DEPENDENCE OF THE FRAGMENTATION UNDER ELECTRON IMPACT OF 2-(δ-METHOXYCARBONYLBUTYL)-3-HYDROXY-4-BENZOYLAMINO-THIOPHANES ON STEREOCHEMICAL FACTORS

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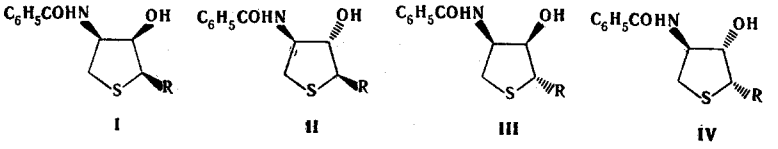
We have previously examined the fragmentation of 3-hydroxy-4-alkylaminothiophanes under electron impact. Differences were noted in the relative intensities of the common ions in the mass spectra of the cis- and trans-isomers of these compounds [1].

In this investigation, the mass spectra of the four possible isomers of 2-(δ-methoxycarbonylbutyl)-3-hydroxy-4-benzoylaminothiophane (I-IV) were studied, the configurations of these isomers having been established by PMR [2]. It is shown that the introduction of a third substituent at $C_{(2)}$ results in fragmentation becoming highly dependent upon the stereochemistry of the thiophanes.



I II III IV

R=(CH2)4COOH

The basic fragmentation processes shown in the scheme above were confirmed by metastable ions (defocusing method). The structures of the ions shown in the scheme are provisional. The compositions of the ions a-m were determined by high-resolution mass spectrometry. Table 1 shows the relative intensities of the peaks due to ions a-f and h in the mass spectra of I-IV, obtained using ionizing electron energies of 75 and 15 eV, and Table 2 presents the complete mass spectra of the thiophanes at 75 eV. Molecular ion peaks (M^+) were observed in the mass spectra of I and II only, at 15 eV (Table 1).

TABLE 1. Peaks Due to Ions M^+, a-f and h in the Mass Spectra of Thiophanes I-IV [Relative Intensities of the Ion Peaks Expressed as a Percentage of the Major Peak (1) and of the Total Ion Current (2)]

Ion	m/e	Compound															
		I				II				III				IV			
		75 eV		15 eV		75 eV		15 eV		75 eV		15 eV		75 eV		15 eV	
		1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
M^+	337	—	—	4,0	2,00	—	—	9,9	3,69	—	—	—	—	—	—	—	—
a	319	—	—	1,9	0,73	—	—	6,9	2,57	1,7	0,39	12,7	5,40	2,3	0,50	11,2	5,12
b	306	5,4	1,27	1,9	0,73	7,6	1,74	—	—	6,8	1,55	2,2	0,94	7,5	1,57	—	—
c	216	27,3	6,70	100,0	38,24	13,4	3,03	45,2	16,83	8,6	1,98	21,1	8,97	2,4	0,50	6,4	2,93
d	198	8,8	2,07	18,7	7,15	16,0	3,87	48,7	18,13	21,4	4,92	56,1	23,86	31,17	6,57	64,3	29,39
e	184	21,8	5,13	19,8	7,56	26,0	5,96	24,6	9,16	17,0	3,92	12,0	5,10	9,7	1,94	4,3	1,97
f	166	19,3	4,54	11,3	4,35	20,8	4,74	4,8	1,79	22,8	5,22	2,0	0,85	29,5	6,13	6,4	2,93
h	122	43,5	12,26	71,9	27,50	47,0	11,10	100,0	37,23	50,0	11,56	100,0	42,54	68,6	14,20	100,0	45,70

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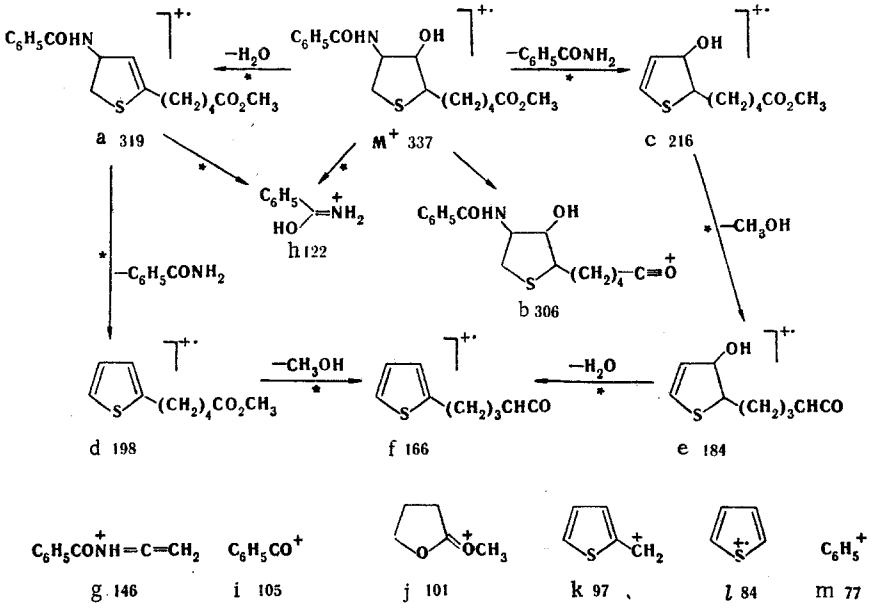
The disintegration of I-IV involving elimination of the substituents from the 3- and 4-positions in the form of neutral fragments also occurs in disubstituted thiophanes [1], but with specific differences for the stereoisomers. One of these processes, namely dehydration to form ion a, is largely suppressed when a substituent is present at $C_{(2)}$. In the disubstituted thiophanes, the peak due to the dehydrated ion is one of the highest in the spectrum at 75 eV, and it is the main peak at 14 eV [1]. In the isomers under investigation, the peak due to ion a does not exceed 12.7% at 15 eV, and it is absent from the spectra of I and II at 75 eV.

Scheme 1*



Competition is observed between the two degradative pathways which involve elimination of substituents from $C_{(3)}$ and $C_{(4)}$. The first of these is dehydration followed by deamidation: $M^+ \rightarrow a \rightarrow d$. The second involves deamidation followed by loss of MeOH: $M^+ \rightarrow c \rightarrow e$. The first pathway becomes increasingly important from I to IV, and the second less important. A criterion which describes the stereochemistry of the molecule is therefore provided by the ratio of the total intensities of the ions formed in these competing fragmentation processes, I_{a+d}/I_{c+e}, where I is the relative intensity of the peak due to the corresponding fragment, which at 15 eV is equal to 0.17 (for I), 0.8 (II), 2.1 (III), and 7.0 (IV).

The stereochemistry of the molecule has its greatest effect on the process of deamidation (pathway $M^+ \rightarrow c$). In passing from I to IV, the intensity of the ion c peak decreases progressively from 100 to 6.4% at 15 eV (Table 1). The deamidation process ($a \rightarrow d$) is also highly dependent on the stereochemistry. There are no metastable transitions for the alternative pathway to ion d (dehydration of ion c). Proceeding from I to IV, the relative intensity of the ion d peak varies inversely as the intensity of the ion c peak. Another stereochemical criterion is therefore provided by the ratio of the intensities of the ion peaks I_c/I_d, which is largely independent of the ionization voltage, and is 3-5 for I, 1 for II, 0.4 for III, and 0.1 for IV. Breakdown to form ion h is less dependent on the stereochemistry of the molecule, the relative intensity of the peak for this ion increasing gradually from I to IV.

In the later stages of fragmentation, the dependence of breakdown on the stereochemistry of the molecule becomes even less marked (for example, in the case of ion f), and it levels out altogether for the formation of ions g and i-m.

The primary breakdown of M^+ to form ion b is virtually independent of the molecular stereochemistry, being due to removal of the terminal MeOH group from the substituent at $C_{(2)}$.

*The numbers underneath the ion structures denote the m/e values. Asterisks denote metastable transitions.

TABLE 2. Mass Spectra of Thiophanes I–IV at 75 eV

Compound	m/e Values (relative intensities of ion peaks as a percentage of the major peak)
I	306 (5,4), 217 (3,0), 216 (27,3), 198 (8,8), 185 (2,4), 184 (21,8), 167 (4,8), 166 (19,3), 156 (5,6), 148 (5,1), 147 (4,2), 146 (3,9), 140 (2,6), 139 (4,9), 138 (3,4), 124 (2,7), 123 (5,7), 122 (43,5), 111 (2,1), 110 (3,6), 106 (8,1), 105 (100,0), 101 (2,5), 98 (3,0), 97 (9,3), 87 (2,9), 85 (2,4), 84 (3,0), 81 (2,3), 78 (4,1), 77 (40,0), 74 (3,7), 67 (2,8), 59 (4,5), 57 (3,5), 55 (7,1), 51 (6,1), 45 (2,9), 41 (5,1)
II	306 (7,6), 216 (13,4), 198 (16,0), 185 (2,8), 184 (26,0), 167 (4,1), 166 (20,8), 156 (7,2), 148 (9,0), 147 (4,8), 146 (3,2), 140 (3,8), 139 (6,3), 138 (3,3), 124 (2,6), 123 (6,4), 122 (47,0), 111 (2,4), 110 (3,2), 106 (8,0), 105 (100,0), 101 (3,8), 98 (2,3), 97 (8,5), 87 (2,8), 85 (1,9), 84 (1,5), 81 (2,0), 78 (3,5), 77 (36,7), 74 (3,1), 67 (2,9), 59 (3,1), 57 (3,9), 55 (7,7), 51 (5,2), 45 (2,6), 41 (6,0)
III	319 (1,7), 306 (6,8), 216 (8,6), 199 (3,3), 198 (21,4), 185 (1,8), 184 (17,0), 167 (6,2), 166 (22,8), 156 (5,2), 148 (5,2), 147 (7,7), 146 (3,0), 140 (3,2), 139 (5,4), 138 (4,2), 124 (2,9), 123 (6,6), 122 (50,3), 111 (2,3), 110 (4,2), 106 (8,7), 105 (100,0), 101 (3,0), 98 (3,9), 97 (9,4), 87 (3,0), 85 (2,1), 84 (1,8), 78 (4,6), 77 (38,5), 74 (3,7), 67 (2,8), 59 (3,2), 57 (3,6), 55 (6,6), 51 (6,0), 45 (3,1), 41 (5,6)
IV	319 (2,3), 306 (7,5), 216 (2,4), 199 (3,8), 198 (31,7), 184 (9,5), 167 (5,1), 166 (29,5), 156 (3,8), 148 (4,5), 147 (5,1), 146 (2,3), 139 (3,7), 138 (4,7), 124 (3,6), 123 (7,5), 122 (68,6), 111 (3,1), 110 (5,7), 106 (8,0), 105 (100,0), 101 (3,2), 98 (3,5), 97 (12,2), 87 (2,7), 84 (2,6), 78 (3,9), 77 (39,6), 74 (3,9), 67 (3,3), 59 (4,1), 57 (4,6), 55 (8,1), 51 (6,0), 45 (5,9), 41 (6,6)

EXPERIMENTAL

The synthesis and properties of the compounds investigated have been described previously [2].

The mass spectra, and the metastable ion spectra obtained by defocusing, were measured on a high-resolution JMS-01-SG2 (Jeol) mass spectrometer with direct introduction of the sample into the ion source at 100–120°C at an ionization chamber temperature of 100°C. The ionizing voltages were 15 and 75 eV, and the emission current was 250 μA.

LITERATURE CITED

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