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SYNTHESIS, THERMAL STABILITY AND MASS SPECTRA OF 2-TRIHALOMETHYL-1,3,5-DITHIAZIN-4-ONES AND THEIR 2,3-DIHYDRO DERIVATIVES

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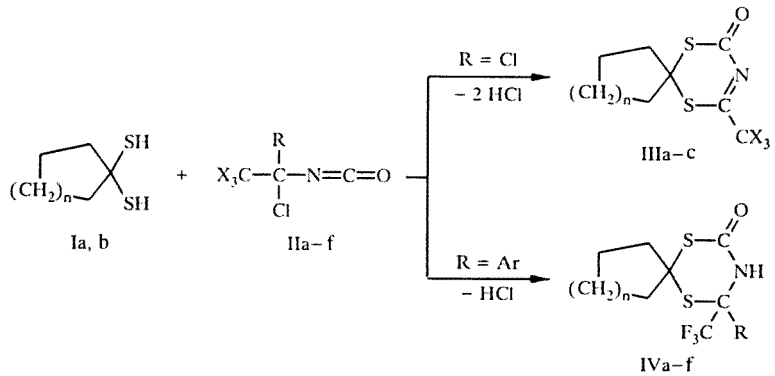
A method has been proposed for the synthesis of 2-trihalomethyl-1,3,5-dithiazines based on the reaction of 1,1,-dithiols with 1,1-dichloro- and 1-chloroalkyl isocyanates. The thermal stability and mass spectra of these compounds were studied.

Geminal dithiols have found common use in the synthesis of various heterocyclic compounds [1]. In particular, the reaction of 1,1-dithiols with N-hydroxymethylthioamides has yielded the first representatives of a new heterocyclic system, 4H-1,3,5-dithiazine [2]. We have shown the promise of using the cyclocondensation of 1,1-dithiols with 1-functionally substituted alkyl isocyanates [3, 4] to give 1,3,5-dithiazines.

Dithiols Ia and Ib react with 1,1-dichloro-2,2,2-trihaloethylisocyanates IIa and IIb in cold benzene in the presence of organic base to give 2-trihalomethyl-1,3,5-dithiazin-4-ones IIIa-IIIc in satisfactory yield (Table 1). The cyclic structure of these products are in accord with their IR spectra (Table 2), which feature carbonyl bands at 1675-1680 cm^{-1}. The ^{19}F NMR spectrum of IIIc shows a singlet for the CF_3 group at 72 ppm, which is typical for CF_3 groups bound to an sp^2-hybridized carbon atom [5]. The ^{13}C NMR spectrum of this compound shows signals for $C_{(4)}$ at 168.6 ppm (q, $^2J_{C-F}$ 37.8 Hz) and $C_{(6)}$ at 170.90 ppm.

The reaction of dithiols Ia and Ib with 1-chloro-2-aryl-2,2,2-trifluoroethyl isocyanates IIc-IIf, which proceeds under analogous conditions, leads to 2,3-dihydro-2-aryl-2-trifluoromethyl-1,3,5-dithiazin-4-ones IVa-IVf (Table 1). The structure of the compounds was demonstrated using IR, PMR, and ^{19}F NMR spectroscopy (Table 2). The lack of thiol group bands in the IR spectra and appearance of ^{19}F NMR signals for the CF_3 groups at 74-76 ppm [6] convincingly confirm the cyclic structure of these compounds.



Ia, IIIa, IVa—c n = 1; Ib, IIIb,c IVd-f n = 2; IIa, IIIa X = Cl; IIb-f , IIIb,cX = F; IIa,b, IVa R = =Cl; IIc, IVd R = C_6H_5; IId, IVe R = 4-ClC_6H_4; IIe, IVb,c,f R = 4-$CH_3C_6H_4$; IIf R = 4-$CH_3OC_6H_4$

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TABLE 1. Properties of IIIa-IIIc and IVa-IVf

Compound	Chemical formula	Found, % / Calculated, %			M_p, °C	Yield, %
		Hal	N	S		
IIIa	$C_8H_8Cl_3NOS_2$	35,08 34,91	4,62 4,60	21,21 21,01	59...60	45
IIIb	$C_9H_{10}Cl_3NOS_2$	33,32 33,38	4,53 4,40	20,27 20,12	65...66	52
IIIc	$C_9H_{10}F_3NOS_2$	21,16 21,33	5,20 5,49	23,81 24,02	60...61	47
IVa	$C_{14}H_{14}F_3NOS_2$	17,32 17,10	4,29 4,20	19,20 19,23	131...132	58
IVb	$C_{15}H_{16}F_3NOS_2$	16,70 16,41	3,86 4,03	18,56 18,46	108...109	64
IVc	$C_{15}H_{16}F_3NO_2S_2$	15,60 15,68	3,79 3,86	17,48 17,64	99...100	52
IVd	$C_{15}H_{16}F_3NOS_2$	16,54 16,41	4,12 4,03	18,29 18,46	153...154	66
IVe	$C_{15}H_{15}ClF_3NOS_2$	—	3,83 3,67	17,01 16,79	117...118	75
IVf	$C_{16}H_{18}F_3NOS_2$	15,43 15,77	4,20 3,88	17,79 17,74	128...129	70

TABLE 2. IR, PMR, ^1H and ^{19}F NMR Spectra of IIIa-IIIc and IVa-IVf

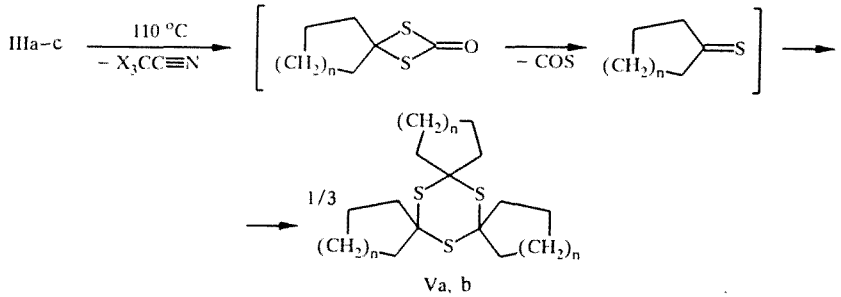
Compound	IR spectrum(KBr), cm^{-1}		NMR spectra, $CDCl_3$, δ, ppm	
	ν_{N-H}	$\nu_{C=O}$	^1H	^{19}F
IIIa	—	1670	2,14...1,55 (8H, m, CH_2)	—
IIIb	—	1675	2,09...1,48 (10H, m, CH_2)	—
IIIc*	—	1680	2,08...1,49 (10H, m, CH_2)	72,3
IVa	3275, 3165	1645	9,04 (1H, s, NH), 7,72...7,44 (5H, m, C_6H_5), 2,17...1,59 (8H, m, CH_2)	75,3
IVb	3270, 3170	1645	8,94 (1H, s, NH), 7,58...7,25 (4H, m, C_6H_4), 2,30 (3H, s, CH_3), 2,12...1,61 (8H, m, CH_2)	76,2
IVc	3270, 3160	1650	8,94 (1H, s, NH), 7,62...6,97 (4H, m, C_6H_4), 3,78 (3H, s, CHO), 2,12...1,61 (8H, m, CH_2)	74,5
IVd	3270, 3160	1645	9,05 (1H, s, NH), 7,58...7,04 (5H, m, C_6H_5), 2,01...1,32 (10H, m, CH_2)	76,3
IVe	3265, 3160	1640	9,08 (1H, s, NH), 7,58...7,33 (4H, m, C_6H_4), 1,99...1,32 (10H, m, CH_2)	76,2
IVf	3270, 3175	1640	9,01 (1H, s, NH), 7,40...7,03 (4H, m, C_6H_4), 2,21 (3H, s, CH_3), 1,91...1,23 (10H, m, CH_2)	76,2

*^{13}C NMR spectrum, $CDCl_3$, δ, ppm (J, Hz): 21.72, 24.45, 39.37, 60.60 (CH_2), 117.30 (CF_3, q, $^1J_{C-F}$ = 280.6 Hz), 168.68 ($C_{(4)}$, q, $^2J_{C-F}$ = 37.8 Hz), 170.90 ($C_{(6)}$).

TABLE 3. Mass Spectra of IIIc and IVd-IVf

Compound	m/z (I, % rel. to I_{max})
IIIc	80 (16), 81 (56), 104 (100), 155 (7), 187 (1), 269 (1)
IVd	78 (27), 81 (52), 104 (7), 114 (100), 121 (23), 190 (14), 273 (14), 316 (1), 347 (3)
IVe	78 (3), 81 (50), 114 (100), 138 (7), 155 (14), 224 (5), 307 (3), 350 (2), 381 (2)
IVf	78 (12), 81 (45), 114 (100), 118 (10), 135 (18), 204 (29), 287 (2), 330 (6), 361 (5)

We have already reported the capacity of Δ^3-1,5-dithia-3-aza-2-trihalomethylbenzocyclononanes [7] and 2-trihalomethyl-1,5,3-benzdithiazepins [8] to undergo facile transannular ring contraction to generate an isocyanate group due to an intramolecular shift of the thio group in the endocyclic azaallyl fragment. Dithiazines IIIa-IIIc are six-membered analogs of this heterocyclic systems and, thus, hold interest in the study of the pathways for their thermal transformations. These dithiazines indeed are thermally labile and readily decompose upon heating for 2 h at reflux in toluene with loss of trihaloacetonitrile and COS to give cycloalkanethiones, which are readily isomerized under the reaction conditions to trithianes Va and Vb. This reaction probably also involves a shift of the thio group in the endocyclic azaallyl system but not to $C_{(4)}$ as in previous cases [7, 8] but to $C_{(6)}$, which leads to elimination of trihaloacetonitrile in the first step and then to loss of COS.



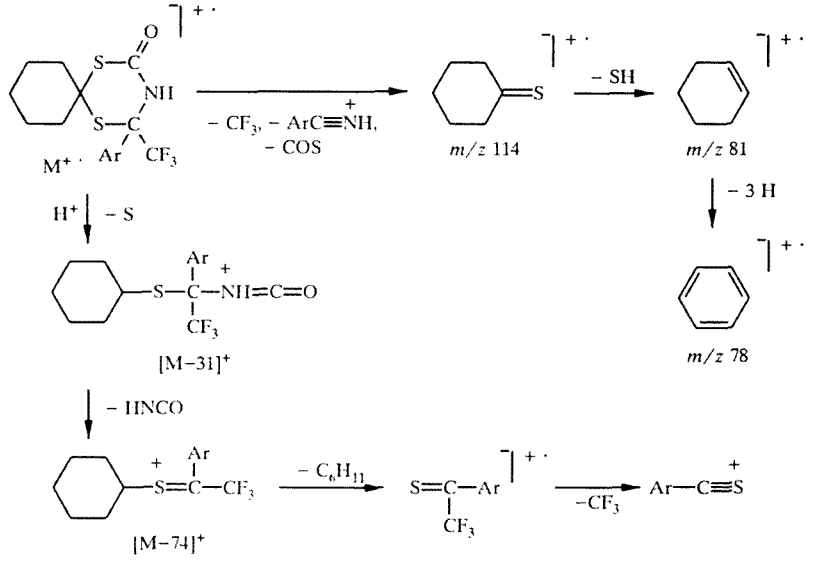
Va, b

V a n = 1, b n = 2

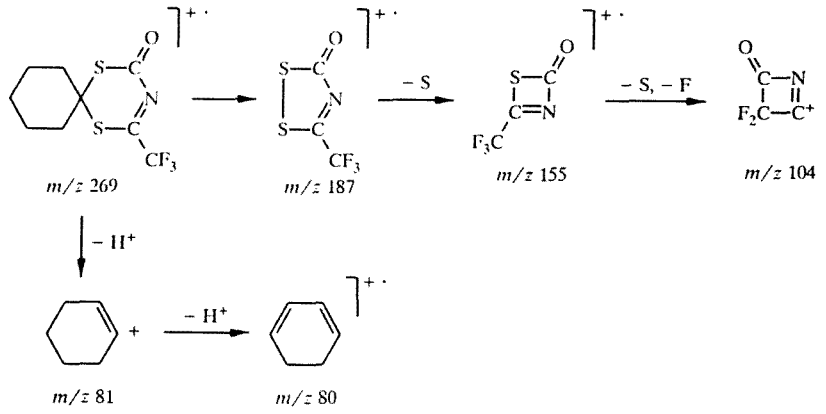
In turn, the lack of azaallyl fragments in 2,3-dihydro-1,3,5-dithiazines IVa-IVf is manifest in their greater thermal stability. These compounds do not undergo significant structural changes in the indicated temperature range or even at 140°C.

The difference in the structures of the heterocyclic fragment between 1,3,5-dithiazines III and IV is manifest not only in their thermal transformations but also in behavior upon electron impact. The mass spectra of IIIc and IVd-IVf are given in Table 3 and show low-intensity molecular ion peaks ($M^{+\cdot}$) (from 1% for IIIc to 5% for IVe). Subsequent fragmentation of $M^{+\cdot}$ for IIIc and IVd-IVf proceeds through different pathways. The fragmentation for IVd-If (Scheme 1) may be represented by two pathways. Pathway 1 is favored since it contains the strongest peaks with *m/z* 114, which may be assigned to cyclohexanethione ions. The formation of such ions most likely is the consequence of successive loss of a CF_3 group [10], $ArC\equiv N^+H$ (*m/z* 104 for IVd, 138 for IVe, and 118 for IVf), and a COS molecule [11]. The loss of the SH group [12] and hydrogen atoms by the cyclohexanethione cation leads to its aromatization. Pathway 2 for the fragmentation of $M^{+\cdot}$ results from initial protonation of the dithiazino ring and subsequent loss of the sulfur atom [13], HNCO molecule [14] to give cations with $[M - 31]^+$ and $[M - 74]^+$ and also thioketone ions $S=C(Ar)CF_3^{+\cdot}$ (*m/z* 273 for IVd, 307 for IVe, and 287 for IVf), which eliminate the CF_3 group and are converted into $S^+\equiv C-Ar$ cations (*m/z* 190 for IVd, 224 for IVe, and 204 for IVf).

Scheme 1



Scheme 2



Cleavage of the S−C−S bond system to give a cyclohexyl carbocation (*m/z* 81) is characteristic for the molecular ion of dithiazine IIIc (*m/z* 269) (Scheme 2). This carbocation undergoes dehydrogenation to give cyclohexadiene (*m/z* 80) and unstable cations 1,2,4-dithiazole (*m/z* 187). Subsequent elimination of sulfur and fluorine atoms is accompanied by formation of an unstable ion (*m/z* 155) and more stable cation (*m/z* 104).

EXPERIMENTAL

The PMR, ^{13}C NMR, and ^{19}F NMR spectra were taken on a Varian Gemini-200 spectrometer with HMDS, TMS, and $CFCl_3$, respectively, as the internal standard. The IR spectra were taken on a UR-20 spectrometer. The mass spectra were taken on an MS-1302 mass spectrometer using direct sample inlet into the ion source. The ionization energy was 70 eV and the emission current was 50 μA. The temperature of the ion source and the inlet block was 80°C.

The elemental analysis data given in Table 1 are in accord with the calculated values.

6,6-Tetramethylene- and 6,6-Pentamethylene-2-trihalomethyl-1,3,5-dithiazin-4-ones (IIIa-IIIc), 2,3-Dihydro-6,6-tetramethylene- and 2,3-Dihydro-6,6-pentamethylene-2-aryl-2-trifluoromethyl-1,3,5-dithiazin-4-ones (IVa-IVf). A sample of 5 mmoles dithiol Ia or Ib was added to a solution of 5 mmoles isocyanate IIa-IIf in 30 ml benzene. Then, a solution of 0.01 mole (for isocyanates Ia and Ib) or 5 mmoles triethylamine (for isocyanates Ic-If) in 10 ml benzene was added with stirring. The reaction mixture was stirred for 3 h and filtered. The filtrate was evaporated. Products IIIa-IIIc and IVc were purified by crystallization from hexane, while the other products were purified by crystallization from hexane−benzene.

Thermolysis of 6,6-Tetramethylene- and 6,6-Pentamethylene-2-trihalomethyl-1,3,5-dithiazin-4-ones (IIIa-IIIc). A solution of 3 moles IIIa-IIIc in 10 ml toluene was heated at reflux for 2 h. In the case of IIIc, the gaseous products were bubbled into 5 ml methanol containing a catalytic amount of sodium methylate. The solvent was evaporated off and the residue was purified by crystallization from methanol to give 0.1 g (34%) 2,2,4,4,6,6-tris(tetramethylene)-1,3,5-trithiane with mp 96-97°C and 0.12-0.14 g (35-41%) 2,2,4,4,6,6-tris(pentamethylene)-1,3,5-trithiane with mp 99-101°C, which is in accord with the data of Jentzsch et al. [9]. Methyl trifluoroiminoacetate was identified by chromatographic analysis of the methanolic solution.

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