Thermochimica Acta, 91 (1985) 173–183
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

SPECTROSCOPIC AND THERMAL CHARACTERIZATION OF SOME 4-GLYCOPYRANOSYLAMINO-PYRIMIDINE DERIVATIVES

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(Received 20 March 1985)

ABSTRACT

The characterization of seven 2-methoxy-4-glycopyranosylamino and 2-methylthio-4-glycopyranosylamino pyrimidine derivatives has been studied by elemental analysis, IR and UV spectra. The spectral data enable us to suppose that all the compounds are in the ketonic tautomeric form in the solid state. The thermal data show that all the compounds are anhydrous, melting at temperatures below their pyrolytic decompositions. The enthalpy values of these processes have been calculated from DSC curves.

INTRODUCTION

Interest in both pyrimidine derivatives and their nucleosides is widespread [1–3]. Recently, this interest has also been extended to some of their metal complexes, in view of their cytostatic influence [4–6]. This is why we have seen fit to complete the spectral study of the 4-glycopyranosylamino-pyrimidine derivatives given in Scheme 1, whose synthesis and ^{1}H NMR spectral study were previously reported [7], and, likewise to carry out the study of their thermal behaviour, as a step in the study of some of their metallic complexes. This report can also be considered as a lengthening of a previous work [8].

EXPERIMENTAL

The synthesis and purification of the seven compounds studied were carried out by methods reported by the authors in a recent paper [7], using analytical reagent grade chemicals.

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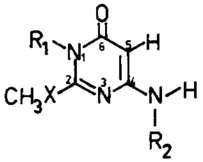

Scheme 1

Compound	R_1	X	R_2
A	H	O	β-Glucopyranosyl
B	CH_3	O	β-Xylopyranosyl
C	CH_3	O	β-Glucopyranosyl
D	H	S	β-Xylopyranosyl
E	H	S	β-Glucopyranosyl
F	CH_3	S	β-Xylopyranosyl
G	CH_3	S	β-Glucopyranosyl

To characterize the compounds obtained, microanalyses of C, H and N were performed at the National Institute of Organic Chemistry (C.S.I.C., Madrid). Data of the analyses and yields are given in Table 1.

Likewise, ^{1}H NMR spectra were obtained with a Hitachi/Perkin-Elmer R-600 FT-NMR spectrometer, using DMSO-d_6 and D_2O as solvents, and TMS as internal standard.

To record the IR spectra in the range 4000–200 cm^{-1}, a Beckman 4250 spectrophotometer was used, starting from the compounds in KBr pellet form. UV spectra in the range 400–200 mn were recorded on a Beckman 25 spectrophotometer, using aqueous solutions of the compounds in all cases.

The thermal analyses were obtained from samples varying in weight from 1.544 to 10.530 mg. TG curves were obtained with a Mettler TG 50 thermobalance, in a static pure air atmosphere, at a heating rate of 10°C min^{-1}. DSC curves were recorded on a Mettler DSC-20 differential scanning calorimeter at the same heating rate as above.

TABLE 1

Analytical and yield data (the analytical data in parentheses are theoretical values)

Compound	%C	%H	%N	Formula	Yield %
A	43.48(43.56)	5.68(8.65)	13.66(13.86)	$C_{11}H_{17}N_3O_7$	44
B	45.66(45.99)	6.19(5.97)	14.22(14.63)	$C_{11}H_{17}N_3O_6$	49
C	45.44(45.42)	5.81(6.04)	12.88(13.24)	$C_{12}H_{19}N_3O_7$	51
D	41.23(41.45)	5.29(5.23)	14.40(14.52)	$C_{10}H_{15}N_3O_5S$	70
E	41.44(41.37)	5.63(5.37)	13.52(13.16)	$C_{11}H_{17}N_3O_6S$	64
F	43.38(43.55)	5.87(5.65)	14.03(13.85)	$C_{11}H_{17}N_3O_5S$	60
G	43.12(43.23)	5.61(5.74)	12.60(12.60)	$C_{12}H_{19}N_3O_6S$	62

RESULTS AND DISCUSSION

The IR spectral data of the seven compounds isolated are given in Table 2.

In all these IR spectra, a group of bands appears which are absent from those of the respective pyrimidine derivatives [9], and can be assigned to the sugar rest. In the high range of frequency values $\nu(OH)$ stretching vibrations appear due to –OH groups. These bands are differentiated from the $\nu(NH)$ bands only in the IR spectra of compounds A and B.

Stretching vibrations, $\nu(C–O)$, of the sugar rests appear in the range 1000–1150 cm^{-1}. All the spectra (except that for compound D) show three bands in the range 740–970 cm^{-1} which could be assigned to three characteristic bands, defined for both α- and β-pyranosic rings [10].

The IR spectra of compounds A, D and E show several bands of medium intensity in the 2500–3000 cm^{-1} range, as for the homologous 5-nitrosopyrimidine derivatives [8]. This fact has been related to molecular interactions by hydrogen bonding through N_1–H groups [11]. The bands appearing in all the IR spectra in the 2800–3000 cm^{-1} range are due to C–H stretching vibrations. $\nu(C_5–H)$ bands are differentiated only in the spectra of compounds B, D and E, where bands appear at 3010, 3040 and 3060 cm^{-1}, respectively.

The strong bands arising in the 1620–1650 cm^{-1} range of the IR spectra, can be assigned to the $\nu(C=O)$ stretching vibration. This feature enables us to suppose that all the compounds are in the ketonic tautomeric form in the solid state.

Finally, the $\nu(C–S)$ stretching vibration has been assigned on the basis of literature data [12].

The UV spectral data of the seven compounds obtained are given in Table 3. Tentative assignments of the bands observed have been made on the basis of literature data for pyrimidine derivatives [13–15].

The TG and DSC curves of the seven compounds obtained are shown in Figs. 1 and 2. The melting and decomposition temperatures, and the weight losses and enthalpies have been calculated from these figures. All the results obtained are given in Table 4.

The TG and DSC curves of the compounds prove their anhydrous character, except for compound D, which suffers a weight loss (3.7%) that can be assigned to weak-linked (18.7 kJ mol^{-1}) non-stoichiometric water. The anhydrous character of these compounds opposes the hydration of some of their 5-nitroso homologues [8]; this feature enables us to suppose that in the last compounds the 5-nitroso groups probably play a large role in the linkage of water via hydrogen bonds.

Two types of processes can be characterized in the TG and DSC curves: melting and pyrolytic decompositions.

The DSC curves of the seven compounds show endothermic effects whose

TABLE 2
IR spectral data

Compound	Assignment (cm^{-1})									
	ν(O–H)	ν(N–H)	ν(C–H) aromatic	ν(C=O)	ν(C=N)	ν(C=C)	ν(C–N)	ν(C–O)	Pyranosic ring	ν(C–S)
A	3520(m)	3280(s,br)	3100(m)	1650(s)	1600(s,br)		1290(s) 1210(m)	1130(m) 1110(m) 1075(s) 1015(s)	940(m) 895(m) 740(w)	—
B	3440(m)	3320(s)	3010(w)	1630(s)	1570(s) 1530(s)		1280(m) 1210(s)	1095(s) 1070(s) 1050(m)	925(w) 890(w) 770(w)	—
C	3360– 3290(w)	3360– 3290(w)	—	1635(s,br)	1550(s,br)		1290(m) 1270(m) 1220(s)	1120(m) 1085(s) 1040(s)	940(w) 900(w) 770(w)	—
D	3420– 3200(m,br)	3420– 3200(s,br)	3040(w)	1650(s)	1595(m) 1555(m)		1285(m) 1240(m,br)	1160(m) 1090(w) 1065(w) 1050(w) 1035(m)	965(m) 890(w)	665

E	3400(s,br)	3270(s,br) 3180(s)	3060(m)	1635(s)	1605(s) 1555(s)	1290(m) 1225(s)	1130(s) 1105(s) 1070(s) 1055(s) 1030(s) 1015(s)	910(w) 890(m) 765(w)	640
F	3400(m,br)	3340(s)	—	1625(s)	1580(s,br) 1530(s,br)	1275(m) 1230(d)	1100(s) 1070(s) 1050(s) 1010(m)	970(m) 895(w) 765(w)	615
G	3420(s)	3280(s,br)	—	1620(s)	1580(s) 1520(s)	1290(m) 1270(m) 1255(m)	1140(w) 1120(m) 1095(s) 1070(s) 1025(s)	910(w) 890(w) 770(w)	630

s, strong; m, medium; w, weak; br, broad.

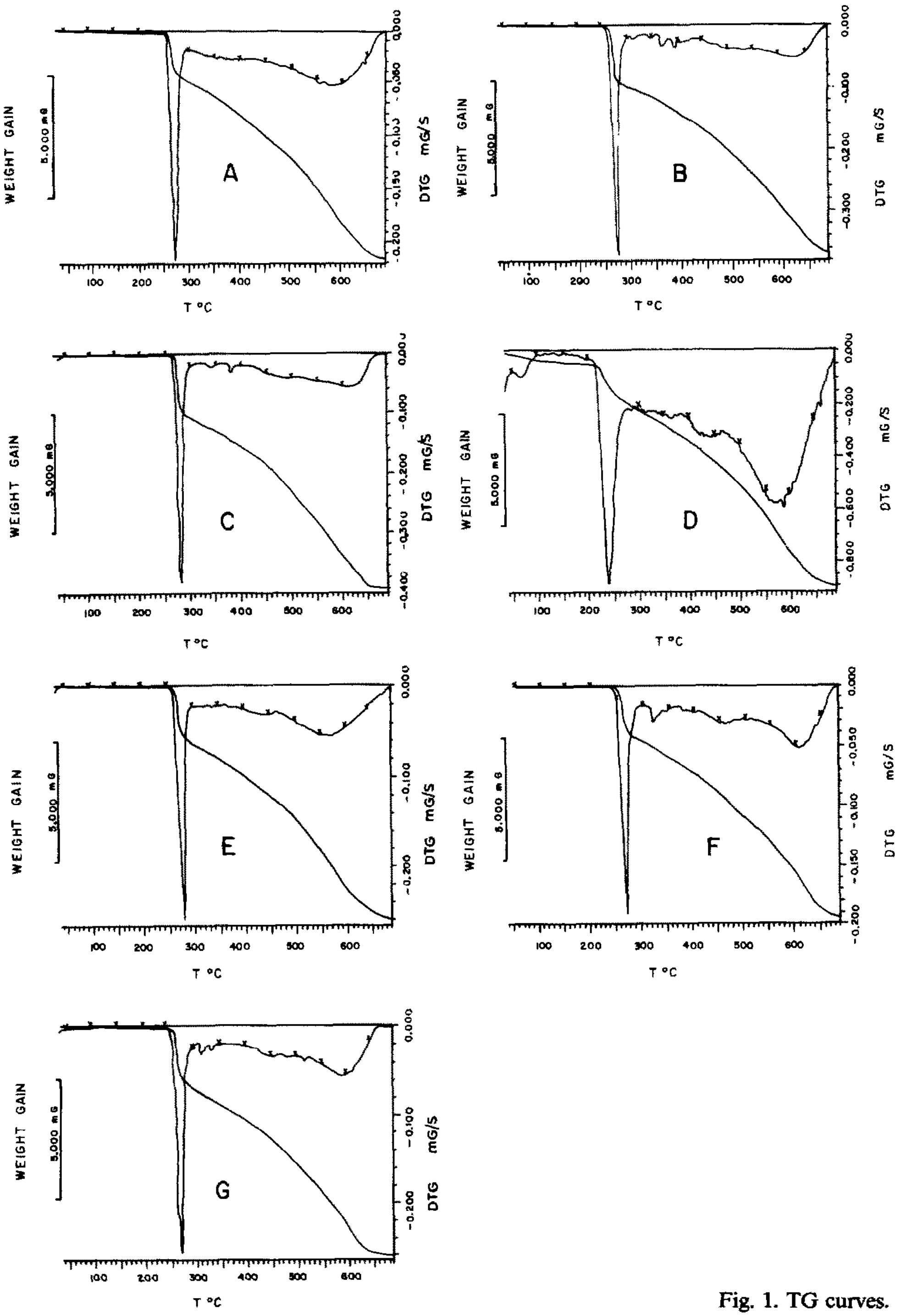

Fig. 1. TG curves.

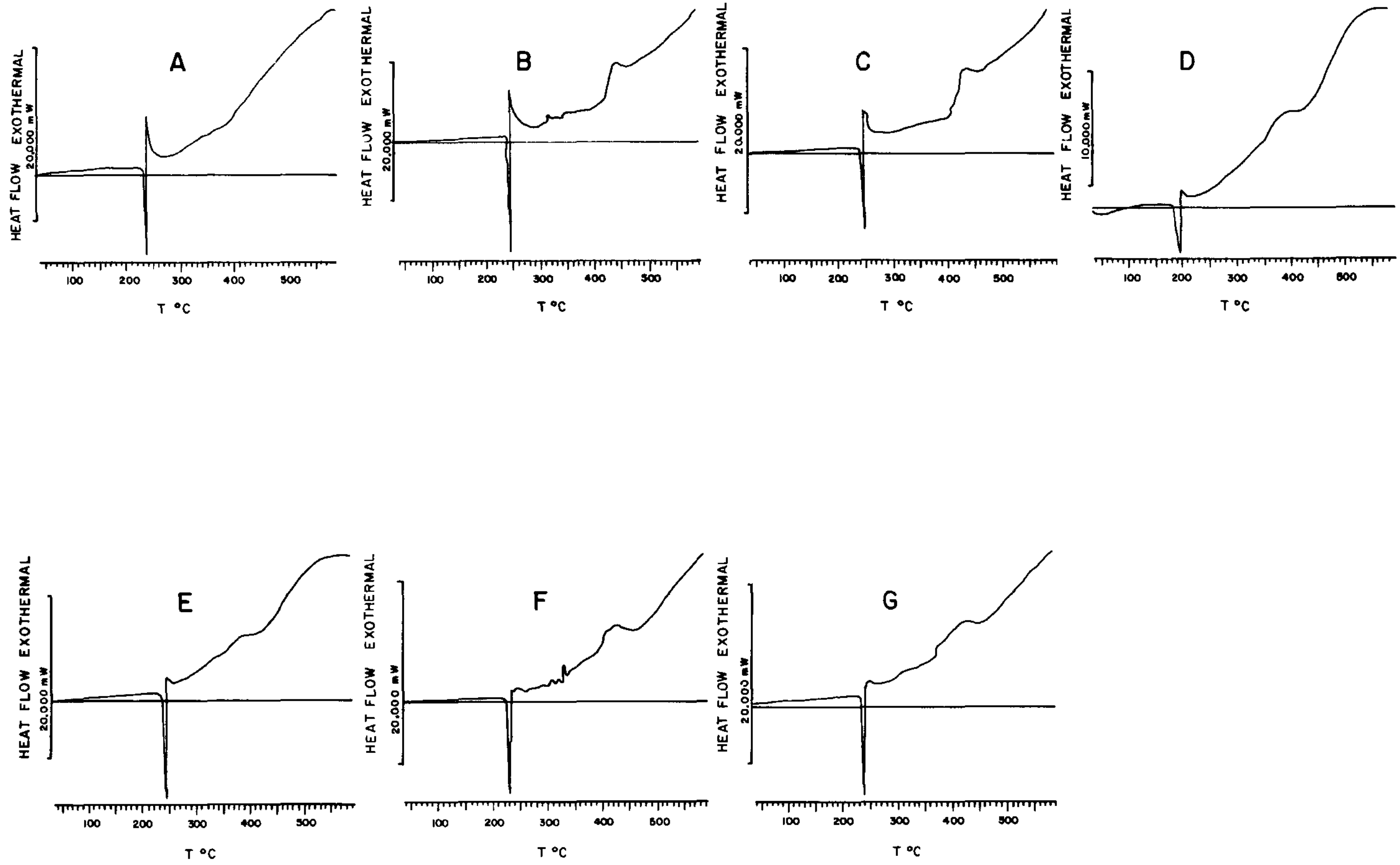

Fig. 2. DSC curves.

TABLE 3
UV data in aqueous solutions

Compound	Conc. (mol^{-1})	λ_{max}(nm)	ξ	Assignment
A	5.28×10^{-5}	214	31.400	$\pi \rightarrow \pi^*$
		266	16.700	$n \rightarrow \pi^*$
B	5.28×10^{-5}	212	25.100	$\pi \rightarrow \pi^*$
		266	15.700	$n \rightarrow \pi^*$
C	4.54×10^{-5}	214	29.100	$\pi \rightarrow \pi^*$
		266	15.400	$n \rightarrow \pi^*$
D	6.50×10^{-5}	217	20.000	$\pi \rightarrow \pi^*$
		236	19.900	$\pi \rightarrow \pi^*$
		280	9.000	$n \rightarrow \pi^*$
E	4.70×10^{-5}	217	24.000	$\pi \rightarrow \pi^*$
		237	23.500	$\pi \rightarrow \pi^*$
		279	10.800	$n \rightarrow \pi^*$
F	3.96×10^{-5}	219	28.600	$\pi \rightarrow \pi^*$
		235	29.200	$\pi \rightarrow \pi^*$
		280	11.000	$n \rightarrow \pi^*$
G	4.50×10^{-5}	219	26.100	$\pi \rightarrow \pi^*$
		235	28.700	$\pi \rightarrow \pi^*$
		278	10.000	$n \rightarrow \pi^*$

peaks are centered at temperatures ranging between 195 and 247°C; no weight losses were observed in the temperature ranges of the endothermic effects. Heating the compounds in capillary tubes proved that these endotherms are due to melting processes (see Table 4). Values of the melting enthalpies are given in Table 4. These values must be considered cautiously since all the compounds start their pyrolytic decompositions immediately after melting.

The characteristic fact that the seven compounds studied show defined melting points below their respective temperatures of pyrolytic decomposition, in opposition to some of their 5-nitroso pyrimidine homologues [8], could be related to the relatively higher intermolecular forces in the last 5-nitroso pyrimidine derivatives, owing to the role of the C_5–NO groups in intermolecular hydrogen bridges.

The DSC and TG plots of the seven compounds studied show that the pyrolytic decompositions start immediately after the melting processes. On the other hand, TG and DSC plots show that no stable intermediate species are formed during the pyrolytic processes. Thus, few available data could be obtained for the decomposition mechanism of the compounds under study.

All the compounds start the weight loss due to pyrolytic decompostion at about 250°C, as can be seen in the TG plots, except that for compound D

TABLE 4

TG and DSC data for the compounds

Compound	Fusion		Other effects	
	T (°C)	ΔH (kJ mol^{-1})	T (°C)	ΔH (kJ mol^{-1})
A	238 [a](237) [b]	28.90	240 exo	−31.60
			346 (w) exo	—
B	244 [a](240) [b]	33.36	247 exo	−49.10
			318 (w) exo	—
			352 (w) exo	—
			432 exo	−61.52
C	247 [a](238) [b]	34.00	250 exo	−28.37
			340 (w) exo	—
			420 (w)	—
			430 exo	−109.11
D	195 [a](191) [b]	23.52	210 exo	−3.58
			277 (w) exo	—
			381 exo	−36.37
			570 (s) exo	—
E	245 [a](242) [b]	39.14	250 exo	−6.78
			373 exo	−15.64
			580 (s) exo	—
F	231 [a](229) [b]	38.02	246 exo	−2.89
			331 (w) exo	—
			427 exo	−62.82
G	240 [a](243) [b]	45.48	253 exo	−7.64
			320 (w) exo	—
			414 exo	−64.68

s, strong; w, weak.

[a] Peak temperature of the endotherm.

[b] Melting temperature values.

(220°C). The DSC plots show exothermic effects (probably due to the oxidation of the previously issued groups) whose energy and temperature values are given in Table 4.

The pyrolytic decomposition of compound A starts at a higher temperature than its homologous 5-nitroso pyrimidine derivative; their DSC and TG plots are very similar [8]. This fact suggests similar mechanisms for their initial pyrolytic decompositions. Thus, compound A could start its decomposition by losing methoxy groups linked to C_2 [16,17]. The higher thermal stability of A could, therefore, be explained on the basis of the absence of the NO group, whose electron-attractive character makes the $O{-}C_2$ bond more labile.

Compounds A, B and C present very similar DSC and TG plots. Thus, it seems evident that all their thermal decompositions follow analogous mechanisms.

Compounds D and E start their pyrolytic decompositions at slightly lower temperatures than their homologous 5-nitroso pyrimidine derivatives; their respective DSC and TG plots are very similar [8]. If we assume the hypothesis that their decomposition mechanism is similar (a mechanism which starts by oxidating -N-H groups linked to C_4), it could be suggested that in the 5-nitroso pyrimidine derivatives the -N-H groups are protected from oxidation by hydrogen bonds to NO groups. This fact has been demonstrated by ^{1}H NMR spectroscopy in DMSO-d_6 [9].

The TG and DSC plots of compounds F and G are also very similar to those of their analogous 5-nitroso pyrimidine derivatives. Thus, their initial decomposition step is, as has been suggested [8], the same as that for 4-amino-1, 6-dihydro-1-methyl-2-methylthio-5-nitroso-6-oxo-pyrimidine (L). This compound starts its pyrolytic decomposition at 244°C by losing $-S-CH_3$ groups. This fact was proved on heating L up to 247°C and immediately obtaining the IR spectrum of the sample in the 4000–200 cm^{-1} range. This spectrum showed the disappearance of only one band, in relation to the spectrum of L, at 685 cm^{-1}, which was assigned to ν(C–S) stretching vibrations [12].

The TG curves of all the compounds are very similar; they show an abrupt weight loss in the same range in which the first exothermic effect takes place (see Table 4). Then, the weight losses continue slowly up to about 500°C. At this temperature, new, abrupt weight losses start. All the samples become completely decomposed in the range 650–690°C.

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