

REACTION OF 2-ALKENYLTHIOBENZIMIDAZOLES WITH IODINE

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The reaction of 2-allylthiobenzimidazole and 2-allylthio-1-methylbenzimidazole with iodine leads to the formation of dihydrothiazolo[3,2-a]benzimidazolium systems.

The reaction of 2-allylthiobenzimidazole (I) with bromine in acetic acid gives the hydrobromide salt of 2-(2,3-dibromopropylthio)benzimidazole, which is cyclized by the action of bases to give 3-bromo-3,4-dihydro-2H-benzimidazolo[2,1-b][1.3]thiazine [1,2]. In the present work, we studied the reaction of allyl sulfide I, 2-allylthio-1-allylbenzimidazole (II), 2-allylthio-1-methylbenzimidazole (III), and 2-styrylthiobenzimidazole (IV) with iodine in various solvents.

Sulfide I was obtained by the allylation of 2-benzimidazolethione (V) using an equimolar amount of allyl bromide in alcohols, DMF, and water. A mixture of sulfides I and II is formed in the case of excess allyl halide.

Sulfides II and III were obtained by the alkylation of sulfide I using allyl bromide, methyl iodide, or dimethyl sulfate in ethanol in the presence of KOH or sodium ethylate as well as in a two-phase system $\text{H}_2\text{O} + \text{KOH} + \text{CCl}_4$ in the presence of tetrabutylammonium bromide.

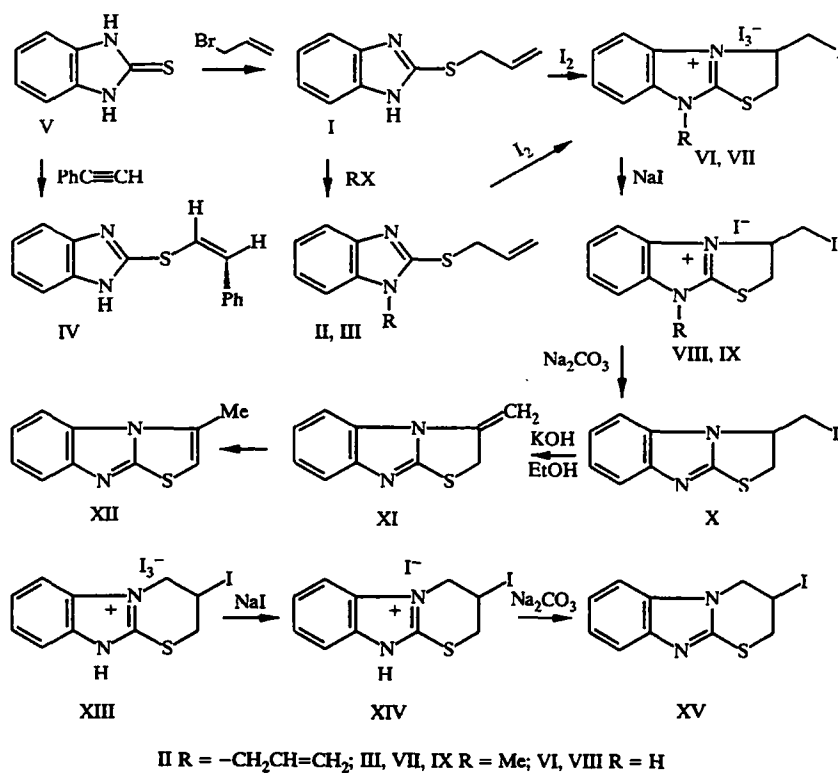


TABLE 1. PMR Spectra of Products in $(\text{CD}_3)_2\text{SO}$

Compound	Chemical shift, ppm, coupling constant, Hz
I*	4,04 (2H, d, $J = 6,8$, SCH_2); 5,25 (2H, m, CH_2); 6,03 (2H, m, CH); 7,11; 7,46 (4H, m, H_{arom})
II	4,90...5,30 (8H, m, SCH_2 , NCH_2 , 2CH_2); 5,70...6,20 (2H, m, 2CH); 7,10...7,50 (4H, m, H_{arom})
III	3,73 (3H, s, CH_3); 4,96 (2H, m, SCH_2); 5,10 (2H, m, CH_2); 5,89 (1H, m, CH); 7,10...7,60 (4H, m, H_{arom})
IV*	6,89 (1H, d, $J = 10,8$, SCH); 7,10...8,70 (10H, m, H_{arom} and $-\text{CH}$)
VI	3,80...4,70 (4H, m, CH_2I , SCH_2); 5,25 (1H, m, 3-H); 7,2...7,9 (4H, m, H_{arom})
VII	3,85 (2H, m, CH_2I); 4,20...5,30 (3H, m, SCH_2 , 3-H); 7,40...7,90 (4H, m, H_{arom})
IX	3,93 (3H, s, CH_3); 3,90 (2H, m, CH_2I); 4,74 (2H, m, SCH_2); 5,23 (1H, m, 3-H); 7,57; 7,82 (4H, m, H_{arom})
X	3,67 (2H, m, CH_2I); 4,30...4,85 (2H, m, SCH_2); 5,13 (1H, m, 3-H); 7,14; 7,47 (4H, m, H_{arom})
XI	3,81 (2H, m, SCH_2); 5,73 (2H, m, $-\text{CH}_2$); 7,10...8,00 (4H, m, H_{arom})
XII	2,74 (3H, d, $J = 1,4$, CH_3); 6,85 (1H, q, $J = 1,4$, 2 -H); 7,10...8,00 (4H, m, H_{arom})

*In $(\text{CD}_3)_2\text{CO}$.

Styryl sulfide IV was synthesized by the reaction of thione V with phenylacetylene in a suspension of KOH in DMSO. Nucleophilic *trans* addition proceeds to give the *cis*-isomer of IV [3].

We have found that, independent of the ratio of starting reagents, the reaction of sulfides I and III with iodine in acetic acid, chloroform, and acetone gives 3-iodomethyl-2,3-dihydro-9H-thiazolo[3,2-*a*]benzimidazolium triiodide (VI) and 3-iodomethyl-9-methyl-2,3-dihydrothiazolo[3,2-*a*]benzimidazolium triiodide (VII), respectively, which have good solubility in acetone. The action of sodium iodide on triiodides VI and VII leads to iodides VIII and IX, which are insoluble in acetone.

Theoretically, the iodocyclization of sulfides I and II may proceed to give products with a thiazine ring (XIII-XV) [1, 2] but, in such case, the PMR signal for the CHI proton (3-H), as in iodocyclohexane [4], should appear at about 4.30 ppm. However, the PMR signal of the NCH proton of the thiazole ring (3-H) appears at 5.13-5.25 ppm in VI-X (Table 1). Further evidence for the formation of a thiazole ring rather than a thiazine ring is found in the formation of a mixture of 3-methyleno-2H-thiazolo[3,2-*a*]benzimidazole (XI) and 3-methylthiazolo[3,2-*a*]benzimidazole (XII) upon the action of KOH in ethanol on 3-iodomethyl-2,3-dihydrothiazolo[3,2-*a*]benzimidazole (X) obtained by the action of sodium carbonate on iodide VIII in water. The PMR spectrum of XII has signals for the methyl group protons at 2.74 ppm and 2-H at 6.85 ppm. Product XII has been obtained by the reaction of thione V with 1,2,3-tribromopropane in DMSO in the presence of KOH and the methyl group signals in the PMR spectrum of this compound appear at 2.50 ppm, while the signal for 2-H appears at 6.70 ppm [5].

In comparison to the starting allylic compounds II and III, the IR spectra of VI-X lack bands for the double bond at 1640 cm^{-1} . In contrast to I and III, sulfides II and IV react with iodine at about 20°C to give complexes, which, upon the action of aqueous sodium thiosulfate, decompose to yield the starting compounds II and IV.

EXPERIMENTAL

The IR spectra were taken on a Specord IR-75 spectrometer for samples in Vaseline, while the PMR spectra were taken on a Tesla BS-417 spectrometer at 100 MHz with TMS as the internal standard. Thin-layer chromatography was carried out on Silufol UV-254 plates with 1:1 ether-hexane as the eluent. The plates were developed with iodine vapor.

2-Allylthioimidazole (I). A sample of 1.5 g (0.01 mole) 2-benzimidazolethione and 0.86 ml (0.01 mole) allyl bromide were added to a solution of 0.56 g (0.01 mole) KOH in 50 ml water and stirred for 1 h. The precipitate was filtered off, dried, and recrystallized from octane. Sulfide I recrystallized from ethanol, 2-propanol, or chloroform-octane contains traces of thione V, which may be eliminated by recrystallization from octane or nonane. The yield of sulfide I was 1.44 g (76%), mp 137°C ($141\text{--}143^\circ\text{C}$ [6]).

2-Allyl-1-allylbenzimidazole (II) and 2-Allylthio-1-methylbenzimidazole (III). A sample of 1.9 g (0.01 mole) sulfide I and 0.01 mole allyl bromide, methyl iodide, or dimethyl sulfate were added to a solution of 0.68 g sodium ethylate in 30 ml ethanol and heated at reflux for 2 h. The solvent was distilled off. The residue was treated with ether and filtered. Ether was distilled off and the residue was recrystallized from hexane.

2-Allylthio-1-allylbenzimidazole (II) was obtained in 85% yield, mp 40°C. Found: C, 67.63; H, 6.15; N, 12.44; S, 13.76%. Calculated for $C_{13}H_{14}N_2S$: C, 67.83; H, 6.09; N, 12.17; S, 13.91%.

2-Allylthio-1-methylbenzimidazole (III) was obtained in 73% yield, mp 48°C. Found: C, 64.28; H, 5.76; N, 13.85; S, 15.46%. Calculated for $C_{11}H_{12}N_2S$: C, 64.67; H, 5.92; N, 13.71; S, 15.70%.

2-Styrylthiobenzimidazole (IV). A mixture of 30 ml DMSO, 1.5 g (0.01 mole) 2-benzimidazolethione, and 0.8 g (0.02 mole) NaOH in 5 ml water and 2.04 g (0.02 mole) phenylacetylene was heated at reflux for 4 h. After cooling, the reaction mixture was poured into 150 ml cold water. The precipitate formed was filtered off and recrystallized from 3:1 octane–2-propane to give 2.4 g (95%) IV, mp 132–135°C. Found: C, 71.05; H, 4.76; N, 11.35; S, 12.53%. Calculated for $C_{15}H_{12}N_2S$: C, 71.40; H, 4.80; N, 11.10; S, 12.70%.

General Procedure for the Synthesis of Triiodides VI and VII. A solution of 0.51 g (2 mmoles) iodine in 10 ml chloroform was added to a solution of 1 mmole I or III in 3 ml chloroform. After 24 h, the precipitate formed was filtered off, dissolved in acetone, and reprecipitated by adding diethyl ether.

3-Iodomethyl-9-H-2,3-dihydrothiazolo[3,2-*a*]benzimidazolium triiodide (VI) was obtained in 96% yield, mp 85–87°C (dec.). Found: S, 4.26; I, 72.84%. Calculated for $C_{10}H_{10}I_4N_2S$: S, 4.58; I, 72.78%.

3-Iodomethyl-9-methyl-2,3-dihydrothiazolo[3,2-*a*]benzimidazolium (VII) was obtained in 84% yield, mp 78–80°C (dec.). Found: S, 4.26; I, 71.62%. Calculated for $C_{11}H_{12}I_4N_2S$: S, 4.51; I, 71.41%.

General Procedure for Synthesis of Iodides VIII and IX. A sample of 0.45 g (3 mmoles) sodium iodide was added to a solution of 1 mmole triiodide VI or VII in 5 ml acetone. The precipitate formed was filtered off, washed with acetone, and dried.

3-Iodomethyl-9H-2,3-dihydrothiazolo[3,2-*a*]benzimidazolium iodide (VIII) was obtained in 97% yield, mp 178–180°C (dec.). Found: S, 6.98; I, 57.42%. Calculated for $C_{10}H_{10}I_2N_2S$: S, 7.21; I, 57.21%.

3-Iodomethyl-9-methyl-2,3-dihydrothiazolo[3,2-*a*]benzimidazolium iodide (IX) was obtained in 94% yield, mp 167–170°C (dec.). Found: S, 6.84; I, 55.73%. Calculated for $C_{11}H_{11}I_2N_2S$: S, 7.02; I, 55.53%.

3-Iodomethyl-2,3-dihydrothiazolo[3,2-*a*]benzimidazole (X). A sample of 0.444 g (1 mmole) iodide VII was added to a solution of 0.17 g (2 mmoles) Na_2CO_3 in 30 ml water and stirred for 2 h. The precipitate was filtered off, washed with water, dried, and recrystallized from octane to give 0.3 g (95%) X, mp 160°C. Found: S, 10.40; I, 40.58%. Calculated for $C_{10}H_9IN_2S$: S, 10.12; I, 40.19%.

REFERENCES

1. N. I. Korotkikh, G. F. Raenko, and O. P. Shvaika, *Khim. Geterotsikl. Soedin.*, No. 3, 410 (1995).
2. N. I. Korotkikh, G. F. Raenko, and O. P. Shvaika, *Zh. Org. Khim.*, **32**, 632 (1996).
3. W. E. Truce and J. A. Simms, *J. Am. Chem. Soc.*, **78**, 2756 (1956).
4. A. Zschunke, *Kernmagnetische Resonanz. Spektroskopie in der Organische Chemie*, Akademie Verlag (1977), p. 63.
5. N. I. Popov, *Khim. Geterotsikl. Soedin.*, No. 4, 567 (1995).
6. M. Kocavar, B. Stanovik, and M. Tisler, *Croat. Chem. Acta*, **45**, 457 (1973).