The Effects of Substitution on the Ultra-violet Absorption Spectra of Phenylpyrimidines.

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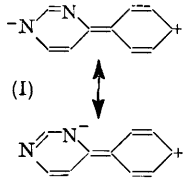
The spectra of 2- and 4-amino- and 2 : 4-diamino-5- and -6-phenylpyrimidines are described. The changes in the spectra resulting from (*a*) replacement of the 2-amino-group by a hydroxyl or mercapto-group, (*b*) substitution in the pyrimidine ring adjacent to the phenyl group, and (*c*) substitution in the phenyl group, are reported. An attempt is made to interpret the observations on the basis of the valency bond resonance concept of the absorption of light.

IN a previous communication (Maggiolo and Russell, *J.*, 1951, 3297), it was shown that the absorption spectra of 5- and 6-phenylpyrimidines could be interpreted if the assumption was made that the forms (I) and (II) made large contributions to the excited states. For any such conjugated resonance form to contribute to a state of a molecule the molecule must be essentially planar and it was shown that interference with the co-planarity of the pyrimidine and phenyl rings by substitution in the positions adjacent to their junction had a profound effect on the spectrum of the resulting compound.



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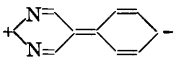

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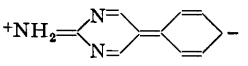

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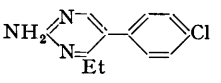


(IV)

The present communication deals with the effect on the spectra of these pyrimidines of substituents, in the 2- and/or the 4-position, capable of conjugation with the chromophoric system. The discussion centres chiefly on amino-compounds but reference is made on occasion to hydroxy- and mercapto-compounds. Braude, Jones, Koch, Richardson, Sondheimer, and Toogood (*J.*, 1949, 1890) restated the principles which govern the effect of substitution on the absorption spectra of organic compounds. The present paper follows these statements closely.

The introduction of 2-amino-group into a 5-phenylpyrimidine causes an increase in both the wave-length and the intensity of absorption (Table 1). A band at longer wave-length and with low intensity also appears. Such a substitution increases the conjugation, by incorporation of the amino-group into the conjugated system, as in (III), and thereby lowers the energy content of the resonance forms contributing mainly to the excited state, thus decreasing the excitation energy. The introduction of an ethyl group at the 6-position of the pyrimidine ring lowers both the wave-length and the intensity of the first band (conjugation band) of the spectrum and intensifies the second peak [see 2-amino-5-*p*-chlorophenyl-4-ethylpyrimidine (IV) in Table 1]. The introduction of the ethyl group does not

prevent the interannular conjugation but it appears to lessen it somewhat. This may be compared with the effect of an ethyl group on the spectrum of diphenyl (Braude, Sondheimer, and Forbes, *Nature*, 1954, **173**, 117). At the same time an increase in the

TABLE 1. *Absorption spectra of some amino-5-phenylpyrimidines.*

Pyrimidine	Absorption (mμ) (10^{-3} ε in parentheses)
5-Phenyl- [a]	Max. 256 (12·1)
2-Amino-5-phenyl-	Max. 263 (17·5); inflexion 300—320 (2·1)
2-Amino-5-*p*-chlorophenyl-4-ethyl-	Max. 252 (16·0); min. 295 (2·5); max. 305 (2·8)
4-Amino-5-phenyl-	Max. 248 (8·6); min. 270 (5·9); max. 282 (6·5)
2 : 4-Diamino-5-phenyl- [b]	Max. 256 (10·5); min. 277 (7·8); max. 294 (8·5)

[a] Maggiolo and Russell, *loc. cit.* [b] Russell and Hitchings, *J. Amer. Chem. Soc.*, 1951, **73**, 3763.

intensity of the long wave-length band is observed. Since this band coincides in wave-length with the bands seen in the spectra of 2-aminopyrimidines not having the 5-phenyl group it is believed to arise from considerable contributions from resonance forms such as (V) to transitions of the pyrimidine part of the molecule from the ground state to excited states. Thus when some hindrance is introduced, in addition to the whole molecule acting

(V)

as a conjugated chromophore each part exhibits its own chromophoric properties. Similar behaviour is reported for some diphenyls by Friedel, Orchin, and Reggel (*J. Amer. Chem. Soc.*, 1948, **70**, 199). The association of different bands in the spectrum with conjugated and unconjugated chromophores provides the key to the interpretation of the spectra of substituted phenylpyrimidines.

The spectra of both 4-amino- and 2 : 4-diamino-5-phenylpyrimidine (VI and VII) show two well-defined bands (Table 1). The origin of these is demonstrated by the introduction of another substituent in the pyrimidine or the phenyl ring adjacent to the ring junction. Thus 2 : 4-diamino-6-ethyl-5-phenylpyrimidine (VIII) shows only one band in its spectrum ($\lambda_{max.}$ 288 mμ, see Table 3), the shorter wave-length band of the conjugated chromophore having been eliminated. This type of spectrum is shown by all 5-phenylpyrimidines with a 4-amino-group and a 6-alkyl group (Table 2). Replacement of one of the *o*-hydrogen

TABLE 2. *Some hindered amino-5-phenylpyrimidines.*

5-Phenylpyrimidine	Absorption (mμ) (10^{-3} ε in parentheses)
2 : 4-Diamino-6-methyl-	Max. 240 (8·0); min. 265 (4·9); max. 288 (8·0)
2 : 4-Diamino-6-methyl-5-*p*-chloro-	Inflexion *ca.* 250 (9·0); min. 265 (800); max. 285 (9·9)
2 : 4-Diamino-6-ethyl-	Inflexion 250 (8·0); min. 265 (6·4); max. 288 (9·5)
2 : 4-Diamino-6-methyl-5-*o*-chloro [a]	Min. 260 (4·9); max. 288 (8·0)

[a] Russell and Hitchings, *loc. cit.*

TABLE 3. 2 : 4-*Diamino*-5-*o*-*substituted phenylpyrimidines.*

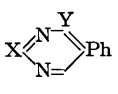
ortho-Substituent	Absorption (mμ) (10^{-3} ε in parentheses)
Hydrogen [a]	Min. 238 (5·5); max. 256 (10·5); min. 277 (4·8); max. 294 (8·5)
Fluorine	Min. 248 (5·8); max. 254 (4·5); min. 275 (5·9); max. 292 (7·0)
Chlorine [a]	Min. 249 (6·5); max. 255 (6·7); min. 272 (5·9); max. 292 (7)
Bromine	Min. 245 (5·5; broad; max. 292 (6·9)
Methyl (*p*-chlorophenyl)	Inflexion 250 (12·5); min. 275 (7·6); max. 290 (8·8)

[a] Russell and Hitchings, *loc. cit.*

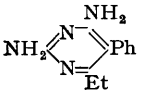
atoms of the benzene ring causes partial or complete loss of the conjugation band (Table 3). It is seen that when the substituent is fluorine or chlorine (IX) the effect is mainly on the intensity of this band with little or no alteration in wave-length, but when the much larger bromine is placed in this position the conjugation band is completely lost and the spectrum resembles that of 2 : 4-diaminopyrimidine with no aryl group at position 5 (Table 4). Since the effect of fluorine and chlorine is in the main on the intensity rather than on the

wave-length of absorption, the transitions must belong to the group described by Braude, Sondheimer, and Forbes (*loc. cit.*) as being between non-planar ground states and planar excited states. Such steric effects are looked upon as comparatively weak. Bromine has a much greater effect, as does an *o*-methyl group in conjunction with *p*-chloro (X). Guy (*J. Chim. phys.*, 1949, **46**, 469) has calculated the effect of variations in the angle of twist (θ) on resonance conjugation in the diphenyl series. For values of θ between 0° and $\pi/8$ the conjugation is little affected; in the range $\pi/8$ to a value between $\pi/4$ and $3\pi/8$ it diminishes rapidly while for greater angles it is completely inhibited. Thus fluorine and chlorine must be placed in the first or second of these groups while bromine and methyl must fall in the third.

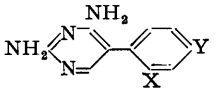
A comparison of the spectra of 2 : 4-diamino-6-methyl-5-phenylpyrimidine and its 5-*p*-chloro-analogue is interesting. The former shows a definite conjugation band ($\lambda_{max.}$ 240; Table 2) which is not shown by the latter. Since the *p*-chlorine atom cannot directly



(VI; X = H, Y = NH_2)
(VII; X = Y = NH_2)



(VIII)



(IX; X = Halogen, Y = H)
(X; X = Me, Y = Cl)

influence the steric situation at the ring junction the observed effect may be due either to electronic influences or to a repulsive force operating on the *o*-hydrogen atoms. If the methyl group is replaced by an ethyl group to give (VIII), the conjugation band is not visible. Braude, Sondheimer, and Forbes (*loc. cit.*) give figures from the diphenyl series which show the steric effect due to ethyl to be greater than that due to methyl. As might be expected, the spectrum of 2 : 4-diamino-5-*o*-chlorophenyl-6-methylpyrimidine (Table 2) is very similiar to that of a 2 : 4-diaminopyrimidine (Table 4). To summarise, one substituent in any of the four positions of a 5-phenylpyrimidine adjacent to the ring junction causes some loss of planarity in the ground state but less in the excited states. When two of these positions are substituted there is a gradation from little effect on the planarity of the excited state to complete loss of planarity in both states while three substituents cause a definite non-planar structure.

TABLE 4. *Absorption spectra of some simple aminopyrimidines.*

Pyrimidine	Absorption (mμ) (10^{-3} ε in parentheses)
2-Amino-	Max. <230 (>13); min. 251 (0·4); max. 296 (3·0)
4-Amino-	Max. 235 (11·5); min. 255 (2·9); max. 270 (3·8)
2 : 4-Diamino-6-methyl-	Max. *ca.* 230 (*ca.* 8·0); min. 253 (1·9); max. 280 (6·9)
2 : 4-Diamino-5-benzyl-6-methyl-	Max. <230 (>16); min. 260 (2·5); max. 288 (7·9)

When the 2-substituent of the pyrimidine ring is changed, the wave-length of the conjugation band increases in the series OH (250 mμ) < NH_2 (260 mμ) < SH (283 mμ). This is the reverse of the order of the electronegativities of the elements O, N, S (Pauling, " The Nature of the Chemical Bond," Cornell Univ. Press, New York, 1943, p. 60). This indicates the importance of structure (II) to the excited states where the atom attached to the 2-position carries a positive charge.

p-Substituents in the phenyl group also have an effect on the wave-length of the conjugation band (Table 5), but this is small except for the *p*-nitrophenyl compound. Here

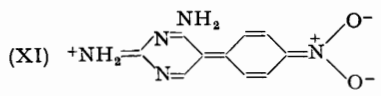
TABLE 5. *Effect of* para-*substituent on wave-length of conjugation band of 2 : 4-diamino-5-phenylpyrimidines.*

p-Substituent	OMe	H	Me	NH_2	Cl	Br	NO_2
$\lambda_{max.}$ (mμ)	259	260	260	265	268	270	345

forms such as (XI) are possible. These structures have a favourable arrangement of electron-donor and electron-acceptor groups. Contributions from forms such as (XI) would be expected to lower the energy of the excited state considerably and so increase the wave-length of the conjugation band. Actually this band falls at 345 mμ in this case. The

origin of this band is demonstrated by introducing a substituent (methyl) in the 6-position. 2 : 4-Diamino-6-methyl-5-*p*-nitrophenylpyrimidine (XII) shows no band at this wave-length [XI : max. 230 (ε 13,400), 295 (ε 6500), 345 (ε 13,400); min. 272 (ε 2700), 311 mμ. XII : max. 231 (ε 13,200), 280 (ε 10,500); min. 255; inflexion 310—340 mμ (ε *ca.* 2500)].

Introduction of an amino-group into the 2- and/or 4-position of 4(6)-phenylpyrimidines causes different phenomena (Table 6). 4-Phenylpyrimidine shows only one intense band at



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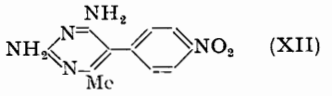


(XII)

273 mμ (Maggiolo and Russell, *loc. cit.*), but 2-amino-4- and 4-amino-2-phenylpyrimidine do not show this band. In the last two compounds the spectrum is resolved into the usual two-banded form of an aminopyrimidine (cf. Table 4). Obviously in the 4(6)-phenylpyrimidines a 2- or 4-substituent cannot combine with the conjugated chromophore to lower the energy of the excited state; rather it favours excited states similar to (V) at the expense of forms such as (I). Since the spectrum owes little or nothing to interannular

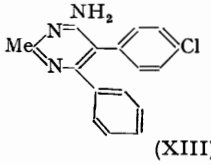
TABLE 6. *Some 4(6)-phenylpyrimidines.*

Pyrimidine	Absorption (mμ) (10^{-3} ε in parentheses)
4-Methyl-6-phenyl- [a]	Max. 243 (18·0)
2-Amino-4-methyl-6-phenyl-	Max. 240 (15·8); min. 278 (2·5); max. 315 (6·0)
2-Amino-5-cyano-4-phenyl- [b]	Max. 255 (23·1); min. 293 (3·2); max. 315 (4·0)
4-Amino-2-methyl-6-phenyl-	Max. 240 (27·0); min. 276 (6·0); max. 288 (7·0)
2 : 4-Diamino-6-phenyl-	Max. 240 (25·0); min. 270 (4·0); max. 305 (8·0)
2 : 4-Diamino-6-*p*-chlorophenyl- [c]	Max. 245 (16·0); min. 275 (2·0); max. 310 (4·0)

[a] Maggiolo and Russell, *loc. cit.* [b] Russell and Whittaker, *J. Amer. Chem. Soc.*, 1952, **74**, 1310. [c] Russell and Hitchings, *loc. cit.*

conjugation, steric hinderance to the coplanarity of the rings has little, if any, effect on the spectrum. The bands in the 4(6)-phenylpyrimidine spectra are all shifted slightly to the longer wave-lengths when compared with those of Table 4.

The spectra of some diphenylpyrimidines were also measured. 4-Amino-5-*p*-chlorophenyl-2-methyl-6-phenylpyrimidine (XIII) showed no evidence of conjugation between the rings [max. <230 (ε 27,000); min. 276 (ε 6500); max. 295 mμ (ε 7400)]. This is not surprising since the ultra-violet spectrum of *o*-terphenyl (XIV) shows no evidence of conjugation (Woods *et al.*, *J. Amer. Chem. Soc.*, 1950, **72**, 3221). The lack of conjugation in *o*-terphenyl is readily understood: Karle and Brockway (*ibid.*, 1944, **66**, 1977) have shown, by electron-diffraction, that rings *a* and *c* are parallel and inclined to ring *b* at an angle of 45°.



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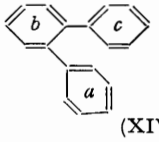

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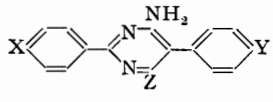

(XV; X = Me, Y = Cl, Z = H)
(XVI; X = Y = H, Z = Me)

The spectrum of 4-amino-5-*p*-chlorophenyl-2-*p*-tolylpyrimidine (XV) shows a strong bifurcate conjugation band [max. 255 (ε 17,000), 267 (ε 16,400), 310 (ε 14,500); min. 262 (ε 16,200), 292 mμ (ε 12,500)]. 4-Amino-6-methyl-2 : 5-diphenylpyrimidine (XVI), on the other hand, shows a spectrum quite similar to that of (XIII), illustrating the steric effects of the 6-methyl group.

EXPERIMENTAL

Compounds.—The majority of the compounds used have been described previously (Russell and Maggiolo, *loc. cit.*; Russell and Hitchings, *loc. cit.*). 2 : 4-Diamino-5-benzyl-6-methylpyrimidine (Table 4) was described by Falco, Du Breuil, and Hitchings (*J. Amer. Chem. Soc.*,

1951, **73**, 3758). Other *compounds* not previously described were prepared by the application of well-known methods. They are listed in the annexed table.

No.	Pyrimidine	M. p.	Formula	Reqd. (%): C	Reqd. (%): H	Found (%): C	Found (%): H
1	2-Amino-5-*p*-chlorophenyl-4-ethyl-	168°	$C_{12}H_{12}N_3Cl$	61·7	5·1	61·9	5·3
2	2 : 4-Diamino-5-*o*-fluorophenyl-	163—164	$C_{10}H_9N_4F$	58·8	4·4	59·0	4·6
3	2 : 4-Diamino-5-(4′-chloro-2′-methylphenyl)-	209	$C_{11}H_{11}N_4Cl$	56·3	4·7	56·6	4·7
4	2-Amino-4-methyl-6-phenyl-	172—173	$C_{11}H_{11}N_3$	71·4	6·0	71·2	6·1
5	4-Amino-2-methyl-6-phenyl-	165	$C_{11}H_{11}N_3$	71·4	6·0	71·6	5·8
6	2 : 4-Diamino-6-phenyl-	162	$C_{10}H_{10}N_4$	64·5	5·4	64·7	5·1

(1) Prep. from 2-amino-5-*p*-chlorophenyl-6-ethyl-4-mercaptopyrimidine (Russell and Whittaker, unpublished work) by reduction with Raney nickel. (2) Prep. by the condensation of α-*o*-fluorophenyl-β-methoxyacrylonitrile with guanidine (cf. Russell and Hitchings, *loc. cit.*). (3) As (2), but from α-(4-chloro-2-methylphenyl)-β-methoxyacrylonitrile. (4) Prep. by the condensation of benzoylacetone and guanidine. (5) Prep. by chlorination and amination of the corresponding hydroxy-compound prepared by the condensation of ethyl benzoylacetate and acetamidine. (6) Prep. from 6-phenyl*iso*cytosine by chlorination and amination.

Spectra.—The ultra-violet absorption spectra were determined with a Beckman model DU quartz spectrophotometer (cell-length 1 cm.). The compounds were in solution (10 mg./l.) in ethanol.

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