CONDENSED HETEROCYCLES.

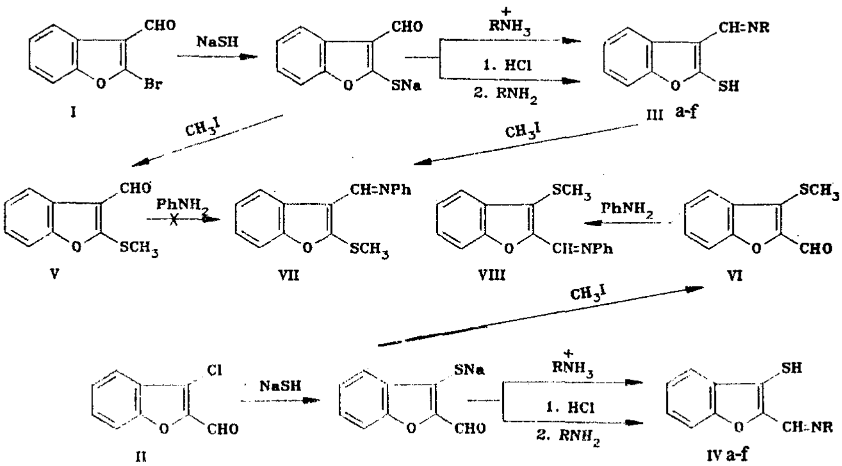
44.* SYNTHESIS AND STRUCTURE OF IMINES OF 2-MERCAPTOBENZO[b]-FURAN-3-CARBALDEHYDES AND 3-MERCAPTOBENZO[b]FURAN-2-CARBALDEHYDES AND THEIR DERIVATIVES

A. F. Vaisburg, V. Yu. Mortikov, and
V. P. Litvinov

UDC: 547.728.1.04:543.422

A number of isomeric mercapto aldimines of benzo[b]furan have been obtained and their structure and properties have been studied in comparison with their benzo[b]-thiophene analogs. It has been shown that the nature of the heterocycle has no substantial influence on the structure and properties of these compounds, in contrast to the initial mercapto and hydroseleno aldehydes. It has been observed that the 2-mercapto or 2-methylthio(methylseleno) groups in benzo[b]furan-3-carbaldehydes are readily replaced by an amino group, while they are not replaced in the isomeric 3-mercapto- and 3-methylthio(methylseleno)benzo[b]furan-2-cabaldehydes.

We have previously synthesized 2-hydroselenobenzo[b]furan-3-carbaldehydes and 3-hydroselenobenzo[b]furan-2-carbaldehydes, have studied their properties and compared them with the properties of the benzo[b]thiophene analogs, and have shown a substantial influence of the nature of the heterocycle [2]. Thus, the hydroseleno (mercapto) aldehydes of benzo[b]thiophene are fairly stable to the action of atmospheric oxygen [3], while the benzo[b]furan hydroseleno (mercapto) aldehydes are rapidly oxidized in the air and are therefore isolated and characterized in the form of diselenides and methylthio (methylseleno) derivatives [2].



III, IV a $R=C_6H_5$, b $R=C_6H_4-CH_3$-p, c $R=C_6H_4-OCH_3$-p, d $R=C_6H_4-CH_3$-o, e $R=C_6H_4-OC_6H_5$-p, f $R=C_4H_9$

---

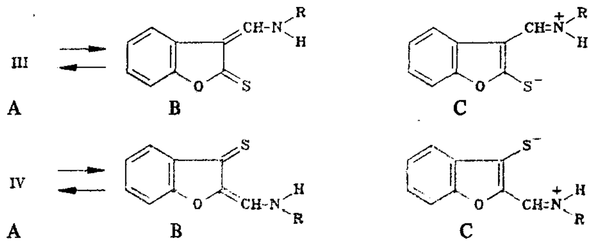
*For communication 43, see [1].

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 598-602, May, 1985. Original article submitted July 2, 1984.

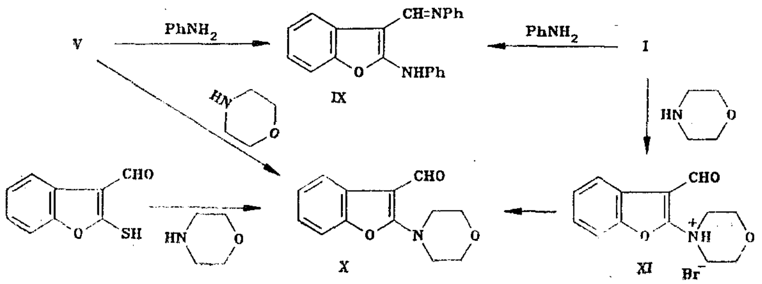
0009-3122/85/2105-0496$09.50

With the aim of studying the influence of the nature of the ring heteroatom on the structure and properties of mercapto aldimines, we have obtained a number of isomeric mercapto aldimines of benzo[b]furan and have studied their structure. The reaction of 2-bromobenzo[b]furan-3-carbaldehyde (I) [4] and of 3-chlorobenzo[b]furan-2-carbaldehyde (II) [5] with sodium hydrogen sulfide gave the sodium salts of the mercapto aldehydes. The addition of the sulfates or hydrochlorides of primary amines to the reaction mixture (method A) or the initial acidification of the reaction mixture followed by the addition of a primary amine to the solution of a mercapto aldehyde in ether (method B) led to the formation of the mercapto aldimines (III) and (IV) with good yields. When methyl iodide was added to the sodium salts of the mercapto aldehydes, their methylthio derivatives (V) and (VI) were formed.

To study the structures of the isomeric mercapto aldimines (III) and (IV), which may exist in various tautomeric forms — for example, IIIA-B, IVA-B or in the form of their equilibrium mixtures — we synthesized compounds (VII) and (VIII) as models of the tautomeric form A. The reaction of the methylthio aldehyde (VI) with aniline gave the imine (VIII), which is a model of the tautomeric form (IVA) [6]. Attempts to obtain the isomeric imine (VII) in a similar manner were unsuccessful.



The reaction of the aldehyde (V) with one or two equivalents of aniline formed 2-phenylamino-3-benzo[b]furylidenephenylamine (IX), which was also obtained from the bromoaldehyde (I). The reaction of 2-mercaptobenzo[b]furan-3-carbaldehyde or the aldehyde (V) with morpholine likewise led to the replacement of the mercapto or methylthio group and to the formation of the amine (X), which was obtained independently by the reaction of the bromoaldehyde (I) with morpholine through the intermediate stage of the formation of the salt (XI).



The reaction of 2-methylselenobenzo[b]furan-3-carbaldehyde [2] with aniline and with morpholine took place similarly, with the formation of compounds (IX) and (X). It must be mentioned that, in contrast to this, in 3-methylthiobenzo[b]furan-2-carbaldehyde (VI) and 3-methylselenobenzo[b]furan-2-carbaldehyde [2] the methylthio or methylseleno group was not replaced by an amino group but the corresponding imines were formed or the initial compound was recovered. The isomeric imine (VII) was obtained by the reaction of the mercapto (IIIa) with methyl iodide in the presence of a base.

In the PMR spectra of the mercapto aldimines (III) and (IV) (Table 2), signals of protons were present in the weak field in the 11.5-14.5 ppm region in the form of broadened doublets and in the 8-8.5 ppm region in the form of doublets with SSCCs J = 13-14 Hz. The nature of the spectra shows the existence of the tautomeric forms (IIIB) and (IVB), which was confirmed by the appearance of additional splitting on passing from the arylimines (IIIa-e) and (IVa-e) to the butylimines (IIIf) and (IVf). Thus, at 11.78 ppm in the spectrum of compound (IIIf) and at 12.81 ppm in that of compound (IVf), the signal of the NH proton appeared in the form of a broadened quartet through interaction with the protons of the α-methylene group of the butyl radical, which, in its turn, interacting with the NH proton, appeared in the form of a quartet at 3.60 and 3.53 ppm, respectively, for the imines (IIIf) and (IVf). At the same time, it may be mentioned that the signals of the NH protons for all the 3-mercapto aldimines

TABLE 1. The Mercapto Aldimines (III) and (IV)

Compound*	Method	mp.† °C	Found, %				Empirical formula	Calculated, %				Yield, %
			C	H	N	S		C	H	N	S	
IIIa	A	198,5—200	70,8	4,4	5,8	12,9	$C_{15}H_{11}NOS$	71,1	4,4	5,5	12,7	68
IIIb	A	210—211,5	72,2	4,9	5,5	12,2	$C_{16}H_{13}NOS$	71,9	4,9	5,2	12,0	71
IIIc	A	187—188,5	67,8	4,5	4,9	11,3	$C_{16}H_{13}NO_2S$	67,8	4,6	4,9	11,3	61
IIId	A	195—197	71,9	5,1	5,2	11,9	$C_{16}H_{13}NOS$	71,9	4,9	5,2	12,0	63
IIIe	B	219,5—221	73,1	4,7	3,8	9,3	$C_{21}H_{15}NO_2S$	73,0	4,4	4,1	9,3	35
IIIf	B	67—68	66,7	6,8	6,2	14,6	$C_{13}H_{15}NOS$	66,9	6,5	6,0	13,7	70
IVa	A	125—126	—	—	—	—	$C_{15}H_{11}NOS$	—	—	—	—	43
IVb	A	155—157	—	—	—	—	$C_{16}H_{13}NOS$	—	—	—	—	75
IVc	A	172—174	—	—	—	—	$C_{16}H_{13}NO_2S$	—	—	—	—	72
IVd	A	151—153	71,8	5,1	5,0	12,0	$C_{16}H_{13}NOS$	71,9	4,9	5,2	12,0	62
IVe	B	135—137,5	73,1	4,2	4,0	9,1	$C_{21}H_{15}NO_2S$	73,0	4,4	4,1	9,3	38
IVf	A	71,5—73	66,9	6,8	6,0	13,8	$C_{13}H_{15}NOS$	66,9	6,5	6,0	13,7	6

---

*Compounds (IVa-c) have been described in [6].

†Compounds (IIIa-d) and (IVc) were crystallized from benzene, (IIIe) and (IVb and d) from $CH_3COC_2H_5$, (IIIf) and (IVa and e) from ether, and (IVf) from methanol.

TABLE 2. Spectral Characteristics of the Mercapto Aldimines (III) and (IV)

Compound	UV spectrum (ethanol) λ_{max}, nm (log ε)	PMR spectra ($CDCl_3$), δ, ppm (TMS)			
		NH, br.d	=CH, d, J, Hz	arom. protons, m	CH_3, s
IIIa	448 (4,35); 289 (4,55); 257 (4,30); 225 (4,23); 202 (4,44)	13,44	8,46 (13,30)	7,55—7,17	—
IIIb	451 (4,43); 290 (4,51); 259 (4,32); 229 (4,27); 202 (4,43)	13,43	8,42 (13,65)	7,58—7,14	2,39
IIIc	460 (4,26); 289 (4,38); 233 (4,17)	13,47	8,35 (13,75)	7,46—6,93	3,85
IIId	450 (4,23); 290 (4,47); 260 (4,27)	13,19	8,52 (13,25)	7,52—7,16	2,54
IIIe	460 (4,25); 294 (4,41); ($CHCl_3$)	13,49	8,40 (14,00)	7,47—7,00	—
IIIf	405 (4,09); 283 (4,27); 266 (4,31); 218 (4,29)	11,78 (br.q)	8,12 (14,30)	7,50—7,08	3,60 (2H, q, CH_2), 1,95—0,97 (7H, m, C_3H_7)
IVa	520 (4,03); 370 (4,12); 294 (4,02); 235 (4,18)	14,52	8,35 (13,00)	8,17—6,76	—
IVb	520 (3,86); 370 (3,91); 304 (3,87); 237 (4,07)	14,45	8,21 (13,00)	7,97—7,14	2,35
IVc	524 (4,00); 376 (4,13); 304 (4,03)	14,58	8,19 (13,30)	8,03—6,90	3,84
IVd	511 (4,36); 367 (4,38); 294 (4,00); 242 (4,17); 204 (4,72)	14,04	8,35 (13,30)	8,06—7,14	2,56
IVe	521 (4,25); 373 (4,21); 244 (4,15)	14,52	8,17 (13,50)	8,03—6,99	—
IVf	463 (4,21); 342 (4,37); 205 (4,33)	12,81 (br.q)	7,84 (13,50)	7,98; 7,57—7,20	3,53 (2H, q, CH_2), 1,85—1,00 (7H, m, C_3H_7)

(IV) were shifted upfield (~1 ppm) as compared with the signals of NH protons of the 2-mercapto aldimines (III) with similar substituents attached to the nitrogen atom. The replacement of an aryl radical by a butyl radical in the aldimines (III) and (IV) led to a shift of the signals of the protons of the NH and CH groups upfield by 1.6 and 0.2-0.4 ppm, respectively.

Analysis of the UV spectra (Table 2) of the mercapto aldimines (III) and (IV) showed that changes in the nature of the solvent (ethanol, chloroform, heptane) and in the temperature (20-60°C) did not appreciably affect the nature of the spectra, which demonstrates the stability of the tautomeric form B. The presence of a long-wave maximum (450-520 nm) in the spectra of the aldimines (III) and (IV) can be explained by the contribution of the bipolar structure C to the tautomeric form B, i.e., by a redistribution of the π-electron density [7].

It must also be mentioned that the long-wave maxima in the UV spectra of the 3-mercapto aldimines (IV) were shifted in the long-wave direction by 50-70 nm as compared with the 2-mercapto aldimines (III). Replacement of the aryl substituent at the nitrogen atom by an alkyl substituent led to a hypsochromic shift of this maximum by approximately 50 nm.

The IR spectra of the imines (VII) and (VIII) each showed the band at 1620 cm^{-1} (C=N) that is characteristic for arylimines. The spectra of the mercapto aldimines (III) and (IV) each contained a band at 1639-1652 cm^{-1} which can be assigned to the stretching vibrations of the $C{=}N^+$ bond [8], and this is in agreement with the indications from the UV spectra on the existence of a contribution of the bipolar structure C to the tautomeric form B. The presence of other bands in the IR spectra of the mercapto aldimines (III) and (IV) does not contradict the information obtained about their structure.

EXPERIMENTAL

IR spectra were recorded on a UR-20 spectrometer (in KBr tablets), and UV spectra on a Specord UV-Vis spectrophotometer. PMR spectra were recorded on Bruker WM-250 and Tesla BS-467 (60 MHz) spectrometers in $CDCl_3$ with TMS as internal standard. The course of the reactions was followed and the individuality of the compounds was checked with the aid of TLC on Silufol UV-254 plates in the $CHCl_3$—hexane (1:1) system.

The 2-Mercapto-3-benzo[b]furfurylidenearyl(alkyl)amines (IIIa-f), and the 3-Mercapto-2-benzo[b]furfurylidenearyl(alkyl)amines (IVa-f). In an atmosphere of argon, 4.7 ml (8.5 mmole) of a 10% aqueous solution of NaSH was added to a hot solution of 5.5 mmole of the haloaldehyde (I) or (II) in 50 ml of methanol. Then the reaction mixture was boiled for 30 min and was cooled to 10°C.

A. A methanolic or aqueous methanolic solution of the hydrochloride or sulfate of the appropriate amine (30 mmole) was added to the mixture and it was stirred for 15 min and was poured into 250 ml of water. The precipitate that deposited was filtered off, dried over P_2O_5, and recrystallized to give the aldimines (IIIa-d) and (IVa-d) (in the case of the aldimine (IVf), the mixture was extracted with chloroform, the extract was dried with $MgSO_4$ and evaporated, and the residue was twice recrystallized from methanol).

B. A mixture was slowly acidified with 20 ml of 5% hydrochloric acid, the resulting precipitate was extracted with ether, and the extract was dried with $MgSO_4$ and was filtered, and then 5.5 mmole of p-phenoxyaniline or n-butylamine was added to it and it was boiled for 10 min and evaporated, and the residue was kept at —10°C for 12 h. The precipitate that had deposited was recrystallized, giving the aldimines (IIIe and f) and (IVe).

The characteristics of compounds (IIIa-f) and IVa-f) are given in Tables 1 and 2.

2-Methylthiobenzo[b]furan-3-carbaldehyde (V). In an atmosphere of argon, 23.5 ml (42.5 mmole) of a 10% aqueous solution of NaSH was added to a hot solution of 6.2 g (27.5 mmole) of the bromoaldehyde (I) in 150 ml of methanol. The mixture was boiled for 30 min and then 9 ml of methyl iodide was added and was followed, after 10 minutes, by 250 ml of water; the mixture was extracted with ether, the extract was dried with $MgSO_4$, filtered, and evaporated, and the residue was recrystallized from ether. Yield 3.49 g (66%), mp 44.5-46°C. IR spectrum: 1665 cm^{-1} (C=O). UV spectrum (ethanol), λ_{max}, nm (log ε): 315 (4.41); 236 (4.56); 206 (4.84). PMR spectrum, ppm: 10.05 (1 H, s, CHO); 8.08-7.00 (4 H, m, arom.); 2.62 (3 H, s, CH_3). Found: C 62.2; H 4.4; S 16.6%. $C_{10}H_8O_2S$. Calculated: C 62.5; H 4.2; S 16.7%.

3-Methylthiobenzo[b]furan-2-carbaldehyde (VI) was obtained in a similar manner to the aldehyde (V) with a yield of 74%, mp 68-69°C (according to the literature [6], mp 72°C, from ethanol). IR spectrum: 1673 cm^{-1} (C=O). UV spectrum (ethanol), λ_{max}, nm (log ε): 310 (4.29), 236 (3.99). PMR spectrum, ppm: 10.02 (1 H, s, CHO); 7.88-7.09 (4 H, m, arom.); 2.56 (3 H, s, CH_3).

3-Methylthio-2-benzo[b]furfurylidenephenylamine (VIII). A solution of 0.6 g (3.1 mmole) of the aldehyde (VI) in 50 ml of benzene was treated with 0.32 ml (3.5 mmole) of aniline. The mixture was boiled for 1 h with a Dean—Stark trap and was cooled, washed with water, and dried with $MgSO_4$, after which the benzene was evaporated off and the residue was recrystallized twice from ether. This gave 0.64 g (77%) of the imine (VIII) with mp 70-71.5°C (according to the literature [6], mp 73°C, in ethanol). IR spectrum: 1618 cm^{-1} (C=N). UV spectrum (ethanol) λ_{max}, nm (log ε): 353 (4.48); 238 (4.14). PMR spectrum, ppm: 8.81 (1 H, s, CH); 7.80-7.02 (9 H, m, arom.); 2.40 (3 H, s, CH_3).

2-Methylthio-3-benzo[b]furfurylidenephenylamine (VII). A solution of 0.44 g (80 mmole) of KOH in 30 ml of hot aqueous methanol (2:1) was treated with 0.4 g (1.6 mmole) of the mercapto aldimine (IIIa), and then 0.1 ml (1.6 mmole) of methyl iodide was added, the mixture was boiled for 5 min and was then treated with 50 ml of water and extracted with ether, after which the extract was dried with $MgSO_4$ and evaporated and the residue was recrystallized from ether. This gave 0.21 g (50%) of compound (VII) with mp 38.5-40.5°C. IR spectrum: 1620 cm^{-1} (C═N). UV spectrum (ethanol), λ_{max}, nm (log ε): 323 (4.16); 282 (4.23); 237 (4.24). PMR spectrum, ppm: 8.78 (1 H, s, CH); 8.56-7.12 (9 H, m, arom.); 2.64 (3 H, s, CH_3). Found: C 71.9, H 5.1; N 5.9; S 12.0%. $C_{16}H_{13}NOS$. Calculated: C 71.9; H 4.9; N 5.2; S 12.0%.

2-Phenylamino-3-benzo[b]furfurylidenephenylamine (IX). A solution of 0.88 g (4.6 mmole) of the aldehyde (V) in 50 ml of benzene was treated with 0.84 ml (9.2 mmole) of aniline. The mixture was boiled with a Dean-Stark trap for 1 h and was then evaporated, and the residue was boiled with 40 ml of ethanol and, after cooling, it was filtered off and recystallized from propanol. This gave 1.12 g (78%) of the amine (IX) with mp 160.5-163°C. When the reaction was performed with one equivalent of aniline, the yield of the amine (IX) was 34%. IR spectrum: 1635, 1668 cm^{-1}. UV spectrum (ethanol) λ_{max}, nm (log ε): 412 (4.70); 285 (4.70); 245 (4.35). PMR spectrum, ppm: 10.9 (1 H, br.s, NH); 8.72 (1 H, s, CH); 7.47-6.69 (14 H, m, arom.). Found: C 80.8; H 5.2; N 8.7%. $C_{21}H_{16}N_2O$. Calculated: C 80.7; H 5.2; N 9.0%.

2-Morpholinobenzo[b]furan-3-carbaldehyde (X). In an atmosphere of argon, 4.7 ml (8.5 mmole) of a 10% aqueous solution of NaSH was added to a hot solution of 1.24 g (5.5 mmole) of the bromo aldehyde (I) in 50 ml of methanol. The mixture was boiled for 30 min and was then cooled to 10°C, and 20 ml of 5% hydrochloric acid was slowly added. The precipitate that deposited was extracted with ether, the extract was dried with $MgSO_4$ and filtered, and 0.5 ml (5.7 mmole) of morpholine was added to it. The resulting solution was boiled for 10 min and was then evaporated and the residue was recrystallized from ethanol. The yield of compound (X) was 0.56 g (41%), mp 125-126.3°C. IR spectrum: 1635 cm^{-1} (C═O). UV spectrum (ethanol), λ_{max}, nm (log ε): 323 (3.96); 291 (3.88); 246 (4.07); 206 (4.03). PMR spectrum (acetone-d_6), ppm: 10.08 (1 H, s, CHO); 8.08-7.00 (4 H, m, arom.); 3.85 (8 H, m, 4 CH_2). Found: C 67.1; H 5.8; N 6.1%. $C_{13}H_{13}NO_3$. Calculated: C 67.5; H 5.7; N 6.1%.

LITERATURE CITED

1. V. P. Litvinov, I. A. Dzhumaev, G. B. Gridunova, V. E. Shklover, Yu. T. Struchkov, and B. M. Zolotarev, Izv. Akad. Nauk SSSR, Ser. Khim., No. 4, 861 (1985).
2. V. P. Litvinov, V. Yu. Mortikov, and A. F. Vaisburg, Khim. Geterotsikl. Soedin., No. 9, 1177 (1984).
3. Ya. L. Gol'dfarb, V. P. Litvinov, and V. Yu. Mortikov, Khim. Geterotsikl. Soedin., No. 7, 898 (1979).
4. V. P. Litvinov, V. Yu. Mortikov, and A. F. Vaisburg, Izv. Akad. Nauk SSSR, Ser. Khim., No. 2, 477 (1984).
5. V. A. Bren', Zh. V. Bren', and V. I. Minkin, Khim. Geterotsikl. Soedin., No. 2, 154 (1973).
6. V. A. Bren', V. I. Usacheva, Zh. V. Bren', B. Ya. Simkin, and V. I. Minkin, Khim. Geterotsikl. Soedin., No. 5, 631 (1974).
7. R. N. Nurmukhametov, O. I. Betin, and D. N. Shigorin, Dokl. Akad. Nauk, 230, 146 (1976).
8. V. Yu. Mortikov, V. P. Litvinov, and Ya. L. Gol'dfarb, Khim. Geterotsikl. Soedin., No. 8, 1052 (1984).