974. *Quinazolines. Part V.*[1] *Covalent Hydration in Quinazoline 3-Oxides.*

By W. L. F. Armarego.

Quinazoline 3-oxide, but not 4-methylquinazoline 3-oxide, forms a covalently hydrated cation in weakly acidic, and an anhydrous cation in strongly acidic, solution. The resonance-stabilised structure (V) for the hydrated cation is postulated. Covalent hydration is demonstrated in five of nine new substituted quinazoline 3-oxides studied. Ionisation constants and ultraviolet and infrared spectra of eleven quinazoline 3-oxides have been measured.

Covalent hydration in aqueous solution in the cation of quinazoline was demonstrated[2] by (i) a large hypsochromic shift (45 mμ), due to loss of conjugation, of the long-wavelength band in the ultraviolet spectrum on protonation, (ii) the rather high basic strength (pK_a 3·51), (iii) the formation of the unstable hydrated neutral species[3] on immediate (<1 second) neutralisation of the hydrated cation, and (iv) the change of ultraviolet spectrum with increasing acidity, owing to dehydration to the anhydrous cation, an effect caused by the decreasing activity of water, so that finally (at H_0 −4·4) a spectrum closely

[1] Part IV, Armarego, *J.*, 1962, 561.
[2] Albert, Armarego, and Spinner, *J.*, 1961, 2689.
[3] Albert, Armarego, and Spinner, *J.*, 1961, 5267.

similar to that of the anhydrous neutral molecule is obtained. Addition of water [2] takes place by addition of hydroxyl at position 4 (as shown by oxidation to 4-hydroxyquinazoline in dilute acid) with formation of a hydrated cation that is stabilised by an amidinium type of resonance (I). The structure (I) for this cation has been conclusively proved.[3] Covalent hydration can be hindered to a large extent by placing a methyl substituent at position 4; [2] so 4-methylquinazoline is a weaker base (pK_a 2·52) than quinazoline and the ultraviolet spectrum of the cation is similar to that of the anhydrous neutral molecule.

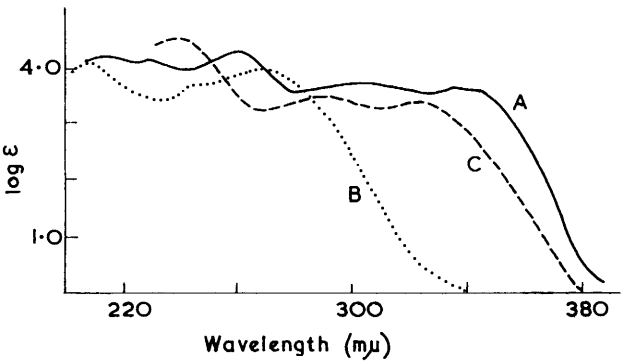


FIG. 1. (A) Neutral molecule (pH 7·0) and (B) cation of quinazoline 3-oxide (H_0 −1·12); (C) cation of 4-methylquinazoline 3-oxide (H_0 −2·06).

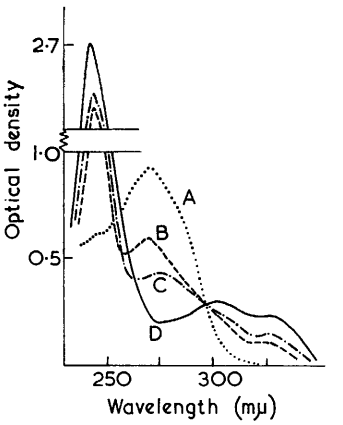
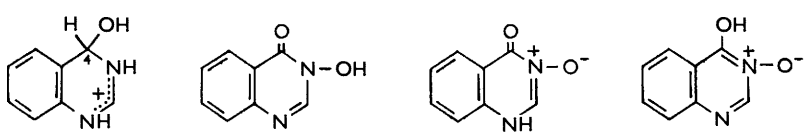


FIG. 2. Effect of acidity (H_2SO_4) on the spectrum of quinazoline 3-oxide.

(A) H_0 −1·12; (B) H_0 −2·06; (C) H_0 −4·40; (D) H_0 −5·65.

It has now been shown that quinazoline 3-oxide undergoes changes analogous to those of quinazoline on protonation. The neutral molecule of this oxide in water is anhydrous because the ultraviolet spectra in water and heptane [4] are closely similar, whereas the spectrum of the cation in aqueous acid reveals a large hypsochromic shift (66 mμ) of the long-wavelength band (336 mμ) present in the neutral molecule (see Fig. 1). The basic strength of quinazoline 3-oxide (pK_a 1·47) is improbably high when compared with that of isoquinoline 2-oxide (pK_a 1·01). The existence of a hydrated neutral molecule of quinazoline 3-oxide could not be demonstrated by rapidly neutralising a solution of the hydrated cation because the large heat evolution and the formation of a considerable amount of inorganic salts led to equivocal results, an effect due to the low pH at which such a very weak base becomes protonated. However, as for the hydrated quinazoline cation, the ultraviolet spectrum of quinazoline 3-oxide cation changes when the acidity is increased, owing to dehydration, and becomes more similar to that of the anhydrous

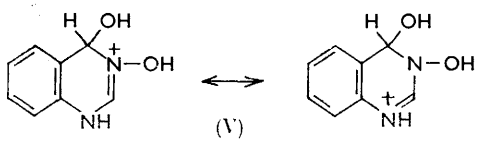


(I) (II) (III) (IV)

neutral molecule at H_0 −5·65 (see Fig. 2). This dehydrating effect is not a special property of sulphuric acid because at similar H_0 values hydrochloric acid produces the same change.

[4] Kubota and Miyazaki, *Chem. and Pharm. Bull.* (*Japan*), 1961, **9**, 498.

Quinazoline 3-oxide with hydrogen peroxide in acetic acid at 60° was reported [5] to give 4-hydroxyquinazoline 3-oxide whose structure was confirmed by reduction to 4-hydroxyquinazoline. This oxidation has now been repeated with one equivalent of hydrogen peroxide in 2·5M-sulphuric acid (to ensure complete formation of the hydrated cation): the oxide crystallised during 24 hr. at 20° in 53% yield. The infrared spectrum shows [6] a strong carbonyl stretching band at 1690 cm.$^{-1}$; thus the structure of the hydroxy-compound is (II) or (III), but not (IV). Structure (II) is the more probable because the formal negative charge on the oxygen atom would provide a better site for the mobile hydrogen atom. By analogy with quinazoline, therefore, the resonance-stabilised structure (V) can be written for the hydrated cation of quinazoline 3-oxide.



(V)

As in quinazoline a 4-methyl group is base-weakening and hinders hydration in the cation of quinazoline 3-oxide (see Table 1). The close similarity of the ultraviolet spectra of the neutral molecule in water and in heptane [4] excludes hydration in this species, and these spectra are also closely similar to that of 4-methylquinazoline 3-oxide cation in aqueous solution but not to that of quinazoline 3-oxide cation (see Fig. 1). Further, the cation spectrum of 4-methylquinazoline 3-oxide does not alter when the acidity is increased to H_0 −4·4.

This study was extended to derivatives in order to see how substituents in the benzene ring affected covalent hydration in the cations, with reference to the pattern previously observed in *Bz*-substituted quinazolines.[1] Nine new substituted quinazoline 3-oxides have been synthesised and some of their physical properties are shown in Table 1.

Ultraviolet Spectra of Substituted Quinazoline 3-Oxides.—The neutral molecules of all the substituted quinazoline 3-oxides listed in Table 1 have properties similar in general to those of the parent substance and are predominantly anhydrous in aqueous solution. The cations of 7-chloro- and 7-methyl-quinazoline 3-oxide are seen to be covalently hydrated because the long-wavelength bands for the neutral molecule were shifted by 86 and 74 mμ, respectively, to shorter wavelength. The cations of 4-methyl- and 4,7-dimethyl-quinazoline 3-oxides show hypsochromic shifts of 18 and 28 mμ, respectively, but these cations are anhydrous as their spectra are only slightly altered when the acidity of the solution is increased to H_0 −4·4. 7-Methoxy- and 4-methyl-7-methoxy-quinazoline 3-oxide cations are also anhydrous since the spectra measured at 2 pH units below their pK_a values and at H_0 −4·14 are closely similar; at H_0 −5·65, however, both substances absorbed at longer wavelengths (see Table 1). This is possibly due to formation of the dication, as was observed for quinazoline and its 4-methyl derivative.[2] These compounds do not decompose on storage for ½ hr. at 25° in sulphuric acid (H_0 −5·65), the single spots obtained on paper chromatography, after four-fold dilution with water, being identical with those of the starting material.

The cation of 5-methoxyquinazoline 3-oxide at H_0 −0·84 is a mixture of anhydrous and hydrated species; this is shown by the fact that the intensity of the long-wavelength band at 378 mμ is low (ε 443) and rises when the acidity is increased to H_0 −4·14. The spectrum at H_0 −5·65 is that of a mixture containing a high proportion of dication and is not that of a decomposition product, as was shown by regeneration of the starting material on dilution. Similarly, 6-methoxyquinazoline 3-oxide cation is a mixture of anhydrous and hydrated species but contains more of the anhydrous species than the 5-isomer does, as estimated by the relative intensities of the long-wavelength bands. At low acidity,

[5] Adachi, *J. Pharm. Soc. Japan*, 1957, **77**, 507.
[6] Dr. Spinner, personal communication.

TABLE 1.

Physical properties of quinazoline 3-oxides.

	Ionisation (H_2O, 20°)		Spectroscopy in water ‖			
Subst.	pK_a	mμ §	Species ¶	$\lambda_{max.}$ (mμ)	log ε	pH or H_0 **
(Parent)	1·47 ± 0·05	344	NM	214 + 230; 259; 300; 336 + *344*	4·21 + 4·15; 4·27; 3·75; 3·61 + *3·60*	7·0
			HC	207; *244* + 270	4·15; *3·74* + 3·92	−1·1
			AC	243; 300; 324	4·44; 3·45; 3·33	−5·65
4-Me	0·06 ± 0·05	256	NM	217 + 232; 255; 297 + *310*; *330* + *343*	4·27 + 4·35; 4·39; 3·79 + *3·70*; *3·51* + *3·44*	7·0
			AC	240; 288; 325	4·60; 3·53; 3·39	−2·06
			AC	241; 290; 327	4·55; 3·52; 3·44	−4·4
7-Me	1·00 ± 0·05 *	355	NM	217; 237; 261; 301; 347	4·30; 4·24; 4·43; 3·76; 3·69	7·0
			HC	215 + *223* + *231*; 249; 273	4·22 + *4·13* + *3·95*; 4·05; 3·87	−1·05
4,7-Me_2	0·40 ± 0·02 †	340	NM	*220* + 238; 256; *287* + 298; 335	*4·28* + 4·41; 4·42; *3·76* + 3·81; 3·60	7·0
			AC	245; 307 + *326*	4·60; 3·69 + *3·52*	−1·4
			AC	248; 314	4·53; 3·67	−4·4
7-Cl	1·49 ± 0·04 ‡	355	NM	219 + 242 + 259; 300 + *315*; 357	4·29 + 4·29 + 4·29; 3·89 + *3·72*; 3·66	6·0
			HC	220 + *224*; *253* + 271 ††	4·34 + *4·32*; *3·82* + 3·90	−1·6
5-MeO	1·20 ± 0·02	345	NM	213 + *232*; 277; 346	4·20 + *4·06*; 4·51; 3·66	7·0
			A + HC	210 + *220* + *234*; 263 + *294*; 378	4·09 + *4·04* + *3·79*; 3·98 + *3·74*; 2·65	−0·84
			DC	209; 267 + *280*; 357 + 417	4·31; 4·33 + *4·22*; 3·05 + 3·30	−5·65
6-MeO	0·58 ± 0·05 †	284	NM	218; *234*; 262; 313; 361	4·09; *4·15*; 4·60; 3·63; 3·59	7·0
			H + AC	209; 256; 285; 363	4·15; 4·25; 3·89; 2·99	−1·38
			AC	209; 255; 286; 365	4·17; 4·42; 3·81; 3·14	−4·9
7-MeO	0·66 ± 0·04 †	380	NM	223; *249* + 263; 300; 360	4·30; *4·31* + 4·35; 3·97; 3·88	5·0
			AC	*216*; 238; 260; 335	*4·23*; 4·20; 4·38; 3·90	−2·0
			DC	215; 275; *343* + 372	4·29; 4·35; *3·75* + 3·84	−5·65
4-Me-7-MeO	0·74 ± 0·03 †	330	NM	*220* + 251; 296 + *307*; 351	*4·22* + 4·49; 3·95 + *3·81*; 3·75	5·0
			AC	207; *239* + 256; 328	4·30; *4·28* + 4·43; 3·91	−1·85
			DC	217; *242* + 274; *335* + 376	4·31; *4·22* + 4·41; *3·69* + 3·86	−5·65
8-MeO	1·21 ± 0·02	280	NM	213; 236; 279; 331	4·36; 4·06; 4·54; 3·57	7·0
			HC	*230*; 266; 302	*3·86*; 3·89; 3·57	−0·87
			AC	266; 344; 381	4·48; 3·17; 3·19	−5·65
4-Me-8-MeO	0·02 ± 0·05 †	276	NM	216; 236; 275; 321	4·30; 4·23; 4·50; 3·58	7·0
			AC	261; *300* + *339* + 360	4·52; *3·11* + *3·33* + 3·35	−2·28
			AC	264 + *281*; *342* + 361	4·43 + *3·81*; *3·28* + 3·29	−4·9
4-HO			NM	220; 255; 310 + *322*	4·50; 4·18; 3·81 + *3·72*	7·0
Isoquinoline N-oxide	1·01 $		NM	218; 250; *287* + 294 + *305*; 337	4·37; 4·55; *3·93* + 3·97 + *3·81*; 2·88	7·0
			AC	212; 234; *272* + 281 + *292*; *320* + 332	4·37; 4·71; *3·46* + 3·52 + *3·37*; *3·49* + 3·56	−1·12

* Readings were taken 3 hr. after mixing. † Optical density of the cation was obtained by extrapolation. ‡ Readings were taken 5 min. after mixing. $ Jaffé and Doak, *J. Amer. Chem. Soc.*, 1955, **77**, 4441. § Analytical wavelength. ‖ Inflexions are in italics. ¶ NM = neutral molecule; HC = hydrated cation; AC = anhydrous cation; A + HC = mixture of anhydrous and hydrated cations; DC = containing a high proportion of anhydrous dication. ** Aqueous sulphuric acid was used for acid solutions. †† 15 min. after mixing.

8-methoxyquinazoline 3-oxide cation is predominantly hydrated, although the hypsochromic shift is only 29 mμ, and this cation is a mixture of hydrated and anhydrous species at H_0 −4·14—its spectrum is intermediate between those measured at H_0 −0·87 and at H_0 −5·65. A similar examination of the cation spectra of 8-methoxy-4-methylquinazoline 3-oxide showed that the cation is predominantly anhydrous at low and high acidity.

The cations of 4-methyl-, 7-chloro-, and 5- and 8-methoxy-quinazoline 3-oxide, therefore,

TABLE 2.

Infrared spectra (KBr disc) near the region 1200—1300 cm.$^{-1}$.*

Quinazoline	1210mw, 1235vw, 1270w, 1308s
Quinazoline 3-oxide	1198s, 1240vw, 1260w, *1283*m, 1335s
4-Methylquinazoline	1255w, 1273w
4-Methylquinazoline 3-oxide	1225vs, *1285*s
7-Methylquinazoline	1205mw
7-Methylquinazoline 3-oxide	1180s, 1260w, *1280*ms
5-Methoxyquinazoline	1218w, 1280s
5-Methoxyquinazoline 3-oxide	1218ms, *1256*vs, 1285s
6-Methoxyquinazoline	1225vs, 1245ms, 1275mw
6-Methoxyquinazoline 3-oxide	1227ms, 1242ms, *1258*s, 1278w
7-Methoxyquinazoline	1222vs, 1275m
7-Methoxyquinazoline 3-oxide	1222s, *1260*w, 1288mw
8-Methoxyquinazoline	1196m, 1219vw, 1270ms
8-Methoxyquinazoline 3-oxide	1190vs, *1251*ms, 1285ms
4-Methoxyquinazoline	1200m, 1305m
4-Methoxyquinazoline 1-oxide	1222ms, *1260*m, 1315s
4,7-Dimethylquinazoline 3-oxide	1214vs, 1220s, 1238w, 1250w, *1283*s
7-Methoxy-4-methylquinazoline 3-oxide	1200s, 1218vs, *1265*s
8-Methoxy-4-methylquinazoline 3-oxide	1197s, 1240vs, *1273*s

* The band intensity ratings are relative within the spectrum and do not permit comparisons between bands in different spectra. The bands probably attributable to the *N*-oxide frequency are in italic type.

are hydrated to the same extent as the corresponding quinazolines, whereas 7-methyl- and 6-methoxy-quinazoline 3-oxide are, respectively, more and less hydrated. A 4-methyl group also inhibits hydration of the cations of substituted *N*-oxides. Thus the general pattern of substituent effect on hydration in the *N*-oxides resembles that in the quinazoline series although the rather high acidities (because of the low pK_a values) necessary to protonate all the *N*-oxide molecules have a dehydrating effect.

Ionisation Constants.—The pK_a values in Table 1 are all equilibrium values and indicate that the 3-oxides are weaker bases than the corresponding quinazolines (cf. ref. 1) by 2—3 pK_a units. The average time for equilibration varied from 5 min. to 3 hr. Although it was shown that equilibrium pK_a values cannot be used for accurate comparative purposes,[7] the values in Table 1 conform to the general hypothesis that covalent hydration is accompanied by an increase in basic strength.

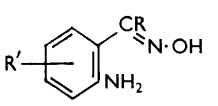
Infrared Spectra.—The *N*-oxide group absorbs in the 1200—1300 cm.$^{-1}$ region.[8] The bands of some quinazoline 3-oxides which appear in this region are given in Table 2, where data for the corresponding available quinazolines are included for comparison. It is seen that in this series the *N*-oxide group absorbs also in this region but that the bands are not always strong.

Synthesis.—All the quinazoline 3-oxides were prepared by the unequivocal method first described by Adachi [5] for the preparation of the parent substance, involving cyclisation of oximes of *o*-aminoaryl carbonyl compounds with boiling triethyl orthoformate (VI ⟶ VII). The time for complete reaction varied from 1 hr. when R = R′ = H to 3 hr. when R = H, R′ = Me. This synthesis was unsatisfactory when the oxime melted below 130° with decomposition (*i.e.*, below the boiling point of triethyl orthoformate): although the oxide (VII; R = H, R′ = 7-Cl) could be obtained in this way it was always contaminated with highly insoluble material, and the oxime (VI; R = Me, R′ = 4-Cl) which decomposes at 98—99° gave only a tar even when the reaction was carried out at 100°.

The starting materials were the substituted *o*-nitrobenzaldehydes or *o*-nitroacetophenones. The former were prepared as described in the literature or from the respective

[7] Armarego, *J.*, 1962, 4094.
[8] Shindo, *Pharm. Bull. Japan*, 1956, **4**, 460; Shindo, *Chem. and Pharm. Bull.* (*Japan*), 1958, **6**, 117; Katritzky, *Quart. Rev.*, 1959, **13**, 353.

o-nitrobenzenediazonium salt and formaldoxime.[9] *o*-Nitroacetophenones were also prepared by the latter method (with acetaldoxime in place of formaldoxime), or by the treatment of the *o*-nitrobenzoyl chloride with ethoxymagnesium malonate followed by



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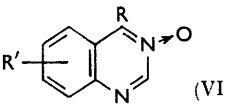

(VII)

hydrolysis.[10] *o*-Nitro-ketones were converted into the oximes by standard procedures and reduced catalytically to the amines (VI).

Experimental

Microanalyses were by Dr. J. E. Fildes and her staff. Evaporations were carried out in a rotary evaporator at 30—40°/15 mm., and the purity of materials was examined as before.[1] Quinazoline 3-oxide,[5] 4-methylquinazoline 3-oxide,[11] 3-,[12] 5-, and 6-methoxy-2-nitrobenzaldehyde,[1] 4-chloro-2-nitrobenzaldehyde,[13] 4-methoxy-2-nitro-aniline [14] and -acetophenone,[10] and 4-methoxyquinazoline 1-oxide [15] were prepared as described in the references cited.

Properties and analyses of the compounds prepared by the following typical methods are given in Table 3.

3-Methoxy-2-nitroacetophenone.—Dry 3-methoxy-2-nitrobenzoic acid (10 g.), phosphorus pentachloride (11·6 g.) (thionyl chloride was unreactive), and a few drops of phosphorus oxychloride were heated at 100° for 10 min. The excess of oxychloride was removed *in vacuo* and the crystalline residue dissolved in benzene (40 ml.) and recovered, and the whole process was repeated. The chloride was added slowly in benzene (40 ml.) to a stirred ethereal solution of ethoxymagnesium malonate [16] (from 10·4 ml. of diethyl malonate), stirring was continued for ½ hr., and the mixture decomposed with 4N-sulphuric acid. The benzene layer was dried (Na_2SO_4) and evaporated to dryness. The residue was refluxed in glacial acetic acid (17 ml.) and sulphuric acid (2·3 ml.; *d* 1·84) diluted with water (17 ml.), for 4 hr. The deposit of the acetophenone obtained on cooling recrystallised from ethanol, then having m. p. 128—130° (lit.,[17] 129—130°) (9·0 g., 91%).

4-Methyl-2-nitroacetophenone Oxime.—4-Amino-3-nitrotoluene (31·2 g.) in 18% hydrochloric acid (90 ml.) was diazotised at −2° to 0° with sodium nitrite (13·4 g.) in water (22 ml.). After 10 min. the solution was filtered, neutralised to Congo Red, and treated with sodium acetate solution. Solutions of (*a*) acetaldoxime (18 g.) in water (20 ml.) and (*b*) copper sulphate (10 g.), hydrated sodium sulphite (1·6 g.), and hydrated sodium acetate (130 g.) in water (120 ml.) were mixed and then added, with stirring, below the surface of the diazonium solution at <15°. After 1 hour's stirring the black insoluble material was separated and refluxed with an excess of hydrochloric acid (225 ml.; *d* 1·18) for 2½ hr., then steam-distilled; the first 3 l. of distillate were neutralised with sodium hydrogen carbonate and extracted with ether. The extract was dried (Na_2SO_4) and on evaporation gave an oil (10·6 g.), b. p. 79—83°/0·4—0·5 mm. This oil gave the oxime (3·3 g., 8%) by the method described below. Although the overall yield is low this method is better than the recorded seven-stage synthesis starting from 4-methylacetophenone.[18]

4-Methoxy- and 4-methyl-2-nitrobenzaldehyde oxime were prepared by the above method but with formaldoxime.

o-*Amino-oximes.*—The *o*-nitro-aldehyde or -ketone (2·0 g.) in ethanol (20 ml.) and hydroxylamine hydrochloride (5·0 g.) in water (20 ml.) were refluxed for 1 hr. On cooling (and dilution

[9] Beech, *J.*, 1954, 1297; see also Bruce and Fryer, *J.*, 1959, 4128.
[10] Osborn and Schofield, *J.*, 1955, 2100.
[11] Adachi, *J. Pharm. Soc. Japan*, 1957, **77**, 514.
[12] Albert and Hampton, *J.*, 1952, 4985.
[13] Spalding, Moersch, Mosher, and Whitmore, *J. Amer. Chem. Soc.*, 1946, **68**, 1596.
[14] Fanta and Tarbell, *Org. Synth.*, 1955, Col. Vol. III, p. 661.
[15] Yamanaka, *Chem. and Pharm. Bull.* (*Japan*), 1959, **7**, 152.
[16] Reynolds and Hauser, *Org. Synth.*, 1950, **30**, 70.
[17] Alford, Irving, Marsh, and Schofield, *J.*, 1952, 3009.
[18] Keneford, Morley, and Simpson, *J.*, 1948, 1702.

with water if necessary), the oxime crystallised (70—90%). The *o*-amino-oximes were prepared (70—90%) by hydrogenating the nitro-oximes (1·0 g.) with 5% palladium–charcoal (0·25 g.) in ethanol (100 ml.) at 1 atm.

Quinazoline 3-Oxides.—The *o*-amino-oximes (1·0 g.) and triethyl orthoformate (3 to 5 ml.) were refluxed for 3 hr. and cooled. The *oxides* (60—90%) were filtered off and recrystallised.

Spectra.—The ultraviolet spectra were measured with a Perkin-Elmer Spectracord instrument, model 4000A, and the maxima were checked with a Hilger Uvispek mark V manual

TABLE 3.

Compound	Cryst. from *	M. p.	Found (%) C	H	N	Formula	Required (%) C	H	N
2-Nitroacetophenone oximes									
3-MeO	C_6H_6	168—170°	51·6	4·9	—†	$C_9H_{10}N_2O_4$	51·4	4·8	13·3
4-MeO	,,	141—143	51·7	4·95	13·4	,,	,,	,,	,,
4-Me	EtOH	186—187	55·65	5·1	—†	$C_9H_{10}N_2O_3$	55·7	5·2	14·4
2-Aminobenzaldehyde oximes									
4-Me	C_6H_6	153—154	64·1	6·65	18·5	$C_8H_{10}N_2O$	64·0	6·7	18·65
5-MeO	EtOH	150 ‡	57·5	5·8	—†	$C_8H_{10}N_2O_2$	57·8	6·1	16·9
6-MeO	A	115—116	57·5	6·2	16·4	,,	,,	,,	,,
2-Aminoacetophenone oximes									
4-Me	A	122—123	66·1	7·1	—†	$C_9H_{12}N_2O$	65·8	7·4	17·1
3-MeO	C_6H_6	118—119	59·9	6·7	15·15	$C_9H_{12}N_2O_2$	60·0	6·7	15·55
Quinazoline 3-oxides									
7-Cl	EtOH	216—218 ‡	52·8	2·9	14·9	$C_8H_5ClN_2O$ §	53·2	2·8	15·5
7-Me	C_6H_6	153—154	67·2	5·05	17·3	$C_9H_8N_2O$	67·5	5·0	17·5
4,7-Me_2	,,	175—176	68·7	5·9	16·05	$C_{10}H_{10}N_2O$	69·0	5·8	16·1
5-MeO	EtOH	183—184	61·5	4·4	15·7	$C_9H_8N_2O_2$	61·4	4·6	15·9
6-MeO	,,	186—187	55·8	5·2	14·2	,, ¶	55·7	5·2	14·4
7-MeO	,,	200—201	61·7	4·8	15·8	,,	61·4	4·6	15·9
8-MeO	$COMe_2$	195—196	61·7	4·6	15·8	,,	,,	,,	,,
7-MeO-4-Me	A	145—146	62·6	5·4	14·45	$C_{10}H_{10}N_2O_2$	63·1	5·3	14·7
8-MeO-4-Me	C_6H_6	198—199	63·5	5·3	14·5	,,	,,	,,	,,

* A = C_6H_6–light petroleum (b. p. 40—60°). † N analyses (Kjeldahl) of oximes were low, even with added glucose. ‡ With decomp. § Found: Cl, 19·6. Reqd.: Cl, 19·6%. ¶ $+H_2O$.

instrument; infrared spectra were taken with a Perkin-Elmer 21 double-beam spectrophotometer. Ionisation constants were determined spectrophotometrically by the method used in this Department.[19]

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[19] Albert and Serjeant, "Ionization Constants," Methuen, London, 1962.