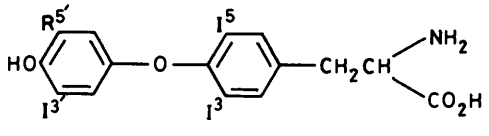
A Study of the Crystal and Molecular Structures of Phenols with only Intermolecular Hydrogen Bonding

Keith Prout* and John Fail and in part Richard M. Jones and Rachael E. Warner
Chemical Crystallography Laboratory, Oxford University, 9 Parks Road, Oxford, OX1 3PD
John C. Emmett
Smith Kline and French Research Ltd., The Frythe, Welwyn, Herts, AL6 9AR

The crystal structures and molecular geometrics of 41 phenols with only intermolecular hydrogen-bonding have been compared and analysed, with the following conclusions. (i) The electronic properties of substituents have effects on the phenolic hydroxy group which are measurable in terms of variations in the endocyclic angle at the phenolic hydroxy group. (ii) For mono-*ortho*-substituted phenols in the crystal the donor hydrogen bond lies on the opposite side of the C–O bond to the *ortho* substituent. (iii) The donor hydrogen bond is not required to be coplanar with the aromatic ring but may deviate by up to 40°. (iv) In di-*ortho*-substituted phenols there is a repulsive steric interaction between the donor hydrogen bond and one *ortho* substituent and this can be described in terms of both an in-plane and out-of-plane distortion of the hydrogen bonding. (v) The acceptor hydrogen bond shows large deviations from the phenolic ring plane and these deviations are greatly increased by *ortho* substitution. The crystal structures of the following compounds have been determined: 2-iodophenol, 2,6-di-isopropylphenol, 2,6-dibromo-4-methylphenol, 4-ethyl-2,6-di-iodophenol, 4-carboxy-2-iodophenol monohydrate, 4-carboxy-2,6-di-iodophenol, 4-carboxy-2,6-di-isopropylphenol, 2-methylsulphonylphenol monohydrate, 4-hydroxy-2-methylsulphonylphenol, 2-iodophenol–1,4-benzoquinone 2:1 molecular complex, 2-methylphenol–1,4-benzoquinone 2:1 molecular complex, 2,4,6-tri-iodophenol–tetramethylpyrazine 2:1 molecular complex, and 4′-hydroxy-4-methyl-2,3′,5′6,-tetraiododiphenyl ether.

The thyroid hormones, L-thyroxine (T_4) (**1**) and L-3,3′,5-tri-iodothyronine (T_3) (**2**), play an important role in the development of the central nervous system, the growth, differentiation, and development of tissue, and the control of metabolic activity, including tissue oxygen consumption and synthesis and metabolism of proteins.[1] The hydrophobic thyroid hormones are bound in the blood to two high-affinity transport proteins, prealbumin (TBPA) and thyroxine-binding globulin (TBG). T_4 binds to these transport proteins more strongly than T_3 and is metabolised in the circulation to T_3, so that the protein-bound T_4 acts as a reservoir for the generation of T_3.[2] The T_3 diffuses or is transported into the cell where it binds high-affinity low-capacity nuclear receptors which are non-histone proteins associated with chromatin DNA.[3]



(**1**) R = I
(**2**) R = H

Structural features that are important for both binding to nuclear receptors and for the production of hormonal effects *in vivo* have been identified.[4] The overall molecular shape is critical, *i.e.* a semi-rigid structure consisting of two mutually perpendicular aromatic rings held in position by an appropriate bridging atom (O, C, or S) and bulky 3,5 substituents are required. A substituent *ortho* to the 3′-position may take up a proximal or distal position, but there is evidence to suggest that the active form of T_3 requires an iodine atom positioned distally. For maximum hormone activity the following substituents, whose relative positions are fixed by the overall semi-rigid structure, are necessary: an anionic side chain in the 1-position, a lipophilic group no larger than iodine in the 3′-position, iodine or bromine in the 3,5-positions and a 4′-hydroxy group. Quantitative structure-activity and structure-binding affinity correlations[5] and theoretical calculations[6] suggest that the un-ionised phenolic hydroxy group acts as a proton donor to the nuclear receptor, and that there are interactive electronic and orientating effects between the hydroxy and its *ortho* substituents, whereas it is the ionised phenolic hydroxy group that binds to the transport proteins. Binding to nuclear receptors is apparently enhanced by substituents which promote proton donation towards the 5′-position and is reduced by 5′-substituents in direct relation to their size.[5] Further support for the important role of the 4′-hydroxy as a proton donor is provided by the recent finding that 3′-acetyl-T_2, possessing a strong intramolecular hydrogen bond, has very weak affinity for the T_3 receptor.[7] The chemical properties of phenols indicate that the hydroxy group is conjugated with the aromatic system and the O–H bond is coplanar with the aromatic ring. The effect of conjugation in stabilising a planar structure has been attributed to the delocalisation of the oxygen *p*-type lone pair; this is likely to be more effective than the delocalisation of the more tightly bound sp^2-type lone pair in an orthogonal structure.[8]

The planarity of phenol has been confirmed by microwave and i.r. spectroscopy.[9] The barrier to rotation about the C–O bond has been shown by microwave spectroscopy to be 13.8[9] and 14.0[10] kJ mol^{-1}, and by i.r. spectroscopy to be 14.5[11] and 14.9[8] kJ mol^{-1}. The rotational barrier has been found to decrease with a π-donor *para* substituent and increase with a π-acceptor *para* substituent.[8] *Ab initio* MO calculations also predict phenol to be planar with a high rotational barrier (21.6 kJ mol^{-1}).[12]

For mono-*ortho*-substituted phenols the hydroxy group remains coplanar, or very nearly so, with the aromatic ring. The

Table 1. Analysis of the hydrogen-bonding environment of the hydroxy group in intramolecularly and intermolecularly hydrogen-bonded phenols (see Figure 1)

R^2	R^3	R^4	R^5	R^6	α(°)	C–(OH) (Å)	θ_1/°	θ_2/°	t_d/°	d_x/Å	d_y/Å	t_a/°	a_x/Å	a_y/Å	d(O–H···O)/Å	d(O···H–O)/Å	pK_a	Ref.
Bu^t	—	Br	—	Bu^t	124(1)	1.37(2)	118(1)	118(1)	—	—	—	—	—	—	No H-bond	—	11.09[53]	25
Bu^t	—	Me	—	Bu^t	122.6(6)	1.375(9)	118.2(6)	119.1(6)	—	—	—	—	—	—	No H-bond	—	12.23[54]	28, 29
Pr^i	—	COOH	—	Pr^i	123.2(3)	1.379(4)	115.8(3)	121.0(3)	33	1.15	1.70	57	1.70	2.31	2.679(7)	2.742(7)	—	(**9**)
Pr^i	—	—	—	Pr^i	122.6(5)	1.408(7)	118.0(6)	119.6(6)	26	0.87	1.94	43	1.53	1.87	2.747(10)	2.735(10)	11.08[54]	(**4**)
Pr^i	—	—	—	Pr^i	122.4(6)	1.382(8)	118.6(6)	118.7(7)	87	2.23	1.41	77	2.21	1.59	2.735(10)	2.747(10)	11.08[54]	(**4**)
Me	—	—	—	Me	122.7(10)	1.37(2)	116.8(10)	120.5(5)	25	0.75	1.82	82	2.80	0.58	2.80	2.80	10.59[55]	20
Me	—	—	—	Me	122.4(7)	1.398(8)	117.5(6)	120.0(6)	29	0.99	1.73	74	2.56	0.56	2.67	2.83	10.59[55]	21
Pr^i	—	—	Me	—	122.5(3)	1.392(3)	117.3(3)	120.2(2)	20	0.81	1.19	70	2.38	0.98	2.703	2.703	—	32
Me	Br	—	—	—	125(1)	1.40(2)	117(1)	118(1)	29	1.29	0.95	74	2.39	1.39	2.78	2.78	9.44[53]	28
Me[a]	Me	—	—	—	122.6(3)	1.402(4)	117.2(3)	120.1(3)	23	0.91	1.17	75	2.73	0.62	2.82	2.82	10.5[55]	28
Me[a]	Me	—	—	—	122.2(5)	1.37(1)	117.9(5)	119.9(5)	22	0.85	1.24	73	2.70	0.45	2.80	2.80	10.5[55]	33
Me	—	—	Me	—	121.5(5)	1.40(1)	117.8(5)	120.7(5)	41	1.84	0.46	68	1.81	1.95	2.80	2.80	10.2[55]	33
Me	—	—	—	—	121.8(3)	1.369(4)	116.2(3)	122.0(3)	0	0.04	1.23	—	—	—	2.798(6)	—	10.28[55]	(**13**)
Me	—	—	—	—	120.8(3)	1.379(4)	117.8(3)	121.4(3)	36	1.64	0.61	—	—	—	2.833(6)	—	10.28[55]	(**13**)
NH_2	—	Cl	—	—	120.0(6)	1.375(9)	117.6(6)	122.4(6)	1	0.06	1.21	—	—	—	2.819[b]	3.137[d]	8.89[53]	34
NH_2	—	—	—	—	119.6(5)	1.368(7)	117.3(5)	121.1(5)	5	0.24	1.23	—	—	—	2.764[b]	3.114[d]	9.40[55]	34
—	Me	Pr^i	—	—	120.2(6)	1.384(8)	117.4(2)	122.3(7)	1	0.07	1.00	14	0.56	1.44	2.858(8)	2.858(8)	—	35
—	—	Me	—	—	120.8(6)	1.39(1)	118.3(7)	120.9(7)	27	0.86	1.62	48	1.91	0.78	2.706	2.661	10.26[55]	36
—	—	Me	—	—	120.6(6)	1.39(1)	118.7(6)	120.5(6)	40	1.65	0.92	48	1.41	1.92	2.661	2.706	10.26[55]	36
—	—	COOH	—	—	120.3(5)	1.36(1)	117.8(5)	121.9(5)	3	0.07	1.21	30	0.73	2.31	2.595	2.823	9.31[55]	37
—	—	COOH	—	—	120.5(2)	1.357(2)	117.9(2)	121.7(2)	3	0.07	1.19	29	0.71	2.29	2.603(2)	2.811(2)	9.31[55]	38
—	—	—	—	—	120.3(7)	1.370(9)	117.1(6)	122.5(7)	—	—	—	—	—	—	2.76(1)	—	9.99[55]	39
—	—	—	—	—	120.2(6)	1.356(6)	118.5(6)	120.2(6)	21	0.81	1.50	—	—	—	2.739(5)	—	9.99[55]	40
—	—	CN	—	—	120.4(4)	1.357(4)	117.8(4)	121.8(4)	6	0.31	1.18	—	—	—	2.819	—	7.95[55]	41
—	—	CN	—	—	119.6(4)	1.344(4)	116.9(4)	123.5(4)	6	0.23	1.26	—	—	—	2.840[b]	—	7.95[55]	41
—	—	Br	—	—	119.1(6)	1.382(7)	118.8(6)	122.2(6)	16	0.67	0.77	15	0.76	1.04	2.84	2.84	9.34[55]	42

—	Cl	—	Cl	—	121.9(7)	1.388(8)	118.1(6)	119.9(6)	23	0.80	1.62	75	2.73	0.46	2.67	2.83	8.25[56]	31
—	Cl	Cl	—	—	121.8(6)	1.395(8)	118.5(6)	119.7(6)	23	0.98	1.22	72	1.87	1.83	2.719(6)	2.719(6)	8.62[56]	43
—	SO_2Me	OH	—	—	119.7(3)	1.369(4)	117.9(3)	122.4(3)	—	—	—	—	—	—	2.862(6)	—	9.33[56]	**(11)**
—	SO_2Me	OH	—	—	119.7(3)	1.369(4)	117.5(3)	122.7(3)	—	—	—	—	—	—	2.885(6)	—	9.33[56]	**(11)**
I	—	—	—	—	120.5(15)	1.38(2)	120.7(15)	118.8(16)	6	0.31	1.05	—	—	—	2.77(2)	—	8.46[55]	**(12)**
I	—	—	—	—	120.0(9)	1.37(1)	118.8(9)	121.2(9)	29	1.28	0.93	71	2.30	1.25	2.78(2)	2.78(2)	8.46[55]	**(3)**
I	—	COOH	—	—	119.0(6)	1.363(6)	119.8(5)	120.5(5)	14	0.64	1.38	24	0.76	2.21	2.817(9)	2.680(9)	—	**(7)**
Cl	Cl	—	—	—	120.3(10)	1.37(1)	117.0(8)	122.7(9)	—	—	—	—	—	—	2.73	2.73	7.71[56]	43
Cl	Cl	—	—	—	122.4(10)	1.38(1)	117.0(9)	120.6(9)	—	—	—	—	—	—	2.83	2.83	7.71[56]	44
Cl	Cl	—	—	—	119.8(10)	1.37(1)	122.9(9)	117.2(9)	—	—	—	—	—	—	2.73	2.73	7.71[56]	44
Cl	—	Cl	—	—	117.9(3)	1.362(5)	123.0(3)	119.1(3)	14	0.55	2.01	50	1.63	1.80	2.82	2.89	7.90[56]	45
Cl	—	Cl	—	—	118.9(3)	1.362(5)	122.6(3)	118.4(3)	40	1.08	2.14	86	2.25	1.86	2.89	2.80	7.90[56]	45
Cl	—	Cl	—	—	118.0(3)	1.364(4)	123.5(3)	118.4(3)	39	0.94	1.92	79	0.06	2.52	2.80	2.82	7.90[56]	45
Cl	—	—	Cl	—	119.(1)	1.38(1)	119(1)	122(1)	42	1.80	0.56	61	1.78	1.80	2.76(1)	2.76(1)	7.51[56]	46
SO_2Me	—	OH	—	—	119.2(3)	1.363(4)	117.9(3)	122.9(3)	18	0.79	0.77	—	—	—	2.748(6)	—	7.3[57]	**(11)**
SO_2Me	—	OH	—	—	117.3(3)	1.352(4)	119.2(3)	123.4(3)	16	0.73	0.82	—	—	—	2.711(6)	—	7.3[57]	**(11)**
SO_2Me	—	—	—	—	118.4(2)	1.353(2)	118.1(2)	123.4(2)	5	0.27	1.04	—	—	—	2.660(4)	—	7.3[57]	**(10)**
I	—	COOH	—	I	119.4(6)	1.361(7)	120.3(3)	120.3(3)	—	—	—	—	—	—	No H-bond	—	—	**(8)**
I	—	COOH	—	I	119.0(6)	1.364(7)	120.5(3)	120.5(3)	—	—	—	—	—	—	No H-bond	—	—	**(8)**
I	—	R	—	I	118.2(5)	1.364(7)	117.6(5)	124.2(5)	—	—	—	—	—	—	2.90(2)	2.90(2)	6.36[58]	**(15)**
I	—	Et	—	I	117.3(6)	1.364(7)	118.6(6)	124.0(6)	33	0.82	2.33	69	2.81	1.39	3.15(2)	3.15(2)	6.41[53]	**(6)**
I	—	I	—	I	116.1(6)	1.341(8)	119(6)	124.8(6)	42	1.30	1.72	—	—	—	2.740(11)	—	—	**(14)**
Br	—	Me	—	Br	118.9(14)	1.37(2)	116.4(4)	124.3(16)	31	0.72	2.02	68	2.74	0.94	2.90(2)	2.90(2)	6.92[53]	**(5)**
Cl	—	—	—	Cl	118(1)	1.38(1)	118(1)	124(1)	36	1.63	1.50	46	1.80	1.73	3.06(1)	3.06(1)	6.78[56]	47
NO_2	—	NO_2	—	—	118.5(5)	1.331(7)	116.7(5)	124.9(5)	—	—	—	—	—	—	1.89(7), 0.94(7)[c]	—	4.09[55]	48
NO_2	—	Cl	—	—	117.2(5)	1.342(6)	117.3(5)	125.5(5)	—	—	—	—	—	—	1.84(7), 0.88(7)[c]	—	6.64[57]	49
Cl	—	NO_2	—	NO_2	116.7(4)	1.333(7)	118.5(4)	124.8(4)	—	—	—	—	—	—	1.66, 1.07[c]	—	2.10[59]	50
NO_2	—	—	—	NO_2	116.0(5)	1.337(7)	120.2(5)	123.8(5)	—	—	—	—	—	—	1.84(5), 0.78(5)[c]	—	3.71[55]	51
NO_2	—	NO_2	—	NO_2	115.3(3)	1.327(3)	119.6(3)	125.0(3)	—	—	—	—	—	—	1.807, 0.86(5)[c]	—	1.02[55]	52

[a] Two structure analyses of same polymorph but with different choice of origin. [b] (O–H · · · N). [c] Intramolecular (O · · · H, H–O). [d] (O · · · H–N).

O–H bond has two conformations, with the hydrogen atom *cis* and *trans* relative to the *ortho* substituent.[13] Studies of models[14] and molecular mechanics calculations[15] suggest that the strain energy produced by repulsion between an *ortho* t-butyl group and a *cis* O–H bond is much less than the resonance energy gained by keeping the O–H bond in the aromatic ring plane. The relative amounts of the *cis* and *trans* conformers have been estimated from their i.r. OH stretching frequencies, OH torsional frequencies,[16,17] and from dipole moment studies.[15] In *o*-alkylphenols the *trans* conformer is said to be preferred, whereas in *o*-halogenophenols it is the *cis* conformer.[18] Of the di-*ortho*-substituted phenols, 2,6-di-t-butylphenols have been examined by several methods. The i.r. OH stretching frequencies in a series of 4-substituted phenols and in a series of 4-substituted 2,6-di-t-butylphenols have very similar linear correlations with the Hammett σ_r constant of the 4-substituent,[14] suggesting that the phenolic OH interacts with the aromatic system in a similar way in both series of phenols and, that, in the 2,6-di-t-butylphenol series, the phenolic OH remains in, or very close to, the ring plane. From polarisability studies it was concluded that the OH bond in 2,6-di-t-butylphenol is $\sim 14°$ out of the ring plane.[19]

The intermolecular hydrogen bonds of *ortho*-substituted phenols, those involved in self-association and those involved in complexation with various ethers and aliphatic amines, have been studied by i.r.[20–23] and n.m.r.[24–26] spectroscopy.

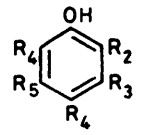
In the liquid state and in concentrated solution in inert solvents, phenols without *ortho* substituents exist as a mixture of free phenol and hydrogen-bonded dimers and polymers.[20] The equilibrium favours the formation of polymers. In mono-*ortho*-substituted phenols, alkyl groups other than t-butyl have only a slight effect on the hydrogen-bonding. In di-*ortho*-substituted phenols the effects are more pronounced and the increase in hindering effect of an alkyl group with increasing branching becomes apparent.[20] The greater the hindering effect of an alkyl group, the more formation of associated states is suppressed. In di-*o*-t-butylphenols little, if any, self-association occurs.[20,24,25]

The effects of *ortho*-substituents on the formation of hydrogen-bonded complexes are very similar to their effects on self-association. Although *o*-alkyl groups, apart from t-butyl, have only small effects on hydrogen bond strengths, there are significant variations in formation constants.[21,22,25,26] The observed trends indicate that complex formaton is sterically hindered by large *ortho*-substituents.

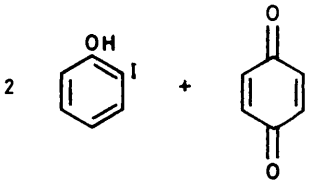
In this work we examine the crystal and molecular structures of phenols with lipophilic alkyl- and halogeno-substituents in the *ortho* position(s) to attempt to correlate the electronic, structural, and hydrogen-bonding properties of these compounds and, in turn, move towards a better understanding of the relationships between structure and nuclear receptor binding of T_3 analogues.

To define those properties relevant to the structure and bonding of the un-ionised phenolic hydroxy group we have analysed structural data from *X*-ray structure analyses of crystals of 41 simple phenols, in which the phenolic hydroxy group is involved in *inter*molecular hydrogen bonding as opposed to *intra*molecular hydrogen bonding. Of these structures, 28 are to be found in the May 1981 release of the Cambridge Crystallographic Data Centre (C.C.D.C.) data-bank[27] and 13 are new structure determinations. A re-examination of the C.C.D.C. data bank in 1985 did not suggest any additions to the original list. These 41 crystal structures represent 51 crystallographically independent phenol molecules.

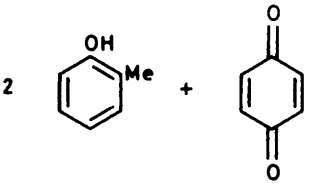
Initially, the new structure analyses examined the phenols not already recorded by the C.C.D.C. with only alkyl- or halogeno-substituents (**3**)—(**6**). Unfortunately these compounds are very volatile, have melting points close to room temperature, and their crystals undergo one or more phase changes on cooling.



(**3**) R_2 = I
(**4**) R_2 = R_6 = Pr^i
(**5**) R_2 = R_6 = Br, R_4 = Me
(**6**) R_2 = R_6 = I, R_4 = Et
(**7**) R_2 = I, R_4 = CO_2H
(**8**) R_2 = R_6 = I, R_4 = CO_2H
(**9**) R_2 = R_6 = Pr^i, R_4 = CO_2H
(**10**) R_2 = SO_2Me
(**11**) R_2 = SO_2Me, R_4 = OH

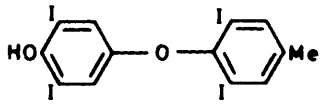


(**12**) 2:1 Molecular complex



(**13**) 2:1 Molecular complex

(**14**) 2:1 Molecular complex



(**15**)

Attention was then turned towards 4-carboxyphenols (**7**)—(**9**), which have much higher melting points. It was expected that the carboxy groups would hydrogen bond to form dimers and the interactions between the phenolic hydroxy groups would follow a similar pattern to those in the alkyl- and halogeno-phenols. The sulphonyl compounds (**10**) and (**11**) were examined because there is evidence that *ortho*-sulphonyl groups do not form intramolecular hydrogen bonds with the phenolic hydroxy group. The complexes of substituted phenols with 1,4-benzoquinone (**12**) and (**13**) were investigated as examples of different phenols interacting with the same hydrogen-bonding substrate. Solid complexes of 2,6-disubstituted phenols with 1,4-benzoquinone could not be prepared, however. The structure of the pyrazine complex (**14**) was examined in the hope that hydrogen-bonding might be so sterically hindered that an iodine–nitrogen lone pair interaction might be seen. Finally, (**15**) is a diphenyl ether analogue of T_4.

Table 2. Crystal data for substituted phenols

Compd.	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)
Formula	C_6H_5IO	$C_{12}H_{18}O$	$C_7H_6Br_2O$	$C_8H_8I_2O$	$C_7H_5IO_3$	$C_7H_4I_2O_3$	$C_{13}H_{18}O_3$	$C_7H_8O_3S$	$C_7H_8O_4S$	$C_{18}H_{14}I_2O_4$	$C_{20}H_{20}O_4$	$C_{10}H_9I_3NO$	$C_{13}H_8I_4O_2$
Mol. wt.	220	178.3	265.9	373.9	273.03	389.9	222	190	188.2	547.9	324.4	539.9	704
M.p./°C	43	18	49—50	29—30	177—178	279—281	147—148	89—90	143—144	Not recorded	17	Not recorded	204—206
Crystal size/ m × 10^{-4}	Not recorded	6 × 5 × 4	5 × 4 × 3	5 × 3 × 0.2	6 × 2 × 2	8 × 3 × 1	5 × 4 × 4	7 × 7 × 5	5 × 5 × 5	Not recorded	4 × 2 × 2	8 × 6 × 4	3 × 2 × 2
Crystal class	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Ortho-rhombic	Ortho-rhombic	Ortho-rhombic	Monoclinic	Ortho-rhombic	Monoclinic	Triclinic	Monoclinic	Triclinic
a/Å	7.162(2)	12.925(2)	11.438(2)	7.964(1)	23.239(3)	22.683(7)	9.562(2)	8.469(2)	7.437(2)	11.911(7)	7.422(3)	12.742(3)	8.467 2(9)
b/Å	4.733(5)	17.894(7)	4.613(4)	4.807(6)	35.150(4)	4.207(1)	9.465(2)	9.660(3)	13.123(4)	5.806(3)	10.147(3)	12.674(3)	8.855 6(10)
c/Å	19.401(6)	20.452(13)	7.603(1)	26.716(3)	4.064(3)	19.397(5)	13.893(3)	11.195(2)	16.421(3)	14.946(8)	11.946(8)	17.232(4)	12.664 2(9)
α/°	90	90	90	90	90	90	90	90	90	90	108.58(4)	90	73.087(7)
β/°	97.69(3)	104.11(2)	97.34(2)	95.05(1)	90	90	90	105.70(4)	90	112.17(7)	94.87(6)	100.26(2)	75.206(7)
γ/°	90	90	90	90	90	90	90	90	90	90	90.87(2)	90	74.625(9)
Space group	$P2_1/n$	$C2/c$	$P2_1$	$P2_1/c$	$Fdd2$	$Pmna$	$Pna2_1$	$P2_1/c$	$Pbc2_1$ [a]	$P2_1/c$	$P\bar{1}$	$C2/c$	$P\bar{1}$
Z	4	16	2	4	16	8	4	4	8	2	2	8	2
D_c/Mg m^{-3}	2.237	1.032	2.220	2.43	2.184	2.798	1.174	1.431	1.558	1.908	1.268	2.619	2.719
F(000)	408	1 568	252	428	2 064	904	480	190	784	520	336	1 944	628
U/Å^3	653	4 587	398	1 019	3 319	1 851	1 257	400	1 603	957	850	2 738	859
Temperature/°C	−65	−40	−75	20	20—24 [b]	20—24 [b]	20—24 [b]	20–24 [b]	20—24 [b]	20—24 [b]	−50	20—24 [b]	20—24 [b]
Radiation	Mo-K_α	Mo-K_α	Mo-K_α	Mo-K_α	Mo-K_α	Mo-K_α	Mo-K_α	Mo-K_α	Mo-K_α	Mo-K_α	Mo-K_α	Mo-K_α	Mo-K_α
μ/m × 10^{-4}	4.75	0.06	10.02	6.07	0.04	6.69	0.07	0.03	0.04		0.08	6.76	7.17
(Sinθ/λ) max.	0.66	0.48	0.6	0.66	0.60		0.59	0.7	0.7	0.6	0.6	0.7	0.64
[c] Total *I*	2 938	2 972	3 065	3 438	1 310	2 707	2 003	2 557	2 561	2 116	2 980	4 102	5 148
[d] Unique *I*	1 128	1 023	924	1 677	943	1 641	809	1 678	1 716	487	1 412	2 194	2 548
Rm/10^{-2}	2.68	4.8	4.6	3.0	2.4	2.3	2.3	3.4	2.00	—	3.44	2.80	1.95
[e] *n*	3	2	3	3	3	3	3	3	2.5	2	2	3	3
R/10^{-2}	5.4	6.8	5.9	4.7	2.1	3.3	3.4	3.3	3.1	4.2	4.8	3.8	2.9
R_w/10^{-2}	7.1	8.4	7.9	6.7	2.4	4.1	3.4	4.3	3.7	4.9	5.5	4.2	3.4
[f] Shift/error	0.00	0.06	0.02		0.02	0.05	0.07	0.04	0.3		0.09	0.02	0.02
[g] Max./e Å^{-3}	2	0.2	2.9		0.7	1.4	0.1	0.3	0.2	—	0.2	1.00	1.00
Ext. para	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
[h] Weights	100, 140, 50	328, 538, 314, 131, 36	279, 421, 289, 113, 56	18, 25, 8	3.75, 4.48, 2.11	72, 97, 35	Unit wts.	27.4, 41.7, 23.9, 12.5, 5.2	33.5, 52.6, 29.8, 11.5, 3.9	Unit wts.	82, 113, 35	19, 27, 9	24, 39, 28 14, 6

[a] Non-standard setting, general positions x, y, z; $\bar{x}, \bar{y}, \frac{1}{2}+z$; $x, \frac{1}{2}-y, \frac{1}{2}+z$; $\bar{x}, \frac{1}{2}+y, z$. [b] Collected at the ambient temperature of the diffractometer room which fluctuates in the range 20—24 °C. [c] Total number of reflections observed. [d] Number of unique reflections with intensity significantly above the background intensity. [e] Criterion for recognising observed reflections $I > n\sigma(I)$. [f] Ratio of maximum least-squares shift to error in final refinement cycle. [g] Maximum height in final difference electron density synthesis. [h] Chebyshev coefficients.

Table 3. Fractional atom co-ordinates ($\times 10^4$) for compounds (**3**)—(**15**)

2-Iodophenol (**3**)

Atom	*x*	*y*	*z*
I(1)	1 860(1)	760(1)	803.1(4)
O(1)	2 780(11)	4 582(14)	2 154(4)
C(1)	4 207(14)	4 779(18)	1 783(5)
C(2)	4 181(12)	3 216(18)	1 177(5)
C(3)	5 702(15)	3 382(21)	805(6)
C(4)	7 189(15)	5 146(27)	1 017(6)
C(5)	7 217(16)	6 688(25)	1 629(7)
C(6)	5 724(15)	6 510(20)	2 011(5)

2,6-Di-isopropylphenol (**4**)

O(1)	3 689(4)	9 495(2)	6 848(7)
C(1)	7 741(5)	9 167(4)	6 470(3)
C(2)	6 844(5)	9 616(3)	6 251(3)
C(3)	5 933(5)	9 286(4)	5 859(4)
C(4)	5 924(5)	9 546(4)	5 686(4)
C(5)	6 817(6)	8 122(4)	5 895(4)
C(6)	7 757(4)	8 422(3)	6 291(3)
C(7)	6 875(5)	10 437(4)	6 429(4)
C(8)	6 405(12)	10 559(6)	7 022(6)
C(9)	6 310(9)	10 932(5)	5 855(6)
C(10)	8 753(5)	7 938(4)	6 534(4)
C(11)	9 216(9)	7 731(8)	5 952(5)
C(12)	8 514(9)	7 252(6)	6 901(7)
O(2)	10 771(4)	9 419(3)	6 775(2)
C(21)	11 356(5)	9 714(4)	6 354(3)
C(22)	12 246(5)	9 332(4)	6 290(4)
C(23)	12 656(6)	9 638(5)	5 694(4)
C(24)	12 549(7)	10 280(5)	5 538(5)
C(25)	11 659(6)	10 650(4)	5 595(4)
C(26)	11 021(5)	10 382(4)	6 005(4)
C(27)	12 550(6)	8 584(5)	6 634(3)
C(28)	13 649(8)	8 557(7)	7 094(5)
C(29)	12 462(12)	7 949(6)	6 139(3)
C(30)	10 036(6)	10 799(4)	6 081(4)
C(31)	9 477(8)	11 245(5)	5 468(5)
C(32)	10 314(9)	11 309(7)	6 681(5)

2,6-Dibromo-4-methylphenol (**5**)

Br(1)	2 738(2)	9 346	2 445(7)
Br(2)	925(2)	2 413(5)	−3 617(2)
O(1)	771(10)	5 300(26)	78(16)
C(1)	1 754(12)	5 996(41)	−698(20)
C(2)	1 966(16)	5 044(43)	−2 351(22)
C(3)	2 960(14)	6 020(41)	−3 046(21)
C(4)	3 707(15)	6 053(37)	−2 224(22)
C(5)	3 506(13)	8 933(40)	−548(18)
C(6)	2 514(15)	8 022(29)	191(22)
C(7)	4 749(15)	9 234(51)	−3 818(22)

4-Ethyl-2,6-di-iodophenol (**6**)

I(2)	8 655.5(6)	−3 826(1)	7 075.5(2)
I(6)	2 638.3(7)	3 740(1)	6 486.6(2)
O(1)	5 078(6)	−554(12)	7 121(2)
C(1)	5 786(8)	−5(14)	6 693(2)
C(2)	7 347(9)	−1 087(14)	6 570(3)
C(3)	8 068(10)	−279(21)	6 142(3)
C(4)	7 269(13)	1 598(21)	5 819(3)
C(5)	5 750(11)	2 660(22)	5 915(3)
C(6)	4 968(9)	1 861(16)	6 347(3)
C(7)	8 147(16)	2 758(35)	5 333(5)
C(8)	7 421(22)	1 499(30)	4 904(7)

4-Carboxy-2-iodophenol (**7**)

I(1)	−404.7(2)	2 026.9(1)	−75
O(1)	−1 638(2)	2 224(1)	3 142(15)
C(1)	−1 488(2)	1 850(1)	3 287(18)
C(2)	−965(2)	1 734(1)	2 062(19)
C(3)	−806(2)	1 355(2)	2 232(24)

Table 3 (*continued*)

Atom	*x*	*y*	*z*
C(4)	−1 169(3)	1 090(2)	3 635(18)
C(5)	−1 697(2)	1 205(1)	4 870(26)
C(6)	−1 858(2)	1 582(2)	4 775(26)
C(7)	−978(3)	686(2)	3 715(20)
O(2)	−1 348(2)	457(1)	5 262(20)
O(3)	−535(2)	573(1)	2 598(21)
O(21)	0	0	−684(21)

4-Carboxy-2,6-di-iodophenol (**8**)

I(1)	2 152.4(2)	1 402(1)	1 354.7(2)
O(1)	1 686(2)	5 000	0
C(1)	2 286(3)	5 000	0
C(2)	2 596(2)	3 521(13)	531(3)
C(3)	3 209(2)	3 510(14)	530(3)
C(4)	3 512(3)	5 000	0
C(5)	4 166(3)	5 000	0
O(2)	4 430(2)	6 388(16)	−489(3)
I(2)	1 331.8(2)	−1 926(1)	2 867.1(2)
O(21)	0	−665(18)	3 328(3)
C(21)	0	−2 320(18)	2 723(4)
C(22)	527(2)	−3 206(13)	2 415(3)
C(23)	531(2)	−4 878(15)	1 796(3)
C(24)	0	−5 708(20)	1 489(4)
C(25)	0	−7 571(22)	836(4)
O(22)	−490(2)	−8 289(16)	567(3)

4-Carboxy-2,6-di-isopropylphenol (**9**)

O(1)	817(3)	−790(3)	−3 144(2)
C(1)	1 143(4)	−201(4)	−2 264(2)
C(2)	2 298(4)	703(4)	−2 254(2)
C(3)	2 655(4)	1 321(4)	−1 383(3)
C(4)	1 890(4)	1 053(4)	−550(3)
C(5)	750(4)	129(4)	−558(3)
C(6)	361(4)	−520(4)	−1 442(3)
C(7)	2 248(4)	1 734(4)	380(3)
O(2)	3 289(4)	2 647(4)	312(2)
O(3)	1 685(3)	1 496(3)	1 133(2)
C(8)	3 139(4)	995(4)	−3 164(3)
C(9)	3 452(6)	2 544(6)	−3 296(4)
C(10)	4 459(6)	142(7)	−3 182(4)
C(11)	−887(4)	−1 511(4)	−1 469(3)
C(12)	−926(5)	−2 546(5)	−639(3)
C(13)	−2 247(5)	−717(6)	−1 514(5)

2-Methylsulphonylphenol (**10**)

S(1)	5 808.4(5)	2 234.4(5)	4 139.3(4)
O(1)	9 274(2)	3 086(1)	5 025(1)
C(1)	9 079(2)	1 975(2)	4 264(2)
C(2)	7 500(2)	1 420(2)	3 814(1)
C(3)	7 227(2)	265(2)	3 047(2)
C(4)	8 507(3)	−334(2)	2 699(2)
C(5)	10 071(3)	222(2)	3 131(2)
C(6)	10 364(2)	1 351(2)	3 913(2)
O(2)	4 354(2)	1 457(2)	3 526(1)
O(3)	5 811(2)	3 673(1)	3 823(2)
C(7)	6 088(3)	2 076(3)	5 744(2)
O(21)	12 403(2)	3 803(2)	5 945(2)

4-Hydroxy-2-methanesulphonylphenol (**11**)

S(1)	8 678.5(9)	1 510.9(5)	7 327.3(5)
O(1)	10 680(4)	3 477(2)	7 311(2)
C(1)	10 799(4)	2 991(2)	8 042(2)
C(2)	9 965(4)	2 042(2)	8 119(2)
C(3)	10 017(4)	1 514(2)	8 862(2)
C(4)	10 903(4)	1 938(2)	9 523(2)
C(5)	11 776(4)	2 876(3)	9 437(2)
C(6)	11 742(5)	3 388(3)	8 701(2)
O(2)	11 002(3)	1 460(2)	10 263(1)
O(3)	8 285(3)	464(2)	7 555(2)
O(4)	7 121(3)	2 149(2)	7 191(2)

Table 3 (*continued*)

Atom	*x*	*y*	*z*
C(7)	10 022(5)	1 500(3)	6 448(2)
S(2)	6 212(2)	968.6(5)	10 392.6(5)
O(21)	4 273(4)	−1 012(2)	10 419(2)
C(21)	4 150(4)	−537(2)	9 690(2)
C(22)	4 969(4)	415(2)	9 587(2)
C(23)	4 896(4)	945(2)	8 855(2)
C(24)	4 009(4)	515(2)	8 201(2)
C(25)	3 161(4)	−427(3)	8 290(2)
C(26)	3 213(5)	−940(3)	9 024(2)
O(22)	3 883(4)	985(2)	7 459(1)
O(23)	6 598(3)	2 010(2)	10 153(2)
O(24)	7 770(3)	337(2)	10 561(2)
C(27)	4 811(5)	1 012(3)	11 255(2)

2-Iodophenol–1,4-benzoquinone 2:1 molecular complex (**12**)

I(1)	2 565(1)	−259(3)	1 672(1)
O(1)	2 997(12)	3 315(22)	3 384(10)
C(1)	2 258(17)	1 562(29)	3 459(13)
C(2)	1 945(15)	−188(30)	2 823(16)
C(3)	1 227(18)	−2 015(36)	2 924(17)
C(4)	827(19)	−1 961(48)	3 688(20)
C(5)	1 154(17)	−84(47)	4 326(14)
C(6)	1 840(19)	1 616(35)	4 221(14)
O(2)	3 659(12)	6 297(23)	4 944(10)
C(21)	4 284(17)	8 081(38)	4 967(14)
C(22)	4 825(17)	8 438(36)	4 241(13)
C(23)	5 467(15)	10 271(34)	4 262(11)

2-Methylphenol–1,4-benzoquinone 2:1 molecular complex (**13**)

O(1)	−1 837(4)	−1 282(3)	5 384(2)
O(2)	1 400(4)	1 555(3)	9 601(3)
C(1)	−1 044(5)	−618(4)	6 346(3)
C(2)	−257(5)	−1 340(4)	2 153(3)
C(3)	560(5)	−621(4)	9 205(3)
C(4)	711(5)	904(4)	8 600(3)
C(5)	−26(5)	1 627(4)	7 789(3)
C(6)	−860(5)	902(4)	6 736(3)
O(21)	−3 381(4)	366(3)	4 109(2)
C(21)	−4 229(5)	−337(4)	3 914(3)
C(22)	−5 000(5)	484(4)	2 370(3)
C(23)	−5 839(5)	−210(4)	1 251(3)
C(24)	−5 925(5)	−1 641(4)	782(3)
C(25)	−5 157(5)	−2 431(4)	1 442(3)
C(26)	−4 212(5)	−1 763(4)	2 568(3)
C(27)	−4 896(6)	2 034(4)	2 821(4)
O(31)	2 686(4)	4 159(3)	11 232(2)
C(31)	1 239(5)	4 565(4)	11 895(3)
C(32)	1 612(5)	5 292(3)	11 599(3)
C(33)	156(5)	5 693(4)	13 762(3)
C(34)	−1 601(5)	5 391(4)	13 274(4)
C(35)	−1 259(5)	4 686(4)	12 974(4)
C(36)	−526(5)	4 278(4)	11 387(3)
C(37)	3 516(5)	5 622(4)	11 657(3)

2,4,6-Tri-iodophenol–tetramethylpyrazine 2:1 molecular complex (**14**)

I(1)	−153.9(5)	9 313.1(4)	8 717.4(5)
I(2)	2 103.5(4)	5 318.8(5)	9 845.6(4)
I(3)	−2 110.5(4)	5 076.0(4)	7 661.2(4)
O(1)	−1 757(4)	7 655(4)	7 840(4)
C(1)	952(5)	7 109(5)	8 264(4)
C(2)	−78(6)	7 660(5)	8 683(5)
C(3)	785(5)	7 174(6)	9 122(5)
C(4)	816(5)	6 084(6)	9 150(4)
C(5)	−22(5)	5 492(6)	8 735(5)
C(6)	−875(5)	6 003(5)	8 284(5)
N(21)	−3 902(4)	7 250(5)	7 615(4)
C(21)	−4 486(5)	7 255(5)	6 883(4)
C(22)	−4 398(6)	7 248(5)	8 232(5)
C(23)	−3 884(7)	7 264(7)	6 213(6)
C(24)	−3 731(7)	7 222(7)	9 037(6)

Table 3 (*continued*)

Atom	*x*	*y*	*z*
4′-Hydroxy-4-methyl-2,3′,5′,6,-tetraiododiphenyl ether (**15**)			
I(1)	−2 502.7(7)	10 996.8(6)	843.9(4)
I(2)	−2 000.5(8)	6 895.1(6)	5 527.7(4)
I(3)	1 579.7(7)	3 059.1(6)	987.2(5)
I(4)	4 587.9(6)	7 781.1(7)	2 018.1(5)
C(1)	−2 910(9)	12 058(8)	4 040(6)
C(2)	−2 885(8)	12 159(8)	2 934(6)
C(3)	−2 581(7)	10 776(7)	2 544(5)
C(4)	−2 315(7)	9 255(7)	3 269(5)
C(5)	−2 380(8)	9 148(7)	4 391(5)
C(6)	−2 669(9)	10 541(9)	4 781(6)
C(7)	−3 205(13)	13 534(10)	4 483(8)
O(1)	−2 083(5)	7 874(5)	2 891(4)
C(21)	−452(7)	7 170(7)	2 469(4)
C(22)	−281(7)	5 844(7)	2 049(5)
C(23)	1 306(8)	5 068(7)	1 622(5)
C(24)	2 720(7)	5 572(7)	1 631(5)
C(25)	2 507(7)	6 911(7)	2 050(5)
C(26)	924(7)	7 717(7)	2 492(5)
O(21)	4 310(5)	4 864(6)	1 223(4)

Results and Discussion

General.—The numbering scheme and various symbols used in the text describing the crystallographic results, and in Table 1, are defined in Figure 1. For consistency the same numbering scheme is used for chemical (*e.g.* 4-hydroxybenzoic acid is referred to as 4-carboxyphenol) and for crystallographic labelling, independent of whatever scheme was used by the original authors. Table 1 presents an analysis of structural data from this and published work on the phenolic hydroxy in an intermolecular hydrogen-bonding environment. Tables 2, 3, and 4 give crystal data, atomic parameters, and bonded distances and interbond angles for the thirteen new analyses. Figures 2 (*a–m*) show the numbered asymmetric unit and the crystal packing in each compound. The location of the asymmetric unit in the crystal packing is indicated by the heavy arrow. For clarity in some diagrams the asymmetric unit has been rotated through a small angle so that all atoms are clearly visible. The details of the structure analysis are given in the Experimental section.

Phenolic Hydrogen-bonding and the Arrangement of the Molecules.—The phenolic hydroxy can act as both a proton donor and a proton acceptor. If the group *ortho* to the phenolic hydroxy is a hydrogen-bond acceptor then an intramolecular hydrogen bond is usually formed, both in the solid state and in solution. For those crystal structures examined, in which the phenolic hydroxy group is the only group capable of forming hydrogen bonds, it invariably acts as both a proton donor and a proton acceptor and links each molecule to two others to form either hydrogen-bonded chains or hydrogen-bonded rings. All but four of these structures consist of chains. The exceptions are hydrogen-bonded tetramers in one form of 4-methylphenol and in 2,6-di-isopropylphenol [Figure 2(b)], and two hexamers 2-isopropyl-5-methylphenol and 3,4-dimethylphenol. Of the hydrogen-bonded chains the most common arrangement is one in which the molecules are related by a two-fold screw axis as in 2-iodophenol [Figure 2(a)]. There is one example, 2,3-dichlorophenol, of a helical arrangement based on a three-fold screw axis and three examples, 3,4-dichlorophenol, 4-isopropyl-3-methylphenol, and 4-isopropylphenol, based on a four-fold screw axis. In addition, four crystals, 2,4-dichlorophenol, 4-methylphenol, 4-chlorophenol, and 3-methylphenol, have

Table 4. Selected interatomic distances and interbond angles with standard deviations calculated from the full variance—covariance matrix in parentheses

2-Iodophenol (**3**)

I(1)–C(2)	2.078(9)	C(3)–C(4)	1.37(2)
O(1)–C(1)	1.37(1)	C(4)–C(5)	1.39(2)
C(1)–C(2)	1.39(1)	C(5)–C(6)	1.38(2)
C(2)–C(3)	1.39(1)	C(6)–C(1)	1.38(1)
O(1)–C(1)–C(2)	118.8(9)	C(1)–C(2)–C(3)	119.3(9)
O(1)–C(1)–C(6)	121.2(9)	C(2)–C(3)–C(4)	120.8(9)
C(2)–C(1)–C(6)	120.0(9)	C(3)–C(4)–C(5)	119.7(9)
I(1)–C(2)–C(1)	120.5(7)	C(4)–C(5)–C(6)	120(1)
I(1)–C(2)–C(3)	120.1(7)	C(5)–C(6)–C(1)	120(1)

2,6-Di-isopropylphenol (**4**)

O(1)–C(1)	1.408(7)	O(2)–C(21)	1.382(8)
C(1)–C(2)	1.392(8)	C(21)–C(22)	1.372(9)
C(2)–C(3)	1.386(6)	C(22)–C(23)	1.373(7)
C(3)–C(4)	1.369(7)	C(23)–C(24)	1.367(7)
C(4)–C(5)	1.360(7)	C(24)–C(25)	1.357(7)
C(5)–C(6)	1.395(7)	C(25)–C(26)	1.395(7)
C(6)–C(1)	1.382(9)	C(26)–C(21)	1.406(9)
C(2)–C(7)	1.511(7)	C(22)–C(27)	1.520(7)
C(7)–C(8)	1.500(8)	C(27)–C(28)	1.500(8)
C(7)–C(9)	1.510(8)	C(27)–C(29)	1.508(8)
C(6)–C(10)	1.529(7)	C(26)–C(30)	1.516(7)
C(10)–C(11)	1.503(8)	C(30)–C(31)	1.517(7)
C(10)–C(12)	1.509(8)	C(30)–C(32)	1.501(8)
O(1)–C(1)–C(2)	118.7(6)	O(2)–C(21)–C(22)	118.0(6)
O(1)–C(1)–C(6)	118.6(6)	O(2)–C(21)–C(26)	119.6(6)
C(6)–C(1)–C(2)	122.6(5)	C(26)–C(21)–C(22)	122.4(6)
C(1)–C(2)–C(3)	117.6(5)	C(21)–C(22)–C(23)	118.3(5)
C(1)–C(2)–C(7)	120.9(5)	C(21)–C(22)–C(27)	121.5(5)
C(7)–C(2)–C(3)	121.6(5)	C(27)–C(22)–C(23)	120.2(5)
C(2)–C(3)–C(4)	120.9(5)	C(22)–C(23)–C(24)	121.1(5)
C(3)–C(4)–C(5)	120.4(5)	C(23)–C(24)–C(25)	120.3(6)
C(4)–C(5)–C(6)	121.3(5)	C(24)–C(25)–C(26)	121.5(5)
C(5)–C(6)–C(1)	117.2(5)	C(25)–C(26)–C(21)	116.3(5)
C(5)–C(6)–C(10)	121.0(5)	C(25)–C(26)–C(30)	121.8(5)
C(10)–C(6)–C(1)	121.8(5)	C(30)–C(26)–C(21)	121.9(5)
C(2)–C(7)–C(8)	110.1(8)	C(22)–C(27)–C(28)	114.6(8)
C(2)–C(7)–C(9)	113.9(7)	C(22)–C(27)–C(29)	112.5(8)
C(8)–C(7)–C(9)	109.1(9)	C(28)–C(27)–C(29)	107.6(8)
C(6)–C(10)–C(11)	110.5(7)	C(26)–C(30)–C(31)	114.6(7)
C(6)–C(10)–C(12)	111.2(7)	C(26)–C(30)–C(32)	110.1(7)
C(11)–C(10)–C(12)	111.3(9)	C(31)–C(30)–C(32)	109.2(7)

2,6-Dibromo-4-methylphenol (**5**)

Br(1)–C(6)	1.88(2)	C(3)–C(4)	1.36(2)
Br(2)–C(2)	1.88(2)	C(4)–C(5)	1.38(2)
O(1)–C(1)	1.37(2)	C(5)–C(6)	1.39(2)
C(1)–C(2)	1.38(2)	C(6)–C(1)	1.39(2)
C(2)–C(3)	1.39(2)	C(4)–C(7)	1.51(2)
O(1)–C(1)–C(2)	124(2)	C(3)–C(4)–C(5)	117(2)
O(1)–C(1)–C(6)	116(1)	C(3)–C(4)–C(7)	123(2)
C(6)–C(1)–C(2)	119(1)	C(7)–C(4)–C(5)	120(2)
C(1)–C(2)–C(3)	119(2)	C(4)–C(5)–C(6)	121(2)
C(1)–C(2)–Br(2)	120(1)	C(5)–C(6)–C(1)	120(1)
Br(2)–C(2)–C(3)	121(1)	C(5)–C(6)–Br(1)	121(1)
C(2)–C(3)–C(4)	123(2)	Br(1)–C(6)–C(1)	119(1)

4-Ethyl-2,6-di-iodophenol (**6**)

I(2)–C(2)	2.086(7)	C(3)–C(4)	1.36(1)
I(6)–C(6)	2.074(7)	C(4)–C(5)	1.36(1)
O(1)–C(1)	1.35(1)	C(4)–C(7)	1.63(2)
C(1)–C(2)	1.41(1)	C(5)–C(6)	1.42(1)
C(1)–C(6)	1.40(1)	C(7)–C(8)	1.37(2)
C(2)–C(3)	1.38(1)		

Table 4 (*continued*)

C(2)–C(1)–O(1)	124.0(6)	C(5)–C(4)–C(3)	119.9(8)
C(6)–C(1)–O(1)	118.6(6)	C(7)–C(4)–C(3)	121.4(9)
C(6)–C(1)–C(2)	117.3(6)	C(7)–C(4)–C(5)	118.3(9)
C(1)–C(2)–I(2)	119.6(5)	C(6)–C(5)–C(4)	121.4(8)
C(3)–C(2)–I(2)	119.3(6)	C(1)–C(6)–I(6)	120.9(6)
C(3)–C(2)–C(1)	121.1(7)	C(5)–C(6)–I(6)	119.2(5)
C(4)–C(3)–C(2)	120.2(7)	C(5)–C(6)–C(1)	119.8(7)

4-Carboxy-2-iodophenol (**7**)

I(1)–C(2)	2.088(5)	C(5)–C(6)	1.379(7)
O(1)–C(1)	1.363(6)	C(6)–C(1)	1.410(8)
C(1)–C(2)	1.376(8)	C(4)–C(7)	1.490(7)
C(2)–C(3)	1.381(7)	C(7)–O(2)	1.338(8)
C(3)–C(4)	1.382(9)	C(7)–O(3)	1.193(8)
C(4)–C(5)	1.386(8)		
O(1)–C(1)–C(2)	119.8(5)	C(3)–C(4)–C(5)	119.6(5)
O(1)–C(1)–C(6)	120.5(5)	C(7)–C(4)–C(5)	122.3(5)
C(2)–C(1)–C(6)	119.7(5)	C(4)–C(5)–C(6)	120.6(6)
C(1)–C(2)–I(1)	120.3(4)	C(5)–C(6)–C(1)	119.2(6)
C(1)–C(2)–C(3)	120.3(5)	C(4)–C(7)–O(2)	113.1(5)
I(1)–C(2)–C(3)	119.4(4)	C(4)–C(7)–O(3)	124.6(6)
C(2)–C(3)–C(4)	120.5(5)	O(2)–C(7)–O(3)	122.3(6)
C(3)–C(4)–C(7)	118.1(5)		

4-Carboxy-2,6-di-iodophenol (**8**)

I(1)–C(1)	2.087(5)	I(2)–C(22)	2.095(5)
O(1)–C(1)	1.361(7)	O(21)–C(21)	1.364(7)
C(1)–C(2)	1.394(5)	C(21)–C(22)	1.388(5)
C(2)–C(3)	1.392(6)	C(22)–C(23)	1.392(6)
C(3)–C(4)	1.385(5)	C(23)–C(24)	1.388(6)
C(4)–C(5)	1.485(7)	C(24)–C(25)	1.489(7)
C(5)–O(2)	1.264(5)	C(25)–O(22)	1.265(5)
O(1)–C(1)–C(2)	120.3(3)	O(21)–C(21)–C(22)	120.5(3)
C(2)–C(1)–C(2^{ii})	119.4(6)	C(22)–C(21)–C(22^{iii})	119.0(6)
C(1)–C(2)–I(1)	120.9(3)	C(21)–C(22)–I(2)	120.1(4)
C(1)–C(2)–C(3)	120.3(5)	C(21)–C(22)–C(23)	120.8(5)
I(1)–C(2)–C(3)	118.8(4)	I(2)–C(22)–C(23)	119.0(4)
C(2)–C(3)–C(4)	119.7(5)	C(22)–C(23)–C(24)	119.5(5)
C(3)–C(4)–C(3^{ii})	120.7(6)	C(23)–C(24)–C(23^{iii})	120.4(6)
C(3)–C(4)–C(5)	119.7(3)	C(23)–C(24)–C(25)	119.8(3)
C(4)–C(5)–O(2)	118.3(4)	C(24)–C(25)–O(22)	118.4(4)
O(2)–C(5)–O(2^{ii})	123.5(7)	O(22)–C(25)–O(22^{iii})	123.1(7)

Symmetry code: (ii) x, $1-y$, $-z$; (iii) $-x$, y, z

4-Carboxy-2,6-di-isopropylphenol (**9**)

O(1)–C(1)	1.379(4)	C(7)–O(2)	1.322(5)
C(1)–C(2)	1.397(5)	C(7)–O(3)	1.198(5)
C(2)–C(3)	1.388(5)	C(2)–C(8)	1.524(5)
C(3)–C(4)	1.393(5)	C(8)–C(9)	1.507(6)
C(4)–C(5)	1.399(5)	C(8)–C(10)	1.498(6)
C(5)–C(6)	1.387(5)	C(6)–C(11)	1.518(5)
C(6)–C(1)	1.399(5)	C(11)–C(12)	1.513(6)
C(4)–C(7)	1.483(5)	C(12)–C(13)	1.503(7)
O(1)–C(1)–C(6)	121.0(3)	C(12)–C(11)–C(13)	109.5(4)
O(1)–C(1)–C(2)	115.8(3)	C(4)–C(5)–C(6)	121.3(3)
C(2)–C(1)–C(6)	123.2(3)	C(5)–C(6)–C(11)	120.4(4)
C(1)–C(2)–C(8)	121.4(3)	C(5)–C(6)–C(1)	117.3(3)
C(1)–C(2)–C(3)	117.5(3)	C(1)–C(6)–C(11)	122.2(3)
C(8)–C(2)–C(3)	121.2(4)	C(4)–C(7)–O(2)	113.3(3)
C(2)–C(3)–C(4)	121.2(3)	C(4)–C(7)–O(3)	125.1(3)
C(3)–C(4)–C(7)	121.5(3)	O(2)–C(7)–O(3)	121.6(4)
C(3)–C(4)–C(5)	119.5(3)	C(2)–C(8)–C(9)	112.5(3)
C(5)–C(4)–C(7)	119.0(3)	C(2)–C(8)–C(10)	111.1(4)
C(6)–C(11)–C(12)	113.6(4)	C(9)–C(8)–C(10)	110.8(4)
C(6)–C(11)–C(13)	111.8(4)		

2-Methylsulphonylphenol (**10**)

S(1)–C(2)	1.757(2)	C(5)–C(6)	1.378(3)
O(1)–C(1)	1.353(2)	C(6)–C(1)	1.391(3)

Table 4 (*continued*)

C(1)–C(2)	1.401(2)	S(1)–O(2)	1.447(1)
C(2)–C(3)	1.389(2)	S(1)–O(3)	1.434(1)
C(3)–C(4)	1.375(3)	S(1)–C(7)	1.754(2)
C(4)–C(5)	1.389(3)		
C(2)–S(1)–O(2)	107.87(8)	C(2)–C(1)–C(6)	118.4(2)
C(2)–S(1)–O(3)	109.07(9)	C(1)–C(2)–S(1)	120.5(1)
C(2)–S(1)–C(7)	106.36(9)	C(1)–C(2)–C(3)	120.8(2)
O(2)–S(1)–O(3)	116.33(9)	S(1)–C(2)–C(3)	118.6(1)
O(2)–S(1)–C(7)	107.6(1)	C(2)–C(3)–C(4)	120.1(2)
O(3)–S(1)–C(7)	109.2(1)	C(3)–C(4)–C(5)	119.3(2)
O(1)–C(1)–C(6)	123.4(2)	C(4)–C(5)–C(6)	121.2(2)
O(1)–C(1)–C(2)	118.1(2)	C(5)–C(6)–C(1)	120.1(2)

4-Hydroxy-2-methylsulphonylphenol (**12**)

S(1)–C(2)	1.758(3)	S(2)–C(22)	1.769(3)
O(1)–C(1)	1.363(4)	O(21)–C(21)	1.352(4)
C(1)–C(2)	1.397(4)	C(21)–C(22)	1.401(4)
C(2)–C(3)	1.404(4)	C(22)–C(23)	1.390(4)
C(3)–C(4)	1.386(4)	C(23)–C(24)	1.382(4)
C(4)–C(5)	1.388(4)	C(24)–C(25)	1.395(4)
C(5)–C(6)	1.388(5)	C(25)–C(26)	1.382(5)
C(6)–C(1)	1.390(4)	C(26)–C(21)	1.400(4)
C(4)–O(2)	1.369(4)	C(24)–O(22)	1.369(4)
S(1)–O(3)	1.454(2)	S(2)–O(23)	1.450(2)
S(1)–O(4)	1.446(2)	S(2)–O(24)	1.451(2)
S(1)–C(7)	1.756(3)	S(2)–C(27)	1.758(4)
O(1)–C(1)–C(6)	122.9(3)	O(21)–C(21)–C(26)	123.4(3)
O(1)–C(1)–C(2)	117.9(3)	O(21)–C(21)–C(22)	119.2(3)
C(2)–C(1)–C(6)	119.2(3)	C(22)–C(21)–C(26)	117.3(3)
C(1)–C(2)–S(1)	121.9(2)	C(21)–C(22)–S(2)	120.2(2)
C(1)–C(2)–C(3)	120.4(3)	C(21)–C(22)–C(23)	122.3(2)
S(1)–C(2)–C(3)	117.6(2)	S(2)–C(22)–C(23)	117.5(2)
C(2)–C(3)–C(4)	119.7(3)	C(22)–C(23)–C(24)	119.1(3)
C(3)–C(4)–O(2)	122.4(3)	C(23)–C(24)–O(22)	122.7(3)
C(3)–C(4)–C(5)	119.7(3)	C(23)–C(24)–C(25)	119.7(3)
C(5)–C(4)–O(2)	117.9(3)	C(25)–C(24)–O(22)	117.5(3)
C(4)–C(5)–C(6)	120.8(3)	C(24)–C(25)–C(26)	120.7(3)
C(5)–C(6)–C(1)	120.2(3)	C(25)–C(26)–C(21)	120.8(3)
C(2)–S(1)–O(3)	107.1(1)	C(22)–S(2)–O(23)	106.7(1)
C(2)–S(1)–O(4)	108.7(1)	C(22)–S(2)–O(24)	109.0(1)
C(2)–S(1)–C(7)	107.6(2)	C(22)–S(2)–C(27)	107.8(1)
O(3)–S(1)–O(4)	115.2(1)	O(23)–S(2)–O(24)	115.6(2)
O(3)–S(1)–C(7)	108.6(2)	O(23)–S(2)–C(27)	107.8(2)
O(4)–S(1)–C(7)	109.4(2)	O(24)–S(2)–C(27)	109.8(2)

2-Iodophenol–1,4-benzoquinone 2:1 molecular complex (**12**)

I(1)–C(2)	2.10(2)	C(4)–C(5)	1.40(3)
O(1)–C(1)	1.38(2)	C(5)–C(6)	1.33(3)
C(1)–C(2)	1.34(2)	O(2)–C(21)	1.27(2)
C(1)–C(6)	1.40(2)	C(21)–C(22)	1.47(2)
C(2)–C(3)	1.41(3)	C(21)–C(23)	1.44(3)
C(3)–C(4)	1.39(3)	C(22)–C(23)	1.30(2)
C(2)–C(1)–O(1)	121(2)	C(6)–C(5)–C(4)	122(2)
C(6)–C(1)–O(1)	119(2)	C(5)–C(6)–C(1)	120(2)
C(6)–C(1)–C(2)	120(2)	C(22)–C(21)–O(2)	121(2)
C(1)–C(2)–I(1)	120(1)	C(23)–C(21)–O(2)	120(2)
C(3)–C(2)–I(1)	119(1)	C(23)–C(21)–C(22)	119(2)
C(3)–C(2)–C(1)	121(2)	C(23)–C(22)–C(21)	121(2)
C(4)–C(3)–C(2)	119(2)	C(22)–C(23)–C(21)	120(2)
C(5)–C(4)–C(3)	119(2)		

2-Methylphenol–1,4-benzoquinone 2:1 molecular complex (**13**)

O(1)–C(1)	1.228(4)	C(3)–C(4)	1.467(5)
O(2)–C(4)	1.231(4)	C(4)–C(5)	1.468(5)
C(1)–C(2)	1.476(5)	C(5)–C(6)	1.333(5)
C(2)–C(3)	1.326(5)	C(6)–C(1)	1.463(5)
O(21)–C(21)	1.369(4)	O(31)–C(31)	1.379(4)
C(21)–C(22)	1.402(5)	C(31)–C(32)	1.396(5)
C(22)–C(23)	1.387(5)	C(32)–C(33)	1.384(5)
C(23)–C(24)	1.378(5)	C(33)–C(34)	1.371(5)
C(24)–C(25)	1.386(5)	C(34)–C(35)	1.385(6)
C(25)–C(26)	1.390(5)	C(35)–C(36)	1.387(6)
C(26)–C(21)	1.372(5)	C(36)–C(31)	1.382(5)
C(22)–C(27)	1.493(5)	C(32)–C(37)	1.496(5)
O(1)–C(1)–C(6)	121.5(3)	C(3)–C(4)–O(2)	120.2(3)
O(1)–C(1)–C(2)	120.5(3)	C(3)–C(4)–C(5)	118.5(3)
C(6)–C(1)–C(2)	117.9(3)	C(5)–C(4)–O(2)	121.3(3)
C(1)–C(2)–C(3)	120.5(3)	C(4)–C(5)–C(6)	120.1(3)
C(2)–C(3)–C(4)	121.3(3)	C(5)–C(6)–C(1)	121.7(3)
O(21)–C(21)–C(26)	122.0(3)	C(33)–C(34)–C(35)	119.8(4)
O(21)–C(21)–C(22)	116.2(3)	C(34)–C(35)–C(36)	119.3(4)
C(26)–C(21)–C(22)	121.8(3)	C(35)–C(36)–C(37)	120.3(3)
C(21)–C(22)–C(27)	120.6(3)	O(31)–C(31)–C(36)	121.4(3)
C(21)–C(22)–C(23)	117.0(3)	O(31)–C(31)–C(32)	117.8(3)
C(23)–C(22)–C(27)	122.4(3)	C(36)–C(31)–C(32)	120.8(3)
C(22)–C(23)–C(24)	121.9(4)	C(31)–C(32)–C(37)	121.3(3)
C(23)–C(24)–C(25)	120.1(4)	C(31)–C(32)–C(33)	117.6(3)
C(24)–C(25)–C(26)	119.2(4)	C(33)–C(32)–C(37)	121.1(3)
C(25)–C(26)–C(21)	120.0(4)	C(32)–C(33)–C(34)	122.2(3)

2,4,6-Tri-iodophenol–tetramethylpyrazine 2:1 molecular complex (**14**)

I(1)–C(2)	2.098(7)	C(5)–C(6)	1.38(1)
I(2)–C(4)	2.091(6)	C(6)–C(1)	1.40(1)
I(3)–C(6)	2.099(7)	N(21)–C(21)	1.35(1)
O(1)–C(1)	1.341(8)	N(21)–C(22)	1.33(1)
C(1)–C(2)	1.40(1)	C(21)–C(22^{ii})	1.40(1)
C(2)–C(3)	1.37(1)	C(21)–C(23)	1.49(1)
C(3)–C(4)	1.38(1)	C(22)–C(24)	1.49(1)
C(4)–C(5)	1.39(1)		
O(1)–C(1)–C(6)	124.8(6)	C(5)–C(4)–I(2)	119.7(5)
O(1)–C(1)–C(2)	119.0(6)	C(4)–C(5)–C(6)	119.4(7)
C(6)–C(1)–C(2)	116.1(6)	C(5)–C(6)–I(3)	118.0(5)
C(1)–C(2)–I(1)	118.4(5)	C(5)–C(6)–C(1)	121.8(6)
C(1)–C(2)–C(3)	123.2(6)	C(1)–C(6)–I(3)	120.2(5)
C(3)–C(2)–I(1)	118.1(5)	C(21)–N(21)–C(22)	119.2(6)
C(2)–C(3)–C(4)	119.0(6)	N(21)–C(21)–C(22^{ii})	120.6(7)
C(3)–C(4)–I(2)	119.9(5)	N(21)–C(21)–C(23)	116.8(6)
C(3)–C(4)–C(5)	120.4(6)	N(21)–C(22)–C(24)	118.0(7)
C(22^{ii})–C(21)–C(23)	122.6(7)	C(21^{ii})–C(22)–C(24)	121.8(8)
N(21)–C(22)–C(21^{ii})	120.2(6)		

Symmetry code: (ii) $-1-x, y, 3/2-z$

4′-Hydroxy-4-methyl-2,3′,5′,6-tetraiododiphenyl ether (**15**)

I(1)–C(1)	2.090(6)	I(3)–C(23)	2.094(6)
I(2)–C(5)	2.093(6)	I(4)–C(25)	2.089(6)
C(1)–C(2)	1.372(9)	C(21)–C(22)	1.385(8)
C(2)–C(3)	1.390(8)	C(22)–C(23)	1.388(8)
C(3)–C(4)	1.390(8)	C(23)–C(24)	1.387(8)
C(4)–C(5)	1.384(8)	C(24)–C(25)	1.387(8)
C(5)–C(6)	1.400(9)	C(25)–C(26)	1.401(8)
C(6)–C(1)	1.395(10)	C(26)–C(21)	1.385(8)
O(1)–C(4)	1.388(7)	O(1)–C(21)	1.394(6)
C(1)–C(7)	1.506(9)	C(24)–O(21)	1.364(7)
C(7)–C(1)–C(2)	122.1(6)	O(1)–C(21)–C(22)	115.6(5)
C(7)–C(1)–C(6)	118.9(6)	O(1)–C(21)–C(26)	122.8(5)
C(6)–C(1)–C(2)	119.1(6)	C(26)–C(21)–C(22)	121.1(5)
C(1)–C(2)–C(3)	120.8(6)	C(21)–C(22)–C(23)	119.0(5)
C(2)–C(3)–I(1)	119.3(4)	C(22)–C(23)–I(3)	119.4(4)
C(2)–C(3)–C(4)	120.8(6)	C(22)–C(23)–C(24)	121.4(5)
I(1)–C(3)–C(4)	119.9(4)	I(3)–C(23)–C(24)	119.2(4)
C(3)–C(4)–O(1)	120.8(5)	C(23)–C(24)–O(21)	124.2(5)
C(3)–C(4)–C(5)	118.6(5)	C(23)–C(24)–C(25)	118.2(5)
O(1)–C(4)–C(5)	120.5(6)	O(21)–C(24)–C(25)	117.6(5)
C(4)–C(5)–I(2)	120.5(4)	C(24)–C(25)–I(2)	119.8(4)
C(4)–C(5)–C(6)	120.7(6)	C(24)–C(25)–C(26)	121.8(5)
I(2)–C(5)–C(6)	118.8(5)	I(4)–C(25)–C(26)	118.4(4)
C(5)–C(6)–C(1)	120.0(6)	C(25)–C(26)–C(21)	118.0(5)
C(4)–O(1)–C(21)	117.4(4)		

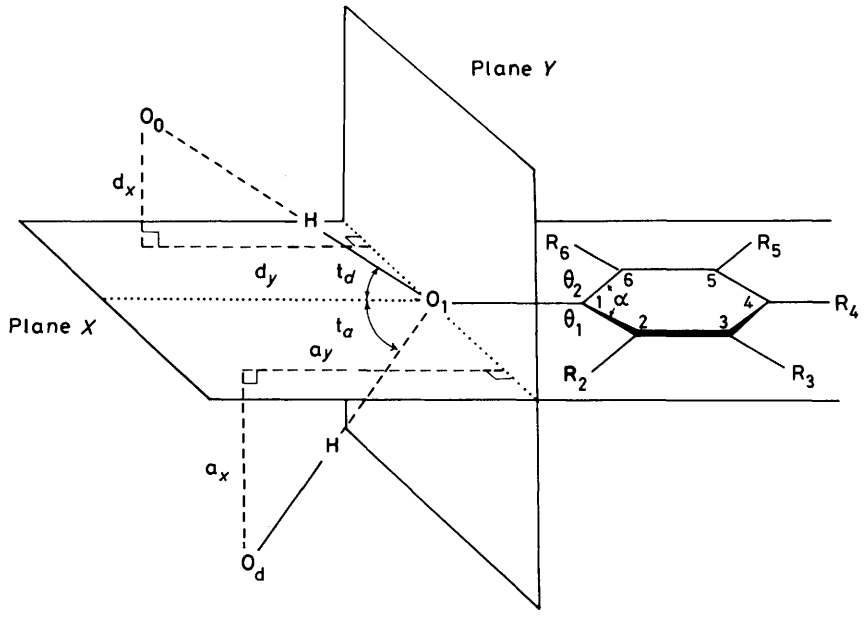


Figure 1. The molecular geometrical parameters referred to in the text and in Table 1 are defined in the Figure. The phenyl ring and the substituent oxygen atom O_1 and the groups R_2 through R_6 lie in the plane X, the plane Y passes through O_1 and is perpendicular to the O_1–C_1 bond

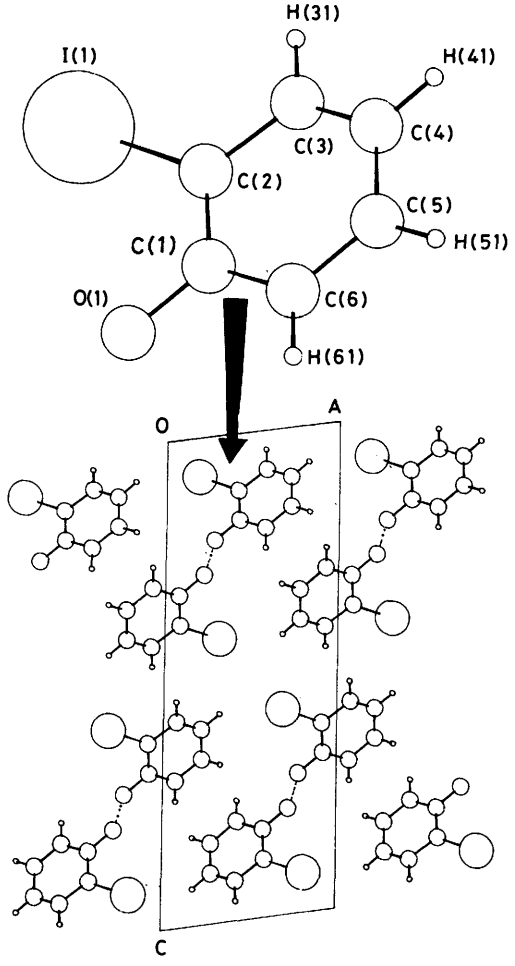


Figure 2(a). 2-Iodophenol (**3**). The crystal packing is shown viewed along *b*. The phenolic OH groups link to form hydrogen-bonded chains along the two-fold screw axes of $P2_1/n$ [O(1) ··· O(1) (−1/2 − *x*, −1/2 + *y*, 1/2 − *z*) 2.78(2) Å]

hydrogen-bonded chains containing more than one crystallographically independent molecule, in arrangements which are close approximations to non-crystallographic three-fold screw axes. When there are other functional groups involved in the hydrogen-bonding, no simple patterns have been detected.

Molecular geometry.—Here the major concern is with the molecular geometry associated with the phenolic hydroxy group of the differently substituted phenols. The most striking variation is that of the internal phenyl ring angle (α in Figure 1 and Table 1) at C(1) the atom carrying the phenolic OH substituent. This angle varies from 115.3—125° (Table 1), and this variation is accompanied by a smaller but significant variation in C–OH bond length.

It has been known for many years that substituents have a measurable effect on benzene ring geometries, with the endocyclic angle, associated with an electron-withdrawing substituent, a few degrees larger than 120°, and at an electron releasing substituent, a few degrees less than 120°. In recent years, a wealth of accurate structural information on mono- and di-(*para*)-substituted benzene derivatives, obtained from *X*-ray structure analyses, has been analysed in detail by Domenicano and co-workers.[59] For any given monosubstituted benzene the observed endocyclic angle (in the range 114—125°) depends markedly upon the electronic properties of the substituent, and for a range of substituents there is a strong linear correlation with Taft's inductive parameter and with Huheey's group electronegativity.[59]

A set of substituent (angular) parameters has been derived by Domenicano and Murray-Rust,[60] by linear regression from crystallographic data for mono and di-(*para*)-substituted compounds, for the prediction of benzene ring endocyclic angles. The benzene ring endocyclic angles observed by *X*-ray diffraction for the phenols in Table 1 were compared with those predicted from the Domenicano and Murray-Rust parameters and it was found that in general the observed values differed from the predicted values by less than the estimated standard deviation of the observed value, even though many of the phenols had three or four substituents, supporting the general predictive capability of these parameters.

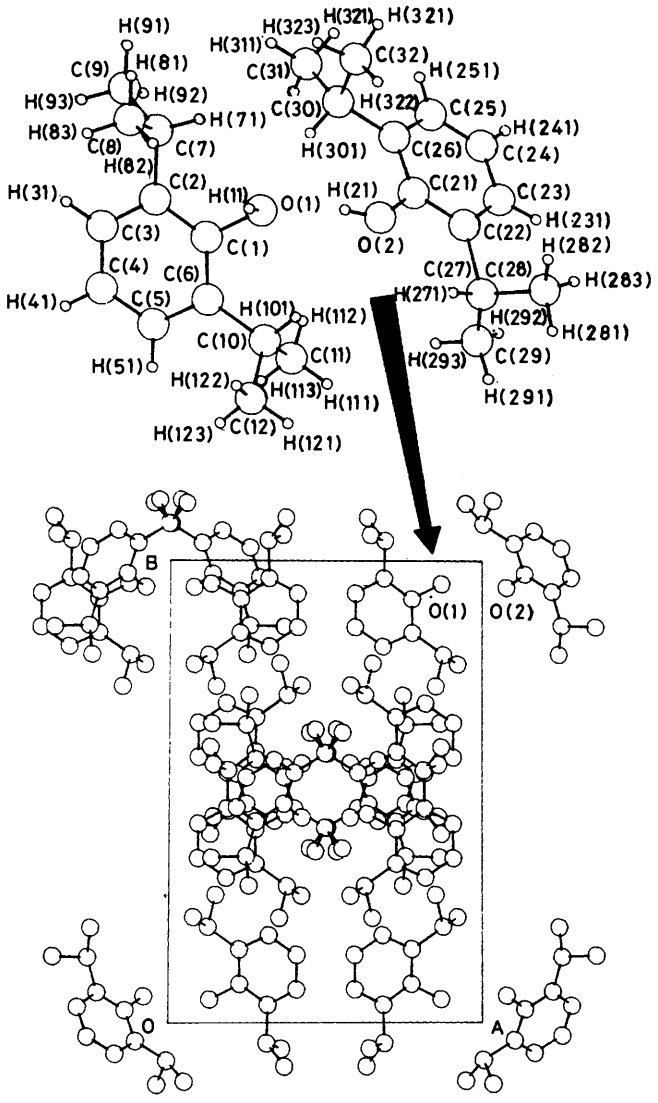


Figure 2(b). 2,6-Di-isopropylphenol (**4**). The crystal packing is shown viewed along the 20.452 Å *c*-axis. The asymmetric unit contains two molecules linked by a H-bond [O(1)···O(2), 2.735(10) Å]. Two asymmetric units link to form a H-bonded tetramer [O(1)···O(2) (2 − *x*, *y*, 3/2 − *z*), 2.747(10) Å] with two-fold symmetry. The asymmetric unit is arrowed, a dimer is to the left of it, and in the centre the full packing is shown

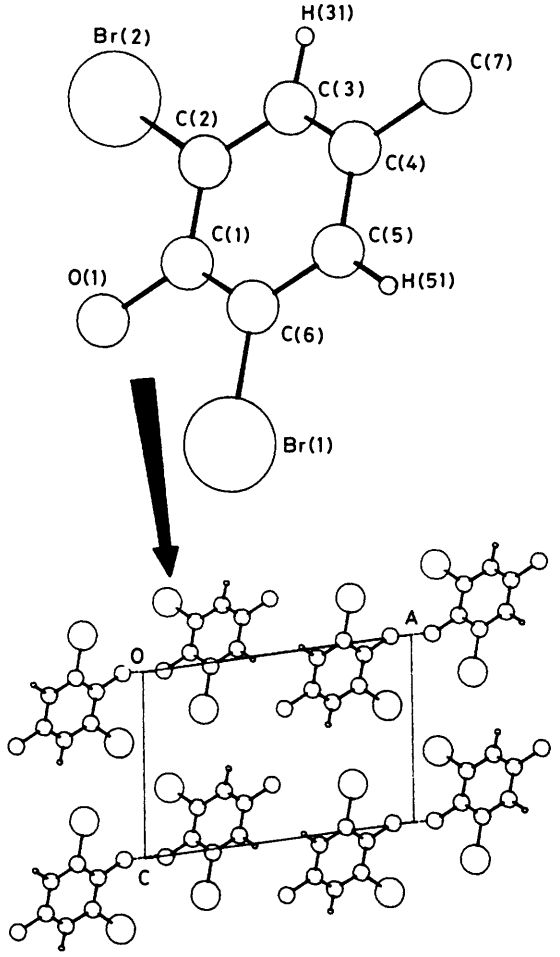


Figure 2(c). 2,6-Dibromo-4-methylphenol (**5**). The crystal packing is shown viewed along *b*. The phenolic OH groups link to form chains along the two-fold screw axes of $P2_1$ [O(1)···O(1) (−*x*, 1/2 + *y*, − *z*) 2.90(2) Å]

If the nature of the substituents is a predictor for the endocyclic angle then, conversely, it might be expected that those properties of a given substituent, *e.g.* a phenolic hydroxy group, which are modified by the presence of other substituents, can be predicted from the observed endocyclic angle. Consequently, the relationships between the endocyclic angle at the phenolic hydroxy, and the C–O bond length, the phenol pK_a, and the ^{13}C chemical shift of the carbon carrying the hydroxy group, were examined.

Figure 3 shows that there is a reasonably good correlation between endocyclic angle at the phenolic hydroxy and the C–OH bond length, with a linear correlation coefficient of 0.80 for 45 data points. Previously, a correlation has been shown between C–OH bond length and the pK_a,[49,61] and for this sample the correlation coefficient is 0.79 for 36 data points. However, the variations in bond length are small and are comparable with the systematic differences in bond length derived from the different magnitudes of thermal motion in the various determinations. An improved linear correlation (0.87 for 38 data points) is found when the endocyclic angle is plotted against the pK_a (Figure 4). There was no correlation between the endocyclic angle and the ^{13}C chemical shift of the carbon carrying the phenolic hydroxy group. (Structures in which the e.s.d. of the endocyclic angle is greater than 1° have been excluded from all the above correlations).

For almost all structures there are small but significaant differences between the two exocyclic ring angles (θ_1 and θ_2 in Figure 1 and Table 1). In every structure where the position of the phenolic hydrogen was located by *X*-ray diffraction, or inferred unambiguously from the hydrogen-bonding pattern, the hydrogen atom was found on the same side of the OH bond as the larger exocyclic angle. This agrees with the studies of the structure of phenols by microwave spectroscopy.[16] In phenols with only *ortho* hydrogen atoms this difference is presumed to be due to repulsion of the phenolic hydrogen by the hydrogen in the 6-position (Figure 1). In mono-*ortho*-substituted phenols the larger C–C–O angle, and, by inference the hydrogen atom, is located on the side of the C–O opposite to the *ortho* substituent, in all but two structures, namely, 2,3-dichlorophenol and 2,4-dichlorophenol. Both structures contain three cystallographically independent molecules. With 2,3-dichlorophenol, one molecule has the larger C–C–O angle on the same side of the

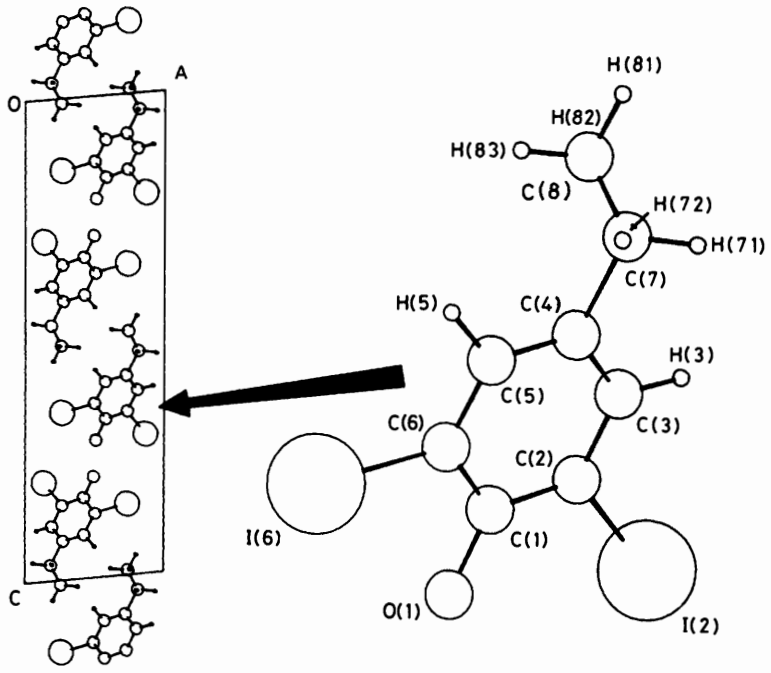


Figure 2(d). 4-Ethyl-2,6-di-iodophenol (**6**). The crystal packing is shown viewed along *b*. The phenolic OH groups link to form chains along the two-fold screw axes of $P2_1/c$ [O(1)···O(1) $(1 - x, 1/2 + y, 3/2 - z)$ 3.15(1) Å] but the hydrogen bond is exceptionally long for O–H···O

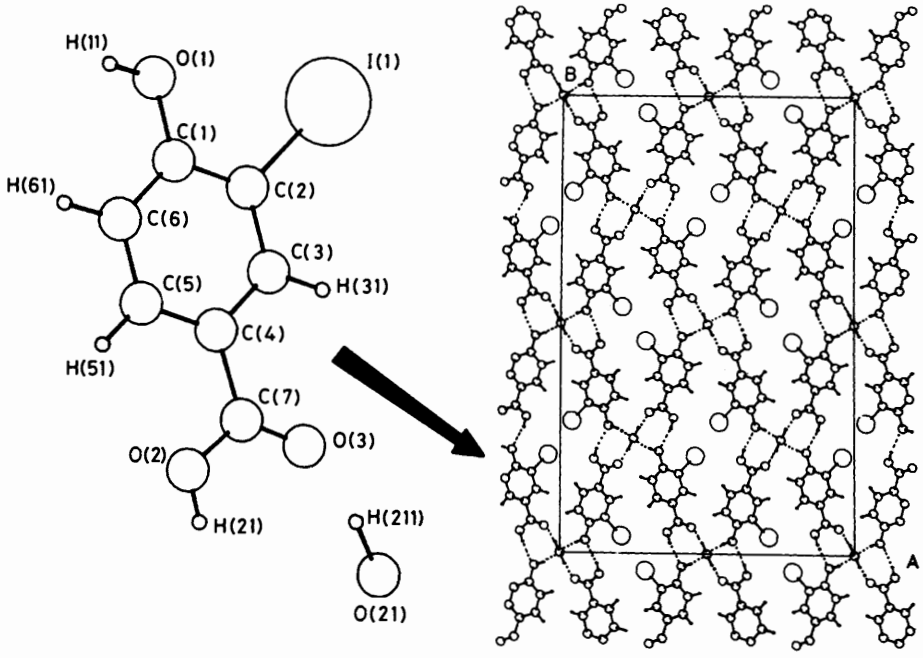


Figure 2(e). 4-Carboxy-2-iodophenol (**7**). The crystal packing is shown viewed along *c* looking along the two-fold axes of *Fdd*2. A water molecule on a two-fold axis forms four hydrogen bonds, two to phenolic OH groups [O(21)···O(1)$(1/4 + x, 1/4 + y, -3/4 + z$ and $-1/4 - x, -1/4 + y, -3/4 + z)$ 2.680(9) Å] and two to carboxylic acid C=O groups [O(21)–O(3) $(x, y, z$, and $-x, -y, z)$ 2.717(9) Å]. These groups are linked into chains by hydrogen bonds from the carboxylic OH groups to the phenol oxygen atoms [O(2)···O(1) $(-1/4 - x, -1/4 + y, 1/4 + z)$ 2.817(9) Å]. The chains are linked into a three-dimensional hydrogen-bonded array because each molecule is hydrogen-bonded to one chain by the phenolic OH and another by the carboxylic acid group

C–O bond as the *ortho* chlorine, and with 2,4-dichlorophenol all three molecules have the larger C–C–O angle on the same side as the *ortho* chlorine. The hydrogen atoms were not located in either structure. However, the presence of the larger C–C–O angle on the same side of the C–O bond as the chlorine suggests that in these cases the phenolic hydrogen is close to the *ortho* chlorine and forms a bifurcated hydrogen bond to it and the phenolic oxygen of a neighbouring molecule. If there is an

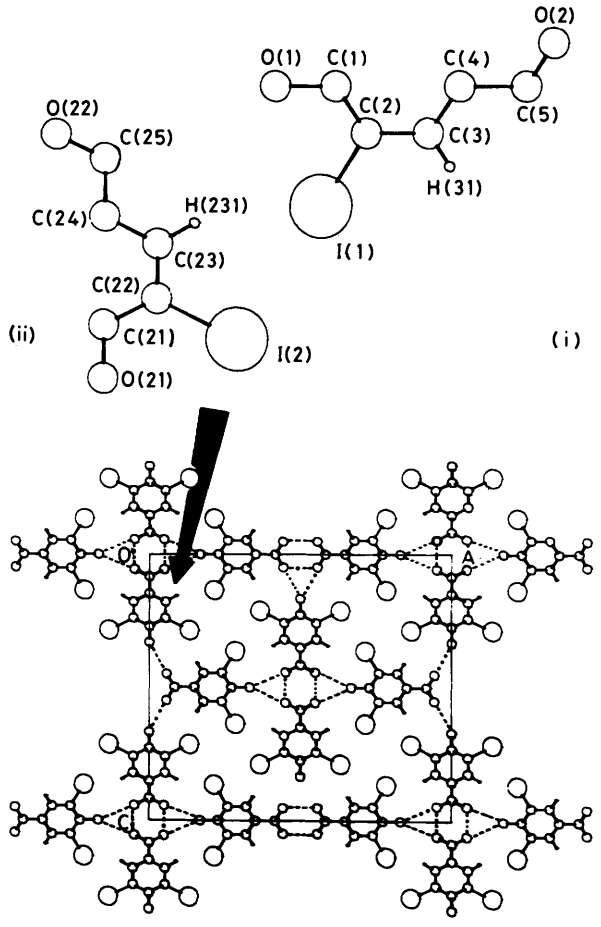


Figure 2(f). 4-Carboxy-2,6-diodophenol (**8**). The crystal packing is shown viewed along *b*. The asymmetric unit contains two 'half molecules'. The molecule (i) containing I(1) is generated by the two-fold axis along *a* at $y = z = 0$ and the molecule (ii) containing I(2) by the mirror plane at $x = 0$ perpendicular to *b*. Molecules (i) and (ii) both form hydrogen-bonded carboxylic acid dimers [O(2)···O(2) $(1 - x, y, z)$ 2.586(9) Å and O(22)···O(22) $(x, -2 - y, -z)$ 2.628(9) Å]. There are long contacts from the phenolic OH groups to the carboxylic acid oxygens [O(1)···O(22) $(-x, -y, -z$ and $-x, 1 + y, z)$ 3.238(10) and O(21)···O(2) $(1/2 - x, 1 - y, 1/2 + z$, and $x - 1/2, 1 - y, 1/2 - z)$ 3.190(10) Å], very long and inappropriate directions to be considered as hydrogen bonds. The packing of the dimers appears to be dominated by the I---I interactions

attractive interaction between the phenolic hydrogen and an *ortho* chlorine it would seem to be weak; it does not occur with two of the three crystallographically independent molecules of 2,3-dichlorophenol,[44] nor in the crystal structure of 2,5-dichlorophenol.[46] In this latter structure, once again the hydrogen atoms were not located, but the larger C–C–O angle is located on the opposite side of the C–O bond to the *ortho* chlorine.

With certain exceptions, *e.g.* when both R_2 and R_6 (Figure 1) are very large, $\Delta\theta$ $(\theta_1 - \theta_2)$ is between 3 and 6° and, in general, as the endocyclic angle (α) gets smaller $\Delta\theta$ increases. Surprisingly, there is little relation between the size of an *ortho* substituent and $\Delta\theta$, although there may be some relationship between the direction of the hydrogen donor hydrogen bond and $\Delta\theta$. Thus, in the structure of the 2:1 molecular complex of 2-methylphenol and 1,4-benzoquinone, which contains two crystallographically independent 2-methylphenol molecules, the donor hydrogen bond of one 2-methylphenol molecule is co-planar with its phenyl ring plane and $\Delta\theta$ is 5.8°, whereas the donor hydrogen bond of the other 2-methylphenol is inclined at ~40° to the phenyl ring plane and $\Delta\theta$ is only 3.6°. Similarly, 2,6-di-isopropylphenol also has two molecules in the crystallographic asymmetric unit with donor hydrogen bonds inclined at 26° and 87° to the phenyl ring plane and $\Delta\theta$ values of 1.6° and 0.1° respectively. Unfortunately, there are insufficient examples to bring statistical verification to support what appears to be a clear causal relationship, that is, as the phenolic hydrogen moves out of the phenyl ring plane its repulsive interaction with the *ortho* group is reduced. In 2,6-di-t-butylphenols[28,29] and 2,6-di-iodophenols, where the hydrogen bonds are either non-existent or very long presumably due to the bulk of the *ortho* substituents, $\Delta\theta$ is very small, suggesting that the phenolic hydrogen atom may lie far from the phenyl ring plane.

Intermolecular Hydrogen-bonding.—In the examples considered the hydrogen bonds are of the type O–H···O and their direction is generally established by the direction of the O···O vector. The angles t_d and t_a in Table 1 are defined as the angle of rotation about the phenolic C–O bond of the donor hydrogen bond O···O vector, and the acceptor hydrogen bond O···O vector, respectively, from the O(1), C(1), C(2), C(6) plane. It is clear that, although there is a relatively high barrier to rotation about the phenolic C–O bond (13 kJ mol^{-1}), there is not a strict requirement for the donor hydrogen bond to be coplanar with the aromatic ring. Only in a few structures does it lie very close to the ring plane and there is an even spread of torsion angles up to about 40° and one outlier of 87°. In di-(*ortho*)-substituted phenols, angle t_d is always greater than 25°. However, apart from this, the deviation of the donor hydrogen bond from the ring plane does not appear to be correlated with any feature of the individual phenols. The phenolic hydrogen has, in this sample of compounds, proved difficult to locate by *X*-ray methods and its position is rarely reported with confidence. For the new structure analyses reported here there are strong indications of the location of the phenolic hydrogen atoms for molecules in eight crystals. For each molecule the difference electron density in a plane perpendicular to the C–O bond, and containing the phenolic hydrogen, is sketched in Figure 5. With one exception, it appears that as the acceptor atom moves out of the ring plane it pulls with it the phenolic hydrogen, but that the phenolic O–H bond is restricted to a maximum deviation from the ring plane of about 15°, and as the acceptor atom moves further out of the ring plane there is an increasing loss of O–H···O collinearity up to a maximum acceptor atom deviation from the ring plane of about 40°.*

Kollman *et al.*[62] in a theoretical study of *ortho*-substituted phenols assumed that the phenolic hydroxy bond would remain coplanar and concluded that movement of the acceptor atom (the oxygen of a water molecule) out of the ring plane would result in a large loss of hydrogen bond energy for rotations of the O···O vector of more than 20°. It would seem reasonable, however, that a small out-of-plane movement of the O–H bond could be accommodated without much loss in resonance energy, since the latter is approximately proportional to the square of the cosine of the C(6), C(1), O(1), H(1) torsion angle. Thus, with a small out-of-plane movement of the phenolic

* Attempts were made to locate the phenolic hydrogen of the perdeuterio derivatives of 2,4,6-tri-iodophenol and 2-iodophenol by neutron powder profile analysis at 4 K. Unfortunately, the 2,4,6-tri-iodophenol diffraction pattern could not be indexed on the basis of the known room temperature unit-cell. It was assumed that, at 4 K, the perdeuterio sample existed in a different phase or mixture of phases. For 2-iodophenol, the phenolic hydrogen atom could not be defined with acceptable accuracy, but the result was generally consistent with the result from the *X*-ray analyses.

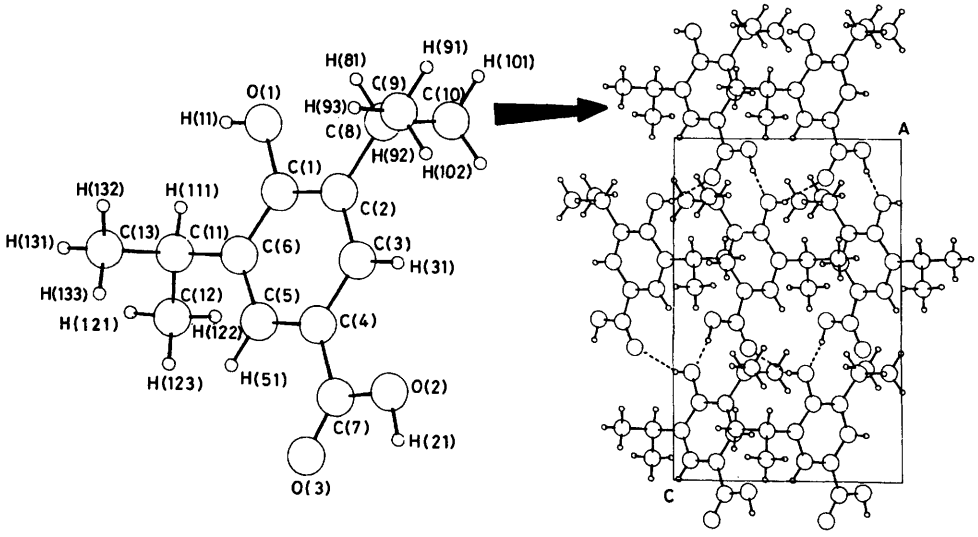


Figure 2(g). 4-Carboxy-2,6-di-isopropylphenyl (**9**). The crystal packing is shown viewed along *b*. Each phenolic OH group is hydrogen-bonded to the carboxylic acid group of two neighbouring molecules [O(1)···O(2) $(1/2 - x, -1/2 + y, -1/2 + z)$ 2.742(7) Å and O(1)···O(3) $(-x, -y, -1/2 + z)$ 2.679(7) Å] to give hydrogen-bonded sheets. The packing contrasts strongly with Figure **2(f)** and highlights the different behaviours in crystal packing of the similarly sized iodo and isopropyl groups

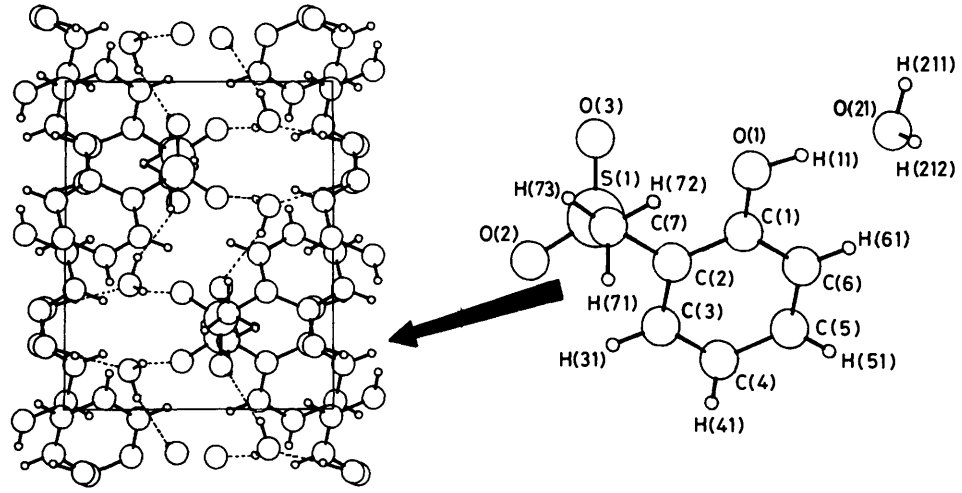


Figure 2(h). 2-Methylsulphonylphenol (**10**). The crystal packing is shown viewed along *c*. There is no intramolecular hydrogen bond between the phenolic OH and the 2-methylsulphonyl group. Instead the OH forms a hydrogen donor hydrogen bond to the water molecule [(O(1)···O(21) 2.660(4) Å]. The water molecule forms two hydrogen bonds to two different sulphonyl oxygen atoms of two neighbouring molecules [O(21)···O(2) $(1 + x, 1/2 - y, 1/2 + z)$ 2.925(5) Å and O(21)···O(3) $(2 - x, 1 - y, 1 - z)$ 2.844(4) Å] and links the 2-methylsulphonylphenols molecules into a three-dimensional network

O–H bond, and a small loss in O–H···O collinearity, the acceptor atom can deviate up to about 40° from the ring plane without a substantial loss in either resonance energy or hydrogen-bond energy. Therefore, it is likely that the detail of the donor hydrogen-bond geometry is determined by crystal packing forces. This would explain the absence of a correlation between the deviation of the donor hydrogen bond from the ring plane and any feature of the individual phenols. This point is exemplified by the crystal structures of the 2:1 molecular complex of 2-methylphenol and *p*-benzoquinone and of 2,6-di-isopropylphenol. Both structures have two crystallographically independent phenol molecules in the asymmetric unit and in both cases the two independent donor hydrogen bonds have very different deviations from their respective ring planes. In the crystal structure of 2,6-di-isopropylphenol the donor hydrogen bond of one molecule lies fairly close to its ring plane (26°), whilst that of the other molecule is almost perpendicular to its plane (87°). This is the only crystal structure in which a donor hydrogen bond and a phenolic hydrogen are approximately perpendicular to the phenol ring plane. Relative to other phenols this compound also has a large phenolic endocyclic angle and a long C–O bond, both of which indicate a decrease in the conjugation of a non-bonding pair on the oxygen with the aromatic ring and a consequent lowering of the rotational barrier about the C–O bond.

The existence of two donor hydrogen bond directions, one coplanar and one perpendicular to the aromatic ring, has also been found in solution for 2,6-di-t-butylphenol. Furthermore,

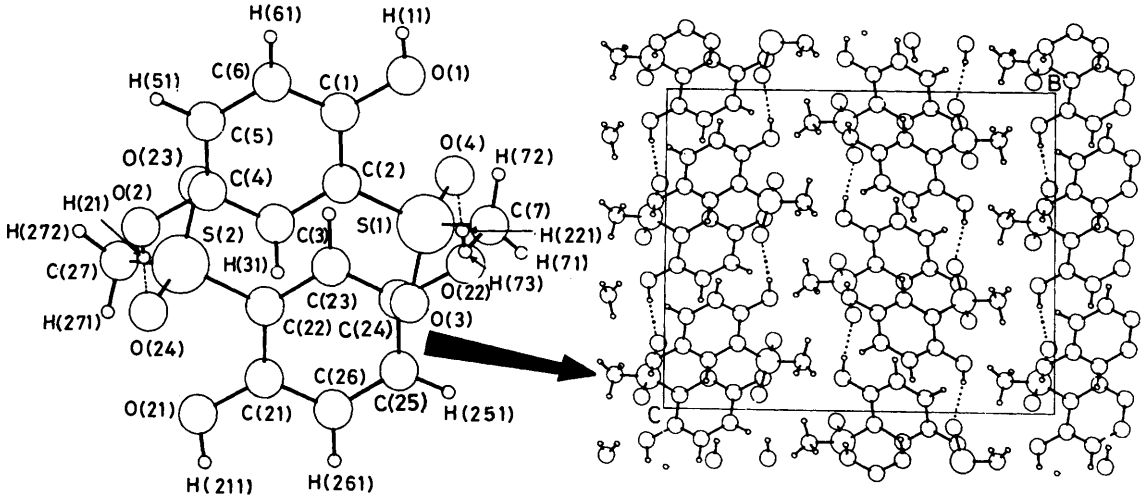


Figure 2(i). 4-Hydroxy-2-methylsulphonylphenol (**11**). The crystal packing is shown viewed along *a*. The asymmetric unit contains two molecules linked to form a hydrogen-bonded dimer with non-crystallographic symmetry centre [O(2)···O(24) 2.862(6) Å and O(22)···O(4) 2.885(6) Å]. The dimers are linked into hydrogen-bonded sheets perpendicular to *c* [O(1)···O(3) $(2 - x, 1/2 + y, z)$ 2.748(6) Å and O(21)···O(23) $(1 - x, -1/2 + y, z)$ 2.711(6) Å]

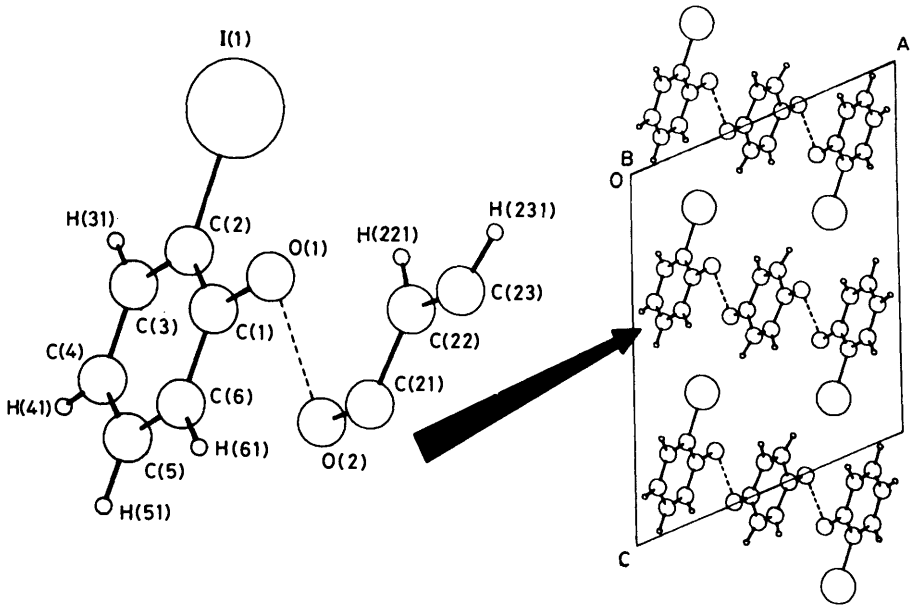


Figure 2(j). 2-Iodophenol–1,4-benzoquinone 2:1 complex (**12**). The crystal packing is shown viewed along *b*. The 1,4-benzoquinone molecules are located at crystallographic symmetry centres in $P2_1/c$ and are linked by hydrogen bonds to two neighbouring 2-iodophenol molecules [O(2)···O(1) 2.77(2) Å]. The crystals are isostructural with the phenol–1,4-benzoquinone 2:1 complex

Kollman *et al.*[62] found that *ortho* substitution on the same side of the molecule as the donor hydrogen bond resulted in a strong repulsive interaction between the *ortho* substituent and an in-plane acceptor atom. This repulsive interaction could be reduced by in-plane bending of the C(1)–O(1)···O angle and most of the hydrogen-bond energy thereby regained. Table 1 gives the deviations of the acceptor atom from (i) the plane defined by the aromatic ring (d_x, Figure 1), and (ii) the plane perpendicular to the C–O bond and containing the phenolic oxygen (d_y, Figure 1). It is found that as d_x decreases then d_y increases and that the largest values for d_y are found when there is an *ortho* substituent on the same side of the molecule as the donor hydrogen bond. These trends are consistent with Kollman's approach, but the overall pattern suggests that hydrogen-bonding overcomes the steric interference of an *ortho* substituent by both an out-of-plane twist and an enlargement of the C–O···O angle. It is also possible that these trends are partly determined by an electronic effect related to changes in the hybridisation of the phenolic oxygen as the hydrogen bond rotates about the C–O bond.

The steric effects of *ortho* substituents are most marked in the crystal structures of 2,6-di-iodo and 2,6-di-t-butylphenols, in which they prevent the formation of phenolic hydrogen bonds. In these structures the sterically hindered phenolic hydroxy group would require to function as both the proton donor and acceptor. In the crystal structure of the 2:1 molecular complex

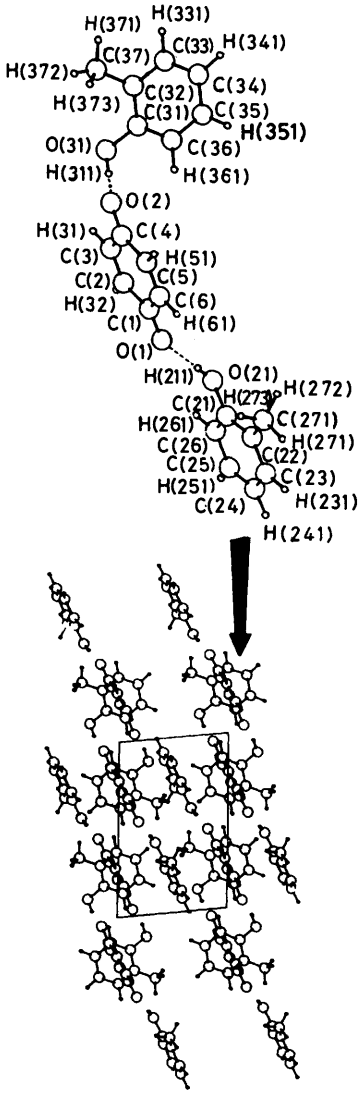


Figure 2(k). 2-Methylphenol–1,4-benzoquinone 2:1 molecule complex (**13**). The crystal packing is shown viewed along *b*. The asymmetric unit contains two 2-methylphenol molecules and one 1,4-benzoquinone forming a hydrogen-bonded complex [O(1)···O(21) 2.798(6), O(2)···O(31) 2.833(6) Å]. The 1,4-benzoquinone molecule and 2-methylphenol [O(21) through C(27) are coplanar and in the packing form alternate donor acceptor stacks parallel to *a*. The second 2-methylphenol [O(31) through C(37)] lies between these stacks with its molecular plane approximately perpendicular to the planes of the molecules in the stack

of 2,4,6-tri-iodophenol and tetramethylpyrazine, the phenolic hydroxy, with two *ortho* iodines, is able to form just one (donor) hydrogen bond to the nitrogen of tetramethylpyrazine. The existence of a strong repulsive interaction between an in plane acceptor atom of a donor hydrogen bond and an *ortho* substituent may explain the lack of success in preparing molecular complexes of di-(*ortho*)-substituted phenols and *p*-benzoquinone. The crystal structures of other phenol–*p*-benzoquinone complexes show a great preference for the hydrogen-bonded molecules to be coplanar.

Kollman *et al.*[62] also studied the hydrogen-bond geometry of the phenolic oxygen acting as a proton acceptor. In this case O···H–O collinearity can be maintained as the donor group moves out of the ring plane and such movement was found to have almost no effect on hydrogen-bond energy (a loss of ~1.5 kJ mol^{-1} for an out-of-plane movement of 45°). The angle of rotation t_a about the phenolic C–O bond of the acceptor O···O vector from the C(2), C(1), O(1) plane is shown in Table 1. There is, unlike the donor bond torsion angles, a continuous spread of angles up to about 86° from the ring plane. *Ortho* substitution on the same side of the molecule as the acceptor hydrogen bond requires $t_a > 60°$ (the only exception occurs in 4-carboxy-2-iodophenol). Thus even in the presence of very bulky *ortho* substituents the acceptor hydrogen bond can form by moving substantially out of the ring plane with very little loss in hydrogen-bond energy.

Table 1 gives the deviations a_x and a_y of the donor atom from the planes (see Figure 1). The overall trend is very similar to that of the acceptor atom deviations; as the donor atom moves closer to the ring plane, so its deviation from the perpendicular plane increases. The effect of *ortho* substitution is also very apparent; not only does the donor atom keep well out of the ring plane, there is also an increase in its distance from the perpendicular plane.

An overall view of the directionality of the phenolic hydrogen bond in the crystal structures of thyroid hormone analogues has been given by Cody.[63] It is consistent with the results of the present study.

Experimental

Data Analyses.—For the earlier analysis of crystallographic data the source was the Cambridge Crystallographic Data Centre (C.C.D.C.) databank (May 1981 release)[27] implemented as the S.E.R.C. supported interactive variant Crystal Structure Search Retrieval (C.S.S.R.) on the Edinburgh (E.R.C.C.) DEC-10.[64] Interactive computer graphics programs of the CHEMGRAF[65] suite, implemented on the E.R.C.C. DEC-10 and the Oxford University VAX11/780 computers, were used in the analysis of the data; SNOOPI to generate the complete hydrogen-bonded units of the structure, and GEOM to tabulate and compare geometry variables for a series of molecules. The data analysis was repeated and extended using the September 1984 C.C.D.C. release implemented on the inhouse VAX11/750, together with Dr. P. Murray-Rust's VAX implementation[66] of the Cambridge search retrieval and data analysis programs. CHEMGRAF was used for graphics.

X-Ray Structure Analysis.—All the phenols used were supplied by Smith Kline and French Research Ltd. *p*-Benzoquinone and tetramethylpyrazine were obtained from Aldrich Chemicals. Weissenberg and/or precession photography was used for a preliminary examination of each sample of crystals and an Enraf-Nonius CAD4 diffractometer for data collection. The unit-cell dimensions and orientation matrix were determined by a least-squares best fit to 25 carefully centred reflexions following the manufacturers recommended procedures. All data were collected by $\omega/2\theta$ scan, scan aperture 4 mm, and graphite-monochromated Mo-K_α radiation. The data were corrected for Lorentz, polarisation, and for compounds containing Br or I, absorption.[67] The Oxford University 2980 and VAX computers were used with MULTAN[68] for direct methods, CHEMGRAF[65] for graphics, and CRYSTALS[69] for all other crystallographic calculations. Scattering factors of non-hydrogen atoms were taken from La-3816.[70] Hydrogen scattering factors and anomolous dispersion corrections were taken from International Tables.[71] After the initial model was established all structures were refined, first with isotropic, and then with anisotropic temperature factors, when a large block approximation to the normal matrix was used the scale parameter the extinction parameter and a 'dummy' U were contained in a separate block. Soft constraints were those of Waser[72] as implemented by Rollett.[73] The weights were determined from truncated Chebyshev[74] polynomials:

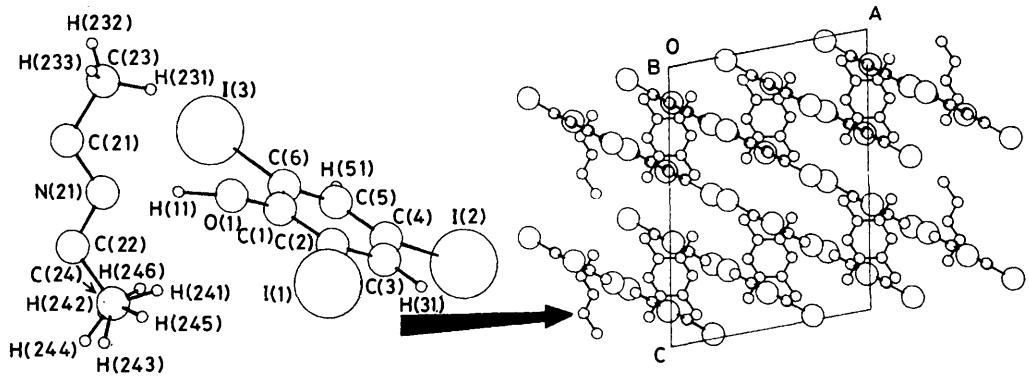


Figure 2(l). 2,4,6-Tri-iodophenol–tetramethylpyrazine 2:1 complex (**14**). The crystal packing is shown viewed along *b*. The tetramethylpyrazine molecules are about the crystallographic two-fold axes of the space group *C*2/*c* and have their molecular planes parallel to the *ac* plane. The 2,4,6-tri-idodophenol molecules are at right angles to those of the tetramethylpyrazine molecules and each pyrazine is hydrogen-bonded to two phenols to give a three-molecule group with two-fold symmetry [N(21) ··· O(1) 2.740(11) Å]

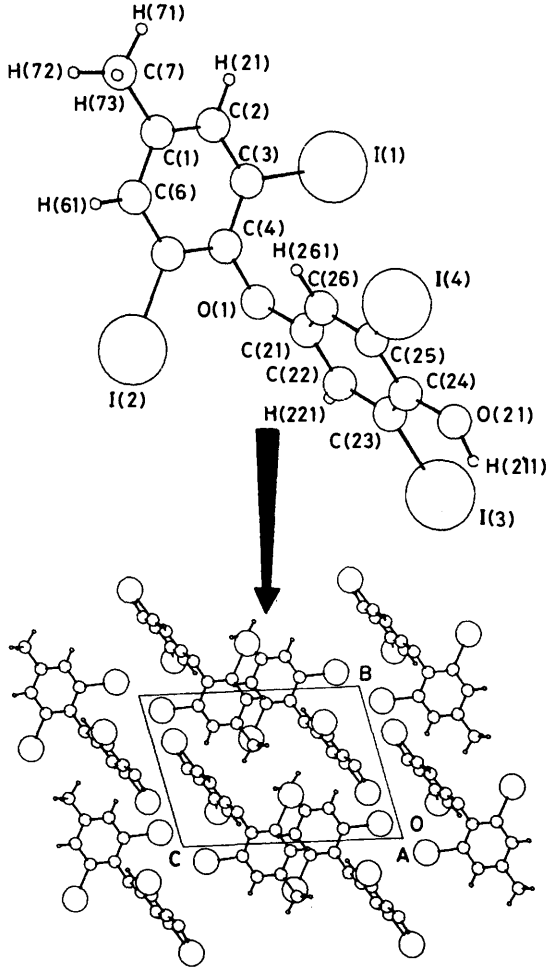


Figure 2(m). 4′-Hydroxy-4-methyl-2,3′,5′,6-tetraiododiphenyl ether (**15**). The crystal is shown viewed along *a*. The molecules are linked to form hydrogen-bonded chains parallel to *a* [O(21) ··· O(21) (1 − *x*, 1 − *y*, −*z*) 2.981(9) Å]

$$\omega = 1/\sum_{r=1}^{n} A_r T_r(|F_o|/|F_o(\text{max.})|)$$

where the coefficients A_r, were determined by a least-squares method which minimises the variation of $w\Delta^2$ with F_o. The atomic co-ordinates of non-hydrogen atoms and selected interatomic distances and interbond angles are recorded in Tables 3 and 4.

2-Iodophenol (**3**). Long colourless needles were grown by sublimation over a period of several months at 3 °C and atmospheric pressure. During preliminary photography it was found that cutting the long needles seriously impaired the diffraction pattern, therefore an uncut needle several millimetres long was used for the data collection. At temperatures below −70 °C the samples lost crystallinity so that −65 °C was chosen for the data collection. The Enraf-Nonius routine NEEDLE, which minimises the *X*-ray path length through a needle crystal, was used to reduce absorption effects.

The structure was determined by Patterson and electron density methods and refined by full-matrix least-squares. The phenyl hydrogen atoms were observed in the difference electron density at $R = 0.056$ but the phenolic hydrogen atom position was obscured by ripples in the difference density of up to 0.5e in the regions where it might be expected. The phenyl hydrogens were placed geometrically and their parameters were not refined. In the final difference electron-density map the highest peaks were 2e Å^{-3} in the immediate vicinity of the iodine atom but otherwise there were no peaks larger than 0.5e Å^{-3}.

2,6-Di-isopropylphenol (**4**). A suitable fragment for *X*-ray data collection was cut from a single crystal sheet obtained by freezing a freshly distilled sample. Because the crystals melt at 18 °C and turn opaque at −45 °C, suggesting a possible phase change, −40 °C was chosen for the data collection.

The structure, which contains two independent molecules in the asymmetric unit, was solved by direct methods using a hand-picked starting set. The refinement was by block diagonal least-squares with one block for the derivatives of the atomic parameters for each molecule. The soft constraint, that for each bonded pair of atoms the difference in the mean square displacement along the bond direction be approximately zero, was applied to the anisotropic thermal parameters. All hydrogen atoms, including the phenolic hydrogen, were located from difference maps but their positions were not refined. The terminal isopropyl carbon atoms have very high temperature factors but there is no residual electron density in the difference synthesis for these regions, indicating that it is adequately modelled. The final electron-density difference map contained no peak higher than 0.2 e Å^{-3}.

2,6-Dibromo-4-methylphenol (**5**). The crystals, colourless cubes obtained by sublimation, were cooled to 198 K (−75 °C) and the data collected in pairs of Friedel equivalents. The frequent large movements of the crystal seemed to reduce the icing of the crystal. In the data reduction Friedel pairs were not

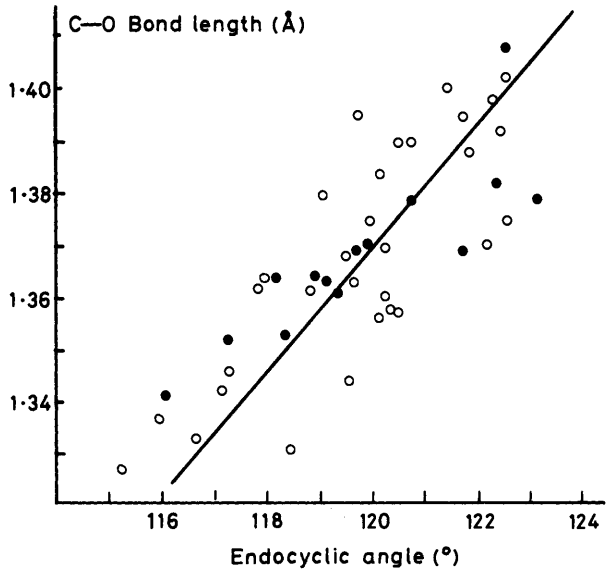


Figure 3. A scatter plot of C–O (Å) bond length *versus* the endocyclic angle (α). The filled circles represent data for the new structures reported in this paper

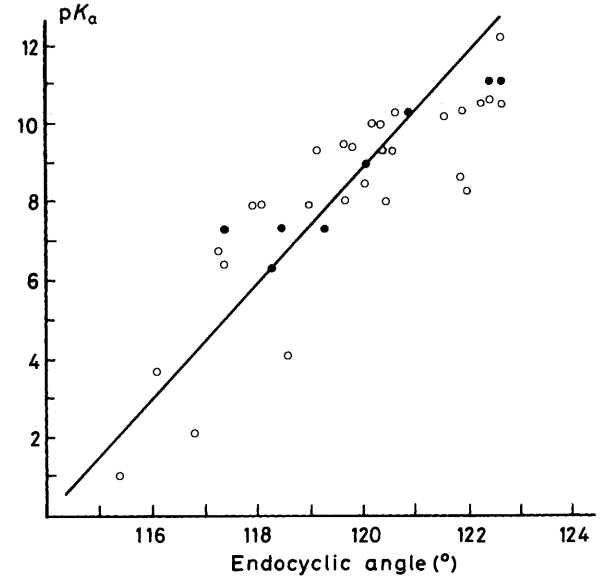


Figure 4. A scatter plot of pK_a *versus* endocyclic angle (α). The filled circles represent data for the new structures reported in this paper

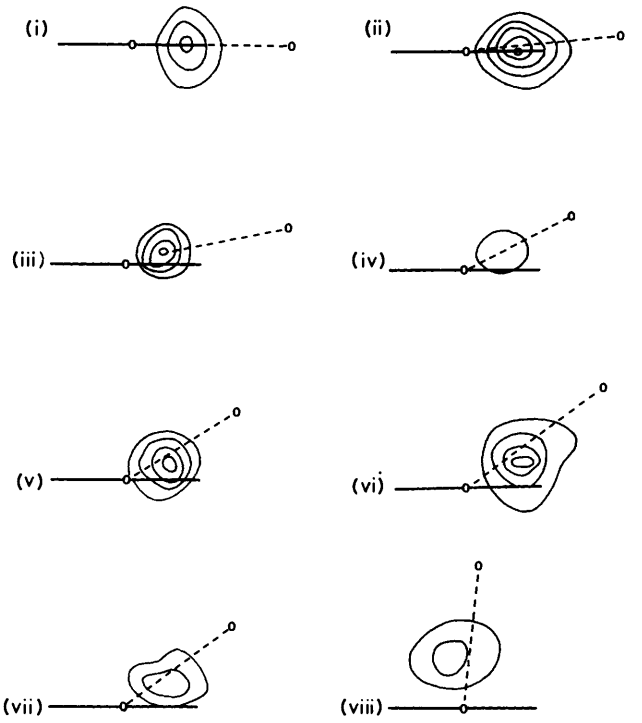


Figure 5. The difference electron density in the plane perpendicular to the C–O bond and containing the phenolic hydrogen for: (i) 2-methylphenol (**13**) at O(21); (ii) 2-methylsulphonylphenyl (**10**); (iii) 4-hydroxy-2-methylsulphonylphenol (**11**) at O(1); (iv) 2,6-di-isopropylphenol (**4**) at O(2); (v) 4-carboxy-2,6-di-isopropylphenol (**9**); (vi) 2-methylphenol (**13**) at O(31); (vii) 2,4,6-tri-iodophenol (**14**); and (viii) 2,6-di-isopropylphenol (**4**) at O(1). The heavy line represents the ring plane and the dashed line the projection of the O···O vector of the hydrogen bond. The electron density above 0.2e Å^{-3} is contoured at intervals of 0.1e Å^{-3}

merged because the space group is polar and the anomalous dispersion of Br is quite large ($\Delta f'' = 2.456$).

The structure was determined by Patterson and electron density methods and was refined by full-matrix least-squares. The origin along the *b*-axis was defined by fixing the *y*-co-ordinate of Br(1). Hydrogen atoms could not be located in the difference electron density at any stage in the refinement and those of the phenyl group were placed geometrically. The structure reported represents the correct absolute configuration of the crystal used.

Reversing the polarity of the structure gives a 0.5% increase in *R*. A 2.9e Å^{-3} peak, in the final difference map, was close to a bromine site.

4-*Ethyl*-2,6-*di-iodophenol* (**6**). After unsuccessful attempts to obtain good quality crystals from an ethanoic acid–H_2O (10:1) mixture and other less promising solvents, crystals were finally obtained by sublimation. At ambient temperature, *i.e.* only about 10 °C below their melting point, the crystals were reasonably good diffractors. The reflections were very broad and tended to overlap in the c^* direction and the data were collected by an ω scan instead of the more usual ω/2θ scan.

The structure was solved by Patterson and electron density methods and refined by full-matrix least-squares. Difficulty was experienced in the location of the carbon atoms of the ethyl groups and at no stage could hydrogen atoms be located in the difference electron density. The hydrogen atoms were placed geometrically and could not be refined. The ethyl carbon atoms, C(7) and C(8), could only be refined with isotropic temperature factors.

Subsequent attempts to obtain a structure at low temperature were unsuccessful. The crystals shatter on cooling below 0 °C, a temperature which is higher than that at which the low-temperature equipment was stable (~ −20 °C).

4-*Carboxy*-2-*iodophenol monohydrate* (**7**). Thin plate-like crystals were grown from a propanol–water (8:1) mixture. The structure was solved by Patterson and electron density methods and refined by full-matrix least-squares with isotropic then anisotropic temperature factors. The origin along the *c*-axis was defined by fixing the *z* co-ordinate of the iodine atom. The water molecule was found on the two-fold axis in a difference synthesis at $R = 0.089$ and all hydrogen atoms in a difference synthesis at $R = 0.033$. The hydrogen atoms were given isotropic temperature factors equivalent to those of the atoms to which

they were bound and were refined with soft constraints (C–H distances to be equal to their mean with an e.s.d. of 0.02 Å, C–C–H angles to be 120 ° with an e.s.d. of 2°).

4-*Carboxy*-2,6-*di-iodophenol* (**8**). Large, thin plate-like crystals were grown from aqueous ethanol. The structure was determined by Patterson and electron density methods. In the structure one molecule was found to lie across a mirror plane and another was about a two-fold axis giving two independent 'half' molecules in the asymmetric unit. The structure was refined by full-matrix least-squares. Phenyl hydrogens were located in the difference synthesis at $R = 0.045$ and were refined with soft constraints (see 4-carboxy-2-iodophenol). The final difference synthesis had diffuse electron density ($\sim 0.5e$ Å^{-3}) in regions where the hydrogens attached to oxygen atoms might be expected. These hydrogen atoms must be disordered in *Pmna* but this was the only indication that the true space group might be of lower symmetry. There were several larger peaks (up to 1.4e Å^{-3}) in the immediate region of the iodine atoms.

4-*Carboxy*-2,6-*di-isopropylphenol* (**9**). Large colourless crystals were grown from a mixture of propanol–water (8:1). The structure was determined by direct methods in space group $Pna2_1$. For the least-squares refinement the origin along the polar axis was defined by constraining the sum of the z co-ordinates to be constant. All hydrogen atoms were located from a difference synthesis at $R = 0.077$. The hydrogens attached to oxygen were placed at their observed positions and the rest were placed geometrically. The methyl hydrogen atoms were given a common isotropic temperature factor and the remaining four hydrogens individual temperature factors, all of which were refined, but the positional parameters were not. $(|F_o| - |F_c|)^2$ was remarkably constant as a function of $|F_o|$ and $\sin\theta/\lambda$ and no improvement on unit weights could be found.

2-*Methylsulphonylphenol monohydrate* (**10**). Crystals were grown as large colourless cubes from a propanol–water (8:1) mixture. The structure was solved by direct methods and refined by full-matrix least-squares. The hydrogen atoms were located in difference syntheses at $R = 0.11$ and $R = 0.05$. All were refined with soft constraints. Four isotropic temperature factors were used, one each for the phenyl, methyl, hydroxy, and water hydrogen atoms.

4-*Hydroxy*-2-*methylsulphonylphenol* (**11**). Large colourless octahedral crystals were grown from aqueous ethanol. After a false start with space group *Pbcm*, the structure was solved by direct methods in the non-centrosymmetric space group $Pbc2_1$, with two molecules to the asymmetric unit. The structure was refined by full-matrix least-squares with the origin along the c-axis, defined by constraining the sum of the z co-ordinates to be zero. Hydrogen atoms were located in difference syntheses calculated at $R = 0.077$ and 0.053. The hydrogen atom parameters were refined with soft constraints, and equivalent bond lengths in the two molecules were constrained to be equal to their mean.

2-*Iodophenol*–1,4-*benzoquinone* 2:1 *molecular complex* (**12**). Thin plate-like crystals were grown from a propanol–water (8:1) mixture. The structure was determined by Patterson and electron density methods. The structure was refined by full-matrix least-squares. Hydrogen atoms were observed in the difference electron density calculated at $R = 0.061$ but were placed geometrically and not refined.

2-*Methylphenol*–1,4-*benzoquinone* 2:1 *molecular complex* (**13**). When a warm dilute solution of a 2:1 molecular ratio of 2-methylphenol and *p*-benzoquinone in light petroleum (b.p. 60—80 °C) was cooled rapidly to 3 °C dark red, volatile, needle crystals of the 2:1 complex were obtained. *X*-ray data were collected at −50 °C using crystals sealed in capillary tubes, the ends of which were packed with an excess of the complex. Even at −50 °C isolated crystals in capillary tubes simply sublimed away.

The structure could not be solved with the available direct method routines. However, it was possible to obtain approximate positions of two six-membered rings from the Patterson function and hence generate a complete structural model by successive electron density syntheses. In the least-squares refinement a block diagonal approximation was used with three large blocks, one each for the derivatives from parameters of the quinone, and the two 2-methylphenol molecules. Hydrogen atoms were observed in a difference synthesis at $R = 0.10$, placed geometrically and included in the model but not refined. If, however, the atom to which a hydrogen was attached moved significantly in the refinement, the hydrogen was relocated.

2,4,6-*Tri-iodophenol–tetramethylpyrazine* 2:1 *molecular complex* (**14**). A large, opaque, irregularly-shaped crystal of the complex was grown by slow evaporation of an acetone solution of 2,4,6-tri-iodophenol (0.135 g) and tetramethylpyrazine (0.039 g). Preliminary diffraction data indicated space group *Cc* or *C*2/*c* and the latter was confirmed by the structure analysis. The structure was solved by direct methods to give the positions of the iodine atoms and subsequent electron density syntheses eventually revealed the complete non-hydrogen skeleton. Hydrogen atoms were observed in the difference electron density at $R = 0.07$, placed geometrically, and their positions adjusted when the atoms to which they were attached moved significantly. The methyl group at C(24) appeared to exist in two conformations.

4′-*Hydroxy*-2,3′,5′,6-*tetraiodo*-4-*methyldiphenyl ether* (**15**). Well formed crystals were obtained from a mixture of chloroform–light petroleum. (b.p. 60—80 °C) The positions of the iodine atoms were deduced from a Patterson function, assuming space group $P\bar{1}$ and the complete non-hydrogen skeleton developed from electron density maps. In the anisotropic least-squares refinement a large block approximation to the normal matrix was used in which the derivatives of parameters of each half of the molecule (divided at the ether linkage) were in separate blocks. The phenyl hydrogen atoms were observed in the difference electron density at $R = 0.045$ but the methyl hydrogens appeared as a torus of unresolved electron density. The phenyl positions of the hydrogen atoms were refined with soft constraints.

References

1 A. H. Greenberg, S. Najjar, and R. M. Blizzard, 'Handbook of Physiology,' Sect. 7; *Endocrinology*, 1974, **3**, 377.
2 J. H. Openheimer, W. H. Dillman, H. L. Schwartz, and H. C. Towle, *Fed. Proc., Fed. Am. Soc. Exp. Biol.*, 1979, **38**, 2154.
3 J. H. Openheimer, H. L. Schwartz, M. I. Surks, D. Koerner, and W. H. Dillman, *Recent Progr. Horm. Res.*, 1976, **32**, 529.
4 E. C. Jorgensen in 'Hormonal Proteins and Peptides,' vol. VI, Thyroid Hormones, ed. C. H. Li, Academic Press, New York, 1978, Chp. 3, p. 108; D. Ellis, J. C. Emmett, P. D. Leeson, and A. H. Underwood, 'C.R.C. Handbook of Hormones, Vitamins and Radiopaques,' ed. M. Verderame, C.R.C. Press, Florida, 1986, Chp. 3, p. 93.
5 S. W. Dietrich, M. B. Bolger, P. A. Kollman, and E. C. Jorgensen, *J. Med. Chem.*, 1977, **20**, 863.
6 T. A. Andrea, S. W. Dietrich, W. J. Murray, D. A. Kollman, and S. Rothenberg, *J. Med. Chem.*, 1979, **22**, 221.
7 M. G. Benson, D. Ellis, J. C. Emmett, P. D. Leeson, N. J. Pearce, V. P. Shah, and A. H. Underwood, *Biochem. Pharmacol.*, 1984, **33**, 3143.
8 L. Radom, W. J. Hehre, S. A. Pople, G. L. Carlson, and W. G. Fateley, *J. Chem. Soc., Chem. Commun.*, 1972, 308.
9 H. Forest and B. P. Dailey, *J. Chem. Phys.*, 1966, **45**, 1736.
10 T. Pedersen, N. W. Larsen, and L. Nygaard, *J. Mol. Struct.*, 1969, **4**, 59.
11 H. D. Bist and D. R. Williams, *Bull. Am. Phys. Soc.*, 1966, **11**, 826.
12 W. J. Hehre, L. Radom, and J. A. Pople, *J. Am. Chem. Soc.*, 1972, **94**, 1496.

13 L. Pauling, *J. Am. Chem. Soc.*, 1936, **58**, 94.
14 K. U. Ingold, *Can. J. Chem.*, 1960, **38**, 1092.
15 N. L. Allinger, J. J. Maul, and M. J. Hiikey, *J. Org. Chem.*, 1971, **36**, 2747.
16 G. L. Carlson, W. G. Fateley, A. S. Manocha, and F. F. Bentely, *J. Phys. Chem.*, 1972, **76**, 1553.
17 G. L. Carlson and W. G. Fateley, *J. Phys. Chem.*, 1973, **77**, 1157.
18 E. A. Allan and L. W. Reeves, *J. Phys. Chem.*, 1962, **66**, 613; E. A. Allan and L. W. Reeves, *ibid.*, 1963, **67**, 591; T. Schaefer, *ibid.*, 1975, **79**, 1888; S. W. Dietrich, E. C. Jorgensen, P. A. Kollman, and S. Rothenberg, *J. Am. Chem. Soc.*, 1976, **98**, 8310.
19 M. J. Aroney, M. G. Corfield, and R. J. W. Le Fevre, *J. Chem. Soc.*, 1964, 2954.
20 N. A. Puttnam, *J. Chem. Soc.*, 1960, 486, 5100.
21 L. J. Bellamy, G. Eglinton, and J. F. Morman, *J. Chem. Soc.*, 1961, 4762.
22 S. Singh and C. N. R. Rao, *J. Am. Chem. Soc.*, 1966, **88**, 2142.
23 L. Farah, G. Giles, D. Wilson, A. Ohno, and R. M. Scott, *J. Phys. Chem.*, 1979, **83**, 2455.
24 B. G. Somers and H. S. Gutowsky, *J. Am. Chem. Soc.*, 1963, **85**, 3065.
25 V. F. Bystrov and V. P. Lezina, *Opt. Spectrosc. (U.S.S.R.)*, 1964, **16**, 542.
26 T. M. Tribble and T. G. Traynham, *J. Am. Chem. Soc.*, 1969, **91**, 379.
27 F. H. Allen, S. H. Bellard, M. D. Brice, B. A. Cartwright, A. Doubleway, H. Higgs, T. Hummelink, B. G. Hummelink-Peters, O. Kennard, W. D. S. Motherwell, J. A. Rodgers, and D. G. Watson, *Acta Crystallogr., Sect. B*, 1979, **35**, 2331.
28 M. Maze-Baudet, *Acta Crystallogr., Sect. B*, 1973, **29**, 602.
29 G. Filippini, C. M. Gramaccioli, A. Mugnoli, and T. Palate, *Cryst. Struct. Commun.*, 1972, **1**, 305.
30 D. Antona, F. Longchambon, M. T. Vandenborre, and P. Becker, *Acta Crystallogr., Sect. B*, 1973, **29**, 1372.
31 C. Bavoux and A. Thozet, *Cryst. Struct. Commun.*, 1980, **9**, 1115.
32 A. Thozet and M. Perrin, *Acta Crystallogr., Sect. B*, 1980, **36**, 1444.
33 A. Neuman and H. Gillier-Pandraud, *Acta Crystallogr., Sect. B*, 1973, **29**, 1017.
34 S. Ashfaquzaman and A. K. Pant, *Acta Crystallogr., Sect. B*, 1979, **35**, 1394.
35 M. Perrin, C. Bavoux, and A. Thozet, *Acta Crystallogr., Sect. B*, 1977, **33**, 3516.
36 C. Bois, *Acta Crystallogr., Sect. B*, 1970, **26**, 2086.
37 K. Fukuyama, K. Ohkara, S. Kashino, and M. Haiso, 1973, *Bull. Chem. Soc. Jpn.*, 1973, **46**, 804.
38 M. Colapietro, A. Domenicano, and C. Marciante, *Acta Crystallogr., Sect. B*, 1979, **35**, 2177.
39 T. T. Harding and S. Wallwork, *Acta Crystallogr.*, 1953, **6**, 791.
40 T. H. Jordan and T. C. W. Mak, *J. Chem. Phys.*, 1970, **52**, 3790.
41 T. Higashi and K. Osaki, *Acta Crystallogr., Sect. B*, 1977, **33**, 607.
42 M. Perrin, S. Rantsordas, and A. Thozet, *Cryst. Struct. Commun.*, 1978, **7**, 59.
43 C. Bavoux, M. Perrin, and A. Thozet, *Acta Crystallogr., Sect. B*, 1980, **36**, 741.
44 C. Bavoux and A. Thozet, *Cryst. Struct. Commun.*, 1976, **5**, 259.
45 C. Bavoux and M. Perrin, *Cryst. Struct. Commun.*, 1979, **8**, 847.
46 C. Bavoux and M. Perrin, *Acta Crystallogr., Sect. B*, 1973, **29**, 666.
47 C. Bavoux and P. Michel, *Acta Crystallogr., Sect. B*, 1974, **30**, 2043.
48 T. Kagawa, R. Kawai, S. Kashino, and M. Haisa, *Acta Crystallogr., Sect. B*, 1976, **32**, 3171.
49 R. Kawai, S. Kashino, and M. Haisa, *Acta Crystallogr., Sect. B*, 1976, **32**, 1972.
50 E. K. Andersen and I. G. K. Andersen, *Acta Crystallogr., Sect. B*, 1975, **31**, 102.
51 F. Iwasaki, M. Sato, and A. Aihara, *Acta Crystallogr., Sect. B*, 1976, **32**, 102.
52 F. H. Herbstein and M. Kuffory, *Acta Crystallogr., Sect. B*, 1976, **32**, 387.
53 H. C. Brown, D. H. McDariel, and O. Hafliger, 'Determination of Organic Structures by Physical Methods,' 1955, ed. E. A. Braude and F. C. Nachod, Academic Press, New York, p. 567—662.
54 G. Kortum, W. Vogel, and V. Andrussow, 'Dissociation Constants of Organic Acids,' Butterworths, London, 1961.
55 J. Drahonovsky and Z. Vacek, *Collect., Czech. Chem. Commun.*, 1971, **36**, 3431.
56 J. C. Emmett, personal communication.
57 G. L. Gemmill, *Arch. Biochem. Biophys.*, 1955, **54**, 359.
58 R. A. Robinson, *J. Res. Natl. Bur. Stand.*, 1967, **71A**, 385.
59 A. Domenicano, A. Vaciago, and C. A. Coulson, *Acta Crystallogr., Sect. B*, 1975, **31**, 221; A. Domenicano, A. Vaciago, and C. A. Coulson, *ibid.*, p. 1630; A. Domenicano and A. Vaciago, *ibid.*, 1979, **35**, 1382; A. Domenicano, P. Mazzeo, and A. Vaciago, *Tetrahedron Lett.*, 1976, 1029.
60 A. Domenicano and P. Murray-Rust, *Tetrahedron Lett.*, 1979, 2283.
61 T. Kagawa, R. Kawai, S. Kashino, and M. Haisa, *Acta Crystallogr., Sect. B*, 1976, **32**, 3171.
62 T. A. Andrea, S. W. Dietrich, W. J. Murray, P. A. Kollman, E. C. Jorgensen, and S. Rothenberg, *J. Med. Chem.*, 1979, **22**, 221.
63 V. Cody, *Acta Crystallogr., Sect. B*, 1981, **37**, 1685.
64 P. A. Machin, D. Froud, J. N. Mills, O. S. Mills, and M. Elder, C.S.S.R.-Crystal Structure Search Retrieval, 1977, Daresbury Laboratory, Science Research Council.
65 E. K. Davies, CHEMGRAF User Manual, 1982, Oxford University.
66 P. Murray-Rust, personal communication.
67 A. C. T. North, D. C. Phillips, and F. S. Mathews, *Acta Crystallogr., Sect. A*, 1968, **24**, 351.
68 P. Main, M. M. Woolfson, L. Lessinger, G. Germain, and J. P. Declerq, MULTAN, 1978, 1980, Univs. of York, England, and Louvain, Belgium.
69 J. R. Carruthers and D. J. Watkin, CRYSTALS User Manual, 1978, 1980, Oxford Univ. Chem. Cryst. Lab.
70 D. T. Cromer and J. B. Mann, Los Alamos Scientific Report, LA-3816, 1968.
71 'International Tables for *X*-ray Crystallography,' Kynoch Press, Birmingham, 1974, vol. IV, p. 202.
72 J. Waser, *Acta Crystallogr.*, 1963, **16**, 1091.
73 J. S. Rollett, in 'Crystallographic Computing,' ed. F. R. Ahmed, Munksguard, 1970, p. 170.
74 J. R. Carruthers and D. J. Watkin, *Acta Crystallogr., Sect. A*, 1979, **35**, 698.

Received 1*st December* 1986; *Paper* 6/2307