MASS-SPECTRAL BEHAVIOR OF BENZOTHIOLACTAMS AND ISOMERIC ω-ARYLALKYL ISOTHIOCYANATES

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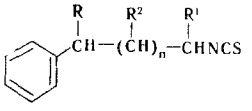
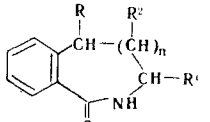
UDC 546.268.6:547:543.422.25.4.6'51

The corresponding five benzothiolactams were obtained by cyclization of racemic arylalkyl isothiocyanates in polyphosphoric acid. The fragmentation of all five pairs of isomeric compounds under the influence of electron impact was investigated thoroughly.

We have previously described the synthesis of (−)-3-methyl-3,4-dihydroisoquinoline-1-thione by cyclization of (+)-α-benzylethyl isothiocyanate in polyphosphoric acid (PPA) [1]. Further study of this reaction showed that ω-isothiocyanates are convenient starting compounds for the synthesis of benzothiolactams with thiolactam rings of various sizes. We synthesized five optically active arylalkyl isothiocyanates (Ia-e) [2]. Using the analogous racemic isothiocynates we synthesized the corresponding five benzothiolactams (IIa-e). The structures of all of the compounds obtained were confirmed by the data from the IR, UV, and PMR spectra.



I a-e



II a-e

I—II a $R=CH_3$, $R^1=H$, n=0; b $R=H$, $R^1=CH_3$, n=0; c $R=CH_3$, $R^1=R^2=H$, n=1; d $R=R^1=H$, $R^2=CH_3$, n=1; e $R=R^2=H$, $R^1=CH_3$, n=1

In order to obtain a more reliable identification and comparison of the starting compounds with an open chain (isothiocyanates Ia-e) and the corresponding isomeric cyclic products (benzothiolactams IIa-e) we made a detailed study of the fragmentation of all five pairs of isomers under the influence of electron impact.

An analysis of the mass-spectral data obtained (Table 1) and a comparison of the intensities of the peaks in the mass spectra of Ia-e and IIa-e (Table 2) make it possible first of all to note that, as expected, cleavage of the benzyl C—C bond in the molecular ions of I to give C_6H_5CHR (F_1) ions, the peaks of which are always maximal, is characteristic for the processes involved in the dissociative ionization of I. Virtually no ions with m/e 72, which are typical for alkyl isothiocyanates [3-5] and undergo the loss of a methyl group to only a very slight extent, are formed in the fragmentation of I. At the same time, intense $(M - HCNS)^+$, $(M-H_2CNS)^+$, and $(M - CH_3NSCH)^+$ ion peaks are frequently observed in the mass spectra of I. In addition, an intense $(M-SH)^+$ ion peak is observed in the mass spectrum of isothiocyanate Ic.

All of these data indicate that processes that involve transfer of hydrogen atoms for the carbon chain to the thiocyanate residue take place to a considerable extent.*

*The absence of mass spectra of selectively deuterated models of Ia-e does not make it possible to give the complete scheme of their fragmentation.

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0009-3122/80/1611-1157$07.50

TABLE 1. Mass Spectra* of ω-Arylalkyl Isothiocyanates Ia-e and Benzothiolactams IIa-e

Compound	m/e values (relative intensities, %)
Ia	177 (1), 118 (75), 117 (50), 115 (14), 106 (6), 105 (100), 103 (45), 95 (9), 91 (8), 82 (35), 81 (63), 80 (65), 79 (41), 78 (30), 77 (49)
Ib	177 (35), 134 (25), 133 (9), 120 (5), 119 (32), 118 (8), 117 (15), 116 (5), 115 (12), 104 (5), 103 (8), 92 (33), 91 (100), 89 (9), 88 (11), 87 (11), 86 (100), 78 (7), 77 (12), 65 (40), 63 (10), 60 (13), 59 (9), 58 (6), 51 (20), 50 (9), 44 (32), 41 (32), 39 (32)
Ic	191 (78), 190 (7), 158 (21), 131 (11), 117 (49), 115 (6), 106 (11), 105 (100), 104 (8), 103 (14), 91 (54), 79 (14), 78 (9), 77 (25)
Id	191 (13), 117 (16), 92 (9), 91 (100)
Ie	191 (68), 177 (6), 132 (8), 131 (6), 117 (40), 105 (5), 97 (7), 91 (100), 86 (19), 84 (18), 83 (11), 82 (7), 81 (6), 77 (7)
IIa	177 (60), 162 (19), 148 (14), 147 (50), 136 (6), 135 (27), 131 (13), 128 (7), 122 (11), 121 (19), 119 (6), 117 (6), 115 (21), 109 (7), 108 (20), 107 (21), 105 (7), 104 (6), 103 (5), 95 (11), 94 (61), 93 (21), 92 (13), 91 (100), 82 (16), 81 (37), 80 (19), 79 (53), 78 (44), 77 (20), 73 (11), 67 (29), 66 (19), 65 (17), 60 (11), 53 (13), 52 (20), 51 (28), 39 (56)
IIb	177 (100), 162 (45), 135 (15), 134 (90), 128 (40), 120 (6), 116 (7), 91 (6), 90 (7), 99 (10), 81 (11), 79 (21), 77 (6)
IIc	191 (100), 162 (13), 161 (34), 148 (18), 147 (34), 131 (11), 130 (27), 129 (36), 128 (30), 127 (6), 121 (12), 117 (13), 109 (6), 104 (8), 103 (20), 102 (8), 93 (8), 91 (16), 89 (7), 79 (8), 78 (9)
IId	191 (100), 190 (8), 176 (10), 162 (5), 161 (15), 158 (30), 148 (5), 147 (24), 143 (6), 134 (10), 131 (7), 130 (7), 129 (32), 121 (6), 117 (12), 116 (35), 115 (22), 91 (12), 90 (5), 89 (12)
IIe	191 (100), 190 (18), 158 (21), 149 (9), 148 (18), 147 (37), 134 (7), 130 (6), 121 (7), 117 (14), 116 (33), 115 (38), 103 (7), 91 (9), 90 (6), 89 (14), 78 (18), 77 (19)

*The molecular ion and the peaks of ions with intensities greater than 5% are presented.

TABLE 2. Intensities of the Peaks of the Characteristic Ions in the Mass Spectra of Ia-e (Σ_{39}%)

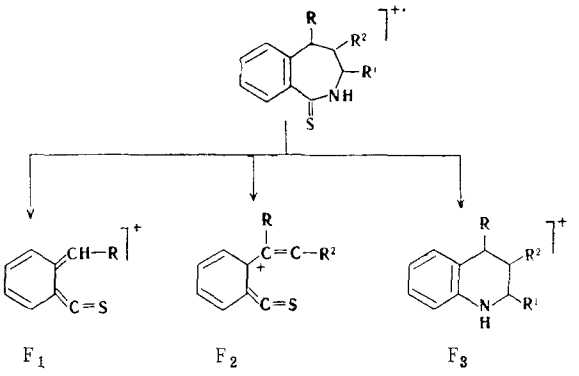
Compound	W_M	$(M-CH_3)^+$	$(M-SH)^+$	$(M-HCNS)^+$	$(M-H_2CNS)^+$	$(M-CH_3NCSH)^+$	$C_6H_5CHR^+$
Ia	0,1	—	—	8,5	5,6	5,1	11,3
Ib	5,7	—	—	1,0	1,9	0,9	12,7
Ic	16,8	0,1	4,1	—	2,2	9,6	19,4
Id	7,5	0,5	0,1	0,4	0,7	0,8	48,5
Ie	15,7	0,1	0,1	1,5	1,1	7,7	19,5

TABLE 3. Intensities of the Peaks of the Characteristic Ions in the Mass Spectra ofBenzothiolactams IIa-e (Σ_{39}%)

Compound	W_M	$(M-CH_3)^+$	$(M-NHCHR^1CHR^2)^+$	$(M-SH)^+$	$(M-CH_3-H_2S)^+$	*m/e* 121, $C_6H_5C{=}S^+$	$(M-CHR^1{=}NH)^+$	$(M-CS)^+$
IIa	6,5	1,7	1,3	0,3	0,6	1,8	1,3	0,3
IIb	21,8	8,2	16,5	0,3	7,2	0,3	—	—
IIc	21,7	0,5	3,3	4,6	0,2	2,2	6,2	6,2
IId	17,8	1,4	1,5	4,6	0,3	0,8	2,2	3,5
IIe	16,9	0,5	1,0	3,4	0,2	1,0	6,2*	6,2*

*A high-resolution mass spectrum is absent.

Intense peaks of hydrocarbon ions are not characteristic, on the other hand, for the mass spectra of IIa-e (Table 3), and the intensities of the peaks of the $(M - CH_3)^+$ and $(M - SH)^+$ ions are considerably higher. The latter are more intense in the spectra of compounds with a seven-membered ring (IIc-e); this is probably associated with the higher percentage of the thiol form in them [6]. In addition to the indicated pathway for II, as well as for their oxygen analogs [7], processes involving fragmentation of the thiolactam ring of the retrodiene fragmentation type with the formation of F_1 ions or the elimination of an NH_2—CHR^1 fragment (the F_2 ion) are characteristic. A third important fragmentation pathway is loss of a CS molecule (the F_3 ion). The compositions of these ions were confirmed in the case of IIc by determination of their elementary compositions by means of the high-resolution mass spectra.



Thus, whereas processes involving retrodiene fragmentation are characteristic for the dissociative ionization of benzolactams, processes involving the formation of fragment ions are typical for the isomeric arylalkyl isothiocyanates. These differences make it possible to confidently identify the examined isomeric compounds.

EXPERIMENTAL

The low-resolution mass spectra were obtained with an MKh-1303 spectrometer at an ionization energy of 50 eV with direct introduction of the substances into the ion source. The high-resolution mass spectra were recorded with a Jeol JMS-01-SG-2 spectrometer at 70 eV.

Isothiocyanates Ia-e were obtained from the corresponding arylalkylamines by the method described in [2]: β-phenylpropyl isothiocyanate (Ia) had bp 127°C (3 mm), α-benzylethyl isothiocyanate (Ib) had bp 111°C (1-2 mm), γ-phenylbutyl isothiocyanate (Ic) had bp 145-147°C (4 mm), γ-phenylisobutyl isothiocyanate (Id) had bp 147-148°C (4 mm), and α-methyl-γ-phenylpropyl isothiocyanate (Ie) had bp 142-144°C (4 mm).

The benzothiolactams were obtained by a general method from isothiocyanates Ia-e by heating with stirring with polyphosphoric acid (PPA) in a weight ratio of 1:40. The reaction temperature was held constant for 8-10 h: 130-140°C for the cyclization of Ia,b and 150-160°C for the cyclization of Ic-e. The reaction mixture was decomposed with ice with cooling and stirring, after which it was extracted with benzene. The benzene extract was washed with sodium bicarbonate solution and water and dried with magnesium sulfate. The benzene was removed by distillation, and the reaction product — a yellow powder or oil — was purified by recrystallization from benzene with heptane or, if this was inadequate, by preparative thin-layer chromatography on aluminum oxide [elution with benzene—acetone (5:1)].

4-Methyl-3,4-dihydroisoquinoline-1-thione (IIa). This compound, with mp 60°C, was obtained in 95% yield. Found: C 67.9; H 6.1%. $C_{10}H_{11}NS$. Calculated: C 67.8; H 6.2%.

3-Methyl-3,4-dihydroisoquinoline-1-thione (IIb). This compound, with mp 131-134°C, was obtained in 100% yield. Found: C 67.9%. $C_{10}H_{11}NS$. Calculated: C 67.8; H 6.2%.

1H-5-Methyl-2,3,4,5-tetrahydrobenz[c]azepine-1-thione (IIc). This compound, with mp 140°C, was obtained in 15% yield. Found: C 69.1; H 6.5%. $C_{11}H_{13}NS$. Calculated: C 69.1; H 6.8%.

1H-4-Methyl-2,3,4,5-tetrahydrobenz[c]azepine-1-thione (IId). This compound, with mp 141°C, was obtained in 20% yield. Found: C 69.4; H 7.5%. $C_{11}H_{13}NS$. Calculated: C 69.1; H 6.8%.

1H-3-Methyl-2,3,4,5-tetrahydrobenz[c]azepine-1-thione (IIe). This compound was obtained in 20% yield and had mp 134°C and M 191. $C_{11}H_{13}NS$. Mass spectrum, m/e: 191 (M^+).

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SOME SIDE REACTIONS IN THE TEMPLATE SYNTHESIS OF MACROCYCLIC COMPOUNDS FROM o-AMINO-o'-HALOAZOPYRAZOLES

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UDC 547.773,778'779:543.422.25+543.51

Pyrazolo[4,5d]-1,2,3-triazoles and 3,4-dimethyl-1,6-diphenyl-dipyrazolo[4,5-b:4',5'-c]-1,6-dihydropyridazine, the structures of which are confirmed by the mass and PMR spectra, were isolated as side products in the preparation of macrocyclic compounds by the template synthesis of o-amino-o'-haloazopyrazoles. The PMR spectra of pyrazolo[4,5-d]-1,2,3-triazoles are examined in comparison with the PMR spectra of the corresponding noncyclic azopyrazoles. All of the compounds obtained were characterized by the results of elementary analysis and data from the IR, UV, mass, and NMR spectra.

Vicinal triazoles are readily formed by cyclization of aromatic o-aminoazo derivatives under both oxidative [1] and reductive [2] conditions. A triazole ring may also be formed in the reaction of an azo group with an o-phenylhydrazono group [3].

In the present research we studied pyrazolo[4,5-d]-1,2,3-triazoles and dipyrazolopyridazine, which were isolated as side products in the preparation of macrocyclic compounds by template synthesis [4, 5].

Azobispyrazoles IIIa-c were obtained by diazotization in hydrochloric acid of 5-amino-4-bromo-3-methyl-1-R-pyrazoles IIa,b and by coupling at pH 1-2 of diazopyrazoles with 5-amino-3-methyl-1-R-pyrazoles Ia,c,d. Diazo coupling of diazopyrazoles with 5-amino-3-methyl-1-R-pyrazoles was also carried out in [6, 7]; however, satisfactory results were not obtained.

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Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1524-1529, November, 1980. Original article submitted December 12, 1979.

0009-3122/80/1611-1160$07.50