Cycloaddition Reactions of Isonitrosoflavanone Esters with Schiff Bases and with Heteroaromatic Rings [1]

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Isonitrosoflavanone toluene-*p*-sulphonate reacts with Schiff bases to form (*o*-hydroxybenzoyl)imidazoles (6); in one case the regioisomeric pyrazole (10) was also isolated. Analogous reactions occur with pyridine and its methyl- and benzo-derivatives to form pyridoimidazoles [*cf.* (11)].

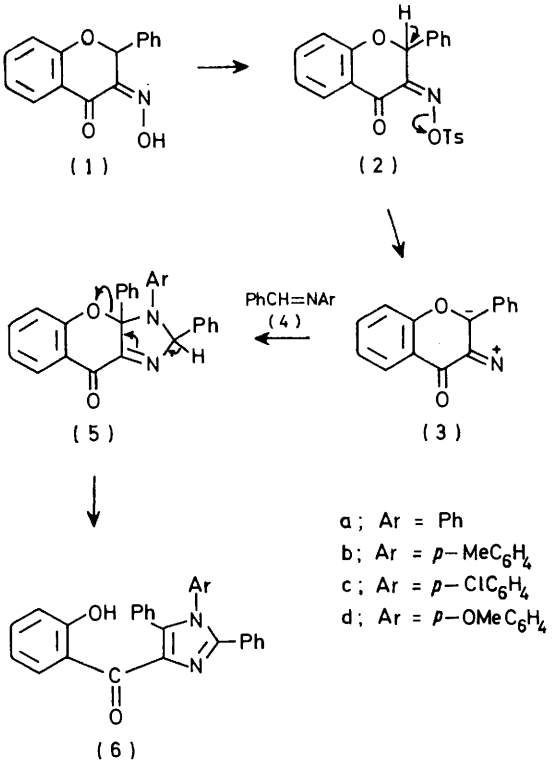
The chemical identities of (6b), (11c), and (13) were elucidated by an *X*-ray diffraction study, although each exhibits some conformational disorder in the crystalline state, associated with a rotation of the hydroxyphenyl moiety. The hydroxy-group can intramolecularly hydrogen-bond with either the carboxylate oxygen atom or the imidazo-moiety nitrogen. In compounds (6b) and (13) the hydroxy-group is primarily H-bonded to the oxygen, and in (11c) to the nitrogen.

ARISING out of a general study of isonitrosoflavanone glucosides by one of us,[2] it was found that isonitrosoflavanone esters reacted at the C=N bond of azaheteroaromatics [1a] and Schiff bases.[1b] The present paper gives full details of this and related work, including details of *X*-ray determinations of the structures of several compounds.

Reactions with Schiff Bases.—Isonitrosoflavanone (1) was converted *in situ* into the corresponding toluene-*p*-sulphonate (2) which reacts smoothly with a series of Schiff bases (4a—d) to yield 4-(*o*-hydroxybenzoyl)-imidazoles (6a—d) in yields of 18—56%. The structure of the *p*-tolyl derivative (6b) was determined unambiguously by *X*-ray crystallography (*vide infra*), those of the other products follow from elemental analysis and from spectral comparisons with (6b). In this respect u.v. spectra were particularly illuminating (see Table 1): each of the compounds shows bands at 213—214 nm ($\log_{10}$ ε 4.40—4.51) and at 263 nm ($\log_{10}$ ε 4.30—4.35) together with a pronounced inflection at 340 nm.

The reaction sequence could involve cycloaddition of the 1,3-dipolar species (3) to the Schiff base (4) to form intermediates (5) which undergo deprotonation and ring-opening to give the products (6). Alternatively the ambident anion (7) may add to the carbon atom of the Schiff base through the nitrogen atom [*cf.* (7b)]. Either sequence could obviously lead to two alternative regioisomers. Although in the cases of Schiff bases (4a—d) only the single imidazole-type regioisomers (6) were isolated, the analogous reaction with Schiff base (8), derived from anisaldehyde and *p*-chloroaniline, formed a separable mixture of the imidazole (9) together with the regioisomeric pyrazole (10). Ultraviolet spectra of (6a), (9), and (10) are shown in Figure 1: whereas that of (9) is similar to those of (6a—d), that of (10) is quite distinct with three peaks at 213 ($\log_{10}$ ε 4.44), 247 ($\log_{10}$ ε 4.34), and 283 nm ($\log_{10}$ ε 4.22). The structural assignments were made on this basis. Previous cycloadditions of azomethines to give imidazole derivatives [3] are of a different type.

Reactions with Pyridines.—Isonitrosoflavanone reacts as its acetate (m.p. 120—123 °C) or as the toluene-*p*-sulphonate or diphenylphosphoryl ester (prepared *in situ*) on heating with pyridine to give a single adduct analogous to those obtained from the Schiff's bases and which could possess structure (11a) or (12a). The presence of a hydroxy-group was indicated by the preparation of a



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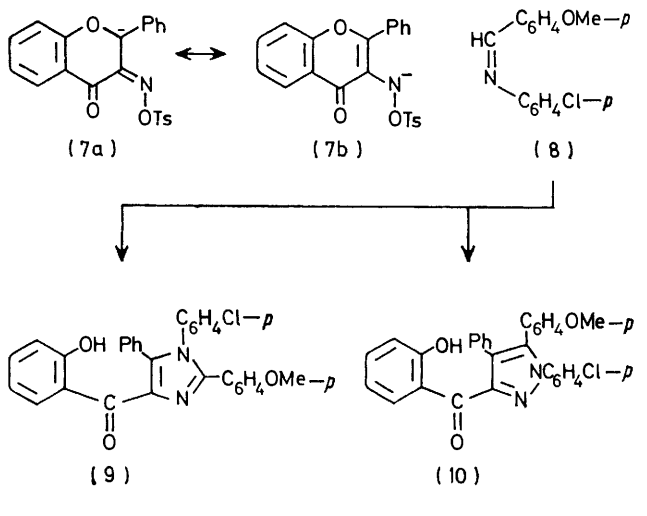
tosylate. The presence of a benzoyl group was indicated by the preparation of an oxime, and reduction with borohydride to the corresponding alcohol. Similarly, β-picoline and γ-picoline gave single adducts for which structures (11b/12b) and (11c/12c), respectively, must be considered.

For the adduct from γ-picoline, structure (11c) was established conclusively by *X*-ray crystallography (*vide*

infra). Ultraviolet (Table 2) and n.m.r. spectral comparisons (Table 3) demonstrate the similarity of all three adducts. Each compound exhibits as the neutral species three bands (or strong inflections) at 229—235



(log ε 4.47—4.55), 247—249 (4.38—4.48), and 352 (3.90—3.93). In the cations, these bands move to 212—225 (4.42—4.45), 269—272 (3.96—3.97), and 313—315 (3.78—3.85). This u.v. evidence strongly supports structures (11a) and (11b).

proton (influenced by the OH-group) shows as a doublet at δ 6.83—6.90 (*J* 9 Hz) and the 5′-proton as a triplet at δ 6.52—6.60 (*J* 7—8 Hz).

The 4-proton is found as a doublet (*J* 7 Hz) at δ 7.84—8.04 in the neutral species and at δ 8.26—8.36 in the cation. The 5-proton is likely to be the most

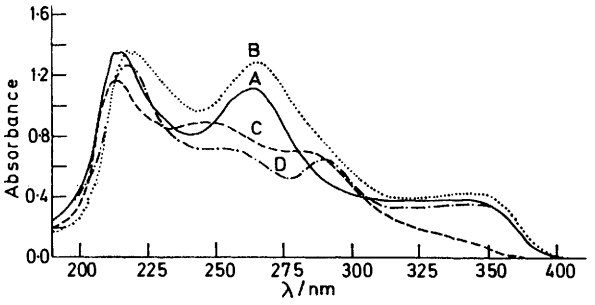


FIGURE 1 U.v. spectra (in EtOH) of: A, 4-(*o*-hydroxybenzoyl)-1,2,5-triphenylimidazole (6a); B, 1-(*p*-chlorophenyl)-4-(*o*-hydroxybenzoyl)-2-(*p*-methoxyphenyl)-5-phenylimidazole (9); C, 1-(*p*-chlorophenyl)-3-(*o*-hydroxybenzoyl)-5-(*p*-methoxyphenyl)-4-phenylpyrazole (10); and D, 2-(*o*-hydroxybenzoyl)-3-phenylimidazo[5,1-*b*]benzothiazole (16)

shielded of those on the pyridine ring: it occurs near δ 7.0 in the neutral molecules and near δ 7.4 in the cations. The 6-proton occurs for (11a) and (11b) near δ 7.4 in the neutral species and δ 7.8 in the cation. The 7-proton occurs as a doublet for (11a) at δ 7.73 in the neutral species and δ 8.18 in the cation; for (11c) the

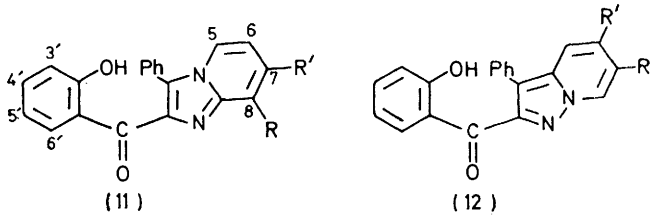
TABLE 1

U.v. spectra of 1,2-disubstituted-4-(*o*-hydroxybenzoyl)-5-phenylimidazoles

Compound	1-Substituent	2-Substituent	λ_{max}/nm	$\log_{10}\varepsilon$	λ_{max}/nm	$\log_{10}\varepsilon$	$\lambda_{infl.}$/nm
(6a)	Ph	Ph	214	4.40	263	4.30	340
(6b)	*p*-MeC_6H_4	Ph	213	4.51	263	4.33	340
(6c)	*p*-ClC_6H_4	Ph	213	4.40	263	4.30	340
(6d)	*p*-$MeOC_6H_4$	Ph	213	4.47	263	4.35	228
							340
(9)	*p*-ClC_6H_4	*p*-$MeOC_6H_4$	218	4.49	265	4.46	346 [a]

[a] Discrete band: $\log_{10}\varepsilon$ 3.97.

Tentative assignments of the n.m.r. spectra for neutral species and cations are given in Table 3. For both of the conformations favoured in the crystal (see later) the 6′-proton should be significantly deshielded: we find it as a doublet at δ 8.54—8.60 (*J* 8 Hz) in the neutral form



a; R = R′ = H; *b*; R = Me, R′ = H; *c*; R = H, R′ = Me

while all the other benzene ring protons (3′, 4′, 5′) absorb near δ 6.8. In the protonated form, the OH can no longer bond to the aza-nitrogen, and the molecule is probably no longer near-planar: consequently the 4′- and 6′-protons both absorb near δ 6.8, whereas the 3′-signal is a singlet at δ 7.45 in the neutral species and at δ 7.84 in the cation.

These detailed n.m.r. assignments also prove that the β-picoline product has the 7-methyl structure (11b) and not the possible isomeric 5-methyl structure (detailed examination of the n.m.r. spectra did suggest a small degree of contamination from the latter isomer).

Reactions with Polycyclic Heteroaromatic Compounds.—Isoquinoline, quinoline, and benzothiazole all react with isonitrosoflavanone toluene-*p*-sulphonate to give single adducts. Again the structure of the adduct from isoquinoline was shown by *X*-ray crystallography to be the imidazole-type regioisomer (13) (*vide infra*). The structure (14) follows for the quinoline adduct from a u.v. comparison (Table 2): the spectra of (13) and (14) are very similar to each other both as neutral forms and as cations; the spectra of the neutral forms are also very similar to those of the pyridine adducts (11a)—(11c).

The structure of the benzothiazole adduct is considerably less certain: the u.v. spectrum differs con-

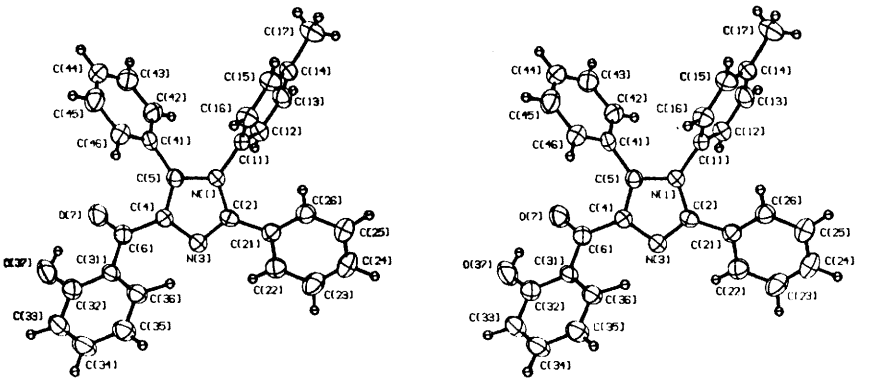
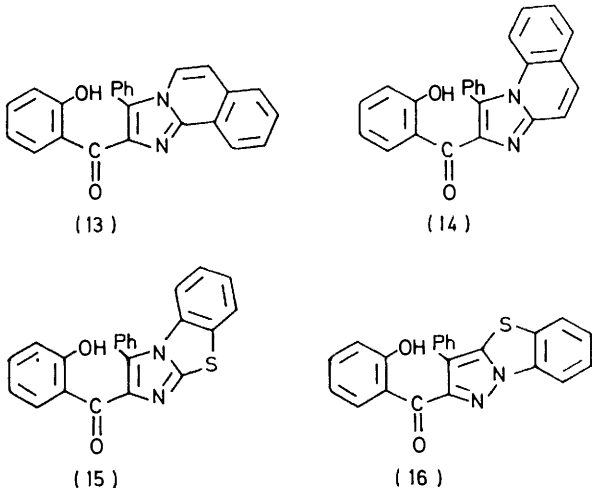


FIGURE 2 Conformation and atom-numbering scheme of 4-(*o*-hydroxybenzoyl)-2,5-diphenyl-1-(*p*-tolyl)imidazole (6b). Hydrogen atoms are numbered according to the non-hydrogen atom to which they are bonded

siderably from those of (13) and (14), and shows much greater similarity with that of the pyrazole (10) (*cf.* Figure 1): we therefore tentatively assign to it structure



(16) rather than (15). The nearest analogy to this ring system appears to arise in the intramolecular cyclisation of 2-(2-quinolyl)cyclohexanone oxime by Hamana *et al.*[4] leading to 7,8-benzo-1,2,3,4-tetrahydropyrido[1,2-*b*]indazole.

Description of the X-*Ray Crystallographic Structures*.—Each of the three structures (6b), (11c), and (13) determined in this series is statically disordered to a small degree. The disorder arises from the ability of the hydroxy-group to serve as an intramolecular proton donor to form a hydrogen bond with either the oxygen atom of the carboxylate group or with the nitrogen atom of the imidazo-moiety. In the structures of 4-(*o*-hydroxybenzoyl)-2,5-diphenyl-1-(*p*-tolyl)imidazole (6b) and 2-(*o*-hydroxybenzoyl)-3-phenylimidazo[2,1-*a*]isoquinoline (13), the hydroxy-groups are primarily hydrogen-bonded to the oxygen atoms (Figures 2 and 3), but there are strong indications that this group is bonded to the nitrogen atom in a few percent of the molecules. However, in the structure of 2-(*o*-hydroxybenzoyl)-7-methyl-3-phenylimidazo[1,2-*a*]pyridine (11c), the hydroxy-group, represented by O(19) in Figure 4, is principally bonded to the nitrogen atom. The disorder is more extensive in this case as evidenced from the electron density maps which show the hydroxy-group, O(19)P in Figure 4 to be bonded to the oxygen atom in approximately 10% of the molecules. Although this disorder is an interesting aspect of the structural studies, it cannot be described or accounted for by a simple model which can be satisfactorily refined by the least-squares method; the difficulty arises because the disorder involves not only a rotation of the hydroxyphenyl group but also a displacement such that the atoms of the two conformations are not exactly superimposed.

Because the effects of the disorder on the overall

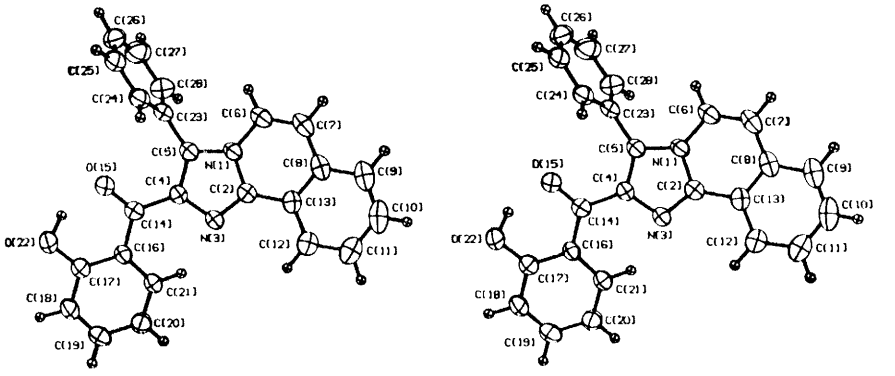


FIGURE 3 Conformation of molecule A (molecule B is similar) and atom-numbering scheme of 2-(*o*-hydroxybenzoyl)-3-phenylimidazo[2,1-*a*]isoquinoline (13)

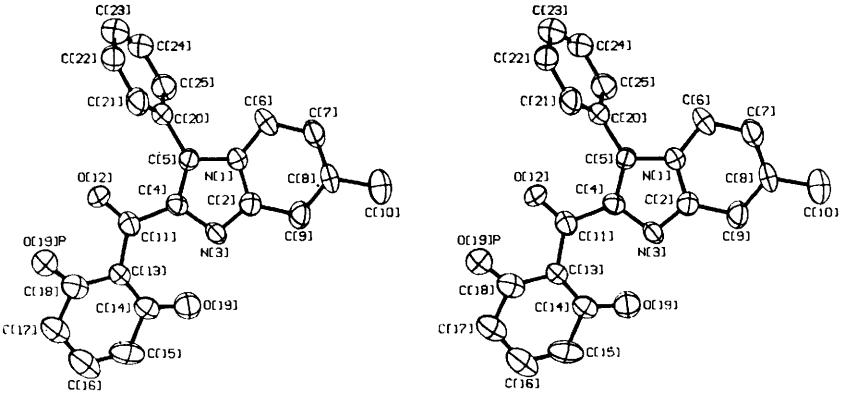


FIGURE 4 Conformation and atom-numbering scheme of 2-(*o*-hydroxybenzoyl)-7-methyl-3-phenylimidazo[1,2-*a*]pyridine (11c). O(19) and O(19)P represent the disordered hydroxy-oxygen atom. The disorder is also manifested in the large thermal ellipsoids of atoms C(15), C(16), and C(17)

geometry of the molecules cannot be ascertained, it is pointless to consider the geometries of these molecules in detail. The imidazo-moieties, however, do not appear to be appreciably affected; the bond distances and angles of these moieties agree well with those of imidazole itself (see Table 4) considering that some bond lengthening is to be expected in the present structures because of steric interactions between the neighbouring substituents. On the other hand, some bond parameters are clearly in error as a result of our attempting to fit an ordered model to a disordered structure. The best example is found in the benzoyl moiety of compound (11c) where the C–C

TABLE 2

U.v. spectra of adducts with heterocycles ($\lambda_{max.}$ and $\log_{10} \varepsilon$)

Compound	Neutral species (EtOH)			Cations (90% EtOH at pH 1)		
(11a)	234 (4.53)	248 (4.40)	352 (3.91)	212 * (4.46)	269 * (3.96)	313 (3.82)
(11b)	229 * (4.47)	247 (4.38)	352 (3.90)	221 * (4.42)	272 (3.97)	314 (3.78)
(11c)	235 (4.55)	249 (4.48)	352 (3.93)	225 * (4.45)	272 (3.97)	315 (3.85)
(13)		252 (4.73)	352 (3.98)		250 (4.61)	305 (3.98)
(14)		252 (4.72)	351 (3.99)		250 (4.60)	302 (3.97)
(16)	218 (4.41)	250 *	290 (4.11)			
			340 *			

* Inflection.

TABLE 3

^{1}H N.m.r. spectra for cycloadducts (chemical shifts p.p.m. on δ scale and coupling constants, Hz)

Cpd.	Species	5	6	7	8	3′	4′	5′	6′
(11a)	Free base	8.04 (d, 7)	[*ca.* 7.2]	[*ca.* 7.5]	7.73 (d, 9)	[*ca.* 6.8]	[*ca.* 6.8]	[*ca.* 6.8]	8.60(d, 8)
	Cation	8.36 (d, 7)	[*ca.* 7.4]	7.85 (t, 7)	8.18 (d, 9)	6.83 (d, 9)	[*ca.* 7.4]	6.60 (t, 8)	[*ca.* 7.4]
(11b)	Free base	7.84 (d, 7)	[*ca.* 6.9]	[*ca.* 7.4]	2.61 (Me)	[*ca.* 6.7]	[*ca.* 6.9]	[*ca.* 6.9]	8.56 (d, 8)
	Cation	8.26 (d, 7)	[*ca.* 7.4]	[*ca.* 7.7]	2.76 (Me)	6.90 (d, 9)	[*ca.* 7.4]	6.60 (t, 8)	[*ca.* 7.4]
(11c)	Free base	7.9 (d, 7)	[*ca.* 6.9]	2.35 (Me)	7.45 (s)	6.60 (d, 7)	[*ca.* 6.8]	[*ca.* 6.8]	8.54 (d, 8)
	Cation	8.28 (d, 6.5)	[*ca.* 7.3]	2.59 (Me)	7.84 (s)	6.88 (d, 9)	[*ca.* 7.3]	6.52 (t, 7)	[*ca.* 7.4]

TABLE 4

Geometries of the ' imidazo '-moieties of (6b), (11c), and (13) compared with that of imidazole [a]

	(6b)	(11c)	(13) [b] Molecule (A)	(13) [b] Molecule (B)	Imidazole
(*a*) Bond distances (Å)					
N(1)–C(2)	1.388(3)	1.36(1)	1.380(3)	1.390(3)	1.349
C(2)–N(3)	1.313(3)	1.31(1)	1.318(3)	1.317(3)	1.326
N(3)–C(4)	1.380(3)	1.40(1)	1.381(3)	1.376(3)	1.378
C(4)–C(5)	1.375(3)	1.35(1)	1.387(3)	1.383(3)	1.358
C(5)–N(1)	1.379(3)	1.41(1)	1.376(3)	1.388(3)	1.369
(*b*) Bond angles (°)					
C(5)–N(1)–C(2)	107.3(2)	106.1(5)	107.8(2)	107.0(2)	107.2
N(1)–C(2)–N(3)	110.9(2)	113.8(6)	111.4(2)	111.6(2)	110.9
C(2)–N(3)–C(4)	105.8(2)	103.8(6)	105.2(2)	105.3(2)	105.4
N(3)–C(4)–C(5)	111.0(2)	111.6(6)	111.1(2)	111.6(2)	109.8
C(4)–C(5)–N(1)	105.0(2)	104.8(6)	104.5(2)	104.5(2)	106.3

[a] S. Martinez-Carrera, *Acta Cryst.*, 1966, **20**, 783. [b] The unit cell of compound (13) has two molecules [(A) and (B)] per asymmetric unit.

bond lengths in the ring vary markedly from 1.33 to 1.48 Å, and where the C(14)–O(19) and C(18)–O(19)P distances are much too short: 1.28 and 1.21 Å, respectively.

EXPERIMENTAL

4-(o-*Hydroxybenzoyl*)-1,2,5-*triphenylimidazole* (6a).—Toluene-*p*-sulphonyl chloride (0.75 g) in CH_2Cl_2 (10 ml) was added dropwise to isonitrosoflavanone (1) and benzylideneaniline (0.71 g) in CH_2Cl_2 (15 ml) and Et_3N (0.5 ml) at −20 °C. When the formation of the toluene-*p*-sulphonyl ester of the isonitroso-compound was complete, as shown by t.l.c. (15—30 min), the mixture was allowed to reach and maintained at 20 °C for 12 h. The CH_2Cl_2 was removed at 40 °C at 15 mmHg, then benzene (10 ml) was added and the whole heated under reflux for 3 h. It was then poured into water (50 ml) at 0 °C, the organic layer separated, and the aqueous layer extracted with MeOAc (10 ml). The combined organic layers were dried ($MgSO_4$) and the solvents evaporated at 40 °C and 15 mmHg. The residue was dissolved in hot EtOH, filtered, evaporated, and benzene and light petroleum added to precipitate the *imidazole* (6a) which separated from MeOH as yellow prisms, m.p. 172—173 °C (0.30 g, 18%). After recrystallisation the m.p. was 177—179 °C (Found: C, 80.7; H, 5.1; N, 6.6. $C_{28}H_{20}N_2O_2$ requires C, 80.7; H, 4.8; N, 6.7%).

The following were prepared similarly: 4-(o-*hydroxybenzoyl*)-2,5-*diphenyl*-1-(p-*tolyl*)*imidazole* (6b) (58%), prisms from EtOH, m.p. 201—203 °C (Found: C, 80.7; H, 5.2; N, 6.9. $C_{29}H_{22}N_2O_2$ requires C, 80.9; H, 5.2; N, 6.5%); 1-(p-*chlorophenyl*)-4-(o-*hydroxybenzoyl*)-2,5-*diphenylimidazole* (6c) (10%), needles from EtOH, m.p. 234—235 °C (Found: C, 75.0; H, 4.7. $C_{28}H_{19}ClN_2O_2$ requires C, 74.6; H, 4.4%); 4-(o-*hydroxybenzoyl*)-1-(p-*methoxyphenyl*)-2,5-*diphenylimidazole* (6d) (22%), yellow needles from EtOH, m.p. 225—226 °C (Found: C, 77.9; H, 5.2; N, 6.4. $C_{29}H_{22}N_2O_3$ requires C, 78.0; H, 5.0; N, 6.3%).

1-(p-*Chlorophenyl*)-4-(o-*hydroxybenzoyl*)-2-(p-*methoxyphenyl*)-5-*phenylimidazole* (9) *and* 1-(p-*Chlorophenyl*)-3-(o-*hydroxybenzoyl*)-5-(p-*methoxyphenyl*)-4-*phenylpyrazole* (10).—Toluene-*p*-sulphonyl chloride (0.75 g) in CH_2Cl_2 (5 ml) was added gradually to isonitrosoflavanone (1) (1 g) in CH_2Cl_2 (15 ml) and Et_3N (1 ml) at −20 °C, and this temperature maintained until the isonitrosoflavanone had disappeared, as shown by t.l.c. (15—30 min). *p*-Methoxybenzylidene-*p*-choroaniline (1 g) and more Et_3N (0.5 ml) were added and the whole heated under reflux for 1 h. The CH_2Cl_2 was removed at 20 °C at 15 mmHg then benzene (15 ml) and Et_3N (0.5 ml) were added and the whole heated under reflux for 3 h. The reaction mixture was poured into water (50 ml), the organic layer separated, and the aqueous layer extracted with benzene (2 × 15 ml). The combined organic layers were dried ($MgSO_4$) and evaporated at 40 °C at 15 mmHg. The semi-solid product was dissolved in hot EtOH. On cooling, the *pyrazole* (10) (0.15 g, 7%) crystallised as prisms, m.p. 204—207 °C (Found: N, 5.8. $C_{29}H_{21}ClN_2O_3$ requires N, 5.8%). When set aside, the mother-liquor deposited the imidazole (9) (0.3 g, 16%) as pale yellow needles, m.p. 212—214 °C (Found: C, 71.2; H, 4.4; N, 5.9. $C_{29}H_{21}ClN_2O_3$ requires C, 71.5; H, 4.4; N, 5.9%).

Isonitrosoflavanone Acetate.—Isonitrosoflavanone (1) (3 g) was treated with Ac_2O (25 ml) at 0 °C for 12 h to give the *acetate* (2.05 g, 60%) which was washed with Et_2O and separated from benzene–light petroleum (b.p. 60—80 °C) as yellow prisms, m.p. 120—122 °C (Found: C, 69.4; H, 4.4; N, 4.8. $C_{17}H_{13}NO_4$ requires C, 69.1; H, 4.4; N, 4.7%).

2-(o-*Hydroxybenzoyl*)-3-*phenylimidazo*[1,2-a]*pyridine* (11a).—Toluene-*p*-sulphonyl chloride (0.75 g) in anhydrous pyridine (5 ml) was added slowly to isonitrosoflavanone (1) (1 g) in anhydrous pyridine (5 ml) at −10 °C. After 30 min, the whole was allowed to come to and maintained at 20 °C for 1 h, and then heated under reflux for 2 h. The cold dark red mixture was poured into H_2O (100 ml) at 0 °C. The oily product was separated, washed with H_2O (3 × 20 ml), and triturated with EtOH (10 ml) to give the *imidazopyridine* (11a) (1.1 g, 90%) which separated from EtOH as prisms, m.p. 150—151 °C (Found: C, 76.3; H, 4.6; N, 8.8 $C_{20}H_{14}N_2O_2$ requires C, 76.4; H, 4.5; N, 8.9%). *Picrate*, m.p. 219—220 °C, needles from EtOH (Found: C, 57.9; H, 3.3; N, 12.5. $C_{26}H_{17}N_5O_9$ requires C, 57.5; H, 3.2; N, 12.9%); *hydrochloride*, m.p. 224—226 °C, prisms from EtOH (Found: C, 68.1; H, 4.2; N, 7.9; Cl, 10.4. $C_{20}H_{15}ClN_2O_2$ requires C, 68.4; H, 4.3; N, 8.0; Cl, 10.1%); *oxime*, m.p. 274—279 °C, prisms from EtOH (Found: C, 72.9; H, 4.8. $C_{20}H_{15}N_3O_2$ requires C, 72.9; H, 4.6%); *toluene*-p-*sulphonate*, m.p. 183—184 °C, plates from EtOH (Found: C, 69.4; H, 4.5; N, 5.8. $C_{27}H_{20}N_2O_4S$ requires C, 69.2; H, 4.3; N, 6.0%).

The following were prepared similarly: 2-(o-*hydroxybenzoyl*)-8-*methyl*-3-*phenylimidazo*[1,2-a]*pyridine* (11b) (from 3-picoline) (58%), yellow needles, m.p. 138—139 °C from EtOH (Found: C, 77.3; H, 5.2; N, 8.4. $C_{21}H_{16}N_2O_2$ requires C, 76.9; H, 4.9; N, 8.5%); 2-(o-*hydroxybenzoyl*)-7-*methyl*-3-*phenylimidazo*[1,2-a]*pyridine* (11c) from 4-picoline (48%) yellow needles, m.p. 108—110 °C from aqueous EtOH or as plates from light petroleum (b.p. 80—100 °C) (Found: C, 76.5; H, 4.9; N, 8.6. $C_{21}H_{16}N_2O_2$ requires C, 76.9; H, 4.9; N, 8.5%).

2-(o,α-*Dihydroxybenzyl*)-3-*phenylimidazo*[1,2-a]*pyridine*.—$NaBH_4$ (0.2 g) in EtOH (70 ml) was added dropwise to the benzoyl derivative (11a) (1 g) in EtOH (70 ml) at −5 °C. After stirring for 2 h at −5 °C, 2N-aqueous HCl was added until pH 4. Volatiles were evaporated to 60 °C at 15 mmHg and H_2O (20 ml) was added. The solid product was crystallised from EtOH to give the *dihydroxy-compound* as a stable *ethanolate* (1.0 g, 90%), needles, m.p. 100—105 °C (Found: C, 72.7; H, 6.4; N, 7.9. $C_{20}H_{16}N_2O_2$,-EtOH requires C, 72.9; H, 6.1; N, 7.7%) (presence of 1 mole of ethanol shown in the ^1H n.m.r. spectrum). The nonsolvated compound had m.p. 144—145 °C and was characterised as the diacetate (90%) (prepared in Ac_2O–pyridine) needles, m.p. 185—186 °C from EtOH (Found: C, 71.9; H, 5.1; N, 6.9. $C_{24}H_{19}N_2O_4$ requires C, 72.0; H, 5.0; N, 7.0%).

2-(o-*Hydroxybenzoyl*)-3-*phenylimidazo*[2,1-a]*isoquinoline* (13).—Toluene-*p*-sulphonyl chloride (1 g) in Me_2CO (5 ml) was added dropwise to isonitrosoflavanone (1) (1 g) in Me_2CO (50 ml) at −10 °C. Isoquinoline (3 g) in Me_2CO (5 ml) was added. After 30 min at −10 °C, the mixture was heated under reflux for 2.5 h. Excess of isoquinoline was removed by steam distillation, the aqueous layer decanted, and the oily residue dissolved in EtOH (20 ml) and Et_2O (20 ml). The solution was dried ($MgSO_4$) and the solvents partially removed under vacuum to yield the *imidazoisoquinoline* (13) (0.3 g, 20%) which separated as yellow plates, m.p. 144—145 °C, from aq. EtOH (Found: C, 78.8; H, 4.2; N, 7.7. $C_{24}H_{16}N_2O_2$ requires C, 79.1; H, 4.4; N, 7.7%).

TABLE 5

	(6b)	(11c)	(13)
(*a*) Crystal data for (6b), (11c), and (13)			
Molecular formula	$C_{29}H_{22}N_2O_2$	$C_{21}H_{16}N_2O_2$	$C_{24}H_{16}N_2O_2$
M	430.51	328.37	364.40
Crystal class	Monoclinic	Orthorhombic	Monoclinic
Space group	$P2_1/n$	$P2_12_12_1$	$P2_1/c$
Z	4	4	8
Unit cell dimensions at −40 °C:			
a/Å	19.277(4)	11 509(2)	11.387(4)
b	9.600(2)	20.358(2)	23.160(9)
c	12.307(2)	7.028(1)	13.784(4)
β/°	92.31(1)		101.00(3)
u/Å^3	2 276	1 647	3 568
D_c at −40 °C (g cm^{-3})	1.256	1.324	1.357
D_m at 23 °C	1.273	1.303	1.333
μ(Mo-K_α)/cm^{-1}	0.86	0.93	0.94
(*b*) Details of the individual data collections and structure refinements			
Dimensions of crystal/mm perpendicular to	0.12 × 0.26 × 0.36 (10$\bar{1}$), (1$\bar{1}$0), (110)	0.23 × 0.25 × 0.25 × 0.48 (010), (110), (1$\bar{1}$0), (001)	0.21 × 0.38 × 0.54 (100), (001), (010)
No. reflections measured	3 350	2 187	5 593
2θ range (°)	4—48	4—55	4—48
No. of reflections used in refinement [$I > 2\sigma(I)$]	2 241	1 612	3 824
No. of variables	386	230	633
R	0.048	0.097	0.042

2-(o-*Hydroxybenzoyl*)-1-*phenylimidazo*[1,2-a]*quinoline* (14).—Isonitrosoflavanone (1) (0.5 g) in freshly distilled quinoline (5 ml) was treated essentially as for the pyridine analogue above, except that after treatment with water the oil was extracted with Et_2O, dried (Mg_2SO_4), and distilled to 75 °C at 0.2 mmHg. The residual *imidazoquinoline* (14) (0.2 g, 27%) separated as yellow plates, m.p. 144—145 °C, from EtOH (Found: C, 78.8; H, 4.6; N, 7.6. $C_{24}H_{16}N_2O_2$ requires C, 79.1; H, 4.4; N, 7.7%).

2-(o-*Hydroxybenzoyl*)-3-*phenylimidazo*[5,1-b]*benzothiazole* (16).—Prepared essentially as for the isoquinoline analogue (13), the *imidazobenzothiazole* (16) (14%) crystallised from EtOH–Me_2CO (1 : 1) as yellow needles, m.p. 196—197 °C (Found: C, 71.3; H, 3.9; N, 7.4; S, 8.6. $C_{22}H_{14}N_2O_2S$ requires C, 71.4; H, 3.8; N, 7.6; S, 8.7%).

TABLE 6

Positional parameters, with estimated standard deviations, for (6b)

Atom	*x*	*y*	*z*
(*a*) For non-hydrogen atoms			
N(1)	0.388 3(1)	0.458 7(2)	0.367 7(2)
C(2)	0.394 0(1)	0.424 8(3)	0.477 4(2)
N(3)	0.353 8(1)	0.504 6(2)	0.534 3(2)
C(4)	0.320 6(1)	0.592 3(3)	0.460 3(2)
C(5)	0.340 7(1)	0.565 4(3)	0.356 5(2)
C(6)	0.264 8(1)	0.687 7(3)	0.491 7(2)
O(7)	0.213 7(1)	0.702 2(2)	0.427 5(1)
C(11)	0.425 5(1)	0.398 2(3)	0.279 4(2)
C(12)	0.408 9(1)	0.266 5(3)	0.242 5(2)
C(13)	0.443 9(2)	0.211 8(3)	0.157 3(2)
C(14)	0.494 4(1)	0.286 9(3)	0.106 0(2)
C(15)	0.510 2(2)	0.418 7(3)	0.144 7(2)
C(16)	0.476 2(1)	0.474 6(3)	0.231 5(2)
C(17)	0.529 4(3)	0.227 6(6)	0.008 2(3)
C(21)	0.436 0(1)	0.311 0(3)	0.526 0(2)
C(22)	0.410 6(2)	0.245 2(3)	0.617 9(2)
C(23)	0.448 5(2)	0.141 5(3)	0.670 5(3)
C(24)	0.511 6(2)	0.102 0(3)	0.632 3(3)
C(25)	0.537 3(2)	0.166 3(3)	0.542 8(2)
C(26)	0.499 9(1)	0.270 9(3)	0.490 5(2)
C(31)	0.269 5(1)	0.765 3(3)	0.594 6(2)
C(32)	0.212 7(1)	0.846 7(3)	0.625 7(2)
C(33)	0.218 3(2)	0.928 1(3)	0.719 0(3)
C(34)	0.278 3(2)	0.927 7(3)	0.780 8(3)
C(35)	0.334 9(2)	0.847 8(3)	0.752 9(2)
C(36)	0.330 2(2)	0.767 4(3)	0.660 3(2)
O(37)	0.152 0(1)	0.850 8(2)	0.568 0(2)
C(41)	0.319 5(1)	0.630 3(3)	0.251 7(2)
C(42)	0.292 1(2)	0.552 3(3)	0.165 7(2)
C(43)	0.268 0(2)	0.616 1(4)	0.070 8(3)
C(44)	0.272 0(2)	0.759 1(4)	0.060 6(3)
C(45)	0.300 3(2)	0.837 5(3)	0.145 0(3)
C(46)	0.323 3(1)	0.773 2(3)	0.240 0(2)
(*b*) For hydrogen atoms			
H(12)	0.373(1)	0.218(2)	0.277(2)
H(13)	0.432(1)	0.122(2)	0.131(2)
H(15)	0.545(1)	0.472(2)	0.111(2)
H(16)	0.488(1)	0.569(2)	0.260(2)
H(17A)	0.567(2)	0.280(4)	−0.013(3)
H(17B)	0.542(2)	0.134(4)	0.019(3)
H(17C)	0.502(2)	0.233(3)	−0.053(3)
H(22)	0.368(1)	0.276(2)	0.639(2)
H(23)	0.428(1)	0.100(3)	0.740(2)
H(24)	0.538(1)	0.026(3)	0.669(2)
H(25)	0.584(1)	0.143(3)	0.514(2)
H(26)	0.518(1)	0.319(2)	0.431(2)
H(33)	0.177(1)	0.985(3)	0.734(2)
H(34)	0.283(1)	0.983(3)	0.844(2)
H(35)	0.373(1)	0.843(2)	0.796(2)
H(36)	0.370(1)	0.689(3)	0.643(2)
H(37)	0.159(2)	0.804(3)	0.513(2)
H(42)	0.288(1)	0.453(2)	0.172(2)
H(43)	0.247(1)	0.558(3)	0.012(2)
H(44)	0.253(1)	0.797(3)	−0.007(2)
H(45)	0.305(1)	0.943(3)	0.139(2)
H(46)	0.338(1)	0.830(3)	0.300(2)

Structural Analysis by X-Ray Single-crystal Diffraction.—Crystals of 4-(*o*-hydroxybenzoyl)-2,5-diphenyl-1-(*p*-tolyl)-imidazole (6b), 2-(*o*-hydroxybenzoyl)-7-methyl-3-phenylimidazo[1,2-*a*]pyridine (11c), and 2-(*o*-hydroxybenzoyl)-3-phenylimidazo[2,1-*a*]isoquinoline (13) were grown by slow evaporation from methanol. Data for the three compounds were collected by use of a Syntex $P2_1$ diffractometer equipped with a low-temperature apparatus which cooled the crystal to −40 °C. The radiation used throughout this study was Mo-K_α monochromated by a graphite crystal (λ 0.710 69 Å). Unit-cell parameters for each crystal were refined by the least-squares method using the Bragg angles of at least 37 reflections; the 2θ values for these reflections ranged from 18 to 25°. Crystal data for the three compounds are given in Table 5(*a*).

Intensity data were collected by the ω-scan technique with a scan range of 1.0°. The scan rate varied from 1.0 to

TABLE 7

Positional parameters, with estimated standard deviations, for (11c)

Atom	*x*	*y*	*z*
N(1)	0.339 0(5)	0.413 9(3)	0.562 3(10)
C(2)	0.238 4(6)	0.446 1(4)	0.600 7(13)
N(3)	0.250 3(6)	0.509 8(3)	0.613 2(9)
C(4)	0.369 4(6)	0.519 9(3)	0.581 3(11)
C(5)	0.425 8(6)	0.462 7(3)	0.548 9(12)
C(6)	0.351 2(7)	0.347 3(3)	0.549 8(12)
C(7)	0.246 2(8)	0.310 9(4)	0.576 9(15)
C(8)	0.142 1(7)	0.339 8(4)	0.616 1(12)
C(9)	0.132 3(7)	0.407 2(4)	0.627 8(14)
C(10)	0.039 4(8)	0.298 1(5)	0.651 0(14)
C(11)	0.421 8(7)	0.587 4(4)	0.581 7(12)
O(12)	0.524 4(4)	0.590 3(2)	0.558 4(11)
C(13)	0.351 1(6)	0.649 0(3)	0.601 6(10)
C(14)	0.235 0(7)	0.658 0(4)	0.570 2(11)
C(15)	0.188 0(9)	0.725 5(5)	0.570 4(14)
C(16)	0.254 1(11)	0.776 8(4)	0.617 0(16)
C(17)	0.376 4(9)	0.767 1(4)	0.659 5(14)
C(18)	0.416 4(8)	0.704 0(4)	0.647 2(13)
O(19)	0.156 4(5)	0.616 1(3)	0.525 1(11)
O(19)P	0.518(3)	0.706 (1)	0.690(4)
C(20)	0.550 4(7)	0.444 3(4)	0.512 4(14)
C(21)	0.631 2(7)	0.455 0(4)	0.663 3(15)
C(22)	0.745 3(7)	0.436 6(4)	0.628 3(20)
C(23)	0.776 9(8)	0.408 3(5)	0.450 4(17)
C(24)	0.695 6(9)	0.397 4(4)	0.319 0(18)
C(25)	0.579 8(8)	0.415 6(4)	0.349 9(13)

5.0° min^{-1} depending upon the number of counts accumulated in a rapid preliminary scan. Backgrounds were measured at both ends of the scan with ω displaced 1.0° from the K_α peak. The intensities of four standard reflections monitored after every 96 reflections showed only statistical variations for compounds (6b) and (11c). The intensities for compound (13) decreased by an average of 1% during data collection and a correction factor, as a function of exposure time, was applied. Intensities were corrected for Lorentz and polarisation effects but not for absorption.

TABLE 8

Positional parameters, with estimated standard deviations, for (13)

Atom	*x*	*y*	*z*
(*a*) For non-hydrogen atoms of molecule (A)			
N(1)	0.419 0(1)	0.158 25(7)	0.298.8(1)
C(2)	0.516 9(2)	0.194 49(9)	0.307 7(1)
N(3)	0.617 7(1)	0.165 12(7)	0.329 4(1)
C(4)	0.583 6(2)	0.107 82(9)	0.326 2(2)
C(5)	0.460 2(2)	0.102 39(9)	0.302 6(2)
C(6)	0.302 1(2)	0.179 06(10)	0.266 5(2)
C(7)	0.284 1(2)	0.236 06(11)	0.260 2(2)
C(8)	0.380 9(2)	0.276 71(10)	0.277 8(2)
C(9)	0.363 6(2)	0.336 69(11)	0.271 3(2)
C(10)	0.458 4(3)	0.373 28(11)	0.288 6(2)
C(11)	0.574 4(2)	0.352 68(11)	0.314 0(2)
C(12)	0.595 4(2)	0.294 39(10)	0.320 8(2)
C(13)	0.499 3(2)	0.255 94(9)	0.302 4(2)
C(14)	0.667 6(2)	0.059 02(10)	0.343 4(2)
O(15)	0.626 3(1)	0.011 04(7)	0.361 0(1)
C(16)	0.796 1(2)	0.064 06(9)	0.341 9(2)
C(17)	0.870 8(2)	0.015 94(10)	0.367 7(2)
C(18)	0.992 7(2)	0.020 22(10)	0.370 2(2)
C(19)	1.041 1(2)	0.070 79(11)	0.345 5(2)
C(20)	0.969 8(2)	0.118 35(9)	0.316 9(2)
C(21)	0.849 1(2)	0.115 00(9)	0.315 1(2)
O(22)	0.828 3(1)	−0.035 76(6)	0.309 6(1)
C(23)	0.379 2(2)	0.052 11(9)	0.290 6(2)
C(24)	0.366 6(2)	0.018 53(10)	0.371 6(2)
C(25)	0.290 7(2)	−0.028 24(10)	0.360 1(2)
C(26)	0.227 0(2)	0.042 47(11)	0.268 3(2)
C(27)	0.238 0(2)	−0.009 46(12)	0.187 5(2)
C(28)	0.313 5(2)	0.038 23(11)	0.198 2(2)

TABLE 8 (*Continued*)

(*b*) For non-hydrogen atoms of molecule (B)			
N(1)	0.575 6(1)	0.267 87(7)	0.063 7(1)
C(2)	0.499 5(2)	0.220 56(10)	0.046 3(2)
N(3)	0.559 6(1)	0.171 75(8)	0.051 2(1)
C(4)	0.678 3(2)	0.187 48(9)	0.071 2(2)
C(5)	0.691 7(2)	0.246 65(9)	0.080 8(2)
C(6)	0.534 2(2)	0.324 13(9)	0.061 9(2)
C(7)	0.415 4(2)	0.333 70(10)	0.042 5(2)
C(8)	0.330 2(2)	0.287 50(10)	0.025 7(2)
C(9)	0.206 3(2)	0.296 88(11)	0.010 5(2)
C(10)	0.128 6(2)	0.250 88(14)	−0.002 6(2)
C(11)	0.171 1(2)	0.194 56(12)	−0.002 3(2)
C(12)	0.292 3(2)	0.184 06(10)	0.012 4(2)
C(13)	0.372 5(2)	0.230 14(10)	0.027 6(1)
C(14)	0.778 8(2)	0.147 82(10)	0.070 7(2)
O(15)	0.877 0(1)	0.170 28(7)	0.064 9(1)
C(16)	0.770 1(2)	0.084 51(9)	0.076 9(2)
C(17)	0.874 8(2)	0.051 82(10)	0.084 1(2)
C(18)	0.872 2(3)	−0.007 68(11)	0.096 9(2)
C(19)	0.766 5(3)	−0.034 77(11)	0.100 2(2)
C(20)	0.661 5(2)	−0.003 75(11)	0.090 1(2)
C(21)	0.663 0(2)	0.055 68(10)	0.079 3(2)
O(22)	0.982 2(2)	0.075 35(8)	0,079 7(1)
C(23)	0.797 5(2)	0.284 48(9)	0.111 1(2)
C(24)	0.828 7(2)	0.325 23(9)	0.047 5(2)
C(25)	0.928 2(2)	0.359 83(9)	0.077 6(2)
C(26)	0.996 4(2)	0.353 94(10)	0.170 3(2)
C(27)	0.965 8(2)	0.313 41(11)	0.234 1(2)
C(28)	0.866 7(2)	0.278 40(9)	0.205 2(2)
(*c*) For hydrogen atoms of molecule (A)			
H(6)	0.241(2)	0.150 3(8)	0.252(1)
H(7)	0.203(2)	0.250 2(8)	0.249(1)
H(9)	0.278(2)	0.351 2(9)	0.255(1)
H(10)	0.446(2)	0.411 4(9)	0.282(2)
H(11)	0.643(2)	0.377 9(8)	0.331(1)
H(12)	0.678(2)	0.279 1(8)	0.339(1)
H(18)	1.040(2)	−0.013 9(9)	0.391(1)
H(19)	1.125(2)	0.073 0(7)	0.348(1)
H(20)	1.001(2)	0.154 3(8)	0.294(1)
H(21)	0.797(1)	0.146 7(7)	0.298(1)
H(22)	0.747(2)	−0.031 1(10)	0.381(2)
H(24)	0.415(2)	0.029 2(8)	0.436(1)
H(25)	0.283(2)	−0.053 3(9)	0.421(1)
H(26)	0.174(2)	−0.074 9(9)	0.259(1)
H(27)	0.192(2)	−0.014 9(9)	0.123(2)
H(28)	0.325(2)	0.061 5(8)	0.141(1)
(*d*) For hydrogen atoms of molecule (B)			
H(6)	0.595(2)	0.354 0(7)	0.077(1)
H(7)	0.386(1)	0.371 2(7)	0.042(1)
H(9)	0.178(2)	0.337 5(9)	0.007(1)
H(10)	0.042(2)	0.257 1(10)	−0.006(2)
H(11)	0.116(2)	0.160 3(8)	−0.013(1)
H(12)	0.324(2)	0.143 4(8)	0.016(1)
H(18)	0.948(2)	−0.029 2(10)	0.108(2)
H(19)	0.769(2)	−0.075 0(8)	0.112(1)
H(20)	0.586(2)	−0.021 8(8)	0.091(1)
H(21)	0.577(1)	0.074 5(7)	0.066(1)
H(22)	0.959(3)	0.119 9(14)	0.073(2)
H(24)	0.782(2)	0.328 0(8)	−0.019(1)
H(25)	0.947(1)	0.388 3(7)	0.031(1)
H(26)	1.068(2)	0.378 2(8)	0.193(1)
H(27)	1.014(2)	0.307 0(9)	0.301(1)
H(28)	0.846(2)	0.248 1(7)	0.250(1)

All the structures were solved by direct methods (MULTAN) and refined by the full-matrix least-squares method. In the initial stages of the refinements, all the non-hydrogen atoms of the imidazo-moieties were assigned carbon scattering factors; those two atoms of each moiety which refined with the lowest isotropic thermal parameters were considered to be nitrogen atoms.

With the completion of two cycles of refinement on the positional and anisotropic thermal parameters of the non-hydrogen atoms, difference maps were calculated in an effort to locate the hydrogen atoms. Until this point, it had been assumed that the three structures were ordered,

even though (6b) and (13) adopted a conformation in which the phenolic hydroxy-group was intramolecularly hydrogen-bonded to the oxygen atom of the carboxylate group while (11c) showed this group to be bonded to the nitrogen atom of the imidazo-moiety. The largest peak in the difference map ot (11c) clearly indicated however that the phenolic oxygen atom, O(19), was disordered; a subsequent difference map, in which O(19) was omitted from the structure-factor calculation, suggested that approximately 90% of the molecules adopted the conformation in which O(19) was hydrogen-bonded to N(3), while 10% had O(19) associated with O(12). As a consequence of the disorder of O(19), and thus of the molecule as a whole, it was impossible to distinguish clearly the locations of the hydrogen atoms and hence they were not included in the refinement. All non-hydrogen atoms were subsequently refined with anisotropic thermal parameters; O(19)P, with an occupation factor of 0.1, was the only exception and was refined with an isotropic parameter.

Difference Fouriers for (6b) and (13) revealed the locations of the hydrogen atoms for these structures. The hydrogen atoms, with isotropic thermal parameters, were then refined along with the non-hydrogen atoms. Although treated as ordered structures, sufficient evidence existed to conclude that both structures were conformationally disordered but to a smaller extent than (11c), probably of the order of a few percent. Such evidence comes in part from the unusual refinement of the hydrogen atoms H(36) of (6b) and of H(21)A and H(21)B of (13). H(36) refined to give an abnormally long (for *X*-ray analysis) C–H distance of 1.10 Å; it was also considerably out of the plane of the benzene ring, deviating by 0.19 Å. H(21)A and B gave somewhat more normal C–H distances of (0.95 and 1.06 Å), but refined with exceptional low thermal parameters. Additional evidence for the disorder was provided by the final difference maps; the largest residual peaks for (13) were found in the neighbourhood of H(21)A and B, while the second largest peak for (6b) was located near H(36). All these peaks had magnitudes of approximately 0.2 eÅ^{-3}.

The numerical details of the various refinements are given in Table 5. Final positional and thermal parameters for (6b), (11c), and (13) are given in Tables 6, 7, and 8 respectively. Computational details can be found elsewhere.[5,*]

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* Structure amplitudes and anisotropic thermal parameters for (6b), (11c), and (13) are given in Supplementary Publication No. SUP 22595 (66 pp.). For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1979, Index issue.

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