2,4-dinitroimidazole. This structure was confirmed by its transformation into 1-methyl-4-nitro-5-chloroimidazole with 2-chloroethanol.[14]

Experimental

Apparatus.—The potentiometric titrations were carried out with a Jonosis Q3 potentiometer. The spectrometric measurements were carried out on a Beckman DK2 spectrometer.

Materials.—The following imidazole derivatives had the melting points and properties reported in the literature and were prepared according to the cited references: **2-Nitro**, m.p. 284° dec.[14]; **4(5)-nitro**, m.p. 308°[3,15]; **1-methyl-4-nitro**, m.p. 133°[16]; **1-methyl-5-nitro**, m.p. 55°[17]; **1-methyl-4-chloro**, b.p. 252°,[18] purified by gas chromatography; **1-methyl-5-chloro**, b.p. 205°[19]; **4(5)-nitro-5(4)-chloro**, m.p. 216°[14]; **1-methyl-4-nitro-5-chloro**, m.p. 148°[14]; **1-methyl-4-chloro-5-nitro**, m.p. 78°[14]; **1-(β-hydroxyethyl)-2-methyl-5-nitro**, m.p. 160°[13b]; and **2,4(5)-dinitro**, m.p. 268°.[14]

1-Methyl-2-nitroimidazole.—To a 4% solution of diazomethane in ethyl ether, 200 mg. of 2-nitroimidazole was added, and the mixture was allowed to react at room temperature overnight. Evaporation of the solvent yielded 130 mg. of a light yellow product, which, after recrystallization from ethanol, melted at 101–102°.

Anal. Calcd. for $C_4H_5N_3O_2$: C, 37.80; H, 3.97; N, 33.06. Found: C, 37.91; H, 4.08; N, 32.95.

1-(β-Hydroxyethyl)-2-nitroimidazole.—A mixture of 2 g. of 2-nitroimidazole silver salt[20] and 8 ml. of 2-bromoethanol in 85 ml. of toluene was refluxed for 14 hr. then evaporated to dryness under reduced pressure. The residue was extracted three times with 50 ml. of boiling water each time, and the collected extracts were evaporated to dryness. The residue, recrystallized from ethyl acetate, yielded 800 mg. of light yellow crystals melting at 157°.

Anal. Calcd. for $C_5H_7N_3O_3$: C, 38.22; H, 4.49; N, 26.74. Found: C, 38.13; H, 4.63; N, 26.95.

1-Methyl-2,4-dinitroimidazole.—2,4(5)-Dinitroimidazole (200 mg.) was treated with diazomethane as described above for the mononitro derivative. By concentration of the solvent, 140 mg. of crystals was obtained, which, after two crystallizations from ethanol, melted at 172°.

Anal. Calcd. for $C_4H_4N_4O_4$: C, 27.92; H, 2.34; N, 32.56. Found: C, 27.87; H, 2.47; N, 32.64.

No traces of the isomeric 1-methyl-2,5-dinitroimidazole could be found in the mother liquor of the crystallization.

1-Methyl-4-nitro-5-chloroimidazole.—A mixture of 680 mg. of 1-methyl-2,4-dinitroimidazole and 10 ml. of 2-chloroethanol was refluxed for 2 hr. The resulting solution was evaporated to dryness under reduced pressure, and the residue was recrystallized from ethanol, yielding 400 mg. of product with m.p. 148° and infrared spectrum identical with that of 1-methyl-4-nitro-5-chloroimidazole obtained as described by Sarasin.[21] No traces of the isomeric 1-methyl-4-chloro-5-nitroimidazole could be detected in the mother liquor of the crystallization.

(14) G. C. Lancini, N. Maggi, and P. Sensi, *Farmaco* (Pavia) *Ed. Sci.*, **18**, 390 (1963).
(15) R. G. Fargher and F. L. Pyman, *J. Chem. Soc.*, **115**, 217 (1919).
(16) W. G. Forsyth and F. L. Pyman, *ibid.*, **127**, 573 (1925).
(17) C. E. Hazeldine, F. L. Pyman, and J. Winchester, *ibid.*, **125**, 1431 (1924).
(18) J. Sarasin, *Helv. Chim. Acta*, **6**, 370 (1923).
(19) F. F. Blicke and H. G. Godt, *J. Am. Chem. Soc.*, **76**, 3654 (1954).
(20) S. Nakamura, *Pharm. Bull.* (Tokyo), **3**, 379 (1955).
(21) J. Sarasin and E. Wegmann, *Helv. Chim. Acta*, **7**, 713 (1924).

Derivatives of 3-Methylthiazolo[3,2-*a*]benzimidazole[1,2]

JOHN J. D'AMICO, ROBERT H. CAMPBELL, AND EARL C. GUINN

Organic Chemicals Division, Rubber Chemicals Research Laboratories, Monsanto Chemical Company, Nitro, West Virginia

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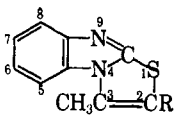
Depending upon reaction conditions, 3-(2-benzimidazolylthio)-2,4-pentanedione (I) or ethyl 2-(2-benzimidazolylthio)acetoacetate (II) when treated with acetic anhydride in pyridine either undergo cyclization or form enol acetates; however, 1-(2-benzimidazolylthio)-2-propanone (III) gives only the enol acetate. A possible mechanism and supporting infrared data are discussed.

As thiazolethiols and 2-mercaptobenzimidazole are known accelerators for the vulcanization of rubber with sulfur and antidegradants for rubber, respectively, it was desirable to prepare a novel heterocyclic compound containing both the thiazolyl and benzimidazolyl moieties. Thiazolo[3,2-*a*]benzimidazol-3(2*H*)-one has been prepared by the dehydration of 2-benzimidazolylthioacetic acid[3,4]; the purpose of this investigation was to prepare compounds having the following structure.



R = H, $COCH_3$, $COOC_2H_5$, COOH, $CHOHCH_3$, $CONHC_6H_5$, CCH_3 (‖ NOH)

The preparation of these new compounds was realized as illustrated in Fig. 1.

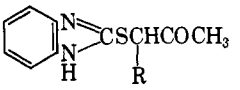
The key intermediates, 3-(2-benzimidazolylthio)-2,4-pentanedione (I), ethyl 2-(2-benzimidazolylthio)-acetoacetate (II), and 1-(2-benzimidazolylthio)-2-propanone (III), required for the synthesis of the new compounds, were prepared by the reaction of the potassium salt of 2-mercaptobenzimidazole with 3-chloro-2,4-pentanedione, ethyl α-chloroacetoacetate, and chloroacetone, respectively. The data are summarized in Table I.

When the mixture containing I, acetic anhydride, and pyridine was heated for only 10 min. at 90–100°, the product isolated in 96% yield was 3-(2-benzimidazolylthio)-4-hydroxy-3-penten-2-one acetate (IV). We had anticipated that acetylation would have occurred on the amino group. However, our postulate was not substantiated since the infrared spectrum revealed that the hydroxyl group was acetylated. However, when this mixture was heated at 90–100° for 3 hr., methyl 3-methylthiazolo[3,2-*a*]benzimidazolyl ketone (V) which contained no ester bonds in the infrared spectrum was obtained in 99% yield. When the mixture was heated at 90–100° for 1 hr., IV and V were ob-

(1) The *Chemical Abstracts'* preferred name for all compounds was kindly furnished by Dr. L. T. Capell of the *Chemical Abstracts'* service.
(2) Presented at the 146th National Meeting of the American Chemical Society, Denver, Colo., January, 1964.
(3) G. F. Buffin and J. D. Kendall, *J. Chem. Soc.*, 361 (1956).
(4) J. A. Van Allan, *J. Org. Chem.*, **21**, 24 (1956).

TABLE I

3-(2-BENZIMIDAZOLYLTHIO)-2,4-PENTANEDIONE (I), ETHYL 2-(2-BENZIMIDAZOLYLTHIO)ACETOACETATE (II), AND 1-(2-BENZIMIDAZOLYLTHIO)-2-PROPANONE (III)



No.	R	% yield, crude	M.p., °C.	Empirical formula	% N Calcd.	% N Found	% S Calcd.	% S Found
I	$-COCH_3$	88.5	185–186[a]	$C_{12}H_{12}N_2O_2S$	11.28	11.19	12.91	12.56
II	$-COOC_2H_5$	71.8	149–150[a]	$C_{13}H_{14}N_2O_3S$	10.07	10.38	11.52	11.26
III	-H	82.2	114–115[a]	$C_{10}H_{10}N_2OS$	13.58	13.66	15.52	15.30

[a] Recrystallization from ethyl alcohol.

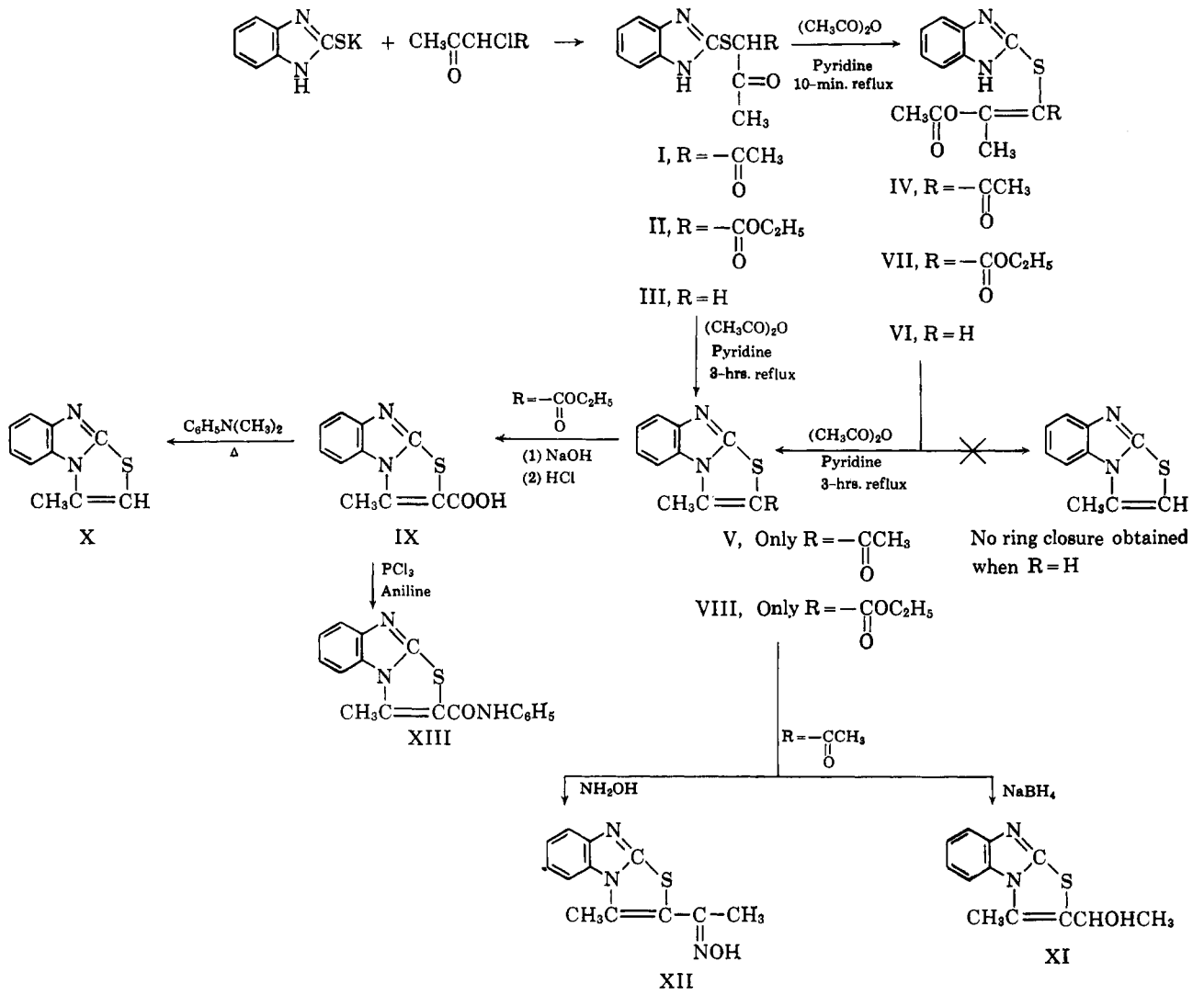


Figure 1

tained in 27.4 and 69.5% yields, respectively. The separation of IV from V was accomplished by cooling the reaction mixture to 0° and collecting V by filtration. Upon the addition of cold water to the filtrate, IV precipitated and was collected by filtration. An attempt to prepare V by heating IV with pyridine alone at 90–100° for 3 hr. failed. However, when pyridine, acetic anhydride, and IV were heated under the same conditions, V was obtained in 97.5% yield.

It was anticipated that the reaction of III with acetic anhydride and pyridine at 90–100° for a period of 4 hr. would yield the desired 3-methylthiazolo[3,2-*a*]benzimidazole (X) but instead 1-(2-benzimidazolylthio)-1-propen-2-ol acetate (VI) was obtained in 99% yield. The infrared spectrum and elemental analysis confirm that no ring closure occurred under these conditions.

The treatment of II with acetic anhydride and pyridine at 90–100° for 10 min. furnished ethyl 2-(2-benzimidazolylthio)-3-hydroxycrotonate acetate (VII) in 99% yield. Because of the great similarity of the infrared spectrum of VII with that of VIII, with only a slight increase in carbonyl and ester absorbance, it was likely that this intermediate was unstable and underwent some ring closure during work-up. Further

TABLE II

INFRARED DATA OF I–XIII

Compound	ν, cm.$^{-1a}$	Assignment
I	3200–2600 (br)	N–H st. and O–H st. (enol)
	1550 (br)	C=O st. (conjugate chelation)
	1393 (s)	Unassigned
II	3340 (w)	N–H st.
	3200 (br)	O–H st. (enolic)
	1730 (m)	C=O st. (ester)
	1590 (s)	C=O st. (conjugate chelation)
	1448 (s)	C–H deformation
	1389 (m)	CH_3 def. (sym.)
	1250 (vs)	C–O st. (ester)
III	3400–2500 (br)	N–H st.
	1712 (m)	C=O st.
	1449 (s)	CH_2 + CH_3 def.
	1361 (s)	CH_3 def. (sym.)
IV	3350 (w)	N–H st.
	1720 (s)	C=O st. (ester)
	1680 (s)	C=O st. (conj. to double bond)
	1610 (s)	C=C st.
	1560 (s)	Unassigned
	1455 (s)	CH_3 def. (asym.)
	1370 (s)	CH_3 def. (sym.)
	1250 (s)	C–O st. (ester)
V	1674 (s)	C=O st. (conj. to double bond)
	1610 (m)	C=C st.
	1560 (s)	Unassigned
	1455 (s)	CH_3 def. (asym.)
	1370 (s)	CH_3 def. (sym.)
	1310 (s)	Unassigned
VI	3400 (w)	N–H st.
	1650 (s)	C=O st. (hydrogen bonded)
	1620 (w)	C=C st.
	1255 (s)	C–O st. (ester)
VIII	1708 (s)	C=O st. (conj. to double bond)
	1612 (m)	C=C st. (conj. to carbonyl)
	1595 (s)	Unassigned
	1455 (m)	CH_2 + CH_3 def.
	1380 (m)	CH_3 def. (sym.)
	1250 (s)	C–O st. (ester)
IX	2353 (m)	O–H st. (H-bonded carboxylic acid)
	1675 (m)	C=O st. (conj. to double bond)
	1315 (m)	Unassigned
X	3110 (w)	C–H st. (fused ring olefin)
	1616 (w)	C=C st.
	1448 (s)	CH_3 def. (asym.) and other unassigned
	1382 (w)	CH_3 def. (sym.)
	1308 (m)	Unassigned
XI	3200 (m)	O–H st. (hydrogen bonded)
	1624 (m)	C=C st.
	1290 (m)	Unassigned
	1087 (s)	O–H def.
XII	2800–2600 (br)	N–O–H associated
	1600 (m)	C=C st. (conj.)
	1400 (s)	Unassigned
XIII	3300 (br)	N–H st. (secondary amide)
	1670 (m)	C=O st. (amide I)
	1610 (w)	C=C (conj. to carbonyl)
	1455 (w)	CH_3 def. (asym.)
	1440 (s)	Unassigned
	1377 (w)	CH_3 def. (sym.)
	694 (m)	C–H out-of-plane def. of monosubstituted phenyl group

[a] br = broad, w = weak, m = medium, s = strong, v = very.

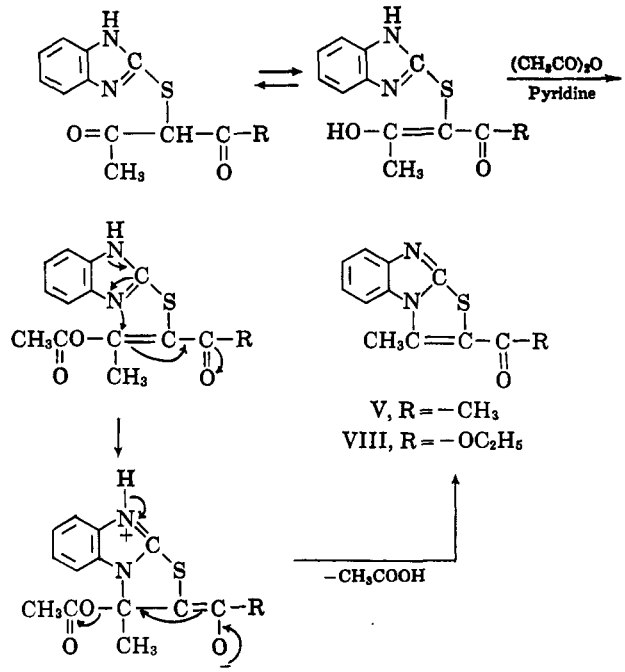


Fig. 2.—Mechanism for V and VIII.

evidence of instability was the evolution of an acetic acid odor upon standing. As expected, the reaction of VII or II in an acetic anhydride–pyridine solution at 90–100° for 3 hr. gave ethyl 3-methylthiazolo[3,2-*a*]-benzimidazole-2-carboxylate (VIII) in 98 and 96.5% yields, respectively.

The saponification of VIII with aqueous sodium hydroxide furnished 3-methylthiazolo[3,2-*a*]benzimidazole-2-carboxylic acid (IX) in 90.5% yield.

The decarboxylation of IX in a dimethylaniline solution at 190–200° furnished 3-methylthiazolo[3,2-*a*]-benzimidazole (X) in 45.3% yield.

The reduction of V with sodium borohydride gave the expected α,3-dimethylthiazolo[3,2-*a*]benzimidazole-2-methanol (XI) in 86.5% yield.

2-Acetyl-3-methylthiazolo[3,2-*a*]benzimidazole oxime (XII) was obtained in 77% yield by the reaction of V with hydroxylamine.

The treatment of IX with phosphorus trichloride and aniline furnished 3-methylthiazolo[3,2-*a*]benzimidazole-2-carboxanilide (XIII) in 64.2% yield.

The mechanism as illustrated in Fig. 2 is offered for the cyclization reactions. The presence of the acetyl of ethoxycarbonyl group in the 2-position facilitated ring closure because of increased resonance stabilization. However, when the above groups were replaced by hydrogen, this phenomenon was not a contributing factor and thus no ring closure occurred.

The infrared spectra of compounds I, VI, IX, XI, and XII were determined from suspensions in Nujol and halocarbon oil. The infrared spectra of compounds II, III, IV, V, VIII, X, and XIII were determined in chloroform (5000 to 830 cm.$^{-1}$) and dimethylformamide solutions (830 to 600 cm.$^{-1}$). A Perkin-Elmer Model 21 spectrophotometer with a sodium chloride prism was used. In all cases the C–H st. (aromatic) and C–H st. (aliphatic) bands were consistent with the proposed structures. Other significant infrared absorption bands of the compounds and assignments where possible are given in Table II.

A medium intensity band in the region 1490 cm.$^{-1}$ consistently appeared in all benzimidazole derivatives and is attributed to skeletal in-plane vibrations of the benzimidazole ring. The C–H out-of-plane deformation bands (region of 750 cm.$^{-1}$) characteristic of *ortho*-substituted phenyl groups were present in all spectra of benzimidazole derivatives. In compound X of Table II the assignment of the higher than normal frequency of 3110 cm.$^{-1}$ was made to the C–H st. of the olefinic group. This was based upon the assumption that the additional strain due to the fused rings induced more s character which resulted in a shorter C–H bond. For the purpose of comparison several frequencies of unassigned absorption bands are given in Table II.

Experimental[5]

3-(2-Benzimidazolylthio)-2,4-pentanedione (I), Ethyl 2-(2-benzimidazolylthio)acetoacetate (II), and 1-(2-Benzimidazolylthio)-2-propanone (III).—A stirred mixture containing 150.2 g. (1.0 mole) of 2-mercaptobenzimidazole, 2000 ml. of ethyl alcohol, and 66 g. (1.0 mole) of 85% potassium hydroxide was heated at 78–80° for 10 min. After cooling the resulting solution to 30°, 1 mole of 3-chloro-2,4-pentanedione, ethyl α-chloroacetoacetate, or chloroacetone was added in one portion. An exothermic reaction set in causing a temperature rise from 30 to 40°. After stirring at 25–30° for 18 hr., the reaction mixture was added to 2000 g. of ice–water. After stirring for 30 min. at 0–10°, the precipitate was collected by filtration, washed with water until free of chloride, and air-dried at 50°. The data are summarized in Table I.

3-(2-Benzimidazolylthio)-4-hydroxy-3-penten-2-one Acetate (IV).—A stirred slurry containing 32 g. (0.129 mole) of I, 65 ml. of pyridine, and 33 ml. of acetic anhydride was heated from 25 to 90° over a 3-min. period. The stirred solution was maintained at 90–100° for only 10 min. and immediately cooled to 0°. To this solution, 1 l. of cold water was added and stirring was continued at 0–5° for 1 hr. The resulting precipitate was collected by filtration, washed with water until neutral to litmus, and air-dried at 25–30°. The product, m.p. 130–132°, was obtained in 96% yield. After recrystallization from ethyl alcohol, it melted at 136–137°.

Anal. Calcd. for $C_{14}H_{14}N_2O_3S$: N, 9.65; S, 11.04. Found: N, 9.64, S, 10.76.

Methyl 3-Methylthiazolo[3,2-*a*]benzimidazolyl Ketone (V). Method 1.—A stirred slurry containing 49.2 g. (0.2 mole) of I, 50 ml. of acetic anhydride, and 100 ml. of pyridine was heated at 95–100° for 3 hr. The solution was cooled to 0° and held at 0–5° for 1 hr. The resulting precipitate was collected by filtration, washed with water until neutral to litmus, and air-dried at 25–30°. The product, m.p. 167–168°, was obtained in 99% yield. After recrystallization from ethyl alcohol the melting point remained unchanged.

Anal. Calcd. for $C_{12}H_{10}N_2OS$: N, 12.17; S, 13.92. Found: N, 12.51; S, 13.70.

Method 2.—A stirred solution containing 22 g. (0.076 mole) of IV, 50 ml. of pyridine, and 25 ml. of acetic anhydride was heated at 95–100° for 3 hr. The product was isolated as described in method 1. The product, m.p. 164–166°, was obtained in 97.5% yield. After recrystallization from ethyl alcohol, it melted at 167–168°. A mixture melting point with the product obtained from method 1 was not depressed and the infrared spectra of the two were superimposable.

Anal. Calcd. for $C_{12}H_{10}N_2OS$: N, 12.17; S, 13.92. Found: N, 12.51; S, 13.92.

3-(2-Benzimidazolylthio)-4-hydroxy-3-penten-2-one Acetate (IV) and Methyl 3-Methylthiazolo[3,2-*a*]benzimidazolyl Ketone (V).—A stirred solution containing 24.9 g. (0.1 mole) of I, 25 ml. of acetic anhydride, and 50 ml. of pyridine was heated at 90–100° for 1 hr. After cooling to 5°, the resulting solid was collected by filtration, washed with 1 l. of water, and air-dried at 25–30°. The product V, m.p. 163–167°, was obtained in 69.5% yield. After recrystallization from ethyl alcohol, it melted at 167–168°. A mixture melting point with product obtained from method 1 or 2 was not depressed, and the infrared spectra of the three products were superimposable. The combined filtrate was filtered and the product was air-dried at 25–30°. The product IV, m.p. 120–126°, was obtained in 27.4% yield. After recrystallization from ethyl alcohol, it melted at 136–137°. A mixture melting point with the product obtained by heating I for only 10 min. was not depressed, and the infrared spectra of the two were superimposable.

1-(2-Benzimidazolylthio)-1-propen-2-ol Acetate (VI).—A stirred solution containing 41.3 g. (0.2 mole) of III, 50 ml. of acetic anhydride, and 100 ml. of pyridine was heated at 90–100° for 4 hr. After cooling to 25°, 1000 ml. of water was added and stirring was continued at 25–30° for an additional 30 min. The precipitate was collected by filtration, washed with water until neutral to litmus, and air-dried at 25–30°. The product, m.p. 155–158°, was obtained in 99% yield. After recrystallization from ethyl alcohol, it melted at 171–172°.

Anal. Calcd. for $C_{12}H_{12}N_2O_2S$: N, 11.28; S, 12.91. Found: N, 11.29; S, 13.30.

Ethyl 2-(2-Benzimidazolylthio)-3-hydroxycrotonate Acetate (VII).—A stirred solution containing 27.9 g. (0.1 mole) of II, 50 ml. of pyridine, and 25 ml. of acetic anhydride was heated from 25 to 90° over a 3-min. period and then maintained at 90–100° for only 10 min. After immediately cooling the stirred solution to 0°, 500 ml. of water and 600 ml. of ethyl ether were added. After stirring for 15 min., the ether solution was separated, washed with water until the washings were neutral to litmus, and dried over sodium sulfate. The ether was removed *in vacuo* at a maximum temperature of 30° at 1–2 mm. The resulting semi-solid was air-dried on a porous plate at 25–30°. The product, m.p. 68–71°, was obtained in 99% yield. After recrystallization from ethyl alcohol, it melted at 88–90°. Upon standing the compound was unstable and liberated acetic acid.

Anal. Calcd. for $C_{15}H_{16}N_2O_4S$: N, 8.75; S, 10.01. Found: N, 9.15; S, 10.10.

Ethyl 3-Methylthiazolo[3,2-*a*]benzimidazole-2-carboxylate (VIII). Method 1.—A stirred solution containing 55.7 g. (0.2 mole) of II, 50 ml. of acetic anhydride, and 100 ml. of pyridine was heated at 90–100° for 3 hr. After cooling to 0°, 1000 g. of ice–water was added and stirring was continued at 0–5° for 30 min. The precipitate was collected by filtration, washed with water until neutral to litmus, and air-dried at 25–30°. The product, m.p. 106–109°, was obtained in 96.5% yield. After recrystallization from ethyl alcohol, it melted at 122–123°.

Anal. Calcd. for $C_{13}H_{12}N_2O_2S$: N, 10.76; S, 12.32. Found: N, 10.67; S, 12.37.

Method 2.—A stirred solution containing 15 g. (0.047 mole) of VII, 25 ml. of acetic anhydride, and 50 ml. of pyridine was heated at 90–100° for 3 hr. After cooling to 0°, 400 g. of ice–water was added and stirring was continued at 0–5° for 30 min. The solid was collected by filtration, washed with water until neutral to litmus, and air-dried at 25–30°. The product, m.p. 115–118°, was obtained in 98% yield. After recrystallization from ethyl alcohol, it melted at 122–123°. A mixture melting point with the product obtained from method 1 was not depressed, and the infrared spectra of the two were superimposable.

Anal. Calcd. for $C_{13}H_{12}N_2O_2S$: N, 10.76; S, 12.32. Found: N, 10.74; S, 12.21.

3-Methylthiazolo[3,2-*a*]benzimidazole-2-carboxylic Acid (IX).—A solution containing 182 g. (0.7 mole) of VIII, 224 g. (1.4 moles) of 25% aqueous sodium hydroxide, and 1600 ml. of ethyl alcohol was stirred at 75–80° for 4 hr. After cooling to 25°, the reaction mixture was added to 4000 g. of ice–water. The stirred solution was made acidic with 220 g. (2.2 moles) of concentrated hydrochloric acid. The resulting precipitate was collected by filtration, washed with water until the washings were neutral to litmus, and air-dried at 50°. The product, m.p. 249–252° dec., was obtained in 90.5% yield. The melting point remained unchanged upon dissolving IX in dilute sodium hydroxide and then reprecipitating from concentrated hydrochloric acid.

Anal. Calcd. for $C_{11}H_8N_2O_2S$: N, 12.06; S, 13.81. Found: N, 12.25; S, 13.75.

3-Methylthiazolo[3,2-*a*]benzimidazole (X).—A stirred solution containing 38 g. (0.17 mole) of IX and 150 ml. of dimethylaniline was heated at 190–200° for 5 hr. After cooling to 25°, 500 ml. of water containing 125 g. (1.25 moles) of concentrated hydrochloric acid was added. A small amount of impurities was removed by filtration. To the stirred filtrate, concentrated ammonium hydroxide was added dropwise until pH 9 was obtained. To this

(5) All melting points were taken upon a Fisher-Johns block and are uncorrected.

stirred slurry, 300 ml. of ethyl ether was added and stirring continued for 15 min. The precipitate was collected by filtration, washed with water until the washings were neutral to litmus, and air-dried at 25–30°. The product, m.p. 162–164°, was obtained in 45.3% yield. After recrystallization from ethyl alcohol, it melted at 165–166°.

Anal. Calcd. for $C_{10}H_8N_2S$: N, 14.88; S, 17.03. Found: N, 14.42; S, 16.93.

α,3-Dimethylthiazolo[3,2-*a*]benzimidazole-2-methanol (XI).—To a stirred solution containing 46.1 g. (0.2 mole) of V in 500 ml. of ethyl alcohol was added dropwise at 65–70° a solution containing 7.6 g. (0.2 mole) of sodium borohydride in 200 ml. of ethyl alcohol over a 30-min. period. The stirred reaction mixture was heated at 75–80° for 2 hr. After cooling to 25°, the reaction mixture was added to 2000 g. of ice–water and stirred at 0–10° for 1 hr. The solid was collected by filtration, washed with water until the washings were neutral to litmus, and air-dried at 25–30°. The product, m.p. 222–228°, was obtained in 86.5% yield. After recrystallization from dimethylformamide, it melted at 227–228°.

Anal. Calcd. for $C_{12}H_{12}N_2OS$: N, 12.06; S, 13.80. Found: N, 12.06, S, 14.12.

2-Acetyl-3-methylthiazolo[3,2-*a*]benzimidazole Oxime (XII).—A stirred slurry containing 46.1 g. (0.2 mole) of V and 500 ml. of ethyl alcohol was heated to 75°. To the cooled stirred solution at 25° was added in one portion 16.4 g. (0.25 mole) of hydroxylamine hydrochloride in 50 ml. of water. A solution containing 17.4 g. (0.125 mole) of potassium carbonate in 60 ml. of water was added dropwise at 25–30° over a 15-min. period. The stirred reaction mixture was heated at 75–80° for 2.5 hr. After cooling to 5°, the precipitate was collected by filtration, washed with water until the washings were neutral to litmus, and air-dried at 25–30°. The product, m.p. 230–234° dec., was obtained in 77% yield. After recrystallization from ethyl alcohol, it melted at 246–247° dec.

Anal. Calcd. for $C_{12}H_{11}N_3OS$: N, 17.13; S, 13.07. Found: N, 16.95; S, 13.16.

3-Methylthiazolo[3,2-*a*]benzimidazole-2-carboxanilide (XIII).—To a stirred slurry containing 34.9 g. (0.15 mole) of IX, 14.1 g. (0.15 mole) of aniline, and 200 ml. of chlorobenzene, 6.9 g. (0.05 mole) of phosphorus trichloride was added dropwise at 80–90° over a 5-min. period. The stirred reaction mixture was heated at 120–130° for 6 hr. After cooling to 25°, 500 ml. of water containing 40 g. (0.25 mole) of 25% aqueous sodium hydroxide was added and stirring was continued for 1 hr. The precipitate was collected by filtration, washed with water until the wash water was neutral to litmus, and air-dried at 25–30°. The product, m.p. 232–233° dec., was obtained in 64.2% yield. The melting point remained unchanged after recrystallization from dimethylformamide.

Anal. Calcd. for $C_{17}H_{13}N_3OS$: N, 13.67. Found: N, 13.40.

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The 1,4-Anhydrohexitols. Synthesis and Periodate Oxidation[1]

ROBERT BARKER

The Department of Biochemistry, University of Tennessee, Memphis, Tennessee

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The 1,4-anhydrohexitols are prepared from the pentoses by application of the nitromethane synthesis followed by reduction and deamination. The rate of "overoxidation" of the 1,4-anhydrohexitols by sodium metaperiodate depends on the rearrangement of the initially formed trialdehyde to a rapidly oxidized form which absorbs at 272 mμ.

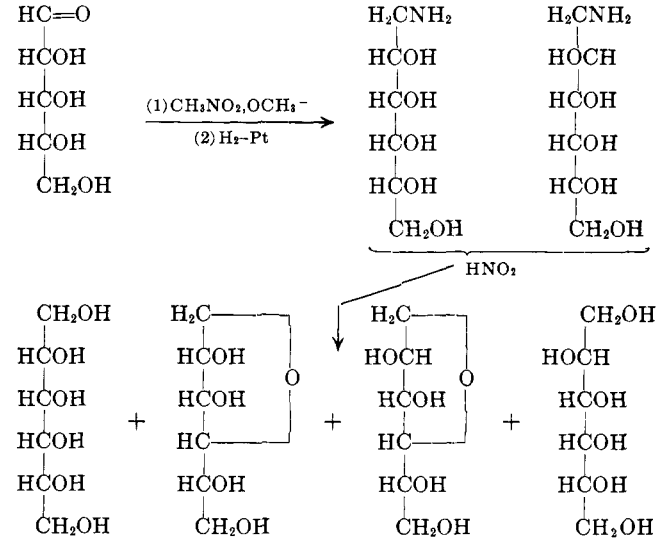
In connection with an investigation of the acid-catalyzed anhydrization of the alditols it was necessary to synthesize those 1,4-anhydrohexitols which are not described in the literature. Most methods of synthesis require the hexose, or a derivative thereof, as starting material and these are not all readily available.[2,3]

In the synthesis reported here, the pentoses, which are readily available, were used as starting materials and the following sequence of reactions was applied to them: pentose → 2-epimeric sodio *aci*-nitro alcohols[4] → 2-epimeric hexitylamines → 2-epimeric hexitols + 2-epimeric 1,4-anhydrohexitols.

The reactions were carried out on D-ribose, D-arabinose, D-lyxose, and D-xylose. In Scheme I the sequence is illustrated using D-ribose as an example.

Paper column chromatography[5] using butanone–water as solvent in all cases gave a fractionation of the products into at least three components. The fastest moving component was an impurity identified as a 1-deoxy-1-(methylnitrosoamino)pentitol.[6] The second and third fractions were the two epimeric 1,4-anhydro-

SCHEME I



hexitols, and the slowest moving component was a mixture of the two epimeric alditols. The 1,4-anhydroalditols from lyxose and xylose were not well-resolved on the column and were separated *via* the isopropylidene derivatives. In all cases one of the pair had *cis* hydroxyl groups in the tetrahydrofuran ring and, therefore, formed a diisopropylidene derivative, whereas the other, having *trans* hydroxyl groups in the ring, could form only a monoisopropylidene deriva-

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(2) L. F. Wiggins, *Advan. Carbohydrate Chem.*, **5**, 191 (1950).

(3) R. K. Ness, H. G. Fletcher, Jr., and C. S. Hudson, *J. Am. Chem. Soc.*, **73**, 3742 (1951).

(4) J. C. Sowden and H. O. L. Fischer, *ibid.*, **67**, 1713 (1945).

(5) LKB, Chro Max Column, Stockholm, Sweden.

(6) R. Barker, in preparation.