116. *Infrared Absorption Spectra of Dimethyl Sulphoxide Solutions. Part I. Heterocyclic Amines.*

By W. K. Thompson.

The spectra of twenty-one 2-aminopyrimidines, twelve 4-aminopyrimidines, five 5-aminopyrimidines, and nine diaminopyrimidines have been recorded from dimethyl sulphoxide solutions. Their spectra have been compared with those several simple amides, anilines, and aminopyridines. A relation has been found between the NH_2 deformation band of similarly substituted 2- and 4-aminopyrimidines. The behaviour of this absorption is discussed with reference to hydrogen bonding, and its separation from superposition on other bands has been achieved in certain cases. For 2-aminopyrimidines the NH_2 deformation seems to fall into one of three groups according to the electrophilic or nucleophilic character of the substituents. Tentative assignments have been made for the NH_2 scissoring vibrations of diaminopyrimidines.

Infrared spectra of pyrimidines have been published by numerous workers but, with few exceptions, the observations were confined to solids. The present report concerns the infrared spectra of substituted aminopyrimidines dissolved in dimethyl sulphoxide which forms very strong hydrogen bonds with compounds containing NH or OH groups [1] and with other substances such as chloroform.[2] Its high solvent power for heterocyclic compounds has been used for infrared [3] and nuclear magnetic resonance studies, and comparisons of compounds so obtained are free from disturbances due to the solid state.

The powerful interaction of dimethyl sulphoxide with the solute is of particular interest in its effect on the vibrations of amino-groups and, here, the deformation frequencies near 6 μ have been singled out for detailed examination (owing to the greater accuracy of wave-number measurements with sodium chloride optics in this region than near 3 μ). Limited observations on simple amides, anilines, and aminopyridines have been made for comparison.

Experimental.—Spectra were obtained with a Perkin-Elmer model 21 spectrophotometer with a rock-salt prism. Calibration employed water vapour and carbon dioxide bands, and wave numbers at about 3400 $cm.^{-1}$ are accurate to at worst ± 33 $cm.^{-1}$. At 1600 $cm.^{-1}$ the corresponding figure is ± 3 $cm.^{-1}$. Dimethyl sulphoxide (from British Drug Houses Ltd.) was stored over potassium hydroxide and, throughout, precautions were taken to minimize the access of atmospheric water to the hygroscopic solvent. Cell path-lengths from 0·025 to 0·1 mm. were found suitable with solutions of ~5% w/v concentration. Compensation of the solvent left the following regions with low instrument response owing to solvent absorption: ~3400 (absorbed water), 3000—2850, 1455—1385, 1330—1290, 1090—990, 965—920, and 710—685 $cm.^{-1}$.

Results and Discussion.—Aminopyrimidines. Table 1 lists NH_2 deformation bands for some 2-, 4-, and 5-aminopyrimidines, placed in order of increasing frequency.

[1] Allen, Beilfuss, Burness, Reynolds, Tinker, and Van Allan, *J. Org. Chem.*, 1959, **24**, 779.
[2] Barnard, Fabian, and Koch, *J.*, 1949, 2442.
[3] Tamres and Searles, jun., *J. Amer. Chem. Soc.*, 1959, **81**, 2100.

Short and Thompson [4] found an unexplained absorption near 3400 cm.$^{-1}$ for some aminopyrimidines. This may be due to an amino-hydrogen atom remaining unbonded in the solid. Davies and Hallam [5] found a band in the free NH region for acetamide in chloroform and concluded that only one NH bond was involved in association. In the present study it was found that this " free " NH band for the solid disappears on dissolution in dimethyl sulphoxide. Since this also occurs when the NH_2 deformation frequency is close to that for the solid the alternative explanation that this band is an

TABLE 1.

2-, 4-, and 5-Aminopyrimidines.

Spectrum No.	2	4	5	6	In Nujol (cm.$^{-1}$)	In Me_2SO (cm.$^{-1}$)	In CCl_4 (cm.$^{-1}$)
1	NH_2	NMe_2	—	Me	1653s	1621s	—
2	NH_2	NEt_2	—	Me	1647s	1623s	—
3	NH_2		—	—	1653s	1629s	1613vs
4	NH_2	OEt	—	Me	1653s	1629s	—
5	NH_2	Me	—	$N<[CH_2]_5$	1656m 1621s	1629m	—
6	NH_2	NHMe	—	Cl	1658s	1631s, sh	—
7	NH_2	Me	—	Me	1639s	1634s	—
8	NH_2	MeS	—	Me	1637s	1634s	—
9	NH_2	OnPr	—	OPr^n	1656s	1634s	—
10	NH_2	NMe_2	—	Cl	1642s	1634s	—
11	NH_2	OPr^i	—	OPr^i	1650s	1634s	—
12	NH_2	OMe	—	OMe	1639s	1634s	—
13	NH_2	Me	—	$O{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$	1669s	1634s	—
14	NH_2	NHPh	—	Cl	1642s	1637s	—
15	NH_2	OMe	—	—	1647s	1639s	—
16	NH_2	Me	—	Cl	1645s	1642s	—
17	NH_2	Me	—	CN	1656s	1642s	—
18	NH_2	Cl	—	Cl	1667s	1645s	1608vs
19	NH_2	Me	NO_2	Me	1637s	1645s	—
20	NH_2	CCl_3	—	CCl_3	1667w 1634vs	1645s	—
21	NH_2	—	NO_2	—	1661s	1656s	—
22	Me	—	—	NHPh	1653s	1626s	—
23	Me	—	N·CHO	NEt_2	1669s	1629m	—
24	—	—	Br	OMe	1653s	1639s	—
25	$N<[CH_2]_5$	—	—	Me	1656s	1642s	—
26	NMe_2	—	—	Cl	1621s	1642s	—
27	—	NH_2	—	—	1661vs	1645s	1613vs
28	Me	NH_2	—	Me	1664s	1645s	—
29	SMe	NH_2	—	Cl	1650s	1645s	—
30	Me	NH_2	Et	Cl	1667s	1647s	—
31	Me	NH_2	—	Cl	1661vs	1647s	—
32	—	NH_2	—	—	1667s	1653s	—
33	Cl	NH_2	—	Cl	1656vs	1658m	—
34	—	OMe	NH_2	OMe	1600vs	1587vs	1600vs
35	Me	OMe	NH_2	OMe	1600vs	1600m *	1613w *
						1587vs	1597vs
36	OMe	OMe	NH_2	Me	1626m, sh 1592s	1626m * 1587vs	1592s–vs
37	$NHPr^i$	Me	NH_2	Me	1634m	1637w–m	—
38	—	Cl	NH_2	Cl	1621s	1639s	1605s

Compound No. 3 absorbed at 1610vs, 1626 * in chloroform solution.
* Inflexion.

overtone of the deformation appears unattractive. The NH stretching vibrations of the aminopyrimidines in dimethyl sulphoxide are otherwise little removed in frequency from the values for the solids. A small variation, comparable with the experimental error, makes the effect of substitution difficult to discern.

In the 1700—1600 cm.$^{-1}$ region a strong band occurs in all the primary aminopyrimidines and is clearly due to an NH_2 deformation. Short and Thompson [4] and Brown

[4] Short and Thompson, *J.*, 1952, 168.
[5] Davies and Hallam, *Trans. Faraday Soc.*, 1951, **47**, 1170.

et al.[6] have shown that this band moves on deuteration: the smaller shifts, in dimethyl sulphoxide, as the degree of association changes, are also consistent with an NH_2 deformation.

The lower deformation frequencies arise with substituents causing an overall donation of electrons to the ring; the highest apparently occur with electron-attracting substituents, *e.g.*: nos. 1—5, 1620—1629 cm.$^{-1}$; 6—15, 1629—1639 cm.$^{-1}$; 16—21, 1642—1656 cm.$^{-1}$.

It is probable that dimethyl sulphoxide normally increases the deformation frequencies above the value found for chloroform or carbon tetrachloride solutions, though few observations on these two solutions have been recorded. In solid 2-amino-4-methyl-6-piperidinopyrimidine bands at 1656 and 1621 cm.$^{-1}$ occur and may be associated with different environments in the crystal. In dimethyl sulphoxide this substance gives rise to only one NH_2 deformation band at 1629 cm.$^{-1}$ with a ring vibration at 1587 cm.$^{-1}$ whereas in carbon tetrachloride solution the ring vibration and NH_2 deformation appear together at 1590 cm.$^{-1}$.

In the case of the 4-aminopyrimidines the average value of the NH_2 deformation frequency is higher by about 7 cm.$^{-1}$ than those in Table 1. In going from (I) to (II) the NH_2 deformation frequency is raised, as shown in Table 2. This suggests that the 4-amino-groups interact more strongly with dimethyl sulphoxide than the 2-amino-groups studied.

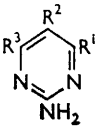
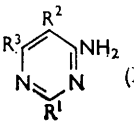
(I)  (II) 

TABLE 2.

R^1 *	Me	Cl	NMe_2	$N<[CH_2]_5$	Me
R^3	Me	Cl	Cl	Me	Cl
δNH_2(2-) (cm.$^{-1}$)	1634	1645	1634	1629	1642
δNH_2(4-) (cm.$^{-1}$)	1645	1658	1642	1642	1647

* R^2 = H.

Too few 5-aminopyrimidines have been studied to justify any general conclusions, but it may be noted that those with electron-donating substituents again have low δNH_2 values.

Anilines and aminopyridines (Table 3) have been observed in dimethyl sulphoxide and

TABLE 3.

No.	Substance	Liquid or Nujol (cm.$^{-1}$)	In Me_2SO (cm.$^{-1}$)	In CCl_4 (cm.$^{-1}$)	In $CHCl_3$ (cm.$^{-1}$)	Ring vibrations: In CCl_4 (cm.$^{-1}$)	Ring vibrations: In Me_2SO (cm.$^{-1}$)
44	2-Aminopyridine	1626s	1634s		1613vs		
45	3-Aminopyridine	1653m * 1634m	1642m		1621vs		
46	4-Aminopyridine	1650s	1645s		1626vs		
47	2,6-$C_6H_3Br_2$·NH_2	1613vs	1618s	1610vs		1553m	1550w
48	2,6-$C_6H_3Cl_2$·NH_2	1616vs	1626s	1616vs		1570s	1562m
49	Aniline	1623s	1639s	1623s		1605s, sh	1608vs 1600ms
50	2,6-$C_6H_3Me_2$·NH_2	1623s	1642s	1621s		1481vs	1600m–s 1481vs
51	*m*-C_6H_4Cl·NH_2	1621vs	1642m	1623vs		1600vs 1592m *	1603vs
52	3,5-$C_6H_3Cl_2$·NH_2	1623s	1645s	1623s		1600vs 1575vs	1600vs 1575vs

Pyridines: The frequencies for the chloroform solutions are in reasonable agreement with those of Angyal and Werner (*J.*, 1952, 2911) who claim an accuracy of 20 cm.$^{-1}$.

Anilines: The δNH_2 value for aniline is 5 cm.$^{-1}$ higher than the (probably correct) value obtained by use of a grating instrument (Tsuboi, *Spectrochim. Acta*, 1960, **16**, 505; Evans, *ibid.*, p. 428).

[6] Brown, Hoerger, and Mason, *J.*, 1955, 4035.

both groups show marked increases in δNH_2 over their condensed phases or carbon tetrachloride solutions. By contrast the primary amides studied give amide II frequencies (Table 4) virtually unaltered in dimethyl sulphoxide, as compared with the condensed phase, indicating a similar degree of association of the amino-groups in the two environments.

TABLE 4.

		In Nujol	In Me_2SO		In $CHCl_3$	
No.	Substance	Amide II ($cm.^{-1}$)	Amide II ($cm.^{-1}$)	Amide I ($cm.^{-1}$)	Amide II ($cm.^{-1}$)	Amide I ($cm.^{-1}$)
39	Acetamide	1639s	1639s	1678vs	1600m–s	1678vs
40	Adipamide	1639s	1634w *	1681vs		
41	Benzamide	1629s–vs	1629m–s	1681vs	1600s?	1681vs
42	Propionamide	1634s	1631s	1684vs	1597m–s	1684vs
43	3,5-Dinitrobenzamide	1637s	1631s	1698s		

N-*Monoacyldiaminopyrimidines*. 2-Amino-5-formamido-4,6-dimethylpyrimidine is of particular interest and is, indeed, the compound which prompted this investigation. A single absorption occurs at 1650 $cm.^{-1}$ in the condensed phase. The highest-frequency ring band is at 1570 $cm.^{-1}$, and the amide II band is probably that at 1506 $cm.^{-1}$. In dimethyl sulphoxide solution bands occur at 1689vs, 1634m, 1572s, and 1513m $cm.^{-1}$, which are interpreted as amide I, amino-deformation, ring vibration, and amide II bands, respectively. The superposition of amide I and amino-deformation bands has, also, been observed by other workers [7] in connection with hydroxyurea, formamide, and phenylacetamide.

Diaminopyrimidines. Short and Thompson [4] published the spectra of several diaminopyrimidines recorded from the condensed phase, but owing to the complexity of the spectra in the region 1400—1650 $cm.^{-1}$ no assignments were made. A comparison of the spectra of some diaminopyrimidines (Table 5) with those of related monoamino- or amino-dialkyl-

TABLE 5.

Diaminopyrimidines.

	Substituents				In	In	Probable ring vibration frequencies				
							In Nujol				In Me_2SO
No.	2	4	5	6	Nujol	Me_2SO					
53	NH_2	NH_2	—	Me	1686m 1653s	1645s * 1626s	1610vs	1553s	1416s	1025w 999w	1592vs 1565s
54	NH_2	Me	NH_2	—	1650s 1605m	— 1623s	1575s			1012m	1567s 1548m *
55	NH_2	Me	NH_2	Me	1658m 1616s	— 1621s	1577vs	1541m *	1395vs		1575vs 1543m *
56	—	NH_2	NH_2	—	1684s 1645s * 1637s	1669m 1634s	1585vs	1572s * 1565m * 1548w, sh 1502vs	1437s		1577vs 1541w–m 1486vs
57	—	NH_2	NH_2	Me	1681s 1653m 1629m	1678m 1631s	1595vs			1023w 998w	1582vs 1548m *
58	Me	NH_2	NH_2	NMe_2	1664s 1626m	1664s 1626s	1585vs	1483s, sh	1422s, sh	1003m 973m	1580vs
59	Me	NH_2	NH_2	NEt_2	1664s 1618m	1664s 1618s	1590vs	1562m *	1418	1000vw	1580vs 1548m *
60	—	NH_2	NH_2	NEt_2	1675m	1667s 1618s	1592vs	1550m *		974m	1580vs 1550m *
61	NMe_2	NH_2	—	NH_2	1634s	1634s	1575vs	1543m *	1399s		1577vs 1546m * 1529m–sh

For compound 60 the 1592vs $cm.^{-1}$ ring band probably also incorporates the 5-amino-group deformation band, shown at 1618s $cm.^{-1}$ for dimethyl sulphoxide solution. Cf. 2,6-dimethylaniline.

amino-pyrimidines in dimethyl sulphoxide has now made it possible to make tentative assignments for the deformation modes of the amino-groups. No diamino-compounds

[7] Davies and Spiers, *Spectrochim. Acta*, 1959, **15**, 487.

containing electron-attracting groups were examined. All the diamines containing a 4-amino-group and no other powerful electron-donating group absorbed at 1681—1686 cm.$^{-1}$ in the condensed phase. Introduction of a dimethylamino-group reduces this frequency to 1664—1674 cm.$^{-1}$ (cf. 4-aminopyrimidines). The degree of hydrogen bonding in dimethyl sulphoxide seems particularly high for 4,5-diaminopyrimidines relative to the 2,6- and 4,6-compounds. Diamines containing a 2-amino-group absorb in the condensed phase at 1650—1658 cm.$^{-1}$, falling to 1621—1626 cm.$^{-1}$ in dimethyl sulphoxide. This is in agreement with the results for 2-aminopyrimidines containing powerful electron-donating groups. Diamines containing a 5-amino-group absorb in the normal range (1618—1631 cm.$^{-1}$) in dimethyl sulphoxide. Classification of diaminopyrimidines in a manner analogous to that for the 2-aminopyrimidines is not possible because of the presence of the second amino-group.

Ring vibrations. Little attempt has been made, in the past, to correlate ring bands with structure for substituted pyrimidines. Katritzky [8] listed frequency ranges for these absorptions: 1590—1555, 1565—1520, 1480—1400, and 1410—1375 cm.$^{-1}$. A band assigned to ring breathing usually occurs near 990 cm.$^{-1}$. Full interpretation of the infrared spectra of substituted pyrimidines has been made more difficult by the absence of Raman data.

For reasons previously stated, only the first two groups of ring frequencies and part of the third can be observed in the present work. All the compounds absorbed between 1570 and 1517 cm.$^{-1}$. For similarly substituted 2- and 4-amino- or dialkylamino-pyrimidines there appears to be no appreciable difference in the position or intensity of the two high-frequency ring bands. These compounds and those containing alkyl or alkoxy-groups, with or without one or two halogen atoms, absorbed very strongly between 1605 and 1572 cm.$^{-1}$. The work of Wiley and Slaymaker [9] supports this observation. Sometimes two bands occur in this range. Halogenopyrimidines containing no powerful electron-donating group exhibit no strong absorption between the C–H stretching region and 1575 cm.$^{-1}$ either in the condensed phase or in dimethyl sulphoxide. An increase in the number of halogen atoms lowers this upper limit to 1520 cm.$^{-1}$. Of the few 5-amino-pyrimidines examined the three which contained alkyl or alkoxy-substituents showed a very strong band at 1587 cm.$^{-1}$; and, as expected, 5-amino-4,6-dichloropyrimidine has its highest-frequency ring band at 1517 cm.$^{-1}$, but unlike the others of the series does not absorb near 1482 cm.$^{-1}$.

In carbon tetrachloride solution all absorbed at 1390—1420m-vs cm.$^{-1}$. Some twenty compounds which did not contain a primary amino-group were examined to help establish the above facts. Attempts to obtain the spectrum of 2,4-dichloro-5-nitropyrimidine in dimethyl sulphoxide were unsuccessful owing to rapid hydrolysis by the water in the sulphoxide. Instead the spectrum of 5-nitrouracil was obtained.

I thank Dr. R. Hull for supplying many of the compounds, Dr. A. Hayes for the sample of 2-amino-4-cyano-6-methylpyrimidine, and Dr. J. M. Pryce for his helpful advice.

IMPERIAL CHEMICAL INDUSTRIES LIMITED, PHARMACEUTICALS DIVISION,
RESEARCH DEPARTMENT, ALDERLEY PARK,
MACCLESFIELD, CHESHIRE.
[Present address: FISONS FERTILIZERS LIMITED, LEVINGTON RESEARCH STATION,
LEVINGTON, IPSWICH, SUFFOLK.] [*Received, August 30th*, 1961.]

[8] Katritzky, *Quart. Rev.*, 1959, **13**, 353.
[9] Wiley and Slaymaker, *J. Amer. Chem. Soc.*, 1957, **79**, 2233.