 H, s, 9-Bu^t), 2.02 (3 H, s, Me), 2.82 (1 H, d, *J* 18 Hz, HC*H*), 3.28 (1 H, d, *J* 18 Hz, *H*CH), 5.99 (1 H, d, *J* 2 Hz, 10-H), and 6.35 (1 H, d, *J* 2 Hz, 8-H), *m/e* 275 (32%, M^+), 260 (22), 219 (28), 206 (28), 204 (25), 177 (13), 149 (22),

* Satisfactory carbon and hydrogen analyses could not be obtained for compounds containing a high percentage of bromine.

91 (16), 76 (11), 57 (100), and 41 (56); (b) 5,7-di-t-butyl-2-methylbenzofuran (42 mg, 9%); (c) 3-bromo-2-methyl-5,7-di-t-butylbenzofuran (50 mg, 8%); (d) 2,4,6-tribromophenol (562 mg); and (e) starting phenolic oxime (150 mg).

(iv) 3-(*p*-Hydroxyphenyl)propan-1-ol (100 mg) and 2,4,4,6-tetrabromocyclohexa-2,5-dienone (800 mg) were dissolved in acetonitrile (20 ml) and left at room temperature for 24 h. The solvent was removed and the residue chromatographed in benzene to give 7,9-dibromo-1-oxaspiro[4.5]deca-6,9-dien-8-one (17) (50 mg, 25%), m.p. 116—118° identical with authentic material prepared from the aforementioned phenol and bromine.

Reactions of 6-*Hydroxy*-6-(2-*hydroxyiminopropyl*)-2,4-*di-t-butylcyclohexa*-2,4-*dienone* (20; R = H).—This oxime was prepared from 6-acetonyl-6-hydroxy-2,4-di-t-butylcyclohexa-2,4-dienone [6] (558 mg), hydroxyammonium chloride (414 mg), and sodium acetate (1 g) in aqueous ethanol by stirring at room temperature for 45 min. The yellow precipitate was collected and water was added to the filtrate to induce further precipitation. The combined solids were washed with water, dried, and crystallised from chloroform to give the *oxime* (450 mg, 76%), m.p. 122—123.5° (Found: C, 69.8; H, 9.5; N, 4.6%. $C_{17}H_{27}NO_3$ requires C, 69.6; H, 9.3; N, 4.8%), $\nu_{max.}$ 3 350br, 1 665, and 1 640 cm^{-1}, $\lambda_{max.}$ 210 and 315 nm (log ε 3.85 and 3.48), δ 1.14 (9 H, s, 2-Bu^t), 1.24 (9 H, s, 4-Bu^t), 1.94 (3 H, s, Me), 2.51 (2 H, q, *J* 13 Hz, CH_2), 4.7 (1 H, s, OH), 6.07 (1 H, d, *J* 4 Hz, 5-H), and 6.92 (1 H, d, *J* 4 Hz, 3-H).

(i) *With hydrogen chloride.* The oxime (20; R = H) (293 mg) was dissolved in 4.7M-hydrogen chloride in ethanol (50 ml) and left for 1 h. Removal of the solvent and chromatography of the residue in chloroform–ether (4 : 1) gave 6-*ethoxy*-6-(2-*hydroxyiminopropyl*)-2,4-*di-t-butylcyclohexa*-2,4-*dienone* (20; R = Et) (150 mg, 46%) as a yellow oil, b.p. 146—148° at 0.19 mmHg (Found: C, 67.9; H, 9.5; N, 4.0%; *M*$^+$, 321.2291. $C_{19}H_{31}NO_3$ requires C, 71.0; H, 9.6; N, 4.3%; *M*, 321.2304), $\nu_{max.}$ (film) 3 300, 1 674, and 1 657 cm^{-1}, $\lambda_{max.}$ 207 and 320 nm (log ε 3.89 and 3.20), δ 1.14 (9 H, s, 2-Bu^t), 1.26 (9 H, s, 4-Bu^t), 1.10—1.28 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.91br (3 H, s, Me), 2.5br (2 H, s, CH_2), 3.2 (2 H, q, *J* 7 Hz, MeCH_2), 5.92 (1 H, d, *J* 4 Hz, 5-H), and 6.9 (1 H, d, *J* 4 Hz, 3-H).

(ii) *With acetic anhydride.* A solution of the oxime (20; R = H) (293 mg) in acetic anhydride (5 ml) was heated at 60 °C for 50 h. Work-up as in (i) gave 6-*acetoxy*-6-(2-*acetoxyiminopropyl*)-2,4-*di-t-butylcyclohexa*-2,4-*dienone* (80 mg, 21%) as a yellow oil, b.p. 135—138° at 0.15 mmHg (Found: C, 66.8; H, 8.5; N, 5.7%; *M*$^+$, 377.2176. $C_{21}H_{31}NO_5$ requires C, 67.6; H, 8.3; N, 3.8%; *M*, 377.2202), $\nu_{max.}$ (film) 1 760 (OAc) and 1 680 and 1 650 cm^{-1} (dienone), $\lambda_{max.}$ 208 and 313 nm (log ε 3.96 and 3.46), δ 1.11 (9 H, s, 2-Bu^t), 1.24 (9 H, s, 4-Bu^t), 2.19br (6 H, s, 2-OAc), 2.16 (3 H, s, Me), 2.68br (2 H, s, CH_2), 5.83 (1 H, d, *J* 4 Hz, 5-H), and 3.04 (1 H, d, *J* 4 Hz, 3-H), and 3,5-di-t-butyl-1,2-benzoquinone (40 mg, 19%).

(iii) *With dicyclohexylcarbodi-imide* (*DCC*). A solution of the oxime (20; R = H) (586 mg) and DCC (412 mg) in dry ether (100 ml) was heated under reflux for 10 min. The mixture was left overnight and filtered. Removal of the solvent from the filtrate left an oil, chromatography of which with chloroform–ether (4 : 1) gave 3,5-di-t-butyl-1,2-benzoquinone (trace) and the starting oxime (500 mg).

Preparation and Cyclisation of 6-*Acetoxy*-6-(2-*hydroxyiminopropyl*)-2,4-*di-t-butylcyclohexa*-2,4-*dienone*.—(i) *Preparation.* A solution of 2-acetonyl-6-hydroxy-2,4-di-t-butylcyclohexa-2,4-dienone [6] (800 mg) in acetic anhydride (8 ml) and pyridine (2 ml) was left at room temperature for 25 h. Water (40 ml) was then added and the mixture was extracted with chloroform. The extracts were shaken successively with saturated aqueous sodium hydrogen carbonate, 2M-sulphuric acid, and water, and dried. Evaporation gave an oil, chromatography of which in chloroform–ether (5 : 1) gave 6-*acetonyl*-6-*acetoxy*-2,4-*di-t-butylcyclohexa*-2,4-*dienone* (581 mg, 63%) as a viscous oil (Found: C, 71.1; H, 9.1. $C_{19}H_{28}O_4$ requires C, 71.2; H, 8.8%), $\nu_{max.}$ (film) 1 745 (OAc), 1 713 (CO), and 1 680 and 1 654 cm^{-1} (dienone), $\lambda_{max.}$ 206 and 313 nm (log ε 4.22 and 3.78), δ 1.14 (9 H, s, 2-Bu^t), 1.26 (9 H, s, 4-Bu^t), 2.08 (3 H, s, Me), 2.2 (3 H, s, Me), 2.74 and 2.79 (2 H, each s, CH_2), 6.03 (1 H, d, *J* 4 Hz, 5-H), and 6.94 (1 H, d, *J* 4 Hz, 3-H), and 3,5-di-t-butyl-1,2-benzoquinone.

The acetoxycyclohexadienone (471 mg), hydroxyammonium chloride (400 mg), and sodium acetate (1 g) were dissolved in ethanol (6 ml) and water (15 ml) and stirred for 1.5 h at room temperature. Water was then added and the ethanol was removed *in vacuo*. The aqueous residue was extracted with chloroform and the extracts were dried. Chromatography in chloroform–ether (4 : 1) of the oil remaining on removal of solvent gave 6-*acetoxy*-6-(2-*hydroxyiminopropyl*)-2,4-*di-t-butylcyclohexa*-2,4-*dienone* (20; R = Ac) (460 mg, 93%) as an oil, b.p. 125—130° at 0.18 mmHg (Found: C, 67.8; H, 8.9; N, 4.1. $C_{19}H_{29}NO_4$ requires C, 68.0; H, 8.7; N, 4.2%), $\nu_{max.}$ (film) 3 300, 1 750 (OAc), and 1 675 and 1 655 cm^{-1} (dienone), $\lambda_{max.}$ 208 and 315 nm (log ε 4.04 and 3.59), δ 1.13 (9 H, s, 2-Bu^t), 1.24 (9 H, s, 4-Bu^t), 1.92 (3 H, s, Me), 2.09 (3 H, s, OAc), 2.53br (2 H, s, CH_2), 5.81 (1 H, d, *J* 4 Hz, 5-H), and 6.94 (1 H, d, *J* 4 Hz, 3-H).

(ii) *Cyclisation.* (*a*) The oxime (20; R = Ac) (125 mg) in triethylamine (40 ml) was heated under reflux for 72 h. Removal of the solvent gave an oil, chromatography of which with chloroform–ether (4 : 1) gave 3-methyl-7,9-di-t-butyl-1-oxa-2-azaspiro[4.5]deca-2,7,9-trien-6-one (4; R = Bu^t) (10 mg, 10%), m.p. 105—106°, identical with an authentic specimen, and the starting oxime (70 mg).

(*b*) The oxime (380 mg) in pyridine (10 ml) was heated at 120—125 °C for 1.5 h. Chloroform (70 ml) was then added and the resulting solution was extracted with 2M-sulphuric acid and water and dried. Removal of the solvent yielded an oil which was chromatographed in chloroform–ether (4 : 1) to give the spirocyclohexadienone (4; R = Bu^t) (25 mg, 8%) and the starting oxime (174 mg, 46%).

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