

- (6) Gammon, B. E., presented at the Advisory Committee Meeting of the Joint Industry-Government Ethylene Project, Boulder, CO, Dec 1978.
 (7) Hejmadi, A. V.; Powers, J. E., private communication, July 1979.
 (8) Kozlov, A., USSR Academy of Sciences, private communication.
 (9) McCarty, R. D.; Jacobsen, R. T. *NBS Tech. Note (U.S.)* 1981, No. 1045.
 (10) Hust, J. G.; McCarty, R. D. *Cryogenics* 1967, 7, 200.

- (11) Goodwin, R. D. *J. Res. Natl. Bur. Stand. Sect. C* 1961, 65, 231.
 (12) Goodwin, R. D.; Weber, L. A. *J. Res. Natl. Bur. Stand. Sect. A* 1969, 73, 15.

Received for review July 27, 1981. Accepted January 19, 1982.

NEW COMPOUNDS

Synthesis and Reactions of 2-Mercaptobenzothiazole Derivatives of Expected Biological Activity. 2[†]

Abou El-Fotooh G. Hammam* and Nabil M. Youssif

National Research Centre, Dokki, Giza, Arab Republic of Egypt

The amides and anilides of benzothiazol-2-ylthioacetic acid and 3-(benzothiazol-2-ylthio)propanoic acid were prepared by the reaction of the corresponding acid chlorides with amines and anilines. Also the arylhydrazones, the cycloalkanone hydrazones, and pyrazoline derivatives were prepared.

The literature (1-3) reveals that substituted benzothiazoles possess anticonvulsant activity and these inhibit monoamine oxidase activity of rat brain homogenate. The following compounds are prepared to test them for biological activity.

Experimental Section

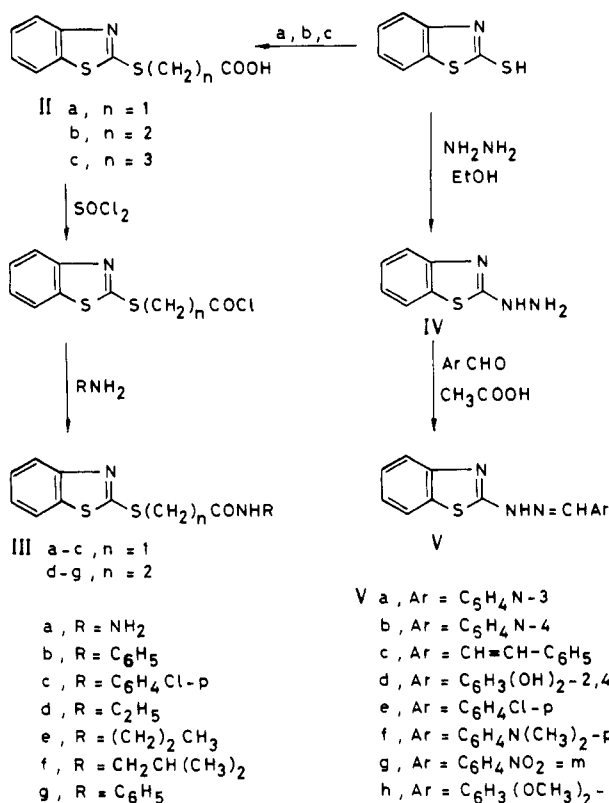
Satisfactory elemental analyses were found.

Benzothiazol-2-ylthioacetic Acid (IIa). A mixture of 1.7 g (0.01 mol) of 2-mercaptobenzothiazole and 0.8 g (0.01 mol) of chloroacetic acid in 50 mL of ethanolic potassium hydroxide (1 g of KOH in 50 mL of ethanol 70%) was refluxed for 3 h. The ethanol was evaporated, and the precipitate formed was dissolved in water and acidified with hydrochloric acid. The precipitate formed was collected and crystallized from ethanol: mp 135 °C; yield 70%.

3-(Benzothiazol-2-ylthio)propanoic Acid (IIb). This compound was prepared as above by replacing the chloroacetic acid with 3-bromopropanoic acid and crystallizing from ethanol: mp 150 °C; yield 83%.

4-(Benzothiazol-2-ylthio)butanoic Acid (IIc). 2-Mercaptobenzothiazole (1.7 g) was dissolved in a solution of 0.3 g of sodium metal in about 15 mL of absolute ethanol. The mixture was refluxed for 3 h. The ethanol was distilled off, and the white mass formed was dissolved in hot water and filtered. The filtrate was acidified with hydrochloric acid. The solid formed was collected and crystallized from ethanol: mp 120 °C; yield 67%. The IR spectra of compounds II showed absorption at 1705 cm⁻¹ (COOH).

Amides (III). General Procedure. A mixture of 2 g of the acid (IIa,b), 5 mL of thionyl chloride, and 20 mL of dry benzene was refluxed for 2 h. The excess of thionyl chloride and benzene was distilled off, and the remaining oil was dissolved in dry benzene, cooled and quickly treated with 2 g of the



a = Chloroacetic acid
 b = 3-bromopropanoic acid
 c = 4-butyrolactone

amine, refluxed for 2 h, and left overnight. The reaction mixture was filtered, the precipitate was washed with ether, and the combined filtrate and washing were extracted with dilute hydrochloric acid and then with sodium carbonate solution. The ethereal solution was dried and evaporated. The residue was triturated with light petroleum ether, and the solid formed was collected and crystallized from the proper solvent (see Table I).

Anilides. The acid chlorides were prepared as in the General Procedure and then treated with aniline and worked up as above (see Table I).

[†] For part 1, see ref 4.

Table I. The Amides and Anilides

compd	mp, °C	solvent ^a	yield, %
IIIa	150	W	83
b	120	E	74
c	200	E	78
d	120	E	68
e	95	W	70
f	100	E	73
g	145	E	68

^a W = water; E = ethanol.Table II. 2-(Arylhiazino)benzothiazole (V) and Cycloalkanone Benzothiazol-2-ylhydrazone (VI)^a

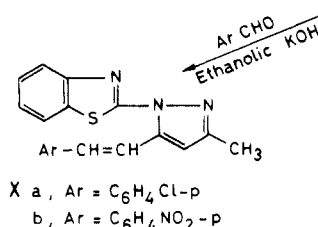
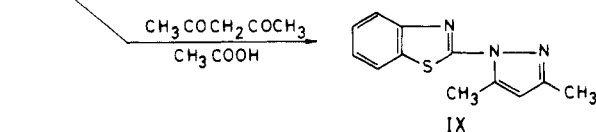
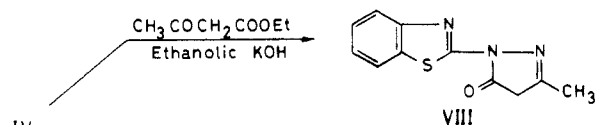
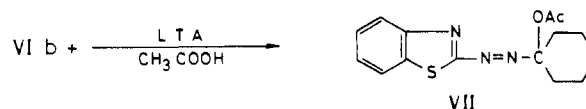
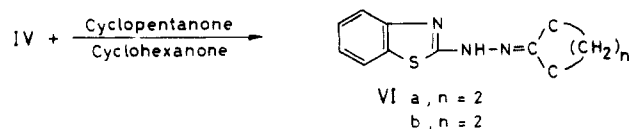
compd	mp, °C	solvent	yield, %
Va	235	E	83
b	230	E	83
c	225	A	91
d	135	E	93
e	260	E	85
f	190	E	80
g	235	E	74
h	250	E	80
VIa	160	E	78
b	140	E	80

^a Satisfactory elemental analyses were found. ^b A = acetic acid; E = ethanol; W = water.

2-(Arylhiazino)benzothiazole (V) and Cycloalkanone Benzothiazol-2-ylhydrazone (VI). Compounds V were prepared (a) by the method of Katz (2) or (b) by refluxing a mixture of 0.01 mol of the appropriate carbonyl compounds and 0.01 mol of compound IV in 20 mL of ethanol for 0.5 h and then allowing the mixture to cool to room temperature. The pale yellow crystals formed were collected and crystallized from the proper solvent (see Table II).

Reaction of VIb with LTA. VIb (1 g) was dissolved in 30 mL of acetic acid, and then 3 g of LTA was added gradually. The mixture was heated with stirring at 50 °C for 2 h, poured into ice water, and then extracted with ether. Ether was distilled off, and the solid formed was crystallized from ethanol to give VII (5): mp 105 °C; yield 68%. The IR spectrum of VII showed absorption at 1660 cm⁻¹ (C=N) and at 1743 cm⁻¹ (OAc). The ¹H NMR of VII (in CDCl₃) showed the cyclohexane protons as a multiplet in the δ 0.7–2.0 region (10 H), OOCCH₃ protons as a singlet at δ 2.15 (3 H), and the aromatic protons as a multiplet in the δ 7.5–8.25 region (4 H).

1-(Benzothiazol-2-yl)-3-methylpyrazol-5-one (VIII). A mixture of 1.5 g of compound IV and 2 mL of ethyl acetoacetate in ethanolic potassium hydroxide (0.6 g of KOH in 50 mL of ethanol) was refluxed for 2 h. The ethanol was distilled off. The solid left behind was washed with dilute hydrochloric acid, collected, and crystallized from ethanol to give VIII: mp 222 °C; yield 63%. The IR spectrum of compound VIII shows absorption at 1620 cm⁻¹ (C=N) and at 1685 cm⁻¹ (C=O). The ¹H NMR of compound VIII (in CDCl₃) showed the



CH₃ protons as a singlet at δ 2.15 (3 H), the CH₂ protons as a singlet at δ 5.25 (2 H), and the aromatic protons as a multiplet in the δ 7.45–8.20 region (4 H).

1-(Benzothiazol-2-yl)-3,5-dimethylpyrazoline (IX). A mixture of 1 g of compound IV and 2 mL of acetylacetone in 10 mL of acetic acid was refluxed for 1 h. The mixture was poured into cold water, and the precipitate formed was collected and crystallized from ethanol: mp 145 °C; yield 70%. The ¹H NMR of compound IX (in CDCl₃) showed the two methyl groups as two singlets at δ 2.35 (3 H) and δ 2.85 (3 H), the =CH proton at δ 6.15 (1 H), and the aromatic protons as a multiplet in the δ 7.45–8.15 region (4 H).

Literature Cited

- (1) Katz, L. J. *Am. Chem. Soc.* **1951**, *73*, 4007.
- (2) Katz, L. J. *Am. Chem. Soc.* **1953**, *75*, 712.
- (3) Singh, S. P.; Misra, R. S.; Parmar, S. S.; Brumleve, S. J. *J. Pharm. Sci.* **1975**, *64*, 1245.
- (4) Hammam, A. G. J. *Chem. Eng. Data* **1979**, *24*, 379.
- (5) Butler, R. N. *J. Chem. Ind.* **1968**, 437.

Received for review May 1, 1981. Revised manuscript received September 4, 1981. Accepted October 1, 1981.