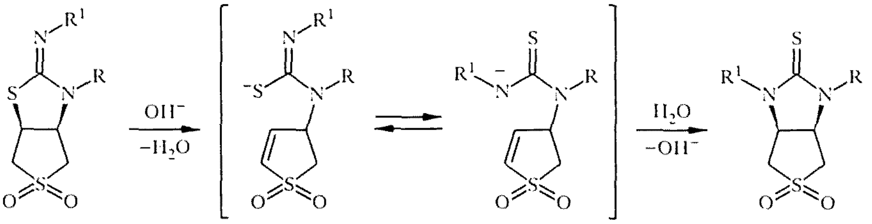
Chemistry of Heterocyclic Compounds, Vol. 30, No. 9, 1994

REARRANGEMENT OF 2-IMINOPERHYDROTHIENO-[3,4-*d*]-THIAZOLE-5,5-DIOXIDES

A. G. Makarenko, P. I. Parkhomenko, A. B. Rozhenko,
A. A. Grigor'ev, M. V. Rybakova, and Yu. V. Bezuglyi

The reaction of 4-bromo-2-thiolene 1,1-dioxide with thiosemicarbazide and thiosemicarbazones gave 2-imino-perhydrothieno[3,4-d]thiazole 5,5-dioxides, which contain a nitrogen function at the imino group. The recyclization of these compounds was studied.

The dissociation—addition reactions of thiolane and thiolene 1,1-dioxides have been studied in considerable detail [1]. A special case of these reactions for 2-iminoperhydrothieno[3,4-*d*]oxazole 5,5-dioxides is base-catalyzed recyclization to give substituted perhydrothieno[3,4-*d*]thiazole 5,5-dioxides [2]. We have studied the recyclization of derivatives of 2-imino-perhydrothieno[3,4-*d*]thiazole 5,5-dioxides (I), previously synthesized in the reaction of 4-bromo-2-thiolene 1,1-dioxide with substituted thiosemicarbazides [3], in alkaline medium as well as the reaction of the hydrochloride salt of 3-chloro-4-amino-thiolane 1,1-dioxide with isothiocyanates in the presence of pyridine [4]. The action of 1 M aq. KOH on dioxides Ia-Ic gives bicyclic 2-thioimidazolidines IIa and IIb in high yield.



Ia-c

IIa, b

I, II a R = Ph, R^1 = H, b R = CH_2—CH=CH_2, R^1 = H, c R = H, R^1 = Ph

The formation of 2-thioimidazolidines IIa and IIb was attributed to opening of the thiazolidine ring at the C—S bond and subsequent intramolecular cyclization by the action of base at the nitrogen atom, leading to *cis* fusion of the bicyclic systems [2, 5]. The structures of these products were indicated by IR and NMR spectroscopy (Tables 1 and 2) and were in accord with literature data [6].

In a study of the synthetic scope of this reaction, we obtained bicyclic iminothiazolidines, containing a nitrogen function at the imino group.

We showed that thiosemicarbazide and thiosemicarbazones react with 4-bromo-2-thiolene 1,1-dioxide (III) upon heating to give perhydrothieno[3,4-*d*]thiazole 5,5-dioxides by analogy to the reaction described for III with thioureas [3] (see Scheme on the following page).

The position of the substituents on the thiazolidine ring in VI and VII was determined from structural data for intermediate isothiosemicarbazonium salts IV and V [7] and the reported behavior of the intramolecular cyclization of 4-substituted 2-thiolene 1,1-dioxides [5] as well as by IR and PMR spectroscopy (Tables 1 and 2).

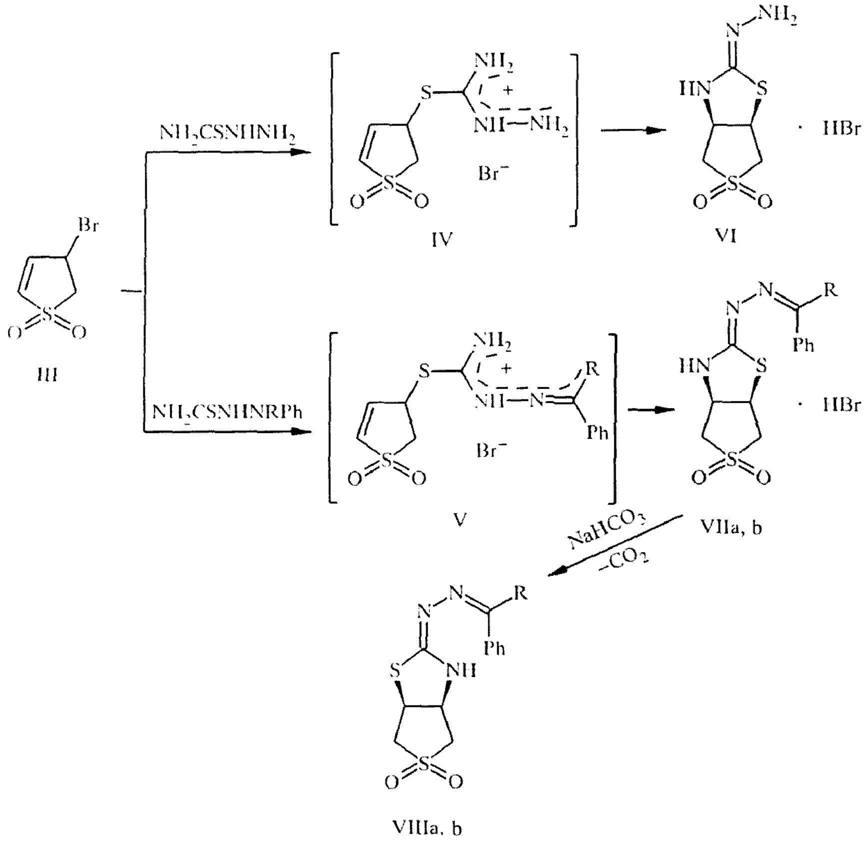
Institute of Bioorganic Chemistry and Petrochemistry, 252160 Kiev. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1274-1277, September, 1994. Original article submitted July 25, 1994.

TABLE 1. Physicochemical Indices of Products Obtained

Compound	Chemical formula	mp, °C	IR spectrum, ν, cm^{-1}	Yield, %
IIa	$C_{11}H_{12}N_2O_2S_2$	277	3160 (NH), 1505 (C–S), 1320, 1110 (SO_2)	85, 91*
IIb	$C_8H_{12}N_2O_2S_2$	207	3200 (NH), 3080, 1640 (C=C), 1480 (C–S), 1320, 1110 (SO_2)	86
VI	$C_5H_9N_3O_2S_2 \cdot HBr$	261 (dec.)	3360, 3260, 3160 (NH), 3000 (N^+H), 1670 (C=N), 1610 (NH), 1315, 1150 (SO_2)	63
VIIa	$C_{12}H_{13}N_3O_2S_2 \cdot HBr$	270 (dec.)	3310 (NH), 3000 (N^+H), 1650 (C=N), 1310, 1150 (SO_2)	54
VIIb	$C_{13}H_{15}N_3O_2S_2 \cdot HBr$	192	3310 (NH), 3000 (N^+H), 1640 (C=N), 1320, 1120 (SO_2)	36
VIIIa	$C_{12}H_{13}N_3O_2S_2$	193	3260 (NH), 1610 (C=N), 1310, 1130 (SO_2)	92
VIIIb	$C_{13}H_{15}N_3O_2S_2$	196	3310 (NH), 1615 (C=N), 1300, 1120 (SO_2)	89
IXa	$C_{12}H_{13}N_3O_2S_2$	262	3200 (NH), 1620 (C=N), 1510 (C–S), 1420 (NH), 1320, 1120 (SO_2)	87
IXb	$C_{13}H_{15}N_3O_2S_2$	259	3200 (NH), 1620 (C=N), 1500 (C–S), 1320, 1130 (SO_2)	86

---

*The yields using Ia and Ib, respectively, are shown.



VII, VIII a R = H, b R = Me

TABLE 2. PMR Spectra of Products Synthesized*

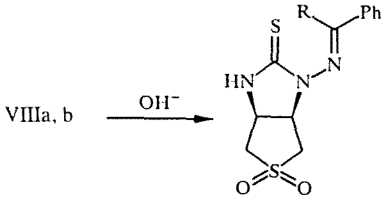
Compound	Chemical shifts, δ, ppm
IIa	2,93...3,24 (2H, m, 4-H), 3,33...3,54 (2H, m, 6-H), 4,74...4,80 (1H, m, 6a-H), 5,33...5,39 (1H, m, 3a-H), 7,42...7,47 (5H, m, Ar), 9,01 (1H, s, NH)
VI	3,40...3,57 (2H, m, 4-H), 3,63...4,01 (2H, m, 6-H), 4,68...4,79 (1H, m, 6a-H), 4,99...5,07 (1H, m, 3a-H), 5,50 (2H, s, NH$_2$), 9,20 (1H, s, NH), 9,73 (1H, s, N$^+$H)
VIIa	3,70...3,77 (2H, m, 4-H), 3,85...3,97 (2H, m, 6-H), 4,94...5,00 (1H, m, 6a-H), 5,61...5,69 (1H, m, 3a-H), 7,50...7,52 (3H, m, Ar), 8,04...8,07 (2H, m, Ar), 8,25 (1H, s, =CH), 9,96 (1H, s, NH), 10,49 (1H, s, N$^+$H)
VIIb	2,45 (3H, s, CH$_3$), 3,50...3,66 (2H, m, 4-H), 3,69...3,75 (2H, m, 6-H), 4,86...4,93 (1H, m, 6a-H), 5,28...5,35 (1H, m, 3a-H), 7,48...7,62 (3H, m, Ar), 7,97...8,01 (2H, m, Ar), 9,24 (1H, s, NH), 9,94 (1H, s, N$^+$H)
VIIIa	3,29...3,58 (2H, m, 4-H), 3,74...4,02 (2H, m, 6-H), 4,58...4,61 (1H, m, 6a-H), 5,14...5,17 (1H, m, 3a-H), 7,39...7,43 (3H, m, Ar), 7,78...7,81 (2H, m, Ar), 8,05 (1H, m.s., NH), 8,20 (1H, s, =CH)
VIIIb	2,29 (3H, s, CH$_3$), 3,23...3,88 (4H, m, CH$_2$—SO$_2$—CH$_2$), 4,28...4,47 (1H, m, 6a-H), 4,65...4,82 (1H, m, 3a-H), 7,36...7,46 (3H, m, Ar), 7,75...7,86 (2H, m, Ar), 8,25$_{(s)}$ + 8,34$_{(s)}$ (1H, NH)
IXa	3,25...3,49 (2H, m, 4-H), 3,57...3,75 (2H, m, 6-H), 4,65...4,83 (1H, m, 6a-H), 5,19...5,24 (1H, m, 3a-H), 7,41...7,44 (3H, m, Ar), 7,73...7,76 (2H, m, Ar), 7,82 (1H, s, =CH), 9,41 (1H, s, NH)
IXb	2,41 (3H, s, CH$_3$), 3,17...3,35 (2H, m, 4-H), 3,41...3,54 (2H, m, 6-H), 4,77...4,81 (1H, m, 6a-H), 4,97...5,00 (1H, m, 3a-H), 7,45...7,50 (3H, m, Ar), 7,85...7,89 (2H, m, Ar), 9,01 (1H, s, NH)

---

*^{13}C NMR spectrum of IIb, ppm: 46.35 ($C_{(4)}$), 50.75 ($C_{(6)}$), 52.10 ($C_{(3a)}$), 52.21 ($C_{(6a)}$), 54.13 (CH_2), 118.26 ($CH_2=$), 132.59 ($CH=$), 181.42 ($C=S$).

The action of sodium bicarbonate on VIIa and VIIb gave azines VIIIa and VIIIb. In contrast to VII, VI does not react with sodium bicarbonate but undergoes tar formation in highly alkaline medium. The IR spectra of VIIa and VIIb show a weak band for the NH group at 3260 cm^{-1} for VIIIa and a medium-intensity band at 3310 cm^{-1} for VIIIb, which probably indicates the existence of hydrogen-bonded chelate in azine VIIIa. The PMR spectrum of VIIIb has a double set of signals with 2:1 integral intensity ratio with the exception of the methyl group singlet at 2.29 ppm. This doubling may be attributed to the existence of E and Z isomers. The lack of reliable criteria and close analogies prevents the specific assignment of the signals to a particular isomer.

Under the recyclization conditions described above, VIIIa and VIIIb are readily converted to the corresponding 2-thioimidazolidines IXa and IXb. This reaction may serve as a method for obtaining previously unreported cyclic thiosemicarbazones condensed with a thiolane 1,1-dioxide ring.



IXa, b

IX a R = H, b R = Me

EXPERIMENTAL

The IR spectra were taken in KBr pellets on a Specord M-80 spectrometer, while the PMR and ^{13}C NMR spectra were taken in DMSO-d_6 relative to HMDS on a Varian VXR-300 spectrometer.

The elemental analysis data were in accord with the calculated values.

***cis*-1-Organylperhydrothieno[3,4-d]imidazole-2-thione-5,5-dioxides (IIa and IIb).** A suspension of 0.01 mole of the corresponding iminothiazolidine Ia-Ic in 20 ml 1 M aq. KOH was stirred for 3 h. The precipitate was filtered off and reprecipitated from a solution in DMF upon adding water.

Hydrobromide Salt of *cis*-1-Hydrazonoperhydrothieno[3,4-d]thiazole-5,5-dioxide (VI). A sample of 1.97 g (0.01 mole) 4-bromo-2-thiolene 1,1-dioxide and 0.91 g (0.01 mole) thiosemicarbazide in 50 ml of a 1:1 mixture of 2-propanol and dioxane was stirred for 3 h at 60-70°C. The mixture was left at room temperature for 24 h. The precipitate was filtered off, washed consecutively with dioxane and 2-propanol, and recrystallized from methanol.

Hydrobromide Salt of *cis*-benzylidenehydrazonoperhydrothieno[3,4-d]thiazole-5,5-dioxide (VIIa) and Hydrobromide Salt of *cis*-2-α-Methylbenzylidenehydrazonoperhydrothieno[3,4-d]thiazole-5,5-dioxide (VIIb) were obtained by analogy to the above procedure. The products were recrystallized from 1:1 water–ethanol. A sample of 0.01 mole hydrobromide VIIIa or VIIIb was dissolved in a minimal amount of water and 0.9 g (0.01 mole) sodium bicarbonate was added. The mixture was stirred until no further gas evolution was noted. The precipitate was filtered off and washed with water to give virtually pure base VIIIa or VIIIb.

***cis*-1-Benzylidenaminoperhydrothieno[3,4-d]imidazole-2-thione-5,5-dioxide (IXa) and *cis*-1-α-Methylbenzylidenaminoperhydrothieno[3,4-d]imidazole-2-thione-5,5-dioxide (IXb)** were obtained by analogy to the synthesis of [3,4-d]imidazole-2-thione 5,5-dioxides IIa and IIb.

REFERENCES

1. T. É. Bezmenova, Chemistry of Thiolene 1,1-Dioxides [in Russian], Naukova Dumka, Kiev (1981), p. 291.
2. G. I. Khaskin and T. É. Bezmenova, Dokl. Akad. Nauk UkrSSR, No. 9, 57 (1981).
3. Yu. V. Bezuglyi, A. A. Tukhar', T. É. Bezmenova, V. P. Foremnaya, A. G. Bratunets, and A. M. Shakhvorost, Khim. Geterotsikl. Soedin., No. 1, 110 (1988).
4. G. I. Khaskin, A. B. Rozhenko, and T. É. Bezmenova, Khim. Geterotsikl. Soedin., No. 3, 424 (1987).
5. T. É. Bezmenova, P. G. Dul'nev, G. I. Khaskin, L. N. Zakharov, V. I. Slutskii, V. I. Kulishov, and Yu. T. Struchkov, Khim. Geterotsikl. Soedin., No. 7, 907 (1981).
6. G. I. Khaskin, T. É. Bezmenova, and P. G. Dul'nev, Khim. Geterotsikl. Soedin., No. 3, 328 (1982).
7. K. N. Zelenin, O. B. Kuznetsova, V. V. Alekseev, V. P. Sergutina, P. B. Terent'ev, and V. V. Ovcharenko, Khim. Geterotsikl. Soedin., No. 11, 1515 (1991).