The Structure of the Cations from 2- and 4-Pyrimidones (1)

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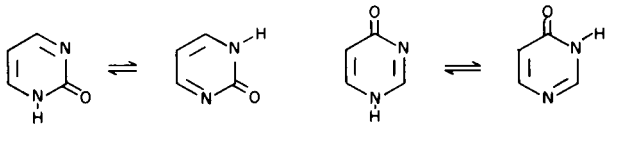
An infrared spectral investigation of a number of pyrimidine and pyrimidone hexachloroantimonates is reported. Typical aromatic absorption bands found in pyrimidinium salts were absent in the pyrimidone cations. 2-And 4-Pyrimidone hexachloroantimonates, as well as their *N*-methyl- and *N,N'*-dimethyl derivatives, exhibit intense carbonyl absorption bands between 1720-1729 cm^{-1} (solid state) which corroborates *N*-protonation of pyrimidones.

The simplest potentially tautomeric "amidic" pyrimidine derivatives are 2- and 4-pyrimidone. A knowledge of their fine structure, as well as that of their salts, assumes significance since this type of "lactam" grouping is prominent in many pyrimidine and purine bases of nucleic acids. Infrared (IR) spectral studies have established that 2- and 4-pyrimidone exist in the solid state and in solutions as the highly hydrogen-bonded cyclic "urea", **1**, and the cyclic *N*-acyl "amidine", **2**, respectively (2-6). The high-frequency C=O stretching modes in **1** and **2** leaves little doubt on this structure assignment.

From a study of 2- and 4-pyrimidone hydrochlorides, Spinner concluded that both bases are protonated on one of the ring nitrogen atoms (7). The evidence was the high-frequency C=O absorption between 1731-1704 (solid) and 1754-1726 (solution) cm^{-1}. Since the use of hexachloroantimonic acid enabled us to distinguish more clearly between *O*- and *N*-protonation in pyridones (8), we sought to apply this technique to 2- and 4-pyrimidone and their *N*-methyl derivatives. This work describes an IR investigation of the hexachloroantimonates of 2- and 4-pyrimidone and a number of 2- and 4- substituted pyrimidines. The use of the complex anion enabled us to handle these salts more readily than the hydrochlorides. Furthermore, there appeared to be less hydrogen-bonding in these crystalline hexachloroantimonates as witnessed by sharper bands in the NH stretching region. Full spectra are recorded (1), but only pertinent bands are discussed below.

2-Pyrimidone Cations.

Partial infrared assignments of pyrimidine, 2-methoxy and 2-chloropyrimidine, 2-pyrimidone, 1-methyl-2-pyrimidone, and 1,3-dimethyl-2-pyrimidone hexachloroantimonates are compiled in Table I. It would be expected that pyrimidine, 2-chloro- and 2-methoxypyrimidine protonate on one of the ring nitrogen atoms and the resulting salt exhibits an NH stretching mode (3150-3250 cm^{-1}). However, 2-pyrimidone, **1**, and its *N*-methyl derivative, **3**, accept the proton on the other ring nitrogen atom to give rise to cations, **4a** and **4b**, respectively. The last two salts show NH stretching vibrations while bands at higher frequencies expected from OH stretching modes were absent



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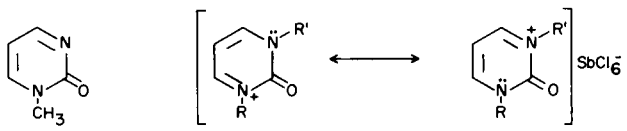

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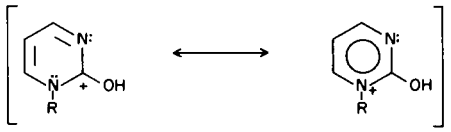
4a: R = R' = H
b: R = CH_3, R' = H
c: R = R' = CH_3



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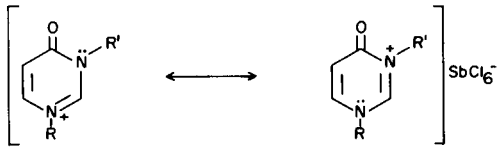

6a: R = CH_3, R' = H
b: R = H, R' = CH_3
c: R = R' = CH_3

TABLE I

Assigned Infrared Absorption Bands (cm^{-1}) of Cations of some 2-Substituted Pyrimidinium and 2-Pyrimidone Hexachloroantimonates (From Nujol and Fluorolube Mulls).

	Pyrimidine	2-Methoxy-pyrimidine	2-Chloro-pyrimidine	2-Pyrimidone	1-Methyl-2-pyrimidone	1,3-Dimethyl-2-pyrimidone
N-H Stretching Mode	3253 s 3158 w	3248 s 3160 s	3202 m	3253 s	3257 w	
C-H Stretching Mode	3080 w	3095 m 3052 w 3030 w	3128 w 3088 m 3051 m	3135 w 3062 w	3123 m 3058 m	3123 w 3067 w
C=O Stretching Modes				1792 vs 1761 s	1748 vs	1762 vs
Ring Modes	1631 m 1617 m	1630 sh	1628 w			
		1605 vs	1602 s 1575 s	1602 s	1602 s	1589 s
	1530 m	1535 m	1508 m	1494 m 1478 w	1509 m 1474 m	1470 w
	1452 s	1435 s	1430 m		1444 m	1420 w

TABLE II

Assigned Infrared Absorption Bands (cm^{-1}) of Cations of some 4-Substituted Pyrimidinium and 4-Pyrimidone Hexachloroantimonates (From Nujol and Fluorolube Mulls).

	4-Methoxy-pyrimidine	4-Chloro-pyrimidine	4-Pyrimidone	3-Methyl-4-pyrimidone	1-Methyl-4-pyrimidone	1,3-Dimethyl-4-pyrimidone
N-H Stretching Modes	3310 s	3248 m-b	3255 m 3180 m	3180 w	3300 m	
C-H Stretching Modes	3147 vw 3100 w 3075 vw	3147 m 3108 m 3065 w	3080 m	3053 m	3095 m	3103 w
C=O Stretching Modes			1730 vs	1719 vs	1750 vs 1720 s	1740 s
Ring Modes	1648 s	1635 w 1612 s	1671 m	1682 s	1685 m	1680 m
	1580 s	1582 s	1576 m 1559 m	1577 m 1551 m	1544 m	
	1500 s				1525 w 1476 w	1498 m
	1424 m	1444 s	1441 m	1421 w	1438 m	

TABLE III

Elemental Analyses and Physical Constants of Pyrimidine and Pyrimidone Hexachloroantimonates.

Hexachloroantimonate	M.P., °C	Formula		Analyses C, %	H, %	N, %
Pyrimidine	249-251	$C_4H_5Cl_6N_2Sb$	Calcd.	11.56	1.21	6.73
			Found	1.52	1.51	6.67
2-Methoxypyrimidine	158-160	$C_5H_7Cl_6N_2OSb$	Calcd.	13.48	1.58	6.29
			Found	13.69	1.82	6.29
2-Chloropyrimidine	155-160	$C_4H_4Cl_7N_2Sb$	Calcd.	10.68	0.90	6.23
			Found	11.24	1.37	6.30
2-Pyrimidone	244-246	$C_4H_5Cl_6N_2OSb$	Calcd.	11.13	1.17	6.49
			Found	11.14	1.19	7.14
1-Methyl-2-pyrimidone	164-166	$C_5H_7Cl_6N_2OSb$	Calcd.	13.48	1.58	6.29
			Found	13.68	1.76	6.53
1,3-Dimethyl-2-pyrimidone	204-206	$C_6H_9Cl_6N_2OSb$	Calcd.	15.68	1.98	6.10
			Found	15.84	2.07	6.10
4-Methoxypyrimidine	90-95	$C_5H_7Cl_6N_2OSb$	Calcd.	13.48	1.58	6.29
			Found	13.48	2.14	6.03
4-Chloropyrimidine	170-175	$C_4H_4Cl_7N_2Sb$	Calcd.	10.68	0.90	6.23
			Found	10.61	1.55	6.16
4-Pyrimidone	253-255	$C_4H_5Cl_6N_2OSb$	Calcd.	11.13	1.17	6.49
			Found	11.50	1.29	6.19
1-Methyl-4-pyrimidone	245-247	$C_5H_7Cl_6N_2OSb$	Calcd.	13.48	1.58	6.29
			Found	13.81	1.72	6.33
3-Methyl-4-pyrimidone	205-207	$C_5H_7Cl_6N_2OSb$	Calcd.	13.48	1.58	6.29
			Found	13.79	1.80	6.57
1,3-Dimethyl-4-pyrimidone	233-237	$C_6H_9Cl_6N_2OSb$	Calcd.	15.68	1.98	6.10
			Found	16.01	2.07	6.10

(9). In **4c**, no NH or OH stretching bands were expected or seen. The outstanding band in the salts, **4a** - **4c**, was the intense high-frequency C=O absorption between 1748 and 1792 cm^{-1}, which was completely absent in the other three aromatic pyrimidinium salts. It is thus evident that **1** and **3** protonate exclusively on the other ring nitrogen atom to produce the symmetrical resonance-stabilized cation, **4**. The process to attach the proton on the carbonyl oxygen of the pyrimidone to produce **5** is not favored since the charge cannot be distributed over both ring nitrogen atoms as in **4**.

Except for the single strong band at about 1600 cm^{-1} all other bands were found to be very weak in the spectra of the 2-pyrimidone cations. The unsubstituted and 2-substituted pyrimidinium cations resemble the IR spectra of the pyridinium cations above 1400 cm^{-1}. As usual, the high frequency aromatic mode near 1630 cm^{-1} is considerably diminished in intensity in 2-chloropyrimidinium hexachloroantimonate. The spectra below 1400 cm^{-1} were rather complex and no further band assignments were made, nor was it possible to determine at present the location of the CH_3 deformation mode (around 1425 cm^{-1}).

4-Pyrimidone Cations

Table II contains assignments for pertinent bands for 4-methoxy- and 4-chloropyrimidinium, and various 4-pyrimidone hexachloroantimonates above 1400 cm^{-1}. The site of protonation is again on the nitrogen since there are absorption bands around 3200 - 3300 cm^{-1} in all species,

except in the 1,3-dimethyl-4-pyrimidone derivative, **6c**, where the quaternary nitrogen atoms already bear alkyl groups. As in the 2-series, the strongest bands in the 4-pyrimidone cations, **6a-6c**, are found above 1700 cm^{-1} (1720-1750 cm^{-1}) and are undoubtedly carbonyl stretching modes. In general, the C=O stretching frequencies are somewhat lower than for isomeric 2-pyrimidone cations. The higher C=O frequency in 2-pyrimidone salts, **4**, is probably due to the sandwiching of the C=O group between two electrophilic ring nitrogen atoms.

There is one other obvious difference between 2- and 4-pyrimidone cations. Whereas the highest ring mode frequency in 2-pyrimidone salt was found at about 1600 cm^{-1}, in 4-pyrimidone cations a strong band was observed between 1670-1680 cm^{-1}. The latter could involve the C=C stretching motion since in cations produced from 1- and 3-methyl-4-pyrimidone on protonation, **6a** and **6b**, and in **6c**, delocalization of the positive charge does not involve the α,β-unsaturated carbonyl system. This is quite in contrast to **4**, where the diene system is considerably more delocalized and not conjugated directly with a C=O group.

The IR spectra of **6a**, **6b** and **6c** below 1600 cm^{-1} are rather undistinguished. The spectrum of the 1,3-dimethyl-4-pyrimidone cation, **6c**, is perhaps unique, being marked by its simplicity. Only a single band of medium intensity is found in the 1400-1650 cm^{-1} region. The aromatic 4-substituted pyrimidinium cations show rather high-frequency absorption in the aromatic region around 1640 cm^{-1}. This is higher than corresponding bands in the 2-pyrimidinium cations. For example, the high-frequency band in the 4-methoxypyrimidine cation appears at 1648 cm^{-1}, while the 2-isomer has a shoulder at 1630 cm^{-1} with a strong band at 1605 cm^{-1}.

EXPERIMENTAL

Starting Materials.

Pyrimidine was synthesized by desulfurizing 2-pyrimidinethione with Raney nickel, modifying the procedure published by Hunt, McOmie, and Sayer (10). 2-Pyrimidone was prepared according to the method of Crosby and Berthold (11). 1-Methyl-2-pyrimidone was obtained using the method of Curd and Richardson (12). 2-Chloropyrimidine was prepared from 2-aminopyrimidine using the procedure of Overberger, Kogon and Minin (13). Raney nickel desulfurization of 2-thiouracil, according to Brown (14), yielded 4-pyrimidone. 4-Chloropyrimidine hydrochloride was obtained from 4-pyrimidone by treatment with phosphoryl chloride (15). Both 1-methyl-4-pyrimidone and 3-methyl-4-pyrimidone were obtained by methylation of 4-pyrimidone (16).

2-Methoxypyrimidine.

The literature method (4) was modified considerably. 2-Chloropyrimidine (12.5 g., 0.11 mole) was dissolved in 60 ml. of tetrahydrofuran. The resulting solution was added dropwise to a to a mixture of sodium methoxide (7.6 g., 0.14 mole) in tetrahydrofuran (125 ml.) over 0.5 hour. The mixture was stirred for an additional 0.5 hour at 25° and then heated under reflux for a like period. The mixture was filtered and the product was obtained by distillation. The yield was 9.0 g. (79%), b.p. 80° (25 mm.)., lit. b.p. 72.5° (22 mm.) (15).

4-Methoxypyrimidine.

4-Chloropyrimidine hydrochloride (freshly prepared, 13.5 g., 0.09 mole) was dissolved in methanol (40 ml.) and added to a solution of sodium methoxide (12.0 g., 0.22 mole) in tetrahydrofuran. On working up the reaction mixture as described above for 2-methoxypyrimidine, afforded 4.2 g., (25%) b.p. 65° (20 mm.); lit. b.p. 69-70° (30 mm.) (4).

Preparation of Hexachloroantimonates.

The salts were prepared by the same general methods described for the pyridinium salts (8). Elemental analyses and physical constants for these salts are given in Table III. Best results were achieved when the salts were filtered and washed on the funnel in a dry-box, transferred into a vacuum desiccator in the dry-box. The dry samples were taken out of the desiccator in dry-box, mulled and mounted in the dry-box before their spectra were determined (8).

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(9) Extreme caution must be exercised to isolate, dry and mull these salts in a dry-box. Spurious OH stretching bands may appear if these salts are handled outside the dry-box.

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