2-Methylselenobenzo[b]furan-3-carbaldehyde (X) was obtained in a similar manner to (IX) with a yield of 67%, mp 38.7-40°C. IR spectrum: 1656 cm^{-1} (C=O). UV spectrum (in ethanol), λ_{max}, nm (log ε): 207 (4.39), 236 (4.19), 323 (3.95). PMR spectrum, ppm: 10.07 (1H, s, CHO), 7.98-7.75 (1H, m, 4-H), 7.47-7.07 (3H, m, Ar), 2.46 (3H, s, CH_4). Found, %: C 50.5, H 3.5, Se 33.5. M^+ 240. $C_{10}H_8O_2Se$. Calculated, %: C 50.2, H 3.4, Se 33.0; mol. wt. 239.

LITERATURE CITED

1. B. M. Zolotarev, V. P. Litvinov, Ya. L. Gol'dfarb, and V. Yu. Mortikov, Khim. Geterosikl. Soedin., No. 8, 1057 (1984).
2. K. Gewald, M. Hentschel, and U. Illigen, J. Prakt. Chem., 316, 1030 (1974).
3. Ya. L. Gol'dfarb, New Directions in Thiophene Chemistry [in Russian], Nauka, Moscow (1976), p. 190.
4. Ya. L. Gol'dfarb, V. P. Litvinov, and V. Yu. Mortikov, Khim. Geterotsikl. Soedin., No. 7, 905 (1979).
5. V. A. Bren', V. I. Usacheva, Zh. V. Bren', B. Ya. Simkin, and V. I. Minkin, Khim. Geterotsikl. Soedin., No. 5, 631 (1974).
6. G. M. Coppola, J. Heterocycl. Chem., 18, 845 (1981).
7. K. Fries and W. Pfaffendorf, Chem. Ber., 43, 212 (1910).
8. Beilst, 17, 309 (1959).
9. R. Royer, P. Demerseman, and I. Rene, Bull. Soc. Chim. Fr., No. 10, 3740 (1970).
10. R. Stoermer and B. Kahlert, Chem. Ber., 35, 1640 (1902).
11. W. Grubenman and H. Erlenmeyer, Helv. Chim. Acta, 31, 78 (1948).
12. Organic Syntheses [Russian translation], IL, Moscow, Coll. 5 (1954), p. 35.

A STUDY OF THE KINETICS OF THE INTERACTION OF BENZOXAZOLINE-2-THIONES WITH BUTYLAMINE

D. Simov, K. Davidkov, and L. Prangova

UDC 547.787.3:541.127

The kinetics of the interaction of butylamine with 5- and 6-substituted benzoxazoline-2-thiones has shown the absence of a correlation between the rate of the reaction and the electronic properties of the substituents. Thus, the mechanism of the nucleophilic opening of the benzoxazoline-2-thione ring differs from those described previously.

It is known that the reaction of benzoxazoline-2-ones and benzoxazoline-2-thiones with nucleophilic agents such as metal hydroxides [1, 2], ammonia [3], or amines [2, 4-7] takes place with the opening of the heterocyclic ring and the formation, in the case of the nitrogenous nucleophiles of substituted o-aminophenols or o-hydroxyphenylureas or the corresponding thio compounds. That is, the nucleophilic attack on these heterocycles is directed to the carbonyl (thione) carbon atom.

In order to elucidate the mechanism of the interaction of benzoxazoline-2-thiones with aliphatic amines, we have studied the kinetics of the reaction of 5- and 6-substituted benzoxazoline-2-thiones (Ia-o) with butylamine. It is known that the reaction of the heterocycle (Ia) with amines takes place with high — frequently quantitative — yields and leads to the unsymmetrical disbustituted thioureas (IIa-o) and trisubstituted thioureas [5-7].

We performed the reaction of compounds (Ia-o) with butylamine at 65°C in butylamine solution, measuring the change in the concentration of the initial heterocycle from the decrease in the intensity of the absorption band in the 280-320 nm region. As can be seen from

Kl. Okhridski Sofia University, Sofia, Bulgaria.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1180-1181, September, 1984. Original article submitted December 14, 1983.

0009-3122/84/2009-0960$08.50

TABLE 1. Number of Measurements (n), Correlation Coefficients (r), Standard Deviations (S), and Rate Constants of the Reactions of Compounds (Ia-o) with Butylamine

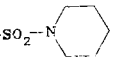
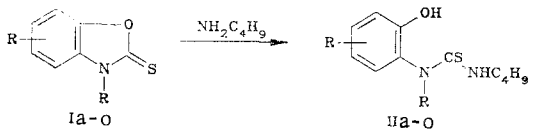
Compound	R	n	r	S	$(k\pm\Delta k)\times10^{-3}$ min^{-1}
Ia	H	17	0,999	0,001	2,49±0,01
Ib	5-I	5	0,999	0,001	4,76±0,04
Ic	5-Cl	13	0,999	0,002	4,57±0,02
Id	5-NO_2	6	0,977	0,008	115,38±0,04
Ie	5-SO_2CH_3	8	0,995	0,014	21,28±0,04
If	5-SO_2NH_2	10	0,990	0,047	7,60±0,32
Ig	6-Cl	12	0,998	0,005	9,31±0,08
Ih	6-Br	14	0,997	0,003	11,85±0,11
Ii	6-SO_2CH_3	9	0,998	0,001	45,74±0,04
Ij	5-SO_2NHCH_3	12	0,997	0,007	10,57±0,11
Ik	5-$SO_2N(CH_3)_2$	8	0,995	0,008	14,13±0,25
Il		8	0,996	0,006	11,32±0,18
Im	5-NH_2	14	0,999	0,003	2,69±0,01
In	5-CH_3	16	0,998	0,005	5,61±0,05
Io	3-CH_3	8	0,998	0,013	224,13±0,04

Table 1, in all cases a good linear dependence of the logarithm of the optical density of the corresponding absorption bands on the time was observed.



Ia-o IIa-o

As analysis of the values of the rate constants obtained shows, in these series of electron-accepting substituents (compounds Ia-i), in the case of the 5-substituted heterocycles a satisfactory, and in the case of the 6-substituted compounds, a good correlation is observed between the values of $\log(k_i/k_o)$ and the McDaniel—Brown σ^- constants of the substituents [8], which permits the assumption of the predominant transmission of the influence of electronic effects through the oxygen atom of the heterocycle. However, as can be seen from the figures in Table 1, the rate constant of the reaction of compound (If) is lower than that of compounds (Ij-l), the donor properties of the substituents of which are higher. In just the same way, the value of k in the case of such donor substituents as CH_3 and NH_2 is higher than for the unsubstituted compound (Ia), and for the 3-methyl-substituted compound (Io) the value of k is two orders of magnitude higher than for compound (Ia), i.e., the taking into account of the electronic effects of both electron-donating and electron-accepting substituents does not permit a direct correlation to be found between the electronic properties of the substituents in the benzene or the heterocyclic nucleus and the rate constants of the opening of the oxazoline-2-thione ring. It follows from this that the mechanism of the interaction of such heterocycles with aliphatic amine has a more complex nature. It has recently been found that when equimolecular amounts of benzoxazoline-2-thiones and primary, secondary, and tertiary amines are mixed in anhydrous diethyl ether or anhydrous ethyl acetate, the saltlike compounds are formed [9], which is apparently the reason for the absence of a correlation. A more detailed investigation of these processes will probably permit the true mechanism of this, at first sight, simple reaction to be discovered in the future.

EXPERIMENTAL

The synthesis of the initial compounds (Ia-o) and also of the final thioureas (IIa-o) was performed by known methods [5-7, 9-12]. The kinetic measurements were performed on a Unicam SP-800 spectrophotometer in closed cells thermostated at 65 ± 0.1°C, in which solutions of the corresponding heterocycles (Ia-o) in freshly distilled n-butylamine at concentrations of $3\text{-}5\cdot10^{-5}$ M were placed. The reaction time was about 120 min.

LITERATURE CITED

1. F. Kalckhof, Chem. Ber., 16, 1825 (1883).
2. V. Kalcheva, Dissertation, Sofia University (1971).
3. S. Chelmicki, J. Prakt. Chem., 42, 442 (1890).
4. R. Desai, R. Hunter, and A. Khalidi, J. Chem. Soc., 1186 (1934).
5. I. Simov and K. Atanasov, Dokl. Bolg. Akad. Nauk, 20, 433 (1967).
6. D. Simov and K. Davidkov, Compt. Rend. Acad. Bulg. Sci., 23, 1361 (1970).
7. K. Davidkov and D. Simov, Compt. Rend. Acad. Bulg. Sci., 26, 777 (1973).
8. V. A. Palm, Principles of the Quantitative Theory of Organic Compounds [in Russian], Khimiya, Leningrad (1967), p. 150.
9. K. Davidkov, Dissertation, Sofia University (1982).
10. J. Dünner, Chem. Ber., 9, 465 (1876).
11. R. Desai, R. Hunter, and A. Khalidi, J. Chem. Soc., 321 (1938).
12. P. Seidel, J. Prakt. Chem., 42, 445 (1890).

SYNTHESIS AND TRANSFORMATIONS OF SULFIDES OF THE THIOPHENE SERIES.

39.* SYNTHESIS AND PHARMACOLOGICAL PROPERTIES OF SOME 2,5-DISUBSTITUTED 3-THIENYLALKYLAMINES

Ya. L. Gol'dfarb, M. A. Kalik, V. K. Zav'yalova, E. F. Lavretskaya, and S. A. Sukhanova

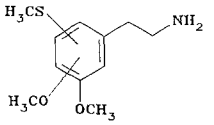
UDC 547.732

A number of isomeric 3-thienylalkylamines containing methylthio and methoxy groups in the α positions of the thiophene ring have been synthesized. It has been shown that they possess a weak activity of the stimulating and antidepressant type.

It is known that substituted phenethylamines are compounds of interest as potential psychotropic agents [2, 3]. Recently [4, 5], it has been shown that the sulfur analogs of natural psychotomimetic agents — mescaline and isomescaline (3,4,5- and 2,3,4-trimethoxyphenethylamines), type (I) — are psychomimetic agents 6-12 times more powerful than mescaline, while the corresponding dithio analogs have no appreciable influence on the central nervous system [5]. It has also been reported that all sulfur analogs of mescaline are readily deaminated by monoamine oxidase and are more suitable for this purpose than the corresponding oxygen compounds [4], although no direct correlation has been detected between the degree of decomposition by the enzyme and the psychotomimetic activity (for man).

Taking into account the frequently observed similarity in the biological activities of thiophene and benzene analogs [6], it appeared desirable to investigate within the plan considered above the corresponding derivatives of the thiophene series.

The present paper describes the synthesis and some psychopharmacological properties of substituted 3-thienyl alkylamines (II-IV) bearing methylthio and methoxy groups in the α positions of the thiophene nucleus.



I

*For communication 38, see [1].

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Scientific-Research Institute for the Biological Testing of Chemical Compounds. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1182-1185, September, 1984. Original article submitted January 10, 1984.

 0009-3122/84/2009-0962$08.50