PREPARATION AND MASS SPECTRA OF HETEROCYCLIC SULFIDES OF THE 5-NITROFURAN SERIES*

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The reaction of heterocyclic thiols RSH wherein R designates 2-benzimidazolyl, 2-benzothiazolyl, 2-benzoxazolyl, 2-benzoselenazolyl, 2-pyrimidinyl, and 2-(4-phenyl-1,3,4-thiodiazole-5-thione-yl), with 5-nitrofurfuryl chloride, bromide, iodide or nitrate in a suitable solvent has furnished the corresponding sulfides, the mass spectra of which are discussed.

In connection with investigations of nitrofuran derivatives, some heterocyclic sulfides have been now synthesized containing the 5-nitrofurfuryl residue in their molecule. From this group, some 5-nitro-2-furyl pyridyl sulfides, furfuryl pyridyl sulfides, and furfuryl 6-nitro-2-benzothiazolyl sulfide have been prepared by Takahashi and coworkers[1]. The preparation of some 5-nitrofurfuryl 2-pyrimidinyl sulfides by reaction of 5-nitrofurfuryl chloride with substituted 2-mercaptopyrimidines in acetonitrile and in the presence of triethylamine has been reported in the patent literature[2]. Some 5-nitro-2-furyl heteroaryl sulfides of a marked antibacterial activity have been obtained by Japanese authors[3] on treatment of 2-bromo-5-nitrofuran with various heterocyclic thiols.

In the synthesis of compounds *I*–*VI*, the appropriate heterocyclic thiols or their salts were treated with 5-nitrofurfuryl halides or other derivatives. The preparation was accomplished by reaction of equimolar amounts of the corresponding dry mercaptide and the 5-nitrofurfuryl derivative such as chloride, bromide, iodide or nitrate in an aromatic hydrocarbon (Method *A*) or by reaction of the corresponding heterocyclic thiol with the 5-nitrofurfuryl derivative in acetone, 2-butanone, dimethylformamide, dimethyl sulfoxide or their mixtures in the presence of alkali metal carbonates (Method *B*) at temperatures ranging from the room temperature to the boiling point temperature of solvents. With the use of Method *A*, the best

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[*] Part L in the series Furan Derivatives; Part IL: This Journal *39*, 767 (1974).

results were obtained at room temperature since tars are obtained as by-products at elevated temperatures. Moreover, the use of an aromatic hydrocarbon as solvent requires a relatively long period of reaction time of 8–12 hours. Notwithstanding, the yields of sulfides are lower than with the use of polar solvents (Method *B*). As it may be seen from Table I, method *B* gives better yields (about 80%) and the reaction time is considerably shorter. The results also depend on the character of the 5-nitrofurfuryl derivative. Thus, with 5-nitrofurfuryl nitrate as reactant, the yields are 30–40% only, even with the use of long reaction periods of time. From 5-nitrofurfuryl halides, better yields are obtained with the bromide and iodide than with the chloride. 5-Nitrofurfuryl nitrate was prepared by nitration of furfuryl alcohol with fuming nitric acid in acetic anhydride[4]. Nitration of furfuryl chloride with acetyl nitrate afforded 5-nitrofurfuryl chloride[5]. 5-Nitrofurfuryl bromide[6] and 5-nitrofurfuryl iodide[7] were prepared by reaction of 5-nitrofurfuryl nitrate with sodium bromide and potassium bromide, resp., in acetone. The present 5-nitrofurfuryl heteroaryl sulfides, their properties, and UV spectra are summarized in Table I. All these sulfides are fairly soluble in polar solvents.

The mass spectra of all the present 5-nitrofurfuryl heteroaryl sulfides have been investigated. The base peaks in mass spectra of compounds *I*–*IV* (Fig. 1) are formed by the $[M—\dot{N}O_2]^{(+)}$ ions. The main fragmentation paths of molecular ions of these compounds are shown on Schemes 1 and 2. The fragment ions, the *m*/*e* value of which is one unit higher than that of *a* ions, are formed by cleavage of the S—C bond in the molecular ion under the simultaneous hydrogen transfer from the neutral fragment. In this way is for example formed the fragment ion of the *m*/*e* 167 value in the case of compound *III* ($X = S$). Its exact mass as well as the exact masses of other fragment ions were measured and their composition confirmed (Table II). The fragment ions of the *b* type are formed by a hydrogen transfer reaction. The further cleavage is analogous to that of benzimidazoles[8], benzothiazoles[9] or benzoselenazoles[10]. The formation of the *m*/*e* 126 fragment ion is obviously accompanied by enlargement to the six-membered ring of a pyrylium ion structure similarly to furan alkyl derivatives[11].

$$M^{+\cdot} \rightarrow [M—\dot{N}O_2]^+ \rightarrow [M—\dot{N}O_2—CO]^+$$

I, *m*/*e* 275	*m*/*e* 229	*m*/*e* 201
II, *m*/*e* 276	*m*/*e* 230	*m*/*e* 202
III, *m*/*e* 292	*m*/*e* 246	*m*/*e* 218
IV, *m*/*e* 340*	*m*/*e* 294*	*m*/*e* 266*

Scheme 1

The mass spectrum of compound *V* is shown on Fig. 2*a*. The base peak is formed by the $[M—\dot{N}O_2]^{(+)}$ ion of *m*/*e* 191 from which the fragment *m*/*e* 163 is obtained by expulsion of CO. Somewhat surprising is the relatively intensive *m/e* 220 peak which is formed by expulsion of the hydroxyl radical from the molecular ion. The

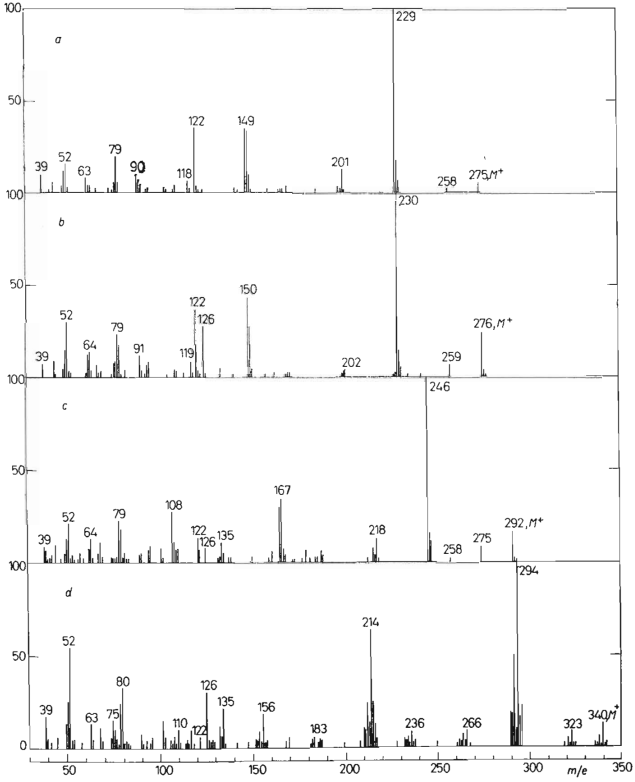
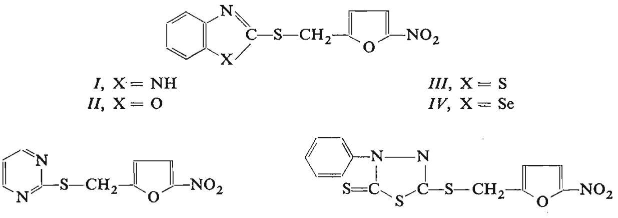


FIG. 1

Mass Spectra

a 5-Nitrofurfuryl 2-benzimidazolyl sulfide (*I*); *b* 5-nitrofurfuryl 2-benzoxazolyl sulfide (*II*); *c* 5-nitrofurfuryl 2-benzothiazolyl sulfide (*III*); *d* 5-nitrofurfuryl 2-benzoselenazolyl sulfide (*IV*).

formation of the m/e 112 fragment ion (Scheme 3) might be explained similarly to compounds *I* and *IV* by cleavage of the S—C bond in the molecular ion and hydrogen transfer to sulfur. Of interest is the formation of the m/e 161 fragment ion. Exact

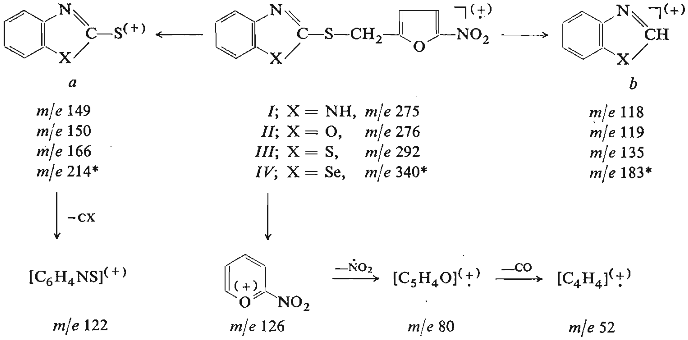


I, X = NH
II, X = O
III, X = S
IV, X = Se

V

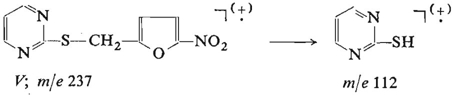
VI

SCHEME 1



* For isotope ^{80}Se.

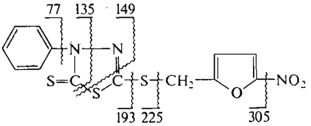
SCHEME 2



SCHEME 3

mass measurements indicate the composition $C_8H_5N_2S$. The difference between this ion and molecular ion is CH_2NO_3. The *m/e* 161 ion can not be formed by a simple bond rupture from the molecular ion. Its formation might be explained by expulsion of the neutral CH_2O fragment from the $[M—\dot{N}O_2]^{(+)}$ fragment ion under a simultaneous migration of atoms.

The mass spectrum of compound *VI* is shown on Fig. 2*b*. The fragment ions *m/e* 319 and *m/e* 305 are formed by expulsion of the sulfur atom or the $\cdot NO_2$ radical



SCHEME 4

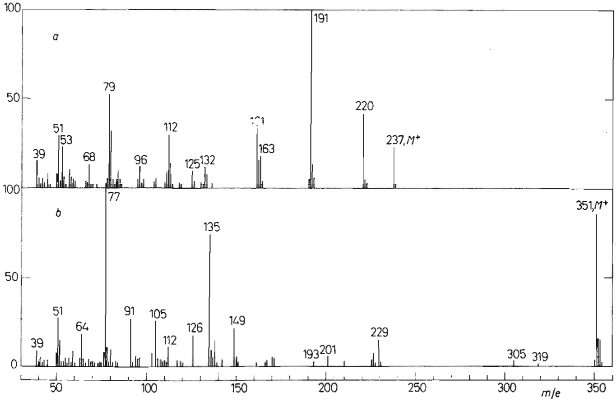


FIG. 2

Mass spectra

a 5-Nitrofurfuryl 2-pyrimidinyl sulfide (*V*); *b* 5-nitrofurfuryl 4-phenyl-1,3,4-thiodiazole-5--thione-2-yl sulfide (*VI*).

from the molecular ion and appear in spectrum of a low relative intensity. The base fragment is in the spectrum represented by the $C_6H_5^+$ ion of *m/e* 77. The other fragmentation paths are shown on Scheme 4.

EXPERIMENTAL

Synthesis of 5-Nitro-2-furfuryl Heteroaryl Sulfides

Method A. To a solution of the corresponding 5-nitrofurfuryl derivative (0·03 mol) in an aromatic hydrocarbon (50 ml) there is added a potassium heteroarylmercaptide (0·03 mol) and the mixture is stirred at room temperature for 8 h under exclusion of atmospheric moisture. The precipitate is collected with suction, washed with ether and water, dried, and recrystallised from ethanol.

Method B. To a mixture of the corresponding heterocyclic thiol (0·01 mol), potassium carbonate (0·01 mol) and 20 ml of acetone (2-butanone, dimethylformamide, dimethyl sulfoxide and the like) there is added with stirring a solution of 5-nitrofurfuryl bromide (0·01 mol) in acetone (10 ml). The reaction mixture is stirred at room temperature for 3 h and the potassium bromide is collected with suction. The filtrate is briefly refluxed with active charcoal, filtered again and diluted under stirring with water to deposit the required sulfide which is collected with suction, washed with ether, and recrystallised from ethanol.

Methods

Electron absorption spectra in the UV region were taken in methanol on a recording Specord UV VIS Zeiss spectrophotometer. Mass spectra were measured on a MAT 111 Varian apparatus operating with a source temperature of 200°C and using the direct insertion (80 eV, 270 μA). Exact measurements were performed on an A.E.I.M.S. 902 S apparatus using the resolving ability 25 000 (10% valley definition) and heptacozafluorotri-n-butylamine as mass reference standard.

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