INVESTIGATION OF AZOLES AND AZINES.

76.* MASS SPECTRA OF 5- AND 6-SUBSTITUTED URACILS

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Peaks of molecular ions that generally have the maximum intensity are observed in the mass spectra of most of the investigated 5- and 6-substituted uracils and 5-substituted orotic acids and their deutero analogs and methylated derivatives. The principal pathway of the fragmentation of the molecular ions is retrodiene fragmentation with the formation of $[O = C_{(4)}C_{(5)}R^5C_{(6)}R_{(6)}N_{(1)}R^1]^+$ (F_1) ions. The stabilities of the latter depend on the nature and position of the substituents attached to the $C_{(5)}$ and $C_{(6)}$ atoms. The fragmentation of the F_1 ions can be realized via four principal pathways (B–E) with the detachment of $N{-}CR^6$ (B), $O{=}C{=}CR^5$ (C), CO (D), and R^6 (E) fragments. The most general pathway for the fragmentation of 5-substituted uracils is pathway C, whereas the most general pathway for 6-substituted uracils is pathway E. In the spectra of 5-substituted orotic acids the intensities of the molecular-ion peaks are high (~100%) only in the case of electron-donor R^5 and decrease sharply with an increase in the electron-acceptor strength of the substituent. The principal pathways of fragmentation of the molecular ions are decarboxylation (F) and retrodiene fragmentation (A), the contribution of which is appreciably smaller. The $M{-}CO_2$ ions formed after decarboxylation undergo fragmentation via a scheme similar to that observed for 5-substituted uracils.

Continuing our search for potentially antitumorigenic compounds among derivatives of natural pyrimidines and our study of their distribution in organs and tissues and metabolism in animal organisms we directed our attention to the fact that at present the literature contains almost no data on the mass spectra of 5- and 6-substituted uracils. The fragmentation of uracil itself under electron impact has been studied in extremely great detail [2]. The mass spectra of 1- and 3-methyluracils [3], 1,3-dimethyluracil, thymine, 6-methyluracil, 5-hydroxymethyluracil [2], 6-aryl- and 2-thio-6-aryluracils [4], and a number of pyrimidine nucleosides [4-7] have been examined. The principal pathways of fragmentation of the enumerated compounds coincide and can be described by scheme 1 proposed in [2].

As the first step of the fragmentation of uracils this scheme includes retrodiene cleavage of the molecular ion (M^+) with the ejection of an $R^3N_{(3)}C_{(2)}O$ or $R^3N_{(3)}C_{(2)}S$ fragment and the formation of, evidently, the most stable F_1 ion. The subsequent fragmentation of the latter proceeds via the four pathways B–E. The mass spectra of uracil-5-carboxylic acid and uracil-6-carboxylic acids, among which interesting physiologically active preparations have recently been detected, have not yet been investigated systematically; only the mass spectra of 5-fluoroorotic acid have been described [8]. Alam and coworkers [8] showed that the initial steps in the fragmentation of this molecule are similar to those observed for uracil and its derivatives and include the detachment of HNCO from the molecular ion via the mechanism of the reverse Diels–Adler reaction with the formation of an ion radical (m/z 131), which subsequently undergoes fragmentation readily via several pathways, in the interpretation of which they permitted a number of inaccuracies. In addition, they noted that decarboxylation with the formation of 5-fluorouracil, which subsequently readily undergoes fragmentation in the same way as uracil, occurs at the experimental temperature (160°C).

*See [1] for Communication 75.

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TABLE 1. Mass Spectra of 5-Mono-, 6-Mono-, and 5,6-Disubstituted Uracils I-III and Their N-Methyl Derivatives IV

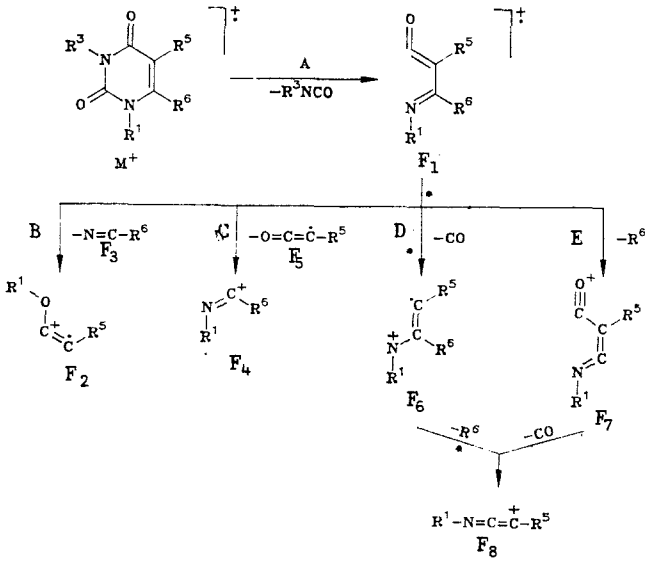
Compound	R^5	R^6	m/z							
			M^+	F_2	F_4	F_1	F_6	F_7	F_8	Other ions*
Ia	NO_2	H	157	114	—	—	—	—	—	70 [M−O, −HNCO, −CO], 40 [M−O, −HNCO, −CO, −NO], 127 [M−NO], 71 [M−NO, −CO, −HNCH], 56 [M−NO, −CO, −HNCO], 67 [M−O, −HNCO, −HNO]
Ib	Br	H	192 190	149 147	122 120	28	—	—	—	—
Ic	Cl	H	148 145	105 103	78 76	28	—	—	—	—
Id	I	H	238	195	168	28	—	—	—	—
Ie	F	H	130	87	60	28	59	—	—	—
If	H	H	112	69	42	28	41	68	40	—
Ig	Me	H	125	83	—	28	55	82	54	—
Ii	NH_2	H	127	84	57	28	56	—	—	—
Ij	$NHCH_2Ph$	H	217	—	—	28	—	—	—	91 [CH_2Ph]
Ik	NHEt	H	155	112	—	28	84	—	83	140 [M−CH_3], 69 [M−CH_3, −HNCO, −CO], 42 [M−CH_3, −HNCO, −CO, −HCN]
Il	NMe_2	H	155	112	—	28	84	111	83	140 [M−CH_3], 97 [M−CH_3, −HNCO], 70 [M−CH_3, −HNCO, −HCN], 69 [M−CH_3, −HNCO, −CO], 42 [M−CH_3, −HNCO, −HNC, −CO], 44 [M−NMe_2]
Im	NEt_2	H	183	140	—	28	112	—	111	168 [M−CH_3], 97 [M−CH_3, −HNCO], 83 [M−CH_3, −HNCO, −CO, −CH_2], 69 [M−CH_3, −HNCO, −CO, −HNCH], 154 [M−C_2H_5], 83 M−C_2H_5, −HNCO, −CO], 56 [HC=NC_2H_5]
In	Morpholino	H	197	154	—	28	126	153	—	179, 166, 140, 139, 138, 112, 95, 41
IIc	H	Cl	148 146	105 103	—	—	—	68	40	111 [M−Cl]
IIe	H	F	130	87	42	—	59	68	—	—
IIg	H	Me	126	83	42	—	—	68	40	—
IIh	H	OMe	142	99	42	—	—	68	—	112 [M−OCH_2], 69 [M−OCH_2, −HNCO], 42 [M−OCH_2, −HNCO, −HCN]
IIi	H	NH_2	127	84	43	—	—	68	—	99 [M−CO]
IIIa	Br	Me	206 204	163 161	122 120	—	—	—	—	122, 120
IIIb	Me	F	144	101	—	46	73	73	54	100 [M−HNCO, −H], 72 [M−HNCO, −H, −CO], 53 [M−HNCO, −H, −CO, −F], 52, 28
IIIc	NH_2	Me	141				70			
IIId	NEt_2	Me	197	154	—	42	126	139	111	182 [M−CH_3], 168 [M−C_2H_5], 183 [M−CH_2], 125 [M−NEt_2], 97 [M−−NEt_2, −CO]
IVa	H	F	144	101	74	60	73	82	—	100 [M−HNCO, −H], 82 [M−HNCO, −F], 72 [M−HNCO, −H, −CO]
IVb	Me	F	158	115	70	60	87	—	68	114 [M−HNCO, −H], 100 [M−HNCO, −H, −CH_3], 86 [M−HNCO, −H, −CO]
IVc	Me	F	172	115	—	60	87	—	68	173, 114 [M−HNCO, −H], 100 [M−HNCO, −CH_6]
IVd	H	Cl	162 160	105 103	—	—	—	68	—	—

*The ions for which the relative intensities are no lower than 10% are presented.

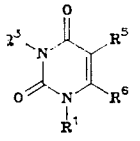
TABLE 2. Intensities of the Peaks of the Characteristic Ions (% of the Total Ion Current) in the Mass Spectra of 5-Mono-, and 6-Mono-, and 5,6-Disubstituted Uracils I-III and Their N-Methyl Derivatives IV

Compound	R^5	R^6	M^+	F_1	F_2	F_4	F_6	F_7	F_8	Other ions
Ia	NO_2	H	43	1	—	—	—	—	—	7 [M−O, HNCO, −CO], 4 [M−O, −HNCO, −CO, −NO], 7 [M−NO], 9 [M−NO, −CO, −HNCH], 9 [M−NO, −CO, −HNCO], 20 [M−O, −HNCO, −HNO]
Ib	Br	H	22 23	16 17	8 9	5	—	—	—	—
Ic	Cl	H	11 27	10 24	9 13	6	—	—	—	—
Id	I	H	62	22	9	7	—	—	—	—
Ie	F	H	56	21	12	8	2	—	—	—
If	H	H	28	22	12	12	8	7	1	—
Ig	Me	H	48	11	—	6	23	3	9	—
Ii	NH_2	H	61	6	3	5	25	—	—	—
Ij	$NHCH_2Ph$	H	47	—	—	6	—	—	—	47 [CH_2Ph]
Ik	NHEt	H	25	1	—	14	3	—	2	40 [M−CH_3], 10 [M−CH_3, −HNCO, −CO], 5 [M−CH_3, −HNCO, −CO, −HCN]
Il	NMe_2	H	28	1	—	16	6	1	3	10 [M−CH_3], 3 [M−CH_3, −HNCO], 3 [M−CH_3, −HNCO, −HCN], 9 [M−CH_3, −HNCO, −CO], 15 [M−CH_3, −HNCO, −HNC, −CO], 5 [M−NMe_2]
Im	NEt_2	H	16	10	—	7	2	—	2	32 [M−CH_3], 3 [M−CH_3, −HNCO], 4 [M−CH_3, −HNCO, −CO, −CH_2], 5 [M−CH_3, −HNCO, −CO, −HNCH], 11 [M−C_2H_5], 4 [M−C_2H_5, −HNCO, −CO], 4 [HC=NC_2H_5]
In	Morpholino	H	12	5	—	9	3	10	—	7, 9, 3, 6, 5, 24, 2, 5
IIc	H	Cl	12 30	10 19	—	—	—	25	1	3 [M−Cl]
IIe	H	F	43	28	2	—	10	17	—	—
IIg	H	Me	41	18	24	—	—	8	9	—
IIh	H	OMe	44	15	7	—	—	10	—	6 [M−OCH_2], 13 [M−OCH_2, −HNCO], 6 [M−OCH_2, −HNCO, −HCN]
IIi	H	NH_2	52	19	4	—	—	17	—	8 [M−CO]
IIIa	Br	Me	21 22	10 11	9 9	—	—	—	—	9, 9
IIIb	Me	F	22	10	—	6	18	18	4	5 [M−HNCO, −H], 7 [M−HNCO, −H, −CO], 2 [M−HNCO, −H, −CO, −F], 3, 4
IIIc	NH_2	Me	75				25			
IIId	NEt_2	Me	16	7	—	7	1	1	4	37 [M−CH_3], 13 [M−C_2H_5], 4 [M−CH_2], 5 [M−NEt_2], 4 [M−NEt_2, −CO]
IVa	H	F	25	18	2,5	1,5	15	9	—	15 [M−HNCO, −H], 9 [M−HNCO, −F], 5 [M−HNCO, −H, −CO]
IVb	Me	F	29	15	2	4	5	—	13	15 [M−HNCO, −H], 4 [M−HNCO, −CH_3], 13 [M−HNCO, −H, −CO]
IVc	Me	F	29	21	—	4	9	—	14	6, 14 [M−HNCO, −H], 4 [M−HNCO, −CH_3]
IVd	H	Cl	17 38	3 19	—	—	—	23	—	

Scheme 1



Most of the investigated spectra (Tables 1-4) are characterized by the existence of an M^+ peak, which has the maximum intensity. The spectra of those compounds in the first steps of the fragmentation of which at least one of the substituents undergoes fragmentation constitute an exception. These include 5-nitro-, 5- and 6-carboxy-, and 5- and 6-butoxycarbonyl uracils Ia, V, and VI and their derivatives, as well as some 5-N-substituted aminouracils (Ij, k, m, n). One should immediately note that the ejection of a halogen does not occur in any of the steps in the fragmentation of 5- and 6-halouracils and 5-haloorotic acids. This process is observed only for 5-iodo- and 6-chlorouracil (Id, IIc), but its contribution is extremely small.



I-VI

I a–g, i–n $R^1=R^2=H$; IIc, e, g–i $R^1=R^3=H$; III a–d $R^1=R^2=H$: IV a, b $R^1=Me$, $R^3=H$, c $R^1=R^2=Me$, d $R^1=H$, $R^3=Me$; V f, p $R^1=R^3=H$; VI a–c, e–h, o, p $R^1=R^3=H$

In conformity with Scheme 1 the molecular ions of most of the investigated I-IV split out $RN_{(3)}C_{(2)}O$ or $MeN_{(3)}C_{(2)}O$ fragments in the case of their 3-methyl derivatives. The stabilities of the resulting F_1 ions depend on the nature of the substituents attached to the $C_{(5)}$ and $C_{(6)}$ atoms. For 5- and 6-substituted uracils, as, on the other hand, for their N-methyl derivatives and for 5,6-disubstituted uracils, the intensities decrease with a decrease in the electron-acceptor capacity of the substituent; the relative intensities of the peaks (as compared with M^+) corresponding to the F_1 ions actually depend linearly on the σ substituent constants:

$$I_{F_1} = (64{,}9 \pm 6{,}6) + (64{,}6 \pm 2{,}2)\sigma \quad (n=15,\ r=0{,}939).$$

The sensitivities to the substituent effect are virtually the same for R^5 and R^6 (σ_p, σ_m).

The pathways of the substituent fragmentation of the F_1 ions under the investigated conditions depend not only and not so much on the nature of the substituent as much as on its position. In the case of 5-halouracils Ib-e, as for uracil (Ia) and thymine (Ig) (see Tables 1 and 2), the F_1 ion is converted primarily to F_2 and F_4 ions (pathways B and C), respectively. The F_4 ion is also observed in the spectra of all (without exception) uracils with electron-donor substituents attached to the $C_{(5)}$ atom; the intensities of the peaks corresponding to the F_4 ions evidently increase somewhat with intensification of the electron-donor capacity of the substituent. The spectra of Ig, j-n do not contain peaks of F_2 ions; an exception to this is 5-aminouracil, in the spectrum of which the corresponding peak is

TABLE 3. *Mass Spectra* of Uracil-5-carboxylic Acid (V) and Uracil-6-carboxylic Acid (VI) and Some of Their Substituted Derivatives

Compound	R^5	R^6	m/z												Other ions
			M^+	F^+	F_1	F_1''	F_6	F_1'	F_6'	F_7'	F_8	F_9	F_{10}	F_{11}	
Vf	COOH	H	156	112	69	68	—	113	—	—	—	—	—	—	139 [M−OH], 45, 44, 43
Vp	COOBu	H	212	—	—	—	—	—	—	—	—	—	—	—	157 [M−C_4H_7], 139 [M−C_4H_7−H_2O], 69 [M−C_4H_7−H_2O, −HNCO, −HNO], 57, 56, 44
VIa	NO_2	COOH	—	157	114	68	86	158	—	113	—	—	—	—	141 [M−CO_2, −O], 127 [M−CO_2, −NO], 115 [M−−HNCO, 99 [M−CO_2, −NO, −CO], 98 [M−CO_2, −O, −HNCO], 71 [M−CO_2, −HNCO, −HNCO], 70 [M−−CO_2, −O, −HNCO, −CO], 69 [M−HNCO, −HNCO, NO_2], 67 [M−CO_2 −O, −HNCO, −HNO], 56 [M−CO_2, −NO, −CO, −HNCO], 53 [M−HNCO, −HNCO, −NO_2, −O], 44, 43, 40
VIb	Br	COOH	206 234	192 190	149 147	68	—	193 191		148 146	218 216	—	—	—	150, 148 [M−HNCO, −HNCO], 122, 120 [M−CO_2, −HNCO, −HCN], 106, 104 [M−HNCO, −HNCO, −CO_2], 44, 40, 28
VIc	Cl	COOH	192 190	148 146	105 103	—		149 147	121 119	104 102	174 172	—	—	—	78, 76, 44, 28 88 [M−HNCO, −HNCO], 69 [M−HNCO, −HNCO, F],
VIe	F	COOH	174	130	87	68	59	131	103	86	156	128	85	57	60 [M−CO_2, −HNCO, −HCN], 58 [M−HNCO, −COOH, −CO]
VIf	H	COOH	156	112	69	68		113	—	—	—	—	—	—	45, 44
VIg	CH_3	COOH	170	126	83	—	55	127	99	82	152	124	81	53	171 [M+1], 153 [M−OH], 125 [M−COOH], 71 [M−−HNCO, −CO, −CO]
VIh	NH_2	COOH	171	127	84	—	56	128	100	—	153	125	82	54	172 [M+1], 72 [M−HNCO, −CO, −CO], 45, 44, 28
VIo	OPh	COOH	248	204	161	—	133	205	—	—	—	—	—	—	105 [M−CO_2, −HNCO, −HCN, −CO], 104 [M−CO_2, −HNCO, −HCN, −CO, −H], 94 [C_5H_5OH], 78 [C_6H_6], 77 [C_6H_5], 45, 44, 43, 28
VIp	H	COOBu	212	—	—	—	—	—	—	—	—	—	—	—	
VII*	H	COOH	170	126	69	68	41	113	85	68	152	124	—	—	171 [M+1], 141 [M−$HNCH_2$], 96
VIII**	H	COOH	172	128	—	—	—	—	—	—	154	126	—	—	173 [M+1], 114 [M−CN], 86 [M−CN, −CO], 69 [M−CN, −COOH], 68 [M−H_2O, −CO, −CN]

*3-Methylorotic acid.

**2-Thioorotic acid.

TABLE 4. Intensities of the Peaks of the Characteristic Ions (% of the Total Ion Current) in the Mass Spectra of Uracil-5-carboxylic Acid (V) and Uracil-6-carboxylic Acid (VI) and Some of Their Derivatives

Compound	R^5	R^6	M^+	F	F_1	F_1''	F_6	F_1'	F_6'	F_7'	F_8'	F_9	F_{10}	F_{11}	Other ions
Vf	COOH	H	27	32	10	6	—	4	—	—	—	—	—	—	5 [M−OH], 6, 10, 3
Vp	COOBu	H	1	—	—	—	—	—	—	—	—	—	—	—	26 [M−C_4H_7], 46 [M−C_4H_7−H_2O], 5 [M−C_4H_7−H_2O, −HNCO, −HNO], 5, 12, 5
VIa	NO_2	COOH	—	19	2	14	2	4	—	1	—	—	—	—	3 [M−CO_2, −O], 6 [M−CO_2, −NO], 1 [M−HNCO, −HNCO], 3 [M−CO_2, −NO, −CO], 2 [M−CO_2, −O, −HNCO], 4 [M−CO_2, −HNCO, −HNCO], 2 [M−CO_2, −O, −HNCO, −CO], 4 [M−HNCO, −HNCO, −NO_2], 3 [M−CO_2, −O, −HNCO, −HNO], 4 [M−CO_2, −NO, −CO, −HNCO], 2 [M−HNCO, −HNCO, $2NO_2$ −O], 10, 8, 3
VIb	Br	COOH	2	13	13	2	—	2	—	2	0,3	—	—	—	2, 1 [M−HNCO, −HNCO], 6, 6 [M−CO_2, −HNCO, −HCN],
			2	14	13			2		1	0,7				1 [M−HNCO, −HNCO, −CO_2], 11, 3, 3
VIc	Cl	COOH	3	8	6	—	—	3	0,7	2,5	0,3	—	—	—	2, 6, 14, 2
			8	18	16			6	1,4	2,5	0,6				
VIe	F	COOH	16	8	5	1	9	3	5	19	1	1	5	5	2 [M−HNCO −HNCO], 2 [M−HNCO, −HNCO, F], 5 [M−CO_2, −HNCO, −HCN], 13 [M−HNCO, −COCH, −CO] 7, 5
VIf	H	COOH	38	2	11	26	—	11	—	—					
VIg	CH_3	COOH	33	5	2	—	5	1	7	9	10	5	3	2	5 [M+1], 7 [M−OH], 3 [M−COOH], 3 [M−HNCO, −CO, −CO]
VIh	NH_2	COOH	27	6	4	—	10	3	6	—	6	5	6	3	3 [M+1], 3 [M−HNCO, −CO, −CO], 4, 11, 3
VIi	OPh	COOH	7	25	6	—	3	6	—	—	—	—	—	—	9 [M−CO_2 −HNCO, −HCN, −CO], 5 [M−CO_2, −HNCO, −HCN, −CO, −H], 7 [C_6H_5OH], 4 [C_6H_6], 3 C_6H_5], 3, 15, 4, 3
VII*	H	COOH	25	1	8	24	—	7	2	24	1	1	—	—	3 [M+1], 3 [M−$HNCH_2$], 1
VIII**	H	COOH	30	4	—	—	—	—	—	—	10	2	—	—	3 [M+1], 5 [M−CN], 5 [M−CN, −CO], 12 [M−CN, −COOH], 29 [M−H_2O, −CO, −CN]

*3-Methylorotic acid.
**2-Thioorotic acid.

present, although its intensity is only 5% of the intensity of the M^+ ion. Other pathways of the fragmentation of F_1 ions with splitting out of OC_2R_5 (pathway C), CO (pathway D), and R^6 (pathway E) fragments are also characteristic for these compounds, as for uracil and thymine. Of course, whereas one can form a judgment regarding pathway E with complete confidence, one should speak cautiously regarding the realization of pathways C and D, since the m/z values of the F_5 and F_6 ions coincide for all of the investigated compounds. For a confident judgment regarding this one must examine the mass spectra of 1,5-disbustituted uracils. Finally, in the spectra of uracils If, g, k-m one observes a low-intensity F_8 peak, which may be formed by splitting out of an F_7 ion or an R^6 radical from the F_6 ion. Fragmentation of the F_1 ion via pathways D and E is not observed for uracils Ia-e with electron-acceptor substituents attached to the $C_{(5)}$ atom.

In the case of 6-substituted uracils (Tables 1 and 2) the most general pathway for the fragmentation of the F_1 ion is pathway E: an extremely intense peak of an F_7 ion (68)* is observed in the spectra of all of the compounds. The remaining pathways are either not realized at all or their contribution is very small.

5,6-Disubstituted uracils IIIa-d undergo fragmentation via the same pathways as the monosubstituted compounds. Since their number was limited, one should not draw rigorous conclusions regarding the preferableness of one or another pathway; one might only note that F_1, F_4, and F_6 ions are observed in the spectra examined.

It must be stated that in most of the investigated cases the formation of an F_1 ion is accompanied by metastable transitions: for example, peaks of metastable ions (113.7 and 72.6, respectively) are observed in the case of 5-bromo- and 5-chlorouracil (Ib, c). The situation is also similar in the conversion of the F_1 ion to F_6 and/or F_7 ions (for example, $m^* = 36.4$ for thymine).

The spectra of many of the investigated compounds have certain peculiarities. Thus in the spectrum of 5-fluorouracil (Ie), in contrast to the other 5-halo derivatives, one observes the appearance of a peak of an ion at 44, which is formed by splitting out of HNCO from the F_1 ion. A similar process also occurs in the case of 6-methyluracil (IIg) – an ion at 40 is formed, which, by the way, distinguishes IIg from thymine.

The behavior of N-methyl derivatives (IV) of 5- and 6-substituted uracils is evidently similar to the behavior of their unmethylated analogs (compare IVa-d with Ib and IIc, e in Tables 1 and 2).

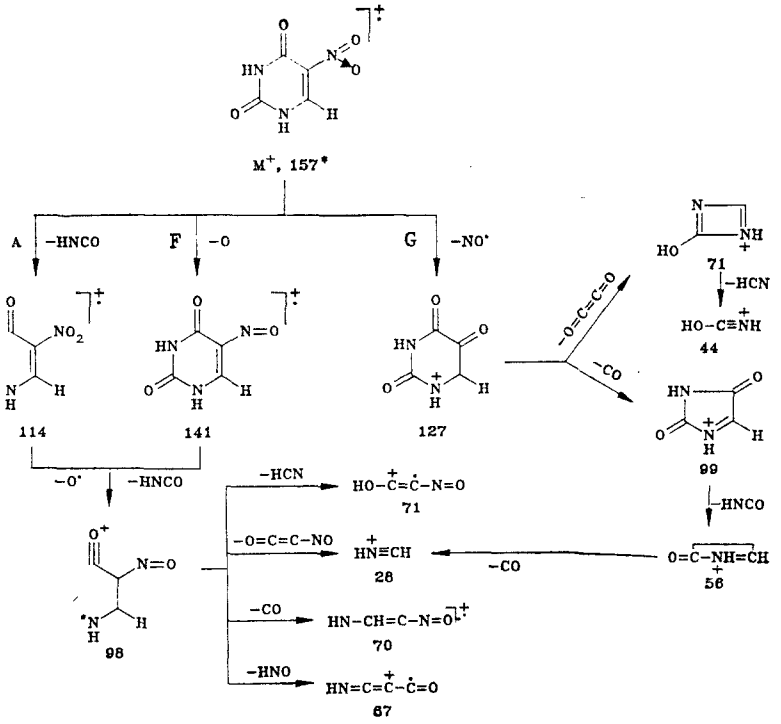
In addition to fragmentation of the pyrimidine ring of uracils I-IV under electron impact, fragmentation of the substituent also occurs. Thus splitting out of a molecule of CH_2O from M^+, which is accompanied by the metastable transition $142 \rightarrow 112$ ($m^* = 88.3$), is observed in the case of 6-methoxyuracil (IIh). The ion at 112 (12%) that is formed in this case subsequently undergoes fragmentation via a pathway similar to pathways A and B.

In the first steps the behavior of 5-nitrouracil (Ia) is similar to that of other compounds: a molecular ion (the peak with the maximum intensity) is formed and then undergoes conversion to F_1 and F_4 ions. However, the principal pathways of the mass-spectrometric fragmentation of the M^* ions are due to cleavage of the nitro group and the resulting fragment ions (see Scheme 2): the splitting out of $O^\cdot$ and $NO^\cdot$ from M^+ leads to the formation of ions at 141 and 127 and is confirmed by metastable transitions similar to what is frequently observed for aromatic nitro compounds [9]. The resulting ions at 114 and 141 subsequently are converted to the same fragment ion at 98 by splitting out of oxygen and retrodiene cleavage. The ion at 98 undergoes all forms of fragmentation that are characteristic for F_1 ions in the general scheme of the mass-spectrometric fragmentation of 5- and 6-substituted uracils (Scheme 1). However, the specific characteristics of nitro compounds are also manifested here: a new pathway – splitting out of HNO with the formation of an ion at 67 – develops. The peak corresponding to this ion has the highest intensity with respect to all of the remaining peaks of fragment ions. The onium ion at 127, which is formed by detachment of NO from M^+, splits out a molecule of CO to give the hydantoin ion at 99, which then loses HNCO and CO successively to give, respectively, the ions at 56 and 28. Another pathway of the fragmentation of the $M - NO^+$ ion is considerably more important if one judges from the overall ion current – the successive detachment of C_2O_2 and HCN with the formation of ions at 71 and 44.

*Here and subsequently, the numbers in the text and in the schemes that characterize the ions are the m/z values.

As expected, this pathway was not encountered among the pyrimidines that we investigated and is possibly manifested in the spectrum of 5-hydroxyuracil.

Scheme 2



The principal process in the fragmentation of 5-alkylaminouracils Ij-m is the detachment of alkyl groups from the molecular ion, which leads to the formation of "pseudomolecular" ions, which then undergo fragmentation via the same pathways (A and C-E) as the starting molecules (see Tables 1 and 2). 5-Morpholinouracil, the fragmentation of which is markedly complicated by fragmentation of the morpholine ring, constitutes an exception. One should also note the appreciable contribution of the detachment of alkylamino and/or dialkylamino groups from the molecular ions of uracils Ij-m.

Carboxy- and butoxycarbonyluracils V and VI, as we have already mentioned, differ appreciably with respect to their behavior not only from other compounds of the investigated series but also from one another. The molecular ion of 5-carboxyuracil is appreciably less stable than that of the 6-carboxy isomer.

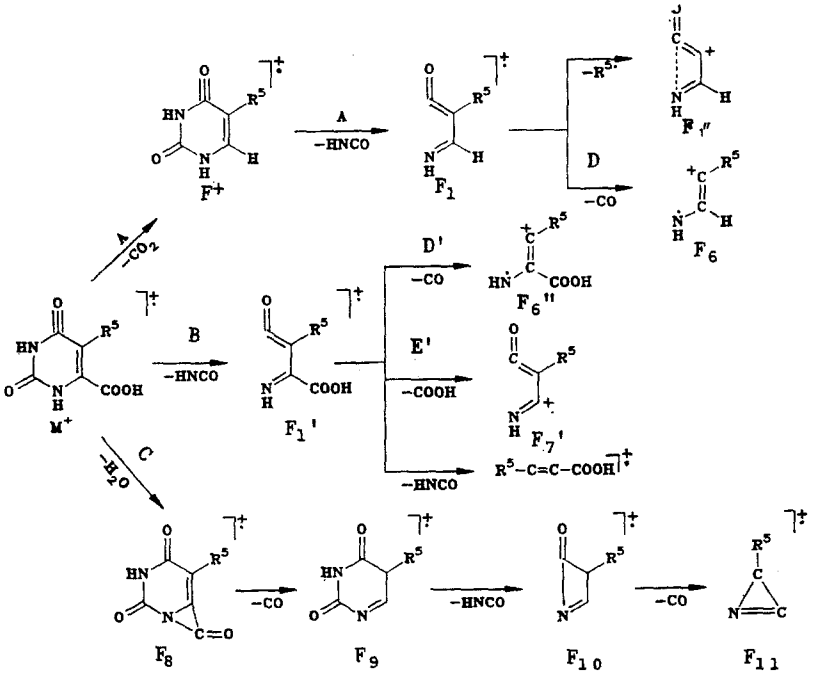
The principal pathways of its fragmentation are decarboxylation (primarily) and dehydrocarboxylation. The latter process is not observed at all in the case of orotic acid under the conditions used. The stabilities of the ions formed as a result of the retrodiene fragmentation of the M^+ ions of carboxy derivatives Vf and VIf differ even more substantially than the stabilities of the M^+ ions. The subsequent pathways of the fragmentation of the $M - HNCO^{+\cdot}$ ions are evidently also different: in the case of orotic acid (VIf) the detachment of CO_2 and COOH groups leads to ions at 69 and 68, respectively. In the case of uracil-5-carboxylic acid ions with these mass numbers are formed not only by the indicated pathways but also as a result of fragmentation of the "pseudomolecular" $[M - CO]^{+\cdot}$ uracil ion. In addition, the detachment of HNC from the F_1 ion also evidently takes place simultaneously.

The fragmentation of butyl esters of uracilcarboxylic acids Vf and VIf is also extremely individual, although it does have common characteristics. The most pronounced difference in them from one another is the difference in the stabilities of the molecular ions: the intensity of the corresponding peak in the spectrum of butyl orotate (VIf) is maximal, whereas in the spectrum of the 5-substituted isomer it is almost minimal. The principal difference in the mass-spectrometric fragmentation of these uracils from the remaining members of the series is the absence of retrodiene fragmentation of the M^+ ions. In the first step in these cases the molecular ions split out a $C_4H_7^{\cdot}$ radical, which is accompanied in both cases by a metastable transition ($m^* = 116.2$): for butyl orotate, in addition, splitting out of $C_4H_8^{\cdot}$ also occurs. A similar pathway of fragmentation of esters with the transfer of two hydrogen atoms from the alkyl fragment of the carbalkoxy group was also previously observed (for ex-

ample, see [10]). Yet another difference in the fragmentation of butyl orotate from its isomer is manifested in the formation of an $[M - HNCONHCO]^{+\cdot}$ ion at 126 with the corresponding metastable transition 212 → 216 ($m^* = 74.8$). The $[M - C_4H_7]^+$ ions in both cases are dehydrated with the formation of an ion at 139, which is most intense for the 5-substituted isomer. Splitting out of a carboxy group from the $[M - C_4H_7]^+$ ion is also possible in both cases, while in the case of butyl orotate dehydroxylation and retrodiene cleavage, which leads to the formation of $[M - C_4H_7 - OH]^+$, $[M - C_4H_7 - HNCO]^+$, and $[M - C_4H_7 - HNCOH]^+$ ions, also occur. The above-presented data on the fragmentation of isomeric uracilcarboxylic acids and their esters constitute evidence for the ease of their identification by means of their mass spectra both in mixtures with one another and in mixtures with other uracils.

Molecular-ion peaks are observed in the mass spectra of 5-substituted orotic acids Vb-h,m and the 3-methyl and 2-thio derivatives VII and VIII, with the exception of the 5-nitro derivative (VIa). Their intensities are maximal in the spectra of the unsubstituted compounds and substances that contain electron-donor substituents. The intensities of the peaks of the molecular ions of the compounds with electron-acceptor substituents decrease sharply in proportion to the increase in the electron-acceptor capacity of the substituent up to zero in the spectra of the nitro derivative. The subsequent fragmentation of the molecular ions of VIb, c, e-h, o proceeds via several pathways, of which one can single out three common pathways A-C. The most important pathway, if one can judge from the overall intensity, is pathway A, which includes decarboxylation and subsequent fragmentation of the resulting "pseudomolecular" F_1 ion in complete conformity with the previously established scheme of the fragmentation of identical M^+ ions of 5-substituted uracils. On the other hand, orotic acid and its derivatives behave like 5,6-disubstituted uracils; evidence for this is provided by pathway B, which includes retrodiene cleavage of the $N_{(3)}-C_{(4)}$ and $N_{(1)}-C_{(6)}$ bonds of the molecular ion. It was somewhat unexpected that the stabilities of the resulting $[M - R^3NCO]$ (F_1) ions are approximately the same for all of the substances: the intensities of the corresponding ions vary over the range 10% to 30% and do not depend on the nature of the substituent attached to the $C_{(5)}$ ion. These ions then also undergo fragmentation via several pathways, splitting out HNCO, COOH, and CO fragments; the ejection of CO is evidently preferable or comparable to splitting out of COOH.

Scheme 3



Pathway C – splitting out of a molecule of water from the molecular ion – is evidently most characteristic for substances (VIg, h, p) with electron-donor substituents. The elimination of H_2O, which probably proceeds through the hydroxy part of the carboxy group and the hydrogen atom in the ortho position relative to the carboxy group (VIa-c, e, f, h, VII, VIII) or the α-hydrogen atom of the substituent attached to the $C_{(5)}$ atom (VIf-h, VII, VIII), as in the case of benzoic acids, leads to the formation of F_8 ions. The latter subsequently

undergo fragmentation with the ejection of CO and HNCO. Finally, it should be noted that a number of errors in the interpretation of the mass spectrum of 5-fluoroorotic acid (VIe) were evidently permitted in [8].

The scheme of the fragmentation of 5-nitroorotic acid (VIa) differs appreciably from that of the remaining derivatives: M^+ peaks and peaks of all ions associated with splitting out of water from the M^+ ions (pathway C) are not observed in the spectrum. In addition, splitting out of $O^\cdot$ and $NO^\cdot$ particles with subsequent fragmentation of the resulting ions (see Tables 3 and 4), as in the fragmentation of 5-nitrouracil (see above), occurs after decarboxylation.

Thus 5- and 6-substituted uracils and their N-alkyl derivatives undergo fragmentation under electron impact via a common scheme; however, the position and nature of the substituent in the uracil ring determine the relative intensities of each of the pathways of this scheme and the development of specific fragmentation pathways associated with cleavage of the substituent itself. Isomeric 5- and 6-substituted uracils can be easily identified by means of their mass spectra.

EXPERIMENTAL

The 5- and 6-substituted uracils and their derivatives investigated in this research were obtained by known methods.

The mass spectra were recorded with an MKh-1303 spectrometer with direct introduction of the samples; the ionizing-electron energy was 30 eV, and the input temperature was 120-150°C.

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