Synthesis and Spectral Studies of 2-Mercaptobenzimidazole Derivatives. II.

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This communication describes synthesis and spectral data of new 2-mercaptobenzimidazole derivatives.

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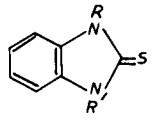
In continuation to our studies (1) on synthesis of new 2-mercaptobenzimidazole (I) derivatives for development of insecticides, new synthetics have been developed under three sets of conditions.

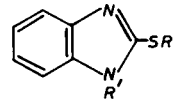
Reactions with α,β-unsaturated esters under anhydrous conditions have yielded *N*-substituted compounds IIa, IIb, IIIa and IIIb. Interaction of I with allyl and benzyl halides in 2-propanol in presence of aqueous sodium bicarbonate has resulted in development of *S*-substituted compounds IVa and Va along with a minor product Vb. While reaction with α-ω-dihalogenoalkanes under identical conditions have yielded α-ω-bis-2-benzimidazolylthioalkanes VI, VII and VIII. In another set of conditions I has been made to react with 2,3-dibromoethane and 1,4-dibromobutane in a mixture of DMF and absolute ethanol by the method of Pujari and co-workers (2). The products were identified as 2,3-dihydrothiazolo[3,2-*a*]benzimidazole and 2,3,4,5-tetrahydrothiazepino[3,2-*a*]benzimidazole, respectively, from their spectroscopic data. Compound IVa has been transformed into IVb *via* Claisen rearrangement.

EXPERIMENTAL

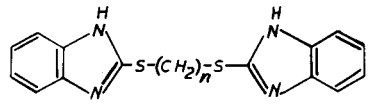
All melting points are uncorrected. The pmr spectra were measured on T-60A Varian using tetramethylsilane as internal reference, the values



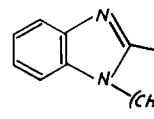
	R	R'
(I)	H	H
(IIa)	CH_2-CH(Me)-CO_2Me	H
(IIb)	CH_2-CH(Me)-CO_2Me	CH_2-CH(Me)-CO_2Me
(IIIa)	CH(Me)-CH_2-CO_2Me	CH(Me)-CH_2-CO_2Me
(IIIb)	CH(Me)-CH_2-CO_2Me	H



	R	R'
(IVa)	CH_2-CH=CH_2	H
(IIIb)	H	CH_2CH=CH_2
(Va)	$CH_2C_6H_5$	H
(Vb)	$CH_2C_6H_5$	$CH_2C_6H_5$



(VI) $n=8$; (VII) $n=4$; (VIII) $n=2$



(IX) $n=2$; (X) $n=4$

are reported in δ units.

Compounds IIa, IIb, IIIa and IIIb were prepared by heating to 100° a solution of 2-mercaptobenzimidazole (I) (0.02 mole) and α,β-unsaturated ester (0.04 mole) in 100 ml of DMF containing 2.0 g of sodium carbonate for 6 hours. After removal of the DMF under reduced pressure, 200 ml of water was added to the residue and the mixture acidified with dilute hydrochloric acid to give the product.

1-(*N*-Carbomethoxy-1-methylethyl)benzimidazole-2-thione (IIa).

The solid obtained after the work up of the reaction of I with methyl methacrylate on crystallization from 95% ethanol gave colourless sandy crystals (18%), 176-178°; pmr (TFA): δ 1.03 (d, 3H, J = 6.5 Hz, CH_3), 2.83-3.34 (m, 1H, CH), 3.40 (s, 3H, OCH_3), 3.83-4.80 (m, 2H, CH_2-N), 7.27 (s, 4H, ArH).

Anal. Calcd. for $C_{12}H_{14}N_2O_2S$: C, 57.60; H, 5.60; N, 11.20. Found: C, 57.48; H, 5.57; N, 11.27.

1,3-(*N,N'*-Dicarbomethoxy-1-methylethyl)benzimidazole-2-thione (IIb).

The mother liquor obtained after the filtration of IIa from the above reaction mixture on purification by column chromatography gave a pure (tlc) gummy material (63%), pmr (carbon tetrachloride): δ 1.33 (d, 6H, J = 7.5 Hz, 2 CH_3), 3.17-3.50 (m, 2H, CH), 3.50 (s, 6H, 2 OCH_3), 4.47 (d, 4H, J = 7 Hz, 2 CH_2-N), 7.28 (s, 4H, ArH).

Anal. Calcd. for $C_{17}H_{22}N_2O_4S$: C, 58.28; H, 6.28; N, 8.00. Found: C, 58.37; H, 6.24; N, 8.15.

1,3-(*N,N'*-Dicarbomethoxy-2-methylethyl)benzimidazole-2-thione (IIIa).

The crude reaction product obtained from the reaction of I with methyl crotonate showed mainly two spots on tlc. Hence, the material was charged over a column containing 150 g of neutral alumina. Ten fractions, consisting of 100 ml each, were collected. Fractions 1-4, eluted with petroleum ether (60-80°) on evaporation of solvent gave a gummy material (52%), pmr (carbon tetrachloride): δ 1.76 (d, 6H, J = 6.0 Hz, 2 CH_3), 3.10 (d, 4H, J = 5.0 Hz, 2 CH_2CO), 3.68 (s, 6H, J = 6.0 Hz, 2 CH_3), 5.71 (q, 2H, J = 6.0 Hz, 2 CH-N), 7.24 (m, 4H, ArH).

Anal. Calcd. for $C_{17}H_{22}N_2O_4S$: C, 58.28; H, 6.28; N, 8.00. Found: C, 58.35; H, 6.31; N, 8.09.

1-(*N*-Carbomethoxy-2-methylethyl)benzimidazole-2-thione (IIIb).

After the isolation of IIIa fractions 7-8 (from above chromatography), eluted with chloroform on removal of solvent gave a colourless gummy material (22%), pmr (carbon tetrachloride): δ 1.73 (d, 3H J = 6.5 Hz, CH_3), 3.0 (d, 2H, J = 5.0 Hz, -CH_2CO), 3.66 (s, 3H, OCH_3) 5.66 (sex, 1H, J = 6.5 and 5.0 Hz - CHN), 7.2 (m, 4H, ArH), 8.10 and 12.10 (s, s, ½ H each collapsed on exchange with deuterium oxide, NH and SH tautomeric).

Anal. Calcd. for $C_{10}H_{14}N_2O_2S$: C, 57.60; H, 5.60; N, 11.20. Found: C, 57.68; H, 5.57; N, 11.11.

Compounds IVa, Va and Vb were prepared by heating to reflux a solution of I (0.02 mole) and allyl bromide (0.02 mole) in case of IVa and benzyl bromide (0.02 mole) in case of Va and Vb in 50 ml of saturated aqueous solution of sodium bicarbonate and 50 ml of 2-propanol for 1 hour. The reaction product in these cases was worked up by removing 2-propanol and then extracting the residue with chloroform. Removal of chloroform gave crude products.

2-Allylthiobenzimidazole (IVa).

The solid obtained was crystallized from 95% ethanol to give colourless fine needles (60%), mp 140-142°; pmr (TFA): δ 3.6 (d, 2H, J = 6.5 Hz, -CH_2-S), 4.83-5.27 (m, 2H, CH_2=), 5.30-5.93 (m, 1H, CH=), 7.25 (s, 4H, ArH).

Anal. Calcd. for $C_{10}H_{10}N_2S$: C, 63.15; H, 5.26; N, 14.73. Found: C, 63.03; H, 5.21; N, 14.58.

2-Benzylthiobenzimidazole (Va).

The crude mixture obtained from the reaction of I with benzyl bromide showed mainly two spots, hence the mixture was subjected to column chromatography over silica gel and the column eluted successively with benzene, chloroform and chloroform-methanol mixtures. Fractions with benzene on removal of the solvent gave pure compound which on crystallisation from 95% ethanol was obtained in the form of fine needles (57%), mp 184-185°; pmr (TFA): δ 4.40 (s, 2H, -CH_2-S), 7.20 (m, 5H, ArH), 7.47 (s, 4H, ArH).

Anal. Calcd. for $C_{14}H_{12}N_2S$: C, 70.00; H, 5.00; N, 11.66. Found: C, 70.09; H, 4.97; N, 11.59.

1-Benzyl-2-benzylthiobenzimidazole (Vb).

The later fractions 3-5 of the above chromatography, eluted with chloroform, on removal of the solvent gave a colourless solid, which on crystallisation from 95% ethanol gave needles (17%) mp 116-117°; pmr (TFA): δ 4.34 (s, 2H, -CH_2-S), 5.13 (s, 2H, CH_2-N), 7.17 (s, 10H, ArH), 7.40 (m, 4H, ArH).

Compounds VI, VII and VIII were obtained by interaction of I and 1,8-dibromooctane, 1,4-dibromobutane and 1,2-dibromoethane, respectively.

1,8-bis(2-Benzimidazolylthio)octane (VI).

On work up and crystallisation from 95% ethanol this compound was obtained as fine needles in 54% yield, mp 239-241°; pmr (TFA): 0.87-1.67 (m, 12H, 6 CH_2), 3.01 (t, 4H, J = 6.0 Hz, 2 CH_2-S), 7.20 (s, 8H, ArH).

Anal. Calcd. for $C_{22}H_{26}N_4S_2$: C, 64.38; H, 6.34; N, 13.65. Found: C, 64.47; H, 6.29; N, 13.51.

1,4-bis(2-Benzimidazolylthio)butane (VII).

It was crystallised from 95% ethanol to give colourless micro crystalline compound (50%), mp 218-220°; pmr (TFA): δ 1.73 (broad, 4H, 2 CH_3), 3.13 (broad, 4H, 2 CH_2-S), 7.27 (s, 8H, ArH).

Anal. Calcd. for $C_{18}H_{18}N_4S_2$: C, 61.02; H, 5.08; N, 15.81. Found: C, 61.19; H, 5.11; N, 15.84.

1,2-bis(Benzimidazolylthio)ethane (VIII).

All physical data given in a previous communication (1).

Compound IX and X were obtained by the procedure adopted by Pujari and co-workers (2) for the preparations of heterocyclic systems containing nitrogen. In this procedure a solution of equimolar concentration of I and α-ω-dihalogenoalkane in 50 ml of anhydrous ethanol and 50 ml of DMF was heated to reflux for 10 hours, cooled and poured onto ice. The hydrobromide thus obtained was neutralized with sodium bicarbonate and free crystallised to give the desired product.

2,3-Dihydrothiazolo[3,2-*a*]benzimidazole (IX).

It was obtained as fine needles from 95% ethanol in 58% yield, mp 116°; pmr (TFA): δ 3.80 (t, 2H, J = 6.0 Hz, CH_2-S), 4.23 (t, 2H, J = 6.0 Hz, CH_2-N), 7.08 (s, 4H, ArH).

Anal. Calcd. for $C_9H_8N_2S$: C, 61.36; H, 4.54; N, 15.91. Found: C, 61.28; H, 4.58; N, 15.91.

3,4,5,6-Tetrahydro-1,3-thiazepino[3,2-*a*]benzimidazole (X).

This compound was obtained in 49% yield from I and 1,4-dibromobutane, mp 133-134°; pmr (TFA): δ 1.93 (m, 4H, 2CH_2), 2.80 (t, 2H, J = −6.0 Hz, CH_2-N), 7.34 (s, 4H, ArH).

Anal. Calcd. for $C_{11}H_{12}N_2S$: C, 64.70; H, 5.88; N, 13.72. Found: C, 64.69; H, 5.83; N, 13.77.

Claisen Rearrangement of 2-Allylthiobenzimidazole (IVb).

A solution of 1.9 g of the compound (0.01 mole) in dimethylaniline was refluxed for 3 hours. On cooling a colourless solid separated which on filtration and subsequent crystallisation from petroleum ether (60-80°) and benzene (1:1) gave 0.95 g of colourless fine needles (50%), mp 115-117°; nmr (TFA): δ 4.70 (d, 2H, J = 6.0 Hz, CH_2-N), 4.83-5.20 (m, 2H, CH_2=), 5.43-6.10 (m, 1H, CH=), 7.08 (s, 4H, ArH).

Anal. Calcd. for $C_{10}H_{10}N_2S$: C, 63.15; H, 5.26; N, 14.74. Found: C, 63.18; H, 5.27; N, 14.69.

REFERENCES AND NOTES

(1) For Part I see: D. B. Saxena, R. K. Khajuria and O. P. Suri, *J. Heterocyclic Chem.*, **19**, 681 (1982).

(2) H. K. Pjari and K. K. Jain, *Indian J. Chem.*, **20B**, 294 (1981).

(3) A. K. Bagrrii, G. F. Galenko and P. M. Kochergin, *Depov. Akad. Nauk Ukr.* RSR Ser B, **9**, 801 (1975); *Chem. Abstr.*, **84**, 43959 (1976).