38. *Infra-red Spectra of Derivatives of Pyrimidine.*

By L. N. Short and H. W. Thompson.

The vibrational spectra between 2 and 25μ of a large number of simple derivatives of pyrimidine have been measured. These include many hydroxy- and amino-derivatives with varying numbers and types of substituent. The spectra have been compared empirically, and partial interpretations have been made on the basis of what is already known about the vibrational frequencies of such key groups as OH, C=O, NH, etc. Particular consideration has been given to the question of keto–enol or lactim–lactam tautomerism which may occur in many of these compounds, and although there are many ambiguities the balance of evidence seems in most cases to favour a ketonic structure for the hydroxy-derivatives, and the presence of amino- rather than imino-forms. The spectra provide reference data which may be useful for analysis and identification.

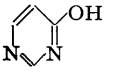
The role of derivatives of pyrimidine in the chemistry of nucleic acids justifies an examination of any method likely to aid their qualitative or quantitative determination or the identification of particular compounds. Spectroscopic methods are obviously relevant, and some ultra-violet absorption measurements have been reported. The greater specificity of infra-red vibrational spectra in relation to nuclear configuration might in principle make these spectra even more useful. There are two limitations, namely, that infra-red measurements with aqueous solutions are effectively impossible, and that the vibrational spectra of such complex compounds may prove too complex for detailed analysis.

However, the vibrational spectra of the solid materials may provide some evidence about outstanding structural problems. One of these concerns the tautomerism which is possible with hydroxy- and amino-derivatives and which may affect their function in metabolism. This tautomerism between ketonic–enolic (lactam–lactim) forms or amino–imino-structures may be influenced by other nuclear substituents. The problem has been studied by several methods with rather indefinite results.

2-Hydroxy- and 4-hydroxy-pyrimidine may have the extreme tautomeric forms (I*a*), (I*b*), and (II*a*), (II*b*), to which will be added various polar structures which may combine


(I*a*)


(I*b*)

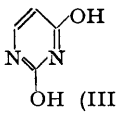

(II*a*)

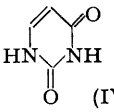

(II*b*)

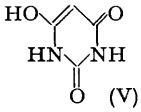
in the final resonance hybrid. From chemical evidence, Arndt (*Rev. Fac. Sci. Istanbul*, 1944, *A*, **2**, 19) concluded that when it is compatible with the maintenance of aromatic character in the ring, the hydroxypyrimidines will have the lactam form. On this basis uracil (2 : 4-dihydroxypyrimidine) (III) will have the structure (IV), and barbituric acid (2 : 4 : 6-trihydroxypyrimidine) will be represented by (V).

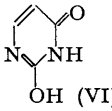
From ultra-violet measurements on ethanol solutions of a series of derivatives, Austin (*J. Amer. Chem. Soc.*, 1934, **56**, 2141) concluded that uracil has structure (VI), but

Loufbourow, Stimson, and Hart (*ibid.*, 1943, **65**, 148) decided from similar measurements in water at different hydrogen-ion concentrations that it is doubly ketonic (IV), a result

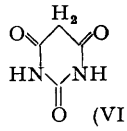

(III)

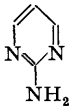

(IV)

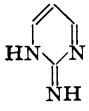

(V)

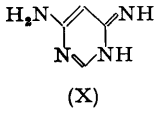

(VI)

confirmed by Marshall and Walker (*J.*, 1951, 1004). The formula (V) for barbituric acid retains some degree of aromatic character, whereas (VII) does not, and 5 : 5-diethylbarbituric acid shows no selective ultra-violet absorption such as would indicate the latter structure.


(VII)


(VIII)


(IX)

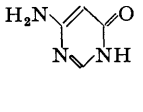

(X)

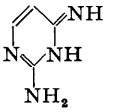
Similarly, 2-aminopyrimidine (VIII) could exist in the imino-form (IX) with which polar structures might participate in the final hybrid, and correspondingly with 4-aminopyrimidine. An amino-group in the 5-position would not be capable of tautomerism.

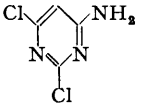
Cavalieri and Bendich (*J. Amer. Chem. Soc.*, 1950, **72**, 2587) have recently argued from some ultra-violet results that 4 : 6-diamino-, 4-hydroxy-2-amino- and 2 : 4-diaminopyrimidine have the structures (X), (XI), and (XII).

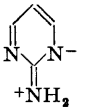
As regards physical properties, the high melting points and low solubilities of the hydroxy-derivatives in non-polar media indicate the participation of polar structures. which may be less marked with the amino-derivatives.

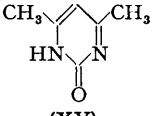
Clews and Cochran (*Acta Cryst.*, 1948, **1**, 4; 1949, **2**, 46) have recently suggested from *X*-ray work that 4-amino-2 : 6-dichloropyrimidine exists in the amino-form (XIII). In this and other compounds (2-amino-4 : 6-dichloro-, 2-amino-4-chloro-6-methyl-, and 4 : 6-diamino-5-bromo-pyrimidine) however a shortening of the extranuclear carbon–nitrogen bond may be explained in terms of an imino-structure or a considerable contribution to the resonance hybrid of the polar forms, such as (XIV). Pitt (*Acta Cryst.*,


(XI)


(XII)


(XIII)


(XIV)


(XV)

1948, **1**, 168), also from *X*-ray data, found that in 2-hydroxy-4 : 6-dimethylpyrimidine, the very short carbon–oxygen distance is compatible with a ketonic form (XV).

Since the vibration frequencies of the C=O and N–H bonds in different types of grouping are now fairly well known, it seemed appropriate to examine the infra-red spectra of some of the simpler derivatives of pyrimidine from this aspect. We have to expect complex and individualistic spectra as a whole, with other complications caused by varying degrees of hydrogen-bridge formation in the different compounds. There is the added difficulty that only the solids can be examined, so that comparisons with dilute solutions cannot be made.

Similar infra-red measurements on some of the simpler pyrimidines and several nucleic acids, nucleotides, and nucleosides have been reported by Brownlie (*J.*, 1950, 3062) and by Blout and Fields (*J. Biol. Chem.*, 1949, **178**, 335; *J. Amer. Chem. Soc.*, 1950, **72**, 479). In so far as they overlap our own in regard to results or interpretation they are discussed below.

Experimental

The compounds examined are listed in Table 1. Many were tested for homogeneity by paper chromatography. When sufficient material was available it was recrystallised, but in no case was any significant change of spectrum found after this process.

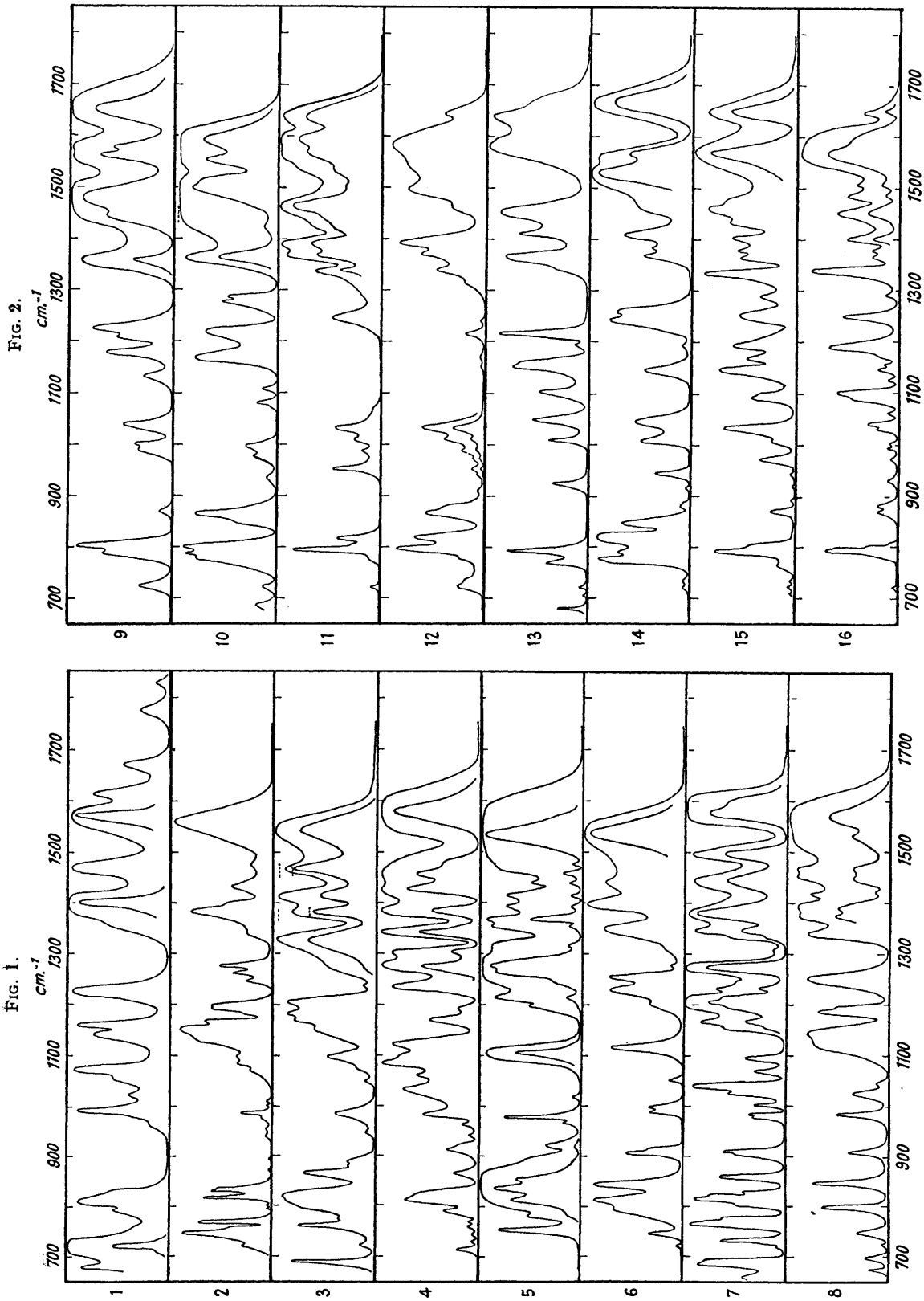

1
2
3
4
5
6
7
8
700
900
1100
1300
1500
1700
cm.-1

FIG. 1.

9
10
11
12
13
14
15
16
700
900
1100
1300
1500
1700
cm.-1

FIG. 2.

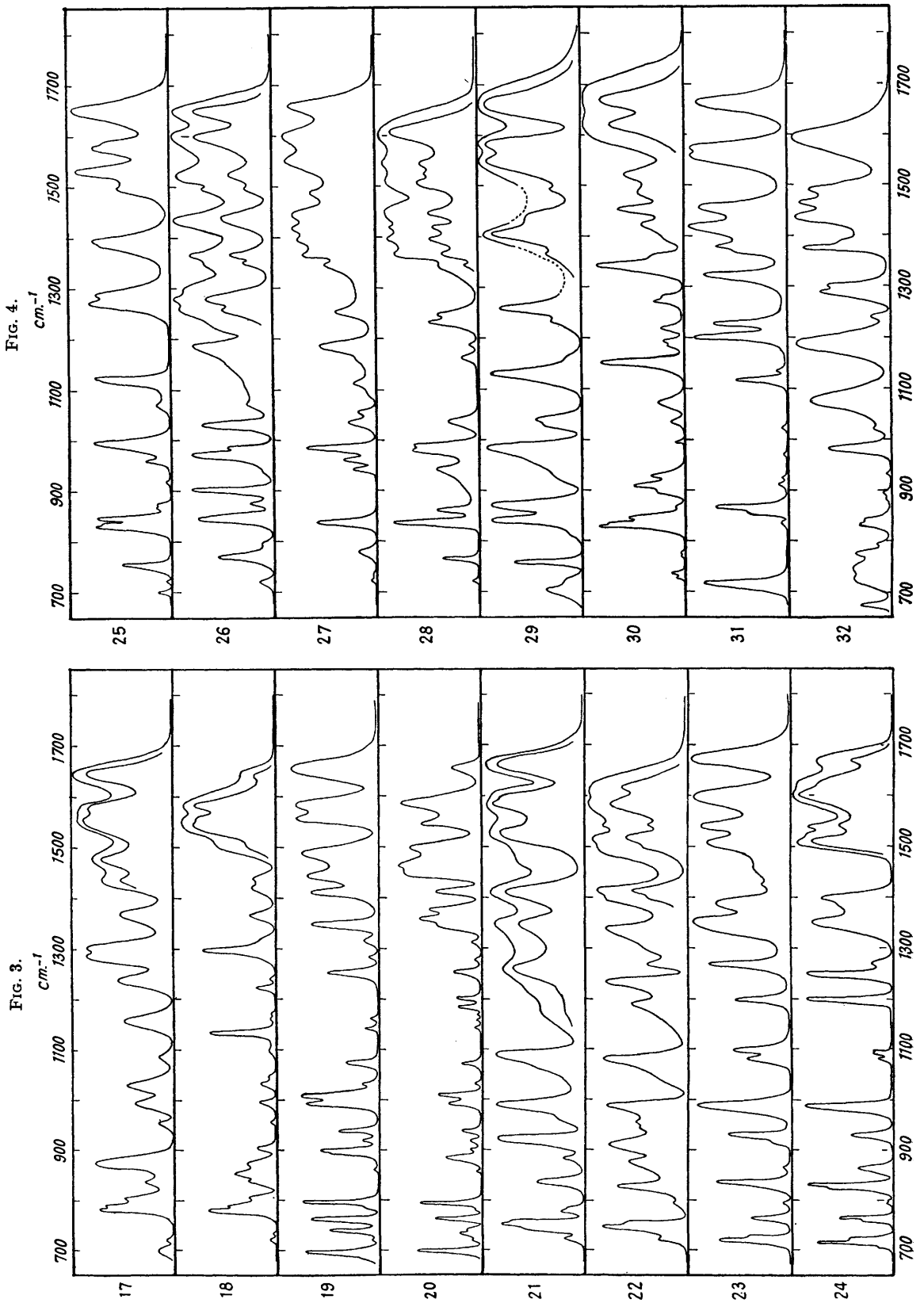

700
900
1100
1300
1500
1700
cm.⁻¹
17
18
19
20
21
22
23
24

FIG. 3.

700
900
1100
1300
1500
1700
cm.⁻¹
25
26
27
28
29
30
31
32

FIG. 4.

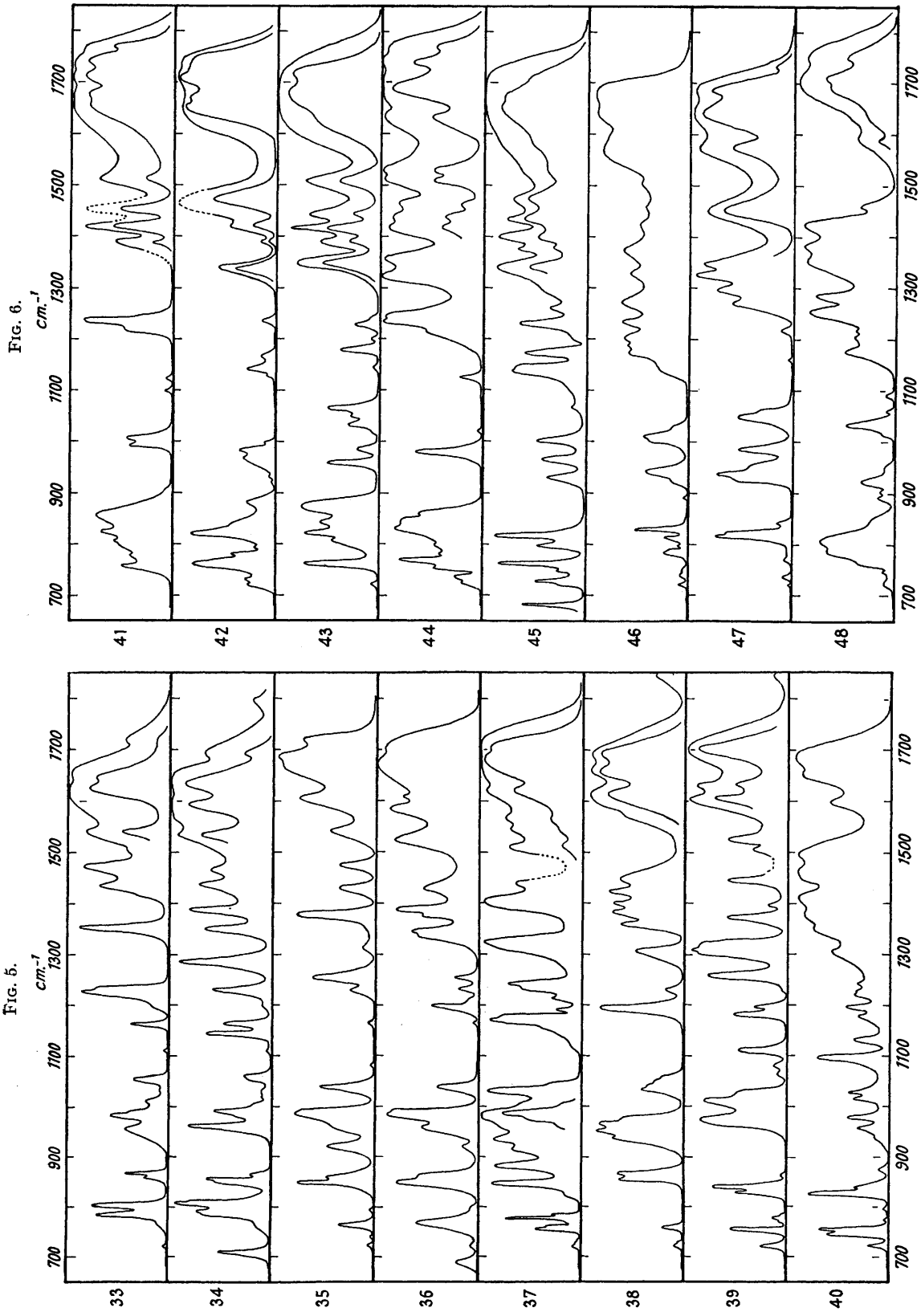

700
900
1100
1300
1500
1700
cm.⁻¹
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48

FIG. 5.

FIG. 6.

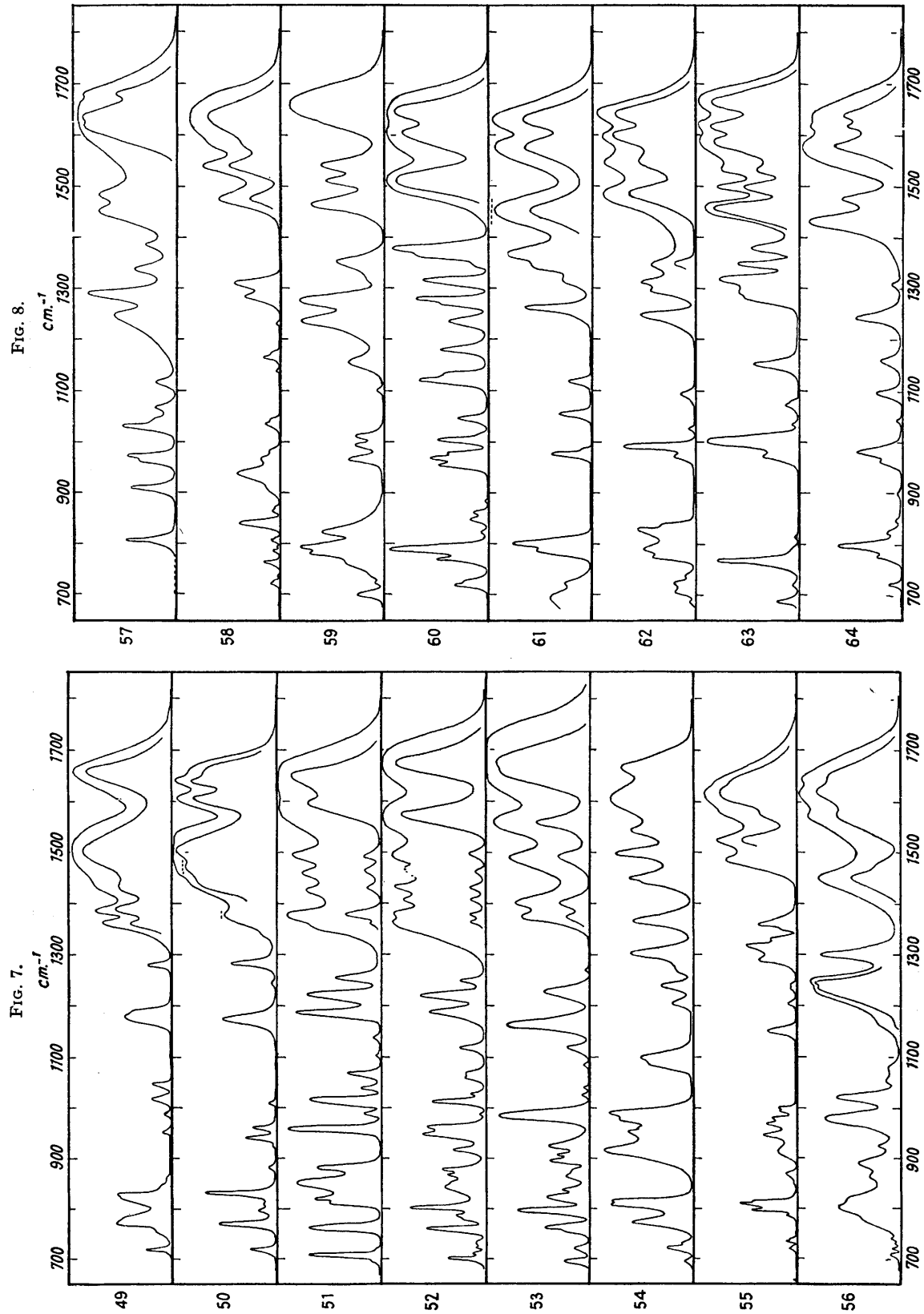

700
900
1100
1300
1500
1700
cm.⁻¹
49
50
51
52
53
54
55
56

FIG. 7.

700
900
1100
1300
1500
1700
cm.⁻¹
57
58
59
60
61
62
63
64

FIG. 8.

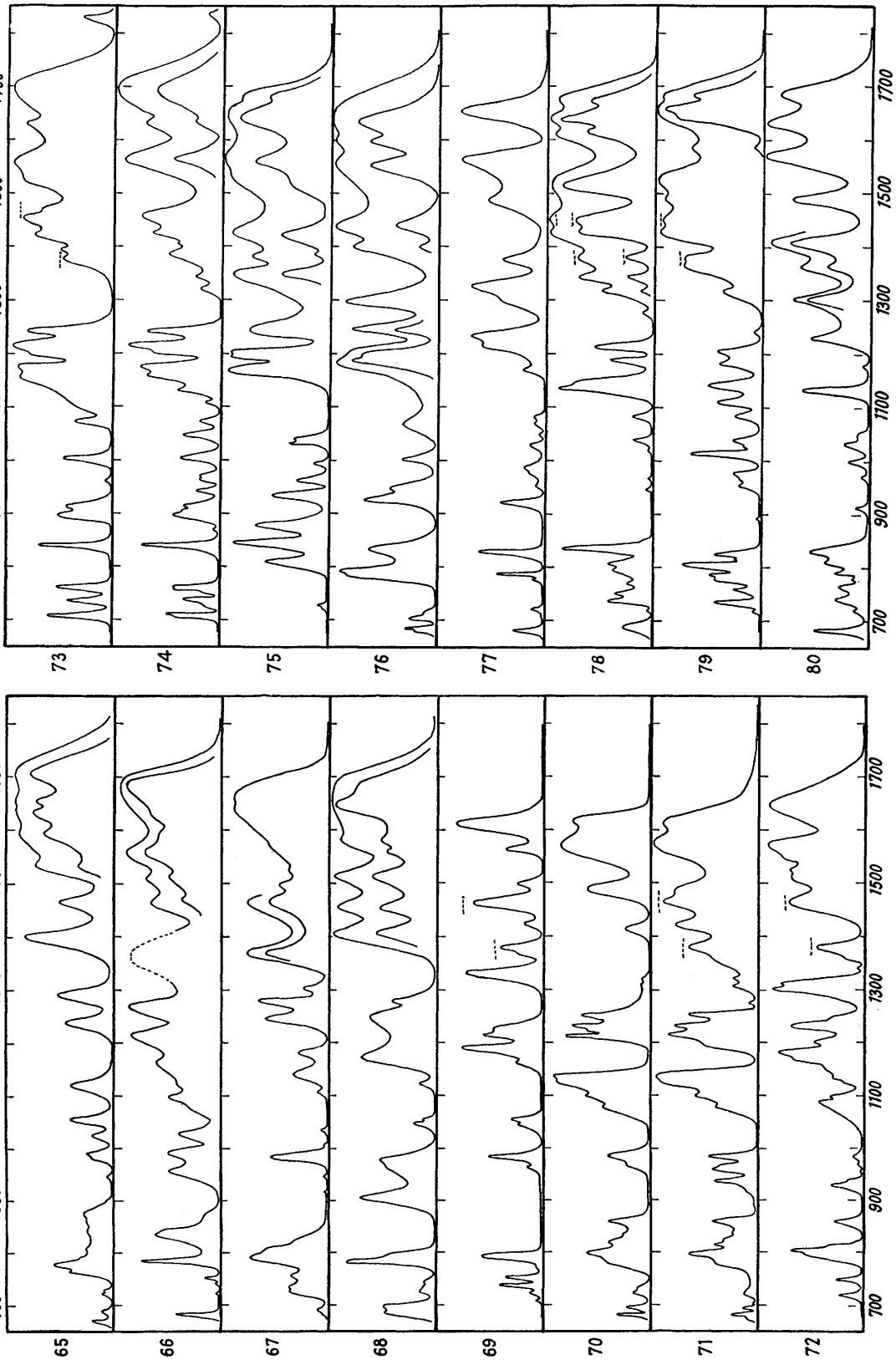

65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
cm.⁻¹
700
900
1100
1300
1500
1700

FIG. 9.

FIG. 10.

FIG. 11.

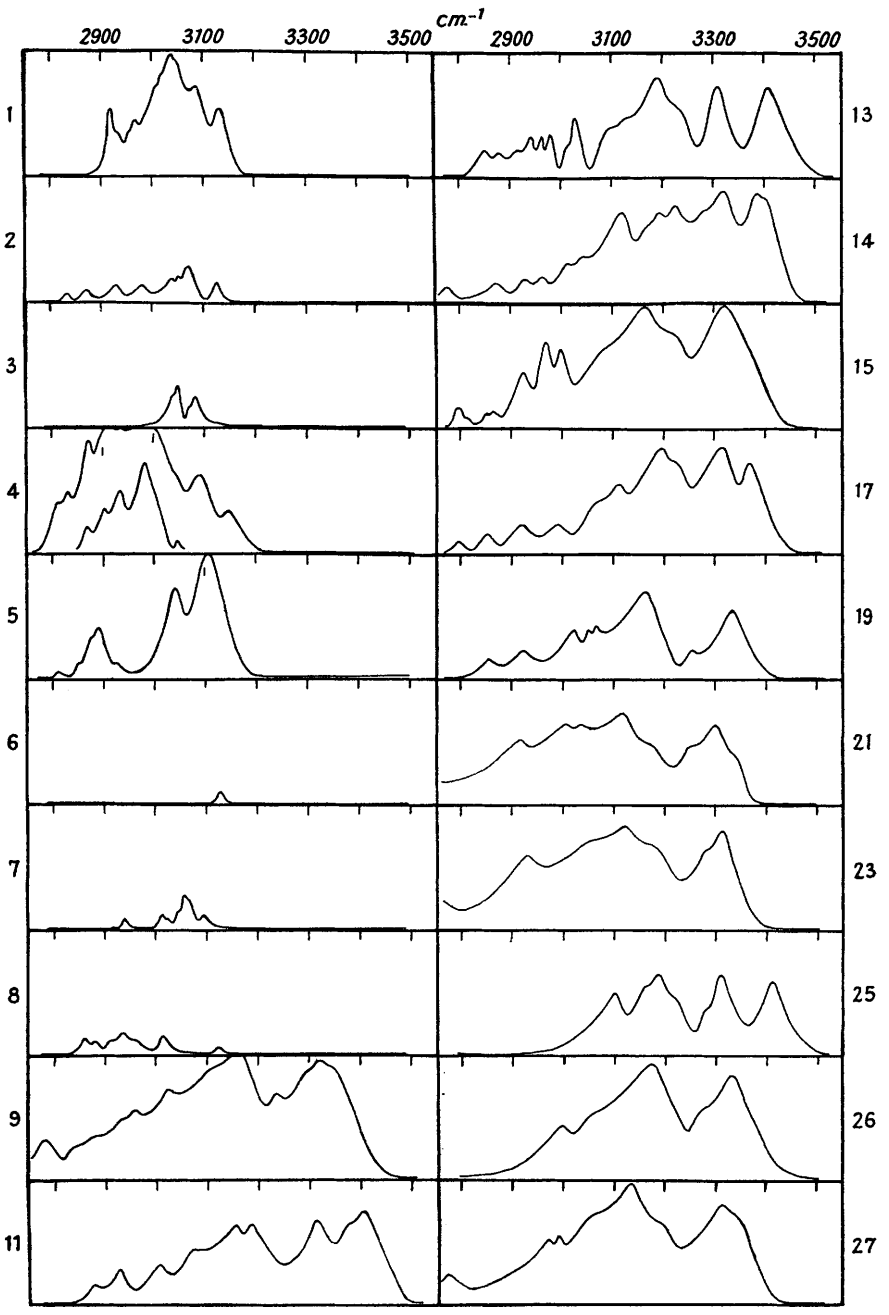
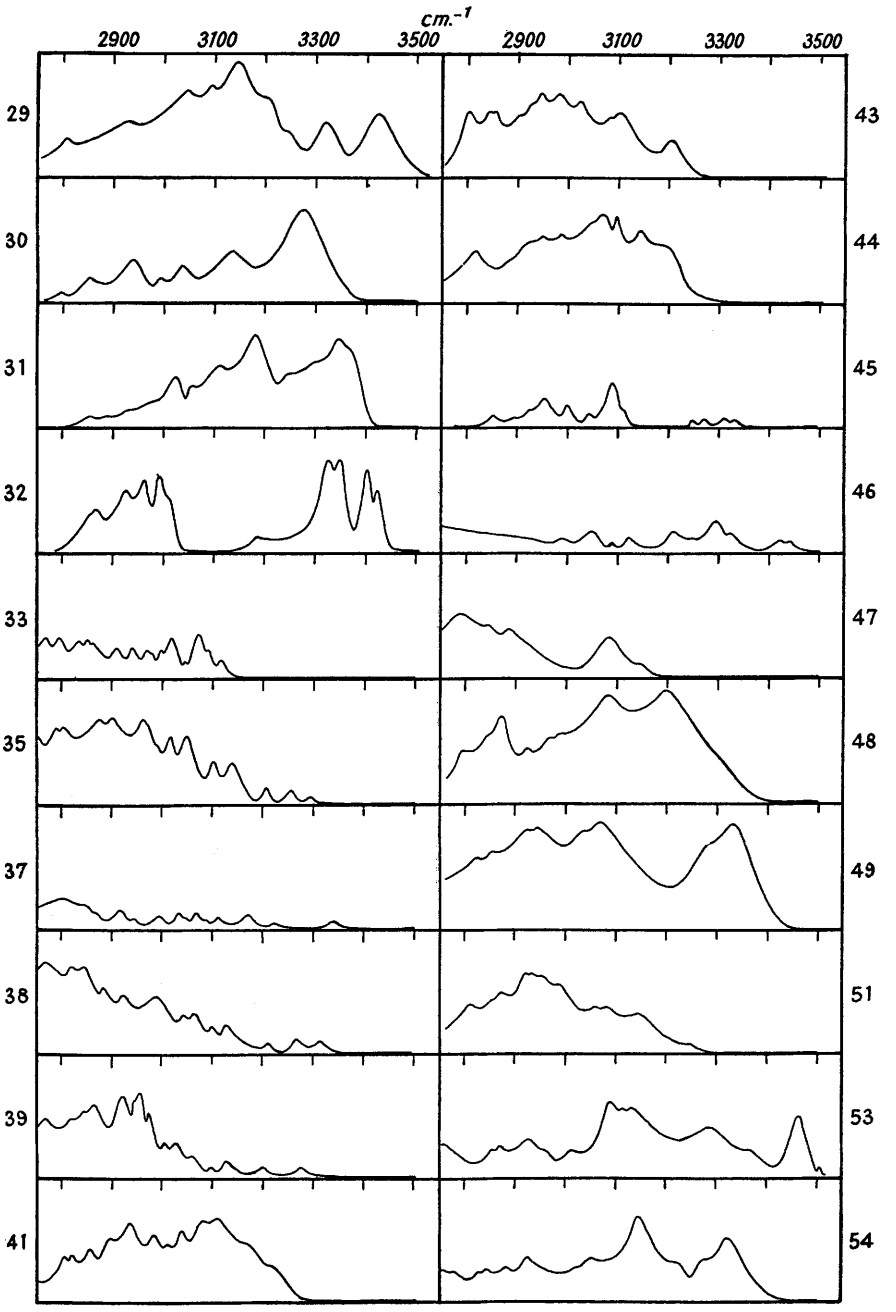

cm.⁻¹
2900
3100
3300
3500
1
2
3
4
5
6
7
8
9
11
13
14
15
17
19
21
23
25
26
27

FIG. 12.


cm.⁻¹
2900
3100
3300
3500
2900
3100
3300
3500
29
30
31
32
33
35
37
38
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41
43
44
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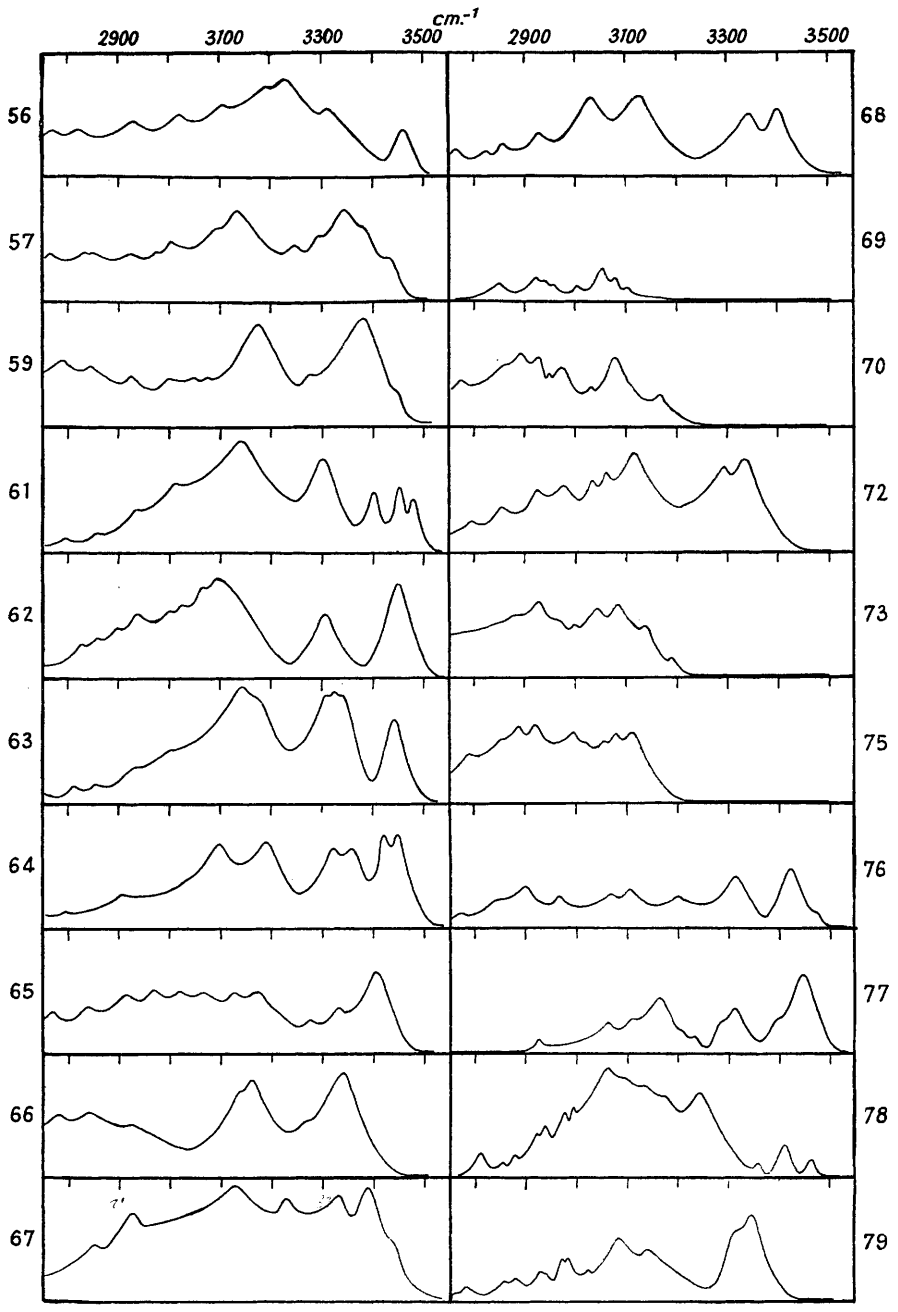
48
49
51
53
54

FIG. 13.


cm.⁻¹
2900
3100
3300
3500
56
57
59
61
62
63
64
65
66
67
68
69
70
72
73
75
76
77
78
79

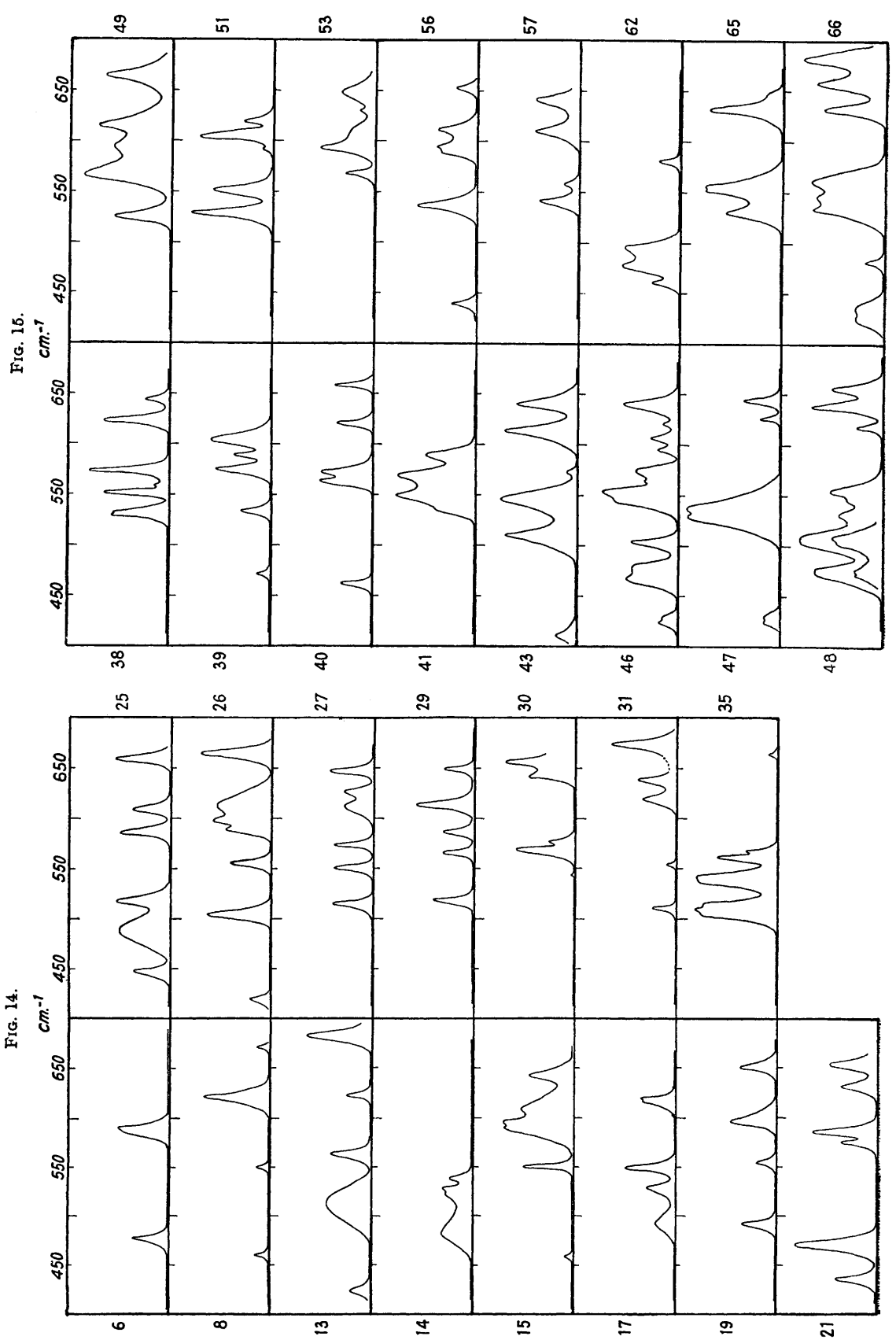
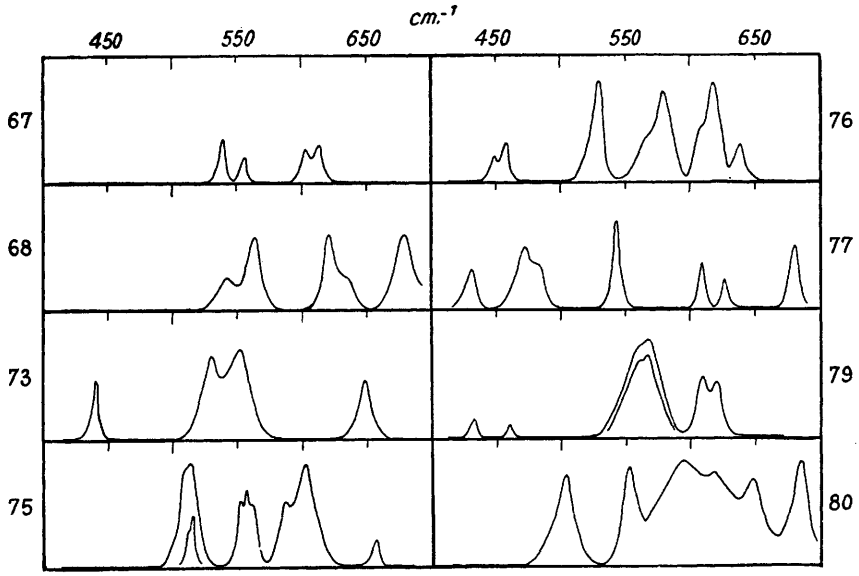

cm.-1
450
550
650
6
8
13
14
15
17
19
21
25
26
27
29
30
31
35

FIG. 14.

cm.-1
450
550
650
38
39
40
41
43
46
47
48
49
51
53
56
57
62
65
66

FIG. 15.

FIG. 16.



The spectra were determined with a Perkin Elmer 12C instrument, prisms of lithium fluoride, sodium chloride, and potassium bromide being used. The compounds were examined as solids suspended in paraffin or perfluorokerosene; in a few cases there was a slight doubt about bands in the narrow region near 7μ where paraffin has strong bands.

Some of the compounds were deuterated by treatment with deuterium oxide. Whilst the extent to which deuteration had occurred was in some cases doubtful, the removal of bands at 3μ and appearance of others near 4μ was a useful indication.

TABLE 1.

No. of spectrum	Substituent(s)		Source [a]	Purity [b]	No. of spectrum of deutero-cpd.
(a) *Monosubstituted pyrimidines*					
2	2-Cl		D	m. p. 63·5—64°	—
9	2-NH_2		A	C	10
31	5-NH_2		G	m. p. 173—174°	—
33	2-OH		E	C	34
35	4-OH		A	R (toluene),	36
69	2-SH		D	m. p. 230°	—
(b) 2 : 4-*Disubstituted pyrimidines*					
	2	4			
3	Cl	Cl	A	R (ether), m. p. 62°	—
4	OC_2H_5	OC_2H_5	C	—	—
7	OC_6H_5	OC_6H_5	E	C	—
23	Cl	NH_2	B	C	24
41	OH	OH	A	C	42
59	OH	NH_2	E	C	60
61	NH_2	NH_2	A	R (toluene), m. p. 143—144°	—
70	SH	SH	E	Anal. pure	71
72	SH	NH_2	E	Anal. pure	—
73	SH	OH	C	I	74
(c) 4 : 6-*Disubstituted pyrimidines*					
	4	6			
21	NH_2	Cl	C	C	22
37	OH	CH_3	C	C	—
46	OH	OH	C	R (water), S	—
54	OH	NH_2	E	C	55
62	NH_2	NH_2	C	C	—

TABLE 1—*continued.*

No. of spectrum	Substituents			Source [a]	Purity [b]	No. of spectrum of deutero-cpd.
(d) 2 : 4 : 6-*Trisubstituted pyrimidines*						
	2	4	6			
5	Cl	Cl	Cl	C	Liquid	—
6	CH_3	Cl	Cl	C	C	—
11	NH_2	CH_3	CH_3	C	R (water), m. p. 149—150°	12
13	NH_2	OCH_3	OCH_3	B	R (toluene), S	—
14	NH_2	Cl	Cl	C	C	—
15	NH_2	CH_3	OC_2H_5	B	R (petrol.), S	16
17	NH_2	CH_3	Cl	C	C	18
25	Cl	NH_2	Cl	C	C	—
26	Cl	NH_2	CH_3	B	C	—
27	CH_3	NH_2	CH_3	C	C	28
29	CH_3	NH_2	Cl	C, B	C	—
30	$NH{\cdot}CH_3$	CH_3	Cl	B	R (toluene), S	—
38	CH_3	OH	CH_3	C	R (water), S	—
43	OH	OH	CH_3	C	C	—
47	CH_3	OH	OH	C	C	—
48	OH	OH	OH	C	I	—
49	NH_2	OH	CH_3	C	C	50
51	$N(CH_3)_2$	OH	CH_3	B	C	52
53	NH_2	OH	Cl	C	C	—
56	SCH_3	OH	NH_2	B	C	—
57	CH_3	OH	NH_2	C	C	58
64	NH_2	NH_2	NH_2	C	R (alcohol)	—
65	OH	OH	NH_2	C	C	—
66	NH_2	OH	OH	C	C	—
67	NH_2	NH_2	OH	C	I	—
68	OH	NH_2	NH_2	C	C	—
75	SH	OH	CH_3	B	C	—
76	SH	OH	NH_2	B	R (alcohol), S	—
77	NH_2	CH_3	CN	B	R (alcohol), S	—
80	NH_2	CH_3	$CO{\cdot}NH_2$	B	C	
(e) *Miscellaneous derivatives*						
1	none			C	—	—
19	4-NH_2, 5-C_6H_5			C	C	20
44	2 : 4-di-OH, 5-NO_2			A	C	—
63	4 : 6-di-NH_2, 5-Br			C	—	—
8	2-CH_3, 4 : 6-di-O·CH_3, 5-NO_2			B	C	—
32	2-CH_3, 4 : 6-di-O·CH_3, 5-NH_2			B	C	—
39	2-S·C_2H_5, 4-OH, 5-C_2H_5, 6-CH_3			B	R (toluene), C	—
40	1 : 4-CH_3, 2-S·CH_3, 6-O			B	I	—
45	1 : 3-CH_3, 2 : 4-di-O			F	C, m. p. 123—124°	—
78	2-NH_2, 3-C_2H_5, 4-CH_3, 6-O			B	C	—
79	1-C_2H_5, 2-NH_2, 4-CH_3, 6-O			B	—	—

[a] Source of materials.—A : Prof. A. Albert, Australian National University. B : Imperial Chemical Industries Limited, Dyestuffs Division. C : Prof. A. R. Todd, Cambridge University. D : Dr. J. F. W. McOmie, Bristol University. E : Dr. D. J. Brown, Australian National University. F : Genatosan Ltd. G : Dr. N. Whittaker, Wellcome Foundation.

[b] Purity.—C : Chromatographically pure. I : Chromatogram not entirely satisfactory. R : Recrystallised. S : Spectrum unchanged after recrystallisation. The melting points are given in some cases.

RESULTS AND DISCUSSION

The spectra are shown in Figs. 1—16.

(1) *Pyrimidine and Simple Non-tautomeric Derivatives.*—It is impossible at present to attempt a complete assignment of the vibration frequencies of pyrimidine, especially in the absence of Raman data. We can, however, draw some analogies with the related molecules, benzene, pyridine, and deuterobenzene.

The spectrum which we have obtained for pyrimidine agrees generally with that indicated by Brownlie (*loc. cit.*), except that we have found a group of bands near 3050 cm.$^{-1}$ not detailed by him, and also a band at 1610 cm.$^{-1}$ rather than 1650 cm.$^{-1}$, and another at 810 cm.$^{-1}$ rather than 825 cm.$^{-1}$. Our spectrum appears to agree with that recorded earlier by Barnes, Gore, Liddel, and Williams (" Infra-red Spectroscopy," p. 97, Reinhold,

New York, 1944). We found a broad, weak band near 3400 cm.$^{-1}$ as distinct from the strong absorption reported by Brownlie, and it appeared to be due to water absorbed by this hygroscopic substance.

Table 2 gives the values of some ring vibrations together with values for the corresponding modes in the related molecules. Values for benzene, deuterobenzene, and

TABLE 2.

Benzene	Monodeuterobenzene	Pyridine	Pyrimidine
992	981	990	991
1010	1009	1028	1024
1485	1418, 1473	1440, 1485	1400, 1461
1595	1576, 1594	1570, 1580	1569, 1610
1693	—	1723?	1670?

(Frequencies in cm.$^{-1}$)

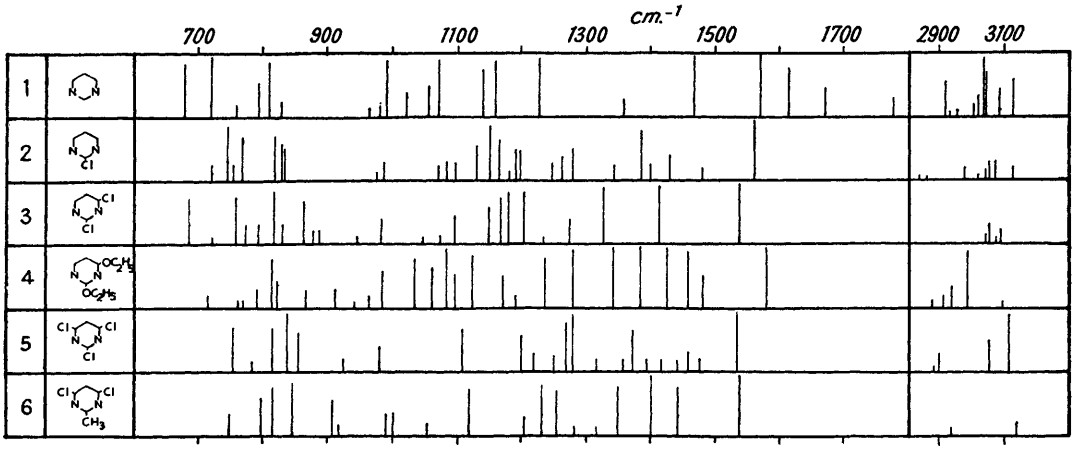
pyridine are taken from the work of Kline and Turkevitch (*J. Chem. Physics*, 1944, **12**, 300). Pyrimidine will possess C_{2v} symmetry, and certain of the twofold degenerate modes in benzene will be split in the same way as in pyridine.

The assignment of frequencies due to bending and deformation of C–H bonds is less obvious, but the following additional similarities are found :

Pyridine	710, 747	1037	1061	1139	1210
Pyrimidine	680, 721	1052	1075	1140, 1165	1220

The spectra of 2-chloro-, 2 : 4-dichloro-, 2 : 4 : 6-trichloro-, 4 : 6-dichloro-2-methyl- and 2 : 4-diethoxy-pyrimidine are compared in Fig. 17.* The most significant feature

FIG. 17.



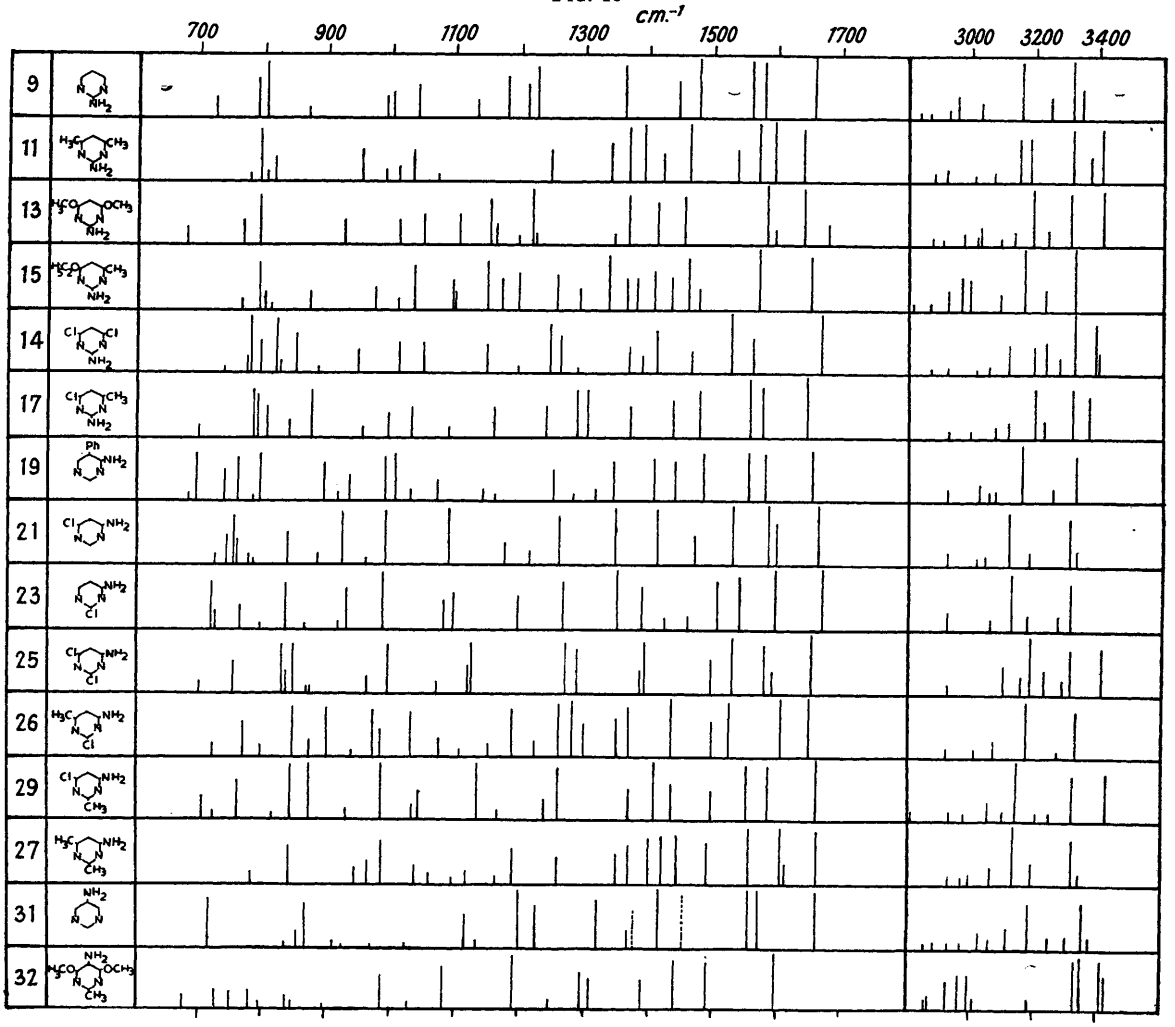
is a strong band in the region 1520—1580 cm.$^{-1}$, which appears to correspond to that at 1569 cm.$^{-1}$ in pyrimidine itself, and has been assigned to a ring vibration. All these compounds have bands near 810 cm.$^{-1}$ and 990 cm.$^{-1}$. The latter is a symmetrical ring vibration, and although the former might have been assigned to a deformation of C–H bonds, its persistence throughout this series rather implies that it may be a ring vibration.

(2) *Monoamino-derivatives.*—The spectra of a number of monoamino-substituted pyrimidines are shown as line drawings in Fig. 18.* All these compounds have marked

* For simplicity the double bonds are not shown in the pyrimidine rings of the formulæ given in Figs. 17—20.

absorption bands at 1500—1700 cm.$^{-1}$ and 3100—3500 cm.$^{-1}$. In the former range of frequency, one or more ring vibrations may occur, corresponding to that near 1550 cm.$^{-1}$ in the simple derivatives discussed above, and deformation vibrations of N–H bonds are also to be expected. The second range of frequency may include certain stretching vibration frequencies of C–H bonds near 3100 cm.$^{-1}$, and the stretching vibration bands of N–H bonds at rather higher frequencies. Combination and overtone bands can occur in both regions, but their relative intensity would probably be low.

FIG. 18.



The spectra as a whole are both complex and individualistic but there are no systematic differences such as to suggest that the 2-amino- and 4-amino-pyrimidines adopt different tautomeric forms. The most marked bands in the higher-frequency range are a pair occurring uniformly near 3150 and 3350 cm.$^{-1}$. These values are rather lower than would be expected for a normal amino-group such as occurs in amines, but they are closely parallel to those near 3180 and 3350 cm.$^{-1}$ found in unsubstituted amides (Richards and Thompson, *J.*, 1947, 1248). If the substituted 2-amino- and 4-amino-pyrimidines exist in the amino-form, and suitable allowance is made for the participating polar structures which are plausible, as well as for the hydrogen bonding, a parallelism with the amides might be expected. The alternative interpretation would be to assign the band at 3150 cm.$^{-1}$ to a C–H vibration, and to suppose that tautomerism in the amino-group has occurred leaving

a side-chain imino-group. This value for the C–H vibration frequency, even in the type of ring concerned, is very high, and this interpretation seems less likely. Moreover, a strong band at 3150 cm.$^{-1}$ only occurs with amino-derivatives. We might alternatively assign it to a ring N–H group, which is carrying a surplus positive charge, somewhat similar to that in amino-acids (Thompson, Nicholson, and Short, *Discuss. Faraday Soc.*, 1950, **9**, 222). This is not in itself very plausible, but in any case the band at 3150 cm.$^{-1}$ is not found with simple hydroxy-pyrimidines in which ketonisation would produce a similar kind of ring NH group.

The most striking feature of the region 1500—1700 cm.$^{-1}$ with monoamino-pyrimidines is a strong band near 1650 cm.$^{-1}$. This lies at higher frequencies than any ring vibration found for the non-tautomeric systems, such as the chloro-derivatives. It is, moreover, removed by deuteration, whereas the other bands from 1500—1600 cm.$^{-1}$ are not much influenced by this treatment. This is further evidence for assigning the band near 1650 cm.$^{-1}$ to a deformation of the amino-group. The similarity with unsubstituted amides is also close in this respect. One or more of the bands between 1500 and 1600 cm.$^{-1}$ will be the analogues of the ring vibration of simple pyrimidines near 1550 cm.$^{-1}$.

By contrast with these simple monoamino-pyrimidines, the 5-amino-4 : 6-dimethoxy-2-methyl derivative shows a markedly different spectrum in the two regions near 6μ and 3μ. This compound can only exist in the amino-form, and its structure is such as to preclude resonance with polar forms. Near 3μ there are strong bands between 3300 and 3430 cm.$^{-1}$ (not at 3150 cm.$^{-1}$), *i.e.* at higher frequencies than with the amino-derivatives just discussed. Also there is no band at 1650 cm.$^{-1}$ corresponding to that suggested already for the deformation of the N–H bond. In this connexion 5-aminopyrimidine is of particular interest since it is almost certainly in the amino-form, amino-imino tautomerism being impossible. The spectrum of this compound in the regions of 3μ and 6μ resembles those of the 2-amino- and the 4-amino-pyrimidines discussed above, and supports the assignment of an amino-structure to these compounds.

When 5-amino-4 : 6-dimethoxy-2-methylpyrimidine is deuterated, the bands near 3μ disappear and others appear near 4μ. Other spectral changes occur below 1300 cm.$^{-1}$, but not noticeably between 1300 and 1700 cm.$^{-1}$. The corresponding nitro-derivative, 4 : 6-dimethoxy-2-methyl 5-nitropyrimidine shows a band at 1571 cm.$^{-1}$ which probably corresponds to that at 1595 cm.$^{-1}$ in the amino-derivatives, and is probably due to a ring vibration.

One peculiar result with the aminopyrimidines is the occurrence in some cases of a strong band near 3400 cm.$^{-1}$, in addition to those between 3150 and 3350 cm.$^{-1}$. This band cannot be correlated with position or type of substituent, or with any other special features in the spectrum of compounds which show it. It might be possible to attribute it to absorbed water, but this is unlikely. The band is almost certainly due to a stretching vibration of N–H bonds, but its exact significance remains obscure.

(3) *Mono-hydroxy-derivatives.*—The spectra of five monohydroxy-pyrimidines are compared in Fig. 19.* Here again there is the possibility of both keto–enol tautomerism and the occurrence of polar forms which may contribute to the final hybrid. Thus, if 2-hydroxypyrimidine exists in the lactim form, we might expect bands of the hydroxyl group, and of the pyrimidine nucleus; if the lactam form occurs, the bands found may simulate those of a monosubstituted amide, with other ring vibrations which may be more or less localised in the C=C and C=N bonds. In either case, the presence of contributing polar forms may affect the situation.

2-Hydroxypyrimidine has a pair of strong bands at 1620—1650 cm.$^{-1}$. In terms of the lactim formula, this absorption would be difficult to explain except as being due to vibrations of the ring, but the values are noticeably higher than those found for ring vibrations in the other simple chloro- or amino-pyrimidines. The alternative would be to explain one band as being due to the deformational vibration of a hydroxyl group, but although the latter seems to vary in frequency in different kinds of molecule, it is improbable that even in the bonded state it could rise to such a high value. A more reasonable interpretation would be to assign one band in this region to the absorption by

* See footnote, p. 181.

a carbonyl group of the lactam form. The apparent doublet at 1620—1650 cm.$^{-1}$ might arise in the lactam form if one ring vibration localised in the C=N bond were raised in value because of changes in bond character resulting from the ketonisation. 2-Hydroxypyrimidine shows no band at frequencies greater than 3200 cm.$^{-1}$, but this does not seem to be conclusive evidence against a lactam form. Monosubstituted amides have a band near 3270 cm.$^{-1}$, but specific conditions of hydrogen bonding could certainly lower this vibration frequency.

FIG. 19.

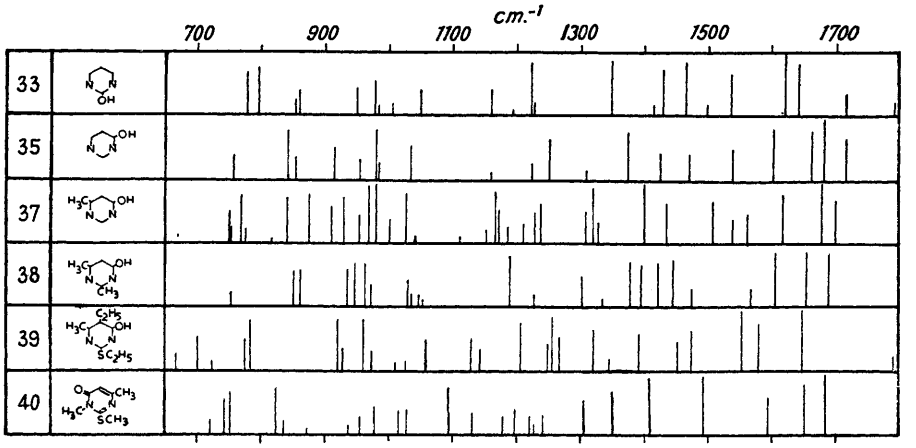
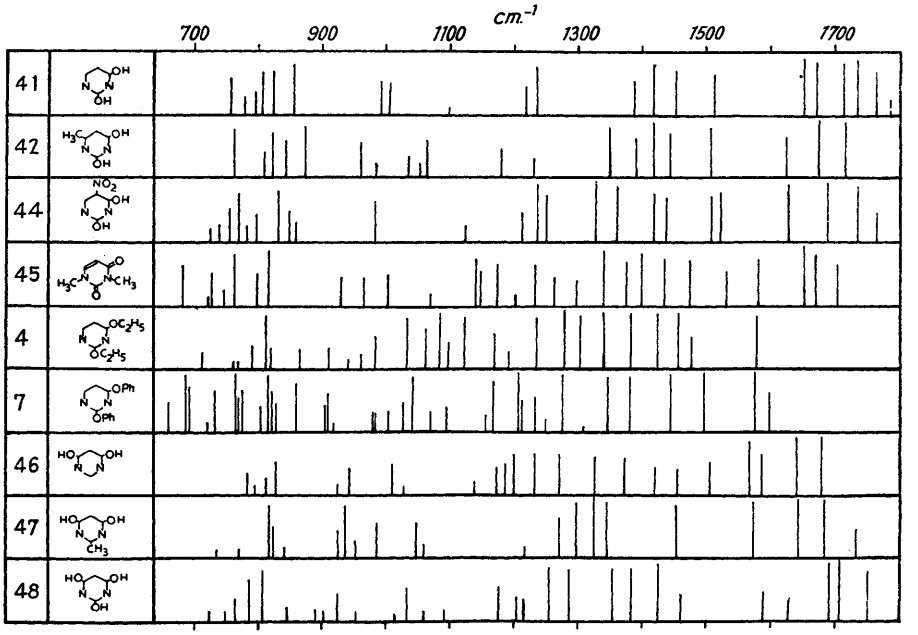


FIG. 20.



Similar arguments apply to 4-hydroxypyrimidine. There are strong bands between 1600 and 1720 cm.$^{-1}$ and their interpretation as ring vibrations of a lactim structure is improbable. It is more reasonable to assume a ketonic formula with ring vibrations raised in value as already indicated. No definite evidence is obtained from the spectrum near 3μ.

Derivatives of 4-hydroxypyrimidine in general behave similarly to the above. It is particularly noteworthy that 1 : 4-dimethyl-2-methylthiopyrimid-6-one is also in line, having strong bands near 1596, 1651, and 1685 cm.$^{-1}$. This compound can only exist in

the ketonic form, and its spectrum in this region is closely parallel to that of 4-hydroxypyrimidine.

(4) *Derivatives with Two or More Tautomeric Groups.*—(a) *Hydroxypyrimidines.* Here the structural problems are even more complex. For example uracil (2 : 4-dihydroxypyrimidine) has six theoretically possible forms, namely the diketonic, dienolic, and four keto–enol forms. The spectra of some hydroxy-derivatives are shown in Fig. 20.*

Uracil has several bands in the range 1640—1770 cm.$^{-1}$ but none between 1510 and 1640 cm.$^{-1}$. By contrast, 2 : 4-diethoxy- and 2 : 4-diphenoxy-pyrimidine have no bands between 1600 and 1800 cm.$^{-1}$. 1 : 3-Dimethyluracil, which must have the lactam structure, has bands between 1640 and 1720 cm.$^{-1}$, which will be due to the carbonyl groups and a possible ring vibration frequency. Partial deuteration of uracil hardly affected the bands at 1653, 1673, 1716, and 1737 cm.$^{-1}$ although that at 1768 cm.$^{-1}$ seemed to disappear. This evidence suggests that uracil exists in a form which is at least partly ketonic, and probably diketonic. On the other hand, the change in the spectrum of uracil between 700 and 1500 cm.$^{-1}$ after deuteration is remarkable, and much more pronounced than with most other compounds. Uracil has a strong band near 1230 cm.$^{-1}$ which is removed by deuteration, and might be attributed to a hydroxyl group.

6-Methyl- and 5-nitro-uracil also each have two strong bands in the region 1670—1740 cm.$^{-1}$ and a third near 1630 cm.$^{-1}$. These compounds do not show a band near 1580 cm.$^{-1}$ found with some derivatives and thought to be a ring frequency.

None of the derivatives of uracil has strong bands above 3200 cm.$^{-1}$ and the feebler bands below this frequency cannot be definitely assigned.

4 : 6-Dihydroxypyrimidine shows a marked spectral difference near 6μ from the 2 : 4-dihydroxy-derivative. It has three strong bands near 1570, 1641, and 1681 cm.$^{-1}$ with a weaker band at 1588 cm.$^{-1}$. There is a close parallelism with 4 : 6-dihydroxy-2-methylpyrimidine; by contrast with uracil there is no band above 1700 cm.$^{-1}$. 2-Methylthio-1 : 6-dimethylpyrimid-6-one, which contains a single carbonyl group, is again closely similar to this respect to 4 : 6-dihydroxypyrimidine, and all this evidence may be consistent with its being singly ketonic, *i.e.*, with one carbonyl and one hydroxyl group. Indirectly, this may support the argument that uracil is diketonic. Incidentally, 4 : 6-dihydroxypyrimidine has a band near 3300 cm.$^{-1}$ which could be due to a bonded-hydroxyl group, although no corresponding band is found with 4 : 6-dihydroxy-2-methylpyrimidine.

One feature of the spectra between 700 and 1500 cm.$^{-1}$ which may serve to differentiate the 2 : 4- and the 4 : 6-dihydroxy-derivative is the occurrence of a fairly marked band near 760 cm.$^{-1}$ with the former class, but not with the latter.

2 : 4 : 6-Trihydroxypyrimidine (barbituric acid) has at least three intense bands in the region 1690—1760 cm.$^{-1}$; these bands are again attributed to carbonyl groups. While the spectrum would be consistent with a structure involving two carbonyl groups and one hydroxyl group, it is impossible to infer this directly. In the region of 3μ the spectrum is somewhat similar to that of 4 : 6-dihydroxypyrimidine, having a pair of strong bands at 3087 and 3204 cm.$^{-1}$. The latter of these could be due to a bonded-hydroxyl group, although again its assignment to an imino-group cannot be excluded.

(b) *Amino-derivatives.* Some di- and tri-aminopyrimidines have been examined. All show a complex group of strong bands at 1400—1650 cm.$^{-1}$, assignment of which is difficult. There are three strong bands at 3125, 3300, and 3450 cm.$^{-1}$. The monoamino-derivatives usually show the first two of these bands, but not that at 3450 cm.$^{-1}$. All three are probably due to stretching vibrations of N–H bonds, and in this connexion Clews and Cochran's *X*-ray measurements (*Acta Cryst.*, 1948, **1**, 4; 1949, **2**, 46) on 4 : 6-diamino-5-bromopyrimidine are interesting, since it was found that the two amino-groups are not equivalent, but bonded differently to adjacent molecules in the crystal. This might account for the spectral differences found between the monoamino- and diamino-derivatives.

(c) *Derivatives with hydroxyl and amino-groups.* Three types of compound containing one amino- and one hydroxy-group have been studied, namely derivatives of 2-amino-4-hydroxy-, 2-hydroxy-4-amino-, and 4-hydroxy-6-amino-pyrimidine.

2-Amino-4-hydroxy-6-methylpyrimidine has strong bands near 1500 cm.$^{-1}$ and

* See footnote p. 181.

1659 cm.$^{-1}$. Partial deuteration leaves the former unchanged and the latter appears to be replaced by a pair at 1605 and 1639 cm.$^{-1}$. The band at 1659 cm.$^{-1}$ may in reality be a double band, one component being shifted to 1605 cm.$^{-1}$. This compound has strong bands at 3068 and 3332 cm.$^{-1}$, corresponding to those at 3160 and 3320 cm.$^{-1}$ with most 2-amino-derivatives, including 2-amino-4-ethoxy-6-methylpyrimidine, and these bands must be due to N–H stretching vibrations. On balance the spectra perhaps favour a form in which the hydroxyl group is ketonised and the amino-group remains unchanged except for hydrogen bonding.

2-Amino-4-hydroxy-6-methyl- and 2-amino-4-ethoxy-6-methyl-pyrimidine have strong bands at 1500—1700 cm.$^{-1}$. In the former case, the band at 1649 cm.$^{-1}$ is probably due to a carbonyl group and is not much affected by deuteration, but the latter compound also has a band near 1650 cm.$^{-1}$ which is removed by deuteration. It is therefore clear that we have a number of overlapping or close-lying bands due to carbonyl and N–H bond vibrations, and possibly also to ring vibrations. The bands near 3μ previously attributed to the amino-group are absent from the spectrum of the dimethylamino-derivatives.

Three compounds were measured in which the amino- and hydroxyl groups occupied the 4- and the 6-position with a non-tautomeric substituent in the 2-position. These were 6-amino-4-hydroxy-, 6-amino-4-hydroxy-2-methylthio-, and 6-amino-4-hydroxy-2-methyl-pyrimidine. In the region 1500—1700 cm.$^{-1}$ a close similarity between the spectra might have been expected, but in fact the strong bands occur at noticeably different positions. With 6-amino-4-hydroxypyrimidine the band at 1664 cm.$^{-1}$ is removed by deuteration, indicating that it is due to N–H or O–H, and by analogy with previous results the former alternative would be expected. In that case, the band at 1610 cm.$^{-1}$ would have to be assigned to the carbonyl group, and this seems an extremely low value although hydrogen bonding might lead to a fall below normal. With 6-amino-4-hydroxy-2-methylpyrimidine a band at 1676 cm.$^{-1}$ is removed by deuteration, and another near 1625 cm.$^{-1}$ persists. A corresponding interpretation might be given, but there is always the possibility that the bands just above 1600 cm.$^{-1}$ may be due to ring vibrations. In the region of 3μ, both the 6-amino-4-hydroxy- and 6-amino-4-hydroxy-2-methyl derivatives have strong bands near 3140 cm.$^{-1}$ and 3340 cm.$^{-1}$, and the 6-amino-4-hydroxy-2-methylthio-derivative has a more complex absorption with bands at higher frequencies. These differences must again originate in differences of polar character of groups, and from special interactions. It therefore seems impossible to decide whether the 6-amino-4-hydroxypyrimidines have a keto-amino-structure or remain in the enolic form.

The spectrum of 4-amino-2-hydroxypyrimidine agrees essentially with that reported by Blout and Fields (*J. Amer. Chem. Soc.*, 1950, **72**, 479), but we have obtained better resolution. These workers assigned the bands at 3425 cm.$^{-1}$ and 3205 cm.$^{-1}$ to O–H and N–H vibrations, but as already stated they are probably more satisfactorily explained as being due to the amino-group as in a solid unsubstituted amide group. There are strong bands at 1507, 1541, and 1659 cm.$^{-1}$, similar to those of 2-hydroxypyrimidine, and the changes produced by deuteration are similar. The evidence is consistent with the occurrence of a keto-amino-form.

The spectrum of 6-amino-2 : 4-dihydroxypyrimidine resembles that of the 2 : 4-dihydroxy-6-methyl derivative between 1500 and 1700 cm.$^{-1}$, and both may exist in the diketonic form. 2-Amino-4 : 6-dihydroxypyrimidine has a strong band near 1680 cm.$^{-1}$ which is absent with the corresponding dimethoxy-derivative and the spectrum is more like that of 4 : 6-dihydroxypyrimidine, possibly a ketonic–enolic structure.

2 : 4-Diamino-6-hydroxy- and 4 : 6-diamino-2-hydroxy-pyrimidine differ from each other in the region of 6μ, although they resemble respectively the 6-hydroxy(4-hydroxy)- and 2-hydroxy-derivatives. There is a difference near 3μ between 4 : 6-diamino-2-hydroxy- and 6-hydroxy-2 : 4-diamino-pyrimidine in that the former has a strong band near 3035 cm.$^{-1}$ in addition to the three bands at higher frequency given by both. A parallel difference arises between 2-hydroxy- and 4-hydroxy-pyrimidine. Although therefore the bulk of the evidence may favour a ketonic form for both 2-hydroxy- and 4-hydroxy-derivatives, there may be a difference between hydroxyl groups in the 2- and the 6-position in some cases.

(d) *Mercaptopyrimidines.* Neither 2-methylthio- nor 2 : 4-dimethylthio-pyrimidine has

bands between 1625 and 1800 cm.$^{-1}$. Comparison of the former with 2-hydroxypyrimidine shows that the latter has a band at 1647 cm.$^{-1}$ in addition to that at 1625 cm.$^{-1}$. This again suggests that 2-hydroxypyrimidine is in the ketonic form. An intense band occurs with 4-hydroxy-2-methylthiopyrimidine at 1695 cm.$^{-1}$, corresponding to that found with 4-hydroxypyrimidine itself. However, no band is found near this frequency with either 4-hydroxy-2-methylthio-6-methyl- or 6-amino-4-hydroxy-2-methylthio-pyrimidine, in spite of a general agreement between the spectra. This would imply that either in these latter compounds the structure is enolic, or the carbonyl group band is weakened or displaced.

(5) *Spectra in the Region* 15—25μ.—Some of the compounds were examined in this range, and the results are shown in the diagrams. Although there are no obvious structural correlations, it seems that this spectral region might well prove valuable for analytical work and for identification.

Conclusions

The complexity and ambiguities of the interpretations given above make it desirable to summarise the main conclusions, as follows :

(i) In the hydroxy- and amino-pyrimidines, either alone or with the addition of other substituents around the pyrimidine ring, the main spectral regions of interest as regards the tautomerism which may occur are at 6μ and 3μ. Unfortunately in both these regions certain ambiguities limit the correlation of bands with structure. Near 6μ, bands are to be expected due to bending modes of N–H bonds, to carbonyl groups, and to ring vibrations. The variation in frequency of these key bands with differences of polar character of bonds and special interactions are such as to preclude many definite assignments. Further, the intensity of ring vibrations of the kind concerned is known, with simple derivatives of benzene for example, to vary from one compound to another in a somewhat unpredictable way. In the region of 3μ, too, ambiguities arise in assigning the stretching vibration frequencies of different kinds of N–H and O–H bond. For all these reasons, it would be unwise to be too dogmatic in making frequency assignments.

(ii) The spectra of different derivatives of pyrimidine are highly characteristic, and since most of the bands are sharp, they might be useful for analysis and identification even though precise structural correlations are obscure.

(iii) It is suggested that the balance of the spectral evidence favours a ketonic structure for the simple 2-hydroxy- and 4-hydroxy-pyrimidines, and probably a diketonic form for the 2 : 4-dihydroxy-derivatives. In 4 : 6-dihydroxypyrimidine one ketonic and one enolic group may be present.

(iv) Amino-substituents are thought in general to exist in the non-tautomerised form, and to have the character of an amido-group.

(v) The electronic effects of different substituent groups may influence the tautomerism and also the quantitative degree of interaction through hydrogen bonding.

(vi) Our conclusions do not agree in some respects with those of Brownlie (*loc. cit.*). He did not measure the simple monohydroxy- and monoamino-derivatives, and other compounds in which tautomerism is prevented by appropriate substitution. These latter measurements provide important evidence. Brownlie appears to have accepted an enolic form and we do not think that his assignment of bands near 3150 cm.$^{-1}$ to the hydroxyl group is satisfactory. Also, in arguing for the imino-structure of certain derivatives, he based some conclusions on the occurrence of only one N–H stretching vibration near 3μ, whereas our results with the same compound indicated a more complicated spectrum in this region. We feel that a clear-cut assignment of frequencies in the way proposed by Brownlie is impossible, and that variations with different derivatives may be marked. If the details of structure of a few simple hydroxylic and amino-derivatives could be established by *X*-ray measurements, so that correlations could be made with the spectrum in these cases, it might assist in a more general interpretation.

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