Synthesis of Heterocyclic Compounds from 3-Acetyl-3-chloropropyl Acetate [1]

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The reaction of the potassium salt of 2-mercaptobenzimidazole with 3-acetyl-3-chloropropyl acetate afforded the novel heterocyclic compound 1. When solutions of 1 in deuteriodimethylsulfoxide or deuteriomethanol were allowed to stand at room temperatures for 15 minutes and 19 days, respectively, ring opening of 1 occurred to give the precursor, 3-acetyl-3-(2-benzimidazolthio)propyl-1-ol. The treatment of 1 with p-fluorophenyl isocyanate furnished the carbanilate 2. The reaction of ammonium dithiocarbamate with the above chloroketone afforded the 2-thiazolethione 3. Possible mechanisms and supporting nmr, ir, mass spectral data for 1-3 and single crystal X-ray analysis for 2 are discussed.
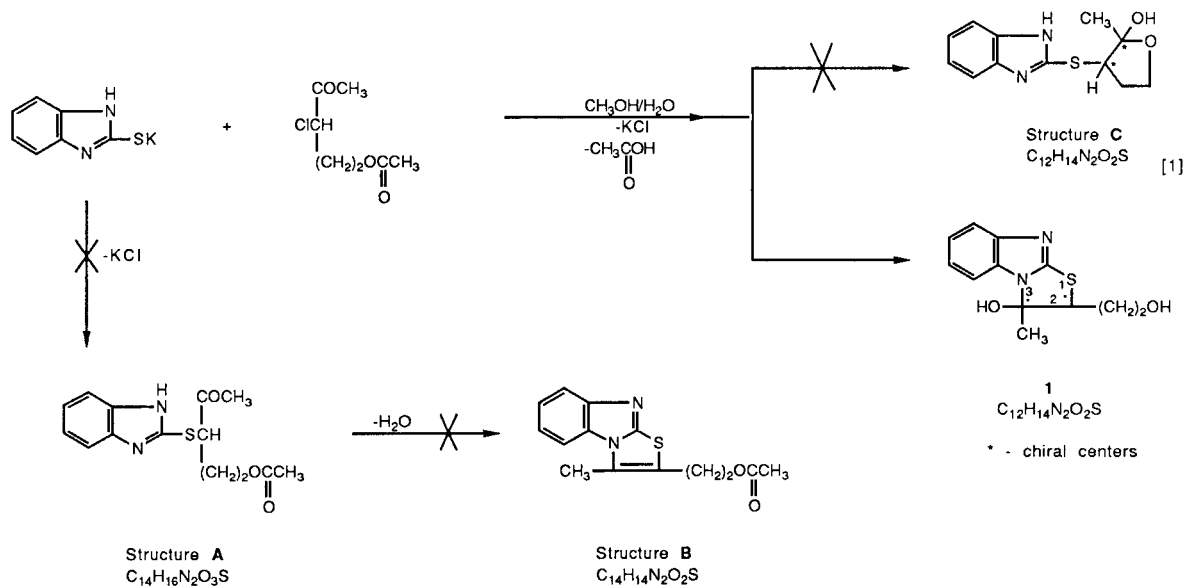
The titled chloroketone and 3-acetyl-3-chloropropyl-1-ol have been used extensively as intermediates in the synthesis of Vitamin B_1 or aneurin [2-9].

In this paper we wish to report the synthesis of novel heterocyclic compounds derived from 3-acetyl-3-chloropropyl acetate.

Based on our previous work in this area of chemistry [10], we anticipated that the reaction of the potassium salt of 2-mercaptobenzimidazole with 3-acetyl-3-chloropropyl acetate [11] would yield products A or B. However, the elemental analysis and molecular weight data ruled out these possible structures. By reviewing the elemental analysis and the mass spectral data the compound isolated in the reaction 1 had a molecular weight of 250 with an empirical formula of $C_{12}H_{14}N_2O_2S$. From these data we considered the possible structures as being 2,3-dihydro-3-

hydroxy-3-methylthiazolo[3,2-a]benzimidazole-2-ethanol (1) or structure C, a cyclic hemi-acetal, which are known to be unstable in the same way as gem-diols.

The ir, nmr and mass spectral data completely substantiated the proposed structure 1 and thus ruled out structure C. The electron impact and isobutane chemical ionization mass spectra furnished the molecular weight data in the form of M^+ 250 and $(M + 1)^+$ 251, respectively. The presence of the intermolecular H-bonded OH (3358 and 3198 cm^{-1}), aromatic CH (3064 and 2996 cm^{-1}), aliphatic CH (2953-2935 cm^{-1}), $-C=N-$ (1688 cm^{-1}), CH_2 deformation of $C-CH_2$ (1477 cm^{-1}), CH_2 deformation of $O-CH_2$ (1443 cm^{-1}), CH_3 (1351 cm^{-1}), aromatic, $C-N$ (1282 cm^{-1}), $C-O$ of tertiary OH (1154 cm^{-1}), benzimidazole ring mode (1066 cm^{-1}) and $C-O$ of primary alcohol (1044 cm^{-1}) absorption bands in potassium bromide ir spectrum afforded

Structure A
$C_{14}H_{16}N_2O_3S$

Structure B
$C_{14}H_{14}N_2O_2S$

Structure C
$C_{12}H_{14}N_2O_2S$ [1]

1
$C_{12}H_{14}N_2O_2S$

* - chiral centers

additional proof for our proposed structure. However when a sample of **1** was dissolved in deuteriodimethylsulfoxide and the solution allowed to stand for only 15 minutes, a considerable number of changes occurred in the ir spectrum. The overlay of the 2% solution and the solid state spectra showed that the benzimidazole ring modes in the 1700 to 1500 cm^{-1} region were changed, but more importantly new bands at 1710, 1423 and 1339 cm^{-1} were formed. These bands are assigned to the methyl ketone carbonyl stretch, the methyl ketone methyl asymmetric deformation, and the methyl ketone methyl symmetric deformation modes, respectively. These changes in the ir spectrum are supporting evidence that the following ring opening occurs. The opening of the ring in the deuteriodimethylsulfoxide solution and the presence of two


[2]
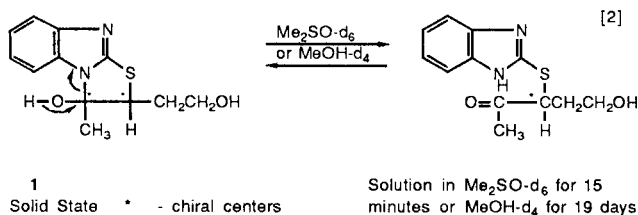
1
Solid State   * - chiral centers

Solution in Me$_2$SO-d$_6$ for 15 minutes or MeOH-d$_4$ for 19 days

chiral centers made the assignment of the chemical shifts of the nmr spectrum very difficult. In order to eliminate the opening of the ring, the polar solvent deuteriodimethylsulfoxide was replaced by the less polar deuteriomethanol. The proton nmr spectra were taken 15 minutes after dissolving **1** in deuteriomethanol and then at various time intervals ranging from 25 minutes to 19 days after sample preparation. After the 19 days study, the deuteriomethanol solution was evaporated to dryness and an ir spectrum of the residue was obtained for comparison to the ir spectrum of **1** prior to dissolving the sample in deuteriomethanol. The nmr spectrum of **1** taken after 15 minutes in solution was in complete agreement for our proposed structure **1**; δ 2.02 (s, 3, a), 2.10-2.30, center 2.20
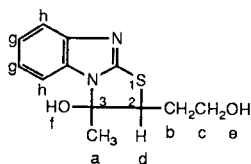

(m, 2, b), 3.70 (t, 2, c), 4.42 (q, 1, d), 4.75 (s, 2, e + f) exchanged with deuterium oxide, 7.00-7.30, center 7.15 (m, 2, g), 7.30-7.70 center 7.50 (m, 2, h). However, the nmr spectrum of **1** after remaining in solution for 19 days furnished evidence for ring opening as illustrated in reaction 2; δ 1.60 (s, 3, a), 1.80-2.50 (br m, 3, b + c), 3.60-4.00 center 3.80 (m, 3, b + d), 4.75 (s, 1, e) exchanged with deuterium oxide 7.00 (s, 1, f) exchanged with deuterium oxide 7.00-7.30 center 7.15 (m, 2, g), 7.30-7.70 center 7.50 (m, 2,

h). The key changes in the spectrum are the appearance of chemical shifts for the methyl protons of the acetyl group at 1.60 ppm and the imino proton of the benzimidazole ring at 7.00 ppm and the disappearance of the methine proton at 4.42 ppm.
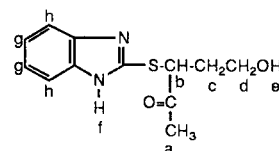

Additional proof for the ring opening process (reaction 2) was obtained from the ir spectrum of **1** after standing in deuteriomethanol solution for 19 days. The ir spectrum of this sample exhibited an extremely strong carbonyl stretch at 1730 cm^{-1} and the loss of the C–O of tertiary OH stretch at 1154 cm^{-1}. Isolation of the precursor, 3-acetyl-3-(2-benzimidazolthio)propyl-1-ol, and its identification by ir and nmr spectral data lends support for the mechanism depicted in Scheme 1.

Scheme 1

Precursor
3-acetyl-3-(2-benzimidazolthio)-
propyl-1-ol.

1
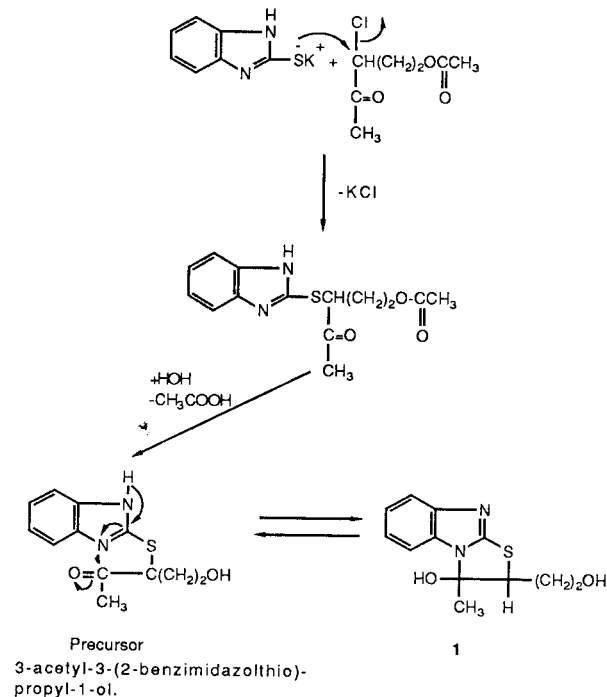
The reaction of **1** with *p*-fluorophenyl isocyanate in a mole/mole ratio afforded 2-(2,3-dihydro-3-hydroxy-3-methyl-2-thiazolo[3,2-*a*]benzimidazolyl)ethyl ester (4-fluorophenyl)carbamic acid (**2**) in a 67% yield. It is noteworthy that in reaction 3 *p*-fluorophenyl isocyanate reacted only with the primary alcohol (2-ethanol) and not with the bulky tertiary alcohol (3-hydroxy-3-methyl). Carbamates or carbanilates can be obtained from tertiary alcohols only with great difficulty. The isocyanate causes dehydration to occur with the formation of the olefin and di-

substituted urea [12]. In order to obtain conclusive and definitive proof for the proposed structure **2** and additional support for our proposed structure **1**, an X-ray crystallographic study was undertaken.
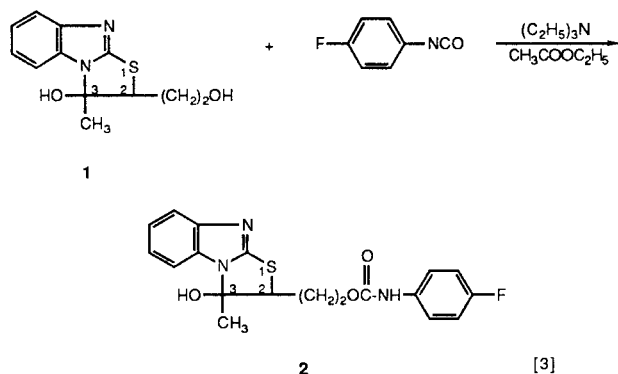
A listing of atomic fractional coordinates and equivalent isotropic thermal factors for all atoms contained in the asymmetric unit can be found in Table I, anisotropic temperature factors in Table II, and bond lengths and angles for non-hydrogen atoms in Tables III and IV. An ORTEP perspective view of **2** is presented in Figure 1, the labeling scheme consistent with that used for Tables I-IV. Bond distances are depicte in Figure 2.

As illustrated in Figure 1, the asymmetric unit contains twenty-seven general position non-hydrogen atoms, comprising two phenyl rings and associated fused five-membered heterocycles. There exist no particularly surprising bond interactions for the structure save the slightly elongated bond between S and C10 of 1.842(5) Å, only slightly different from a normal value of approximately 1.780 Å for a sulfur-sp^3 carbon bond distance. The most obvious structural feature present in this molecule is the striking coplanarity of the three rings made up of atoms contained in the phenyl substituent labeled C2 through
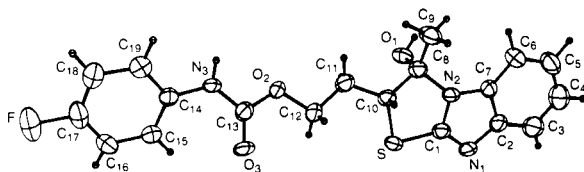

Figure 1. An Ortep drawing showing the molecular configuration of **2**.
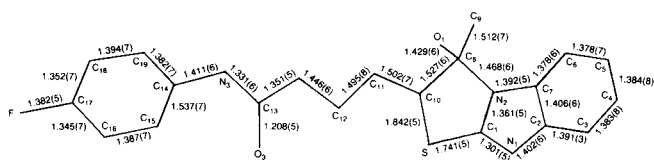

Figure 2. Selected bond distances for **2**.

Table I

Atomic Fractional Coordinates for Crystalline **2** [a]

Atom	x	y	z	B(Å)^3
S	0.4650(3)	0.52383(11)	0.29002(6)	3.82(3)
F1	−1.1215(8)	0.6330(4)	0.0214(1)	6.9(1)
O1	0.6106(7)	0.8093(3)	0.2999(1)	3.6(1)
O2	−0.1100(8)	0.7057(4)	0.1979(1)	3.76(9)
O3	−0.2852(8)	0.5339(3)	0.1703(1)	4.5(1)
N1	0.7867(9)	0.4902(4)	0.3610(2)	3.7(1)
N2	0.5681(8)	0.6654(4)	0.3553(1)	2.8(1)
N3	−0.4137(9)	0.7232(4)	0.1496(2)	3.3(1)
C1	0.6253(10)	0.5537(5)	0.3386(2)	2.9(1)
C2	0.8488(11)	0.5679(6)	0.3958(2)	3.5(1)
C3	1.0184(13)	0.5493(6)	0.4299(2)	5.3(2)
C4	1.0447(14)	0.6409(7)	0.4607(2)	5.9(2)
C5	0.9089(14)	0.7482(6)	0.4574(2)	4.8(2)
C6	0.7414(13)	0.7695(6)	0.4238(2)	4.1(2)
C7	0.7147(11)	0.6782(5)	0.3928(2)	2.9(1)
C8	0.4324(11)	0.7501(5)	0.3264(2)	3.1(1)
C9	0.2745(12)	0.8399(6)	0.3509(2)	4.1(2)
C10	0.2806(10)	0.6642(5)	0.2970(2)	2.9(1)
C11	0.1851(11)	0.7190(5)	0.2552(2)	3.4(1)
C12	0.0417(12)	0.6317(5)	0.2269(2)	4.2(2)
C13	−0.2729(11)	0.6443(5)	0.1720(2)	3.3(1)
C14	−0.5955(10)	0.6940(5)	0.1176(2)	2.9(1)
C15	−0.5809(11)	0.5915(5)	0.0917(2)	3.4(1)
C16	−0.7621(12)	0.5698(6)	0.0600(2)	3.9(2)
C17	−0.9431(11)	0.6529(6)	0.0535(2)	4.1(2)
C18	−0.9688(13)	0.7545(6)	0.0781(2)	4.6(2)
C19	−0.7893(12)	0.7750(6)	0.1105(2)	3.7(1)
H1	0.665(9)	0.870(4)	0.313(1)	4(1)*
H3N	−0.409(8)	0.786(4)	0.154(1)	2(1)*
H3C	1.101(11)	0.486(5)	0.432(2)	6(2)*
H4	1.162(12)	0.632(6)	0.485(2)	8(2)*
H5	0.926(9)	0.814(5)	0.479(1)	4(1)*
H6	0.634(7)	0.847(3)	0.422(1)	0.8(9)*
H9A	0.151(9)	0.797(5)	0.377(2)	4(1)*
H9B	0.146(9)	0.873(4)	0.331(2)	4(1)*
H9C	0.373(8)	0.891(4)	0.365(1)	3(1)*
H10	0.139(7)	0.637(3)	0.313(1)	0.7(9)*
H11A	0.310(7)	0.747(3)	0.243(1)	0.8(9)*
H11B	0.098(10)	0.793(5)	0.262(2)	5(1)*
H12A	−0.040(8)	0.602(4)	0.245(1)	2(1)*
H12B	0.159(11)	0.568(6)	0.210(2)	7(2)*
H15	−0.449(8)	0.538(4)	0.097(1)	2(1)*
H16	−0.751(8)	0.512(4)	0.042(1)	2(1)*
H18	−1.083(9)	0.812(5)	0.072(2)	4(1)*
H19	−0.816(11)	0.841(5)	0.131(2)	7(2)*

[a] Starred atoms were refined isotropically. Anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as: (4/3) * [a^2 * B(1,1) + b^2 * B(2,2) + c^2 * B(3,3) + ab(cos γ) * B(1,2) + ac(cos β) * B(1,3) + bc(cos α) * B(2,3)].

Table II

Anisotropic Thermal Parameters for Crystalline **2** [a]

Atom	B11	B22	B33	B12	B13	B23
S	5.02(8)	2.02(6)	4.32(7)	0.31(7)	−1.90(6)	−0.65(7)
F1	6.8(2)	8.3(3)	5.5(2)	−0.3(2)	−3.4(2)	−1.0(2)
O1	3.8(2)	2.4(2)	4.6(2)	−0.6(2)	−0.1(2)	−0.7(2)
O2	4.9(2)	2.3(2)	3.9(2)	−0.3(2)	−2.3(2)	0.5(2)
O3	5.4(2)	1.6(2)	6.5(2)	−0.7(2)	−2.6(2)	0.8(2)
N1	5.0(3)	2.0(2)	4.1(2)	0.5(2)	−1.9(2)	0.1(2)
N2	3.2(2)	1.9(2)	3.2(2)	0.6(2)	−0.6(2)	−0.4(2)
N3	3.6(2)	1.5(2)	4.7(2)	−0.2(2)	−1.8(2)	0.0(2)
C1	2.9(3)	2.3(3)	3.6(3)	−0.2(2)	−0.5(2)	0.0(2)
C2	4.1(3)	2.9(3)	3.5(3)	−0.1(3)	−1.3(2)	0.3(2)
C3	6.3(4)	4.2(4)	5.2(3)	0.8(3)	−2.5(3)	−0.1(3)
C4	6.2(4)	6.5(4)	4.8(3)	0.3(4)	−2.9(3)	−0.2(3)
C5	5.5(4)	5.1(4)	3.8(3)	0.0(3)	−1.0(3)	−1.4(3)
C6	5.3(4)	3.6(3)	3.5(3)	0.2(3)	0.2(3)	−0.9(3)
C7	3.5(3)	2.8(3)	2.6(3)	−0.5(2)	−0.3(2)	0.1(2)
C8	3.6(3)	2.5(3)	3.1(3)	−0.3(3)	0.2(3)	−0.0(2)
C9	4.0(3)	3.4(3)	4.8(3)	1.0(3)	−0.9(3)	−1.6(3)
C10	2.9(3)	2.2(2)	3.5(3)	−0.6(2)	−0.6(2)	0.3(2)
C11	3.4(3)	2.7(3)	4.1(3)	−0.3(3)	−0.6(3)	0.5(3)
C12	5.4(3)	2.9(3)	4.2(3)	−0.6(3)	−2.4(3)	0.6(3)
C13	3.3(3)	2.8(3)	3.6(3)	−0.4(2)	−0.9(2)	0.7(3)
C14	3.1(3)	2.4(3)	3.1(3)	−0.6(2)	−0.4(2)	0.5(2)
C15	3.9(3)	2.5(3)	3.7(3)	−0.2(3)	−0.6(3)	0.4(3)
C16	4.7(3)	3.1(3)	3.9(3)	−0.8(3)	−0.8(3)	−0.6(3)
C17	3.4(3)	5.2(4)	3.6(3)	−0.8(3)	−1.0(3)	0.0(3)
C18	4.4(3)	4.8(4)	4.5(3)	0.8(3)	−1.4(3)	−0.0(3)
C19	3.8(3)	3.3(3)	3.9(3)	0.2(3)	−0.4(3)	−0.1(3)

[a] The form of the anisotropic thermal parameter is:
$\exp[-0.25 \{h^2 a^2 B(1,1) + k^2 b^2 B(2,2) + l^2 c^2 B(3,3) + 2hkabB(1,2) + 2hlacB(1,3) + 2klbcB(2,3)\}]$ where a,b, and c are reciprocal lattice constants.

Table III

Interatomic Bond Lengths for Non-Hydrogen Atoms in Crystalline **2** [a]

Interaction	Distance (Å)	Average [b]
S – C1	1.741(5)	
S – C10	1.842(5)	
C1 – N1	1.301(5)	
C1 – N2	1.361(5)	
N1 – C2	1.402(6)	
C2 – C3	1.391(7)	
C3 – C4	1.383(8)	
C4 – C5	1.384(8)	
C5 – C6	1.378(7)	1.388(7,7,18,6)
C6 – C7	1.387(6)	
C7 – C2	1.406(6)	
C7 – N2	1.392(5)	
N2 – C8	1.468(6)	

Interaction	Distance (Å)	Average [b]
C8 – C9	1.512(7)	
C8 – O1	1.429(6)	
C8 – C10	1.527(6)	
C10 – C11	1.502(7)	
C11 – C12	1.495(8)	
C12 – O2	1.446(6)	
O2 – C13	1.351(5)	
C13 – O3	1.208(5)	
C13 – N3	1.331(6)	
N3 – C14	1.411(6)	
C14 – C15	1.376(7)	
C15 – C16	1.387(7)	
C16 – C17	1.345(7)	
C17 – C18	1.352(7)	1.373(7,16,28,6)
C18 – C19	1.394(7)	
C19 – C14	1.382(7)	
C17 – F1	1.382(5)	

[a] Numbers in parentheses are the estimated standard deviations in the least significant digit. [b] Where averaged, numbers in parentheses represent the average standard deviation, average deviation from the mean, maximum deviation, and the number of interactions averaged.

C7, the five-membered ring containing C2, C7, N1, N2 and C1, and the third cycle made up of C1, S, C10, C8 and N2. Dihedral angles between each of these mean planes are no larger than 0.6°, but there appears to be no extended conjugation for the twelve-atom fused system from consideration of the associated bond distances. Moreover, the crystal structure shows that all non-hydrogen atoms are planar to within ±0.007Å. In conclusion, since **2** was derived by the reaction of **1** with *p*-fluorophenyl isocyanate (reaction 3), the X-ray crystallographic study afforded conclusive proof for both structures **1** and **2**. Moreover, the ir and mass spectral data provided additional support for structure **2**. The electron impact and isobutane chemical ionization mass spectra furnished the molecular weight data in the form of M^+ 387 and $(M+1)^+$ 388, respectively. The presence of NH and OH (3420 cm⁻¹), aromatic CH (3151 and 3095 cm⁻¹), ArNH (C=O)O- (1733 cm⁻¹, CHCl₃ solution and 1694 cm⁻¹, solid state), Ar–C–F (1218 cm⁻¹), and C–O of tertiary alcohol (1075 cm⁻¹) absorptions bands in the ir spectrum furnished additional evidence for structure **2**. However, due to the insolubility of compound **2** in most common solvents including methanol, the nmr spectral data comparable to that obtained for compound **1** could not be obtained. However, the nmr spectra was obtained in deuteriodimethyl sulfoxide which exhibited the same complexity as that of compound **1** and was indicative of the same ring opening process as shown in reaction 2.

The reaction of 3-acetyl-3-chloropropyl acetate with ammonium dithiocarbamate afforded 4-methyl-5-(β-acetoxyethyl)-2-thiazolethione (**3**) in 71% yield. A British patent

$$NH_2CSNH_4 + CH_3C-CH(CH_2)_2OCCH_3$$

[4]

3
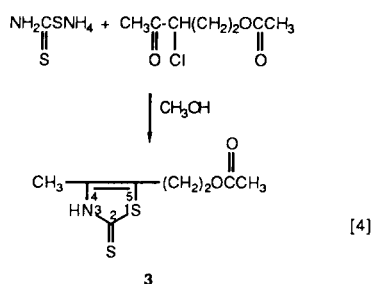
[13] mentioned **3** as an intermediate but gave no details as to its preparation. Analysis and nmr spectral data confirmed the proposed structure **3**. As noted in reaction 4, the ester group in the 5 position was not hydrolyzed to the alcohol moiety [2-ethanol]. The proposed mechanism of reaction 4 is depicted in Scheme 2.

Scheme 2

3
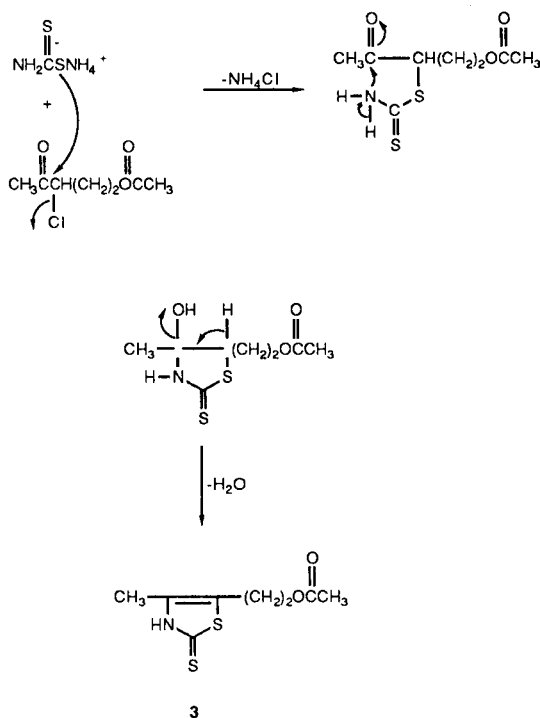
EXPERIMENTAL

The nmr spectra for **1** and **3** were obtained with an Varian EM-390 90 MHz and Varian T-60 nmr spectrophotometer, respectively. The chemical shifts are reported in δ using tetramethylsilane as an internal reference. All melting points were taken upon a Fisher-Johns block and are uncorrected. The electron impact spectra for **1** and **2** were determined with a Varian-MAT CH-7A mass spectrophotometer operating at an ionizing potential of 70 eV using a dirct insertion probe technique with a source temperature of 250°. This instrument was operated in the ClMS mode to obtain the chemical ionization mass spectra of **1** and **2**. The infrared spectra of **1** and **2** were obtained with a Beckman IR-12 spectrophotometer. The X-ray for **2** was determined by using a Syntex P2 diffractometer.

Table IV

Bond Angles for Non-Hydrogen Atoms in Crystalline **2** [a]

Interaction	Angle (deg)	Interaction	Angle (deg)
C1 – S – C10	90.1 (2)	S – C10 – C8	107.2 (3)
		S – C10 – C11	114.0 (4)
S – C1 – N1	132.1 (4)	C8 – C10 – C11	115.6 (4)
S – C1 – N2	112.4 (3)		
N1 – C1 – N2	115.5 (4)	C10 – C11 – C12	114.2 (5)
N1 – C2 – C3	129.1 (5)	O2 – C12 – C11	106.5 (5)
N1 – C2 – C7	74.0 (3)		
C3 – C2 – C7	120.3 (5)	C12 – O2 – C13	116.2 (4)
C2 – C3 – C4	117.8 (6)	O2 – C13 – O3	123.6 (5)
		O2 – C13 – N3	110.0 (4)
C3 – C4 – C5	121.0 (6)	O3 – C13 – N3	126.4 (5)
C4 – C5 – C6	122.4 (6)	C13 – N3 – C14	126.5 (5)
C5 – C6 – C7	116.9 (6)	N3 – C14 – C15	122.7 (5)
		N3 – C14 – C19	118.5 (5)
C6 – C7 – C2	121.6 (5)	C15 – C14 – C19	118.7 (5)
C6 – C7 – N2	133.8 (5)		
		C14 – C15 – C16	119.9 (6)
C7 – N2 – C8	135.0 (4)		
C7 – N2 – C1	105.9 (4)	C15 – C16 – C17	119.2 (6)
C1 – N2 – C8	116.6 (4)		
		F1 – C17 – C16	119.6 (5)
O1 – C8 – C9	112.7 (5)	F1 – C17 – C18	116.8 (5)
O1 – C8 – C10	107.4 (4)	C16 – C17 – C18	123.5 (5)
O1 – C8 – N2	107.3 (4)		
N2 – C8 – C9	112.6 (4)	C17 – C18 – C19	117.0 (6)
N2 – C8 – C10	103.0 (4)		
C9 – C8 – C10	113.2 (5)	C18 – C19 – C14	121.5 (6)

[a] Numbers in parentheses are the estimated standard deviations in the least significant digit.
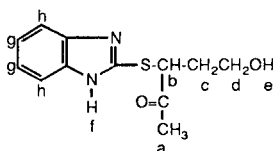
2,3-Dihydro-3-hydroxy-3-methylthiazolo[3,2-*a*]benzimidazole-2-ethanol (1).

A stirred charge containing 90.2 g (0.6 mole) of 2-mercaptobenzimidazole, 39.6 g (0.6 mole) of 85% potassium hydroxide and 1200 ml of methanol was heated at reflux for 15 minutes. After cooling the stirred solution to 20°, 107.2 g (0.6 mole) of 3-acetyl-3-chlorpropyl acetate [11] was added in one portion. An exothermic reaction set in causing a temperature rise from 20° to 35° over a 1 minute period. The reaction mixture was stirred at 25-30° for 24 hours. The reaction mixture was added to 4000 g of stirred ice-water and stirring continued at 0-10° for 5 hours. During this period the semi-solid which first formed turned to a crystalline solid. The solid was collected by filtration, washed with 500 ml of water and air-dried at 25-30°. The crude **1**, mp 126-128°, was obtained in 74% yield. After recrystallization from ethyl acetate **1** melted at 128-129°; ir (potassium bromide): 3358 and 3198 (intermolecular H-bonded OH), 3064 and 2996 (ArCH), 2953-2835 (alip CH), 1688 (C=N), 1611 (Ar ring), 1477 (CH$_2$ deform of C-CH$_2$), 1443 CH$_2$ deform of O-CH$_2$), 1351 (CH$_3$ sym deform), 1282 (ArC-N), 1154 (C-O of *t*-OH), 1066 (benzimidazole ring mode, 1044 (C-O of primary OH) and 742 (CH wag on *o*-subst Ar ring) cm⁻¹. Ir (2% solution by weight in deuteriodimethylsulfoxide): 1710 (CO of CH$_3$CO-), 1423 (CH$_3$ asym of CH$_3$CO-) and 1339 (CH$_3$ syn of CH$_3$CO) cm⁻¹. Ir (after 19 days in deuteriomethanol and sol-

vent removed by evaporation) 1730 ($-COCH_3$) cm^{-1} and the loss of the C-O of tertiary alcohol stretch at 1154 cm^{-1}; electron impact ms: m/e (relative intensity) 250 (25) M$^+$, 232 (12), 219 (15), 207 (10), 189 (16), 177 (66), 164 (58), 163 (25), 161 (26), 150 (100), 122 (21), 118 (18), and 43 (93); isobutane chemical ms: m/e 251 (M + 1)$^+$; nmr (after 15 minutes in deuteriomethanol): δ 2.02 (s, 3, a); 2.10-2.30 center 2.20 (m, 2, b), 3.70 (t, 2, c), 4.42 (q, 1, d), 4.75 (s, 2, e + f) exchanged with deuterium oxide, 7.00-7.30 center 7.15 (m, 2, g), 7.30-7.70 center 7.50 (m, 2, h);
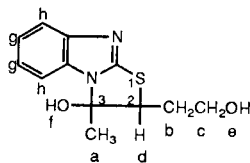
nmr (after 19 days in deuteriomethanol): δ 1.60 (s, 3, a), 1.80-2.50 (br m, 3, b + c), 3.60-4.00 center 3.80 (m, 3, b + d), 4.75 (s, 1, e) exchanged with deuterium oxide 7.00 (s, 1, f) exchanged with deuterium oxide, 7.00-7.30 center 7.15 (m, 2, g), 7.30-7.70 center 7.50 (m, 2, f).

Anal. Calcd. for $C_{12}H_{14}N_2O_2S$: C, 57.58; H, 5.64; N, 11.19; O, 12.78; S, 12.81. Found: C, 57.68; H, 5.71; N, 11.29; O, 12.94; S, 12.82.

2-(2,3-Dihydro-3-hydroxy-3-methyl-2-thiazolo[3,2-a]benzimidazolyl)-ethyl Ester (4-Fluorophenyl)carbamic Acid (2).

To a stirred slurry containing 25 g (0.1 mole) of **1**, 1 ml of triethylamine and 100 ml of ethyl acetate, 13.7 g (0.1 mole) of *p*-fluorophenyl isocyanate was added in one portion. The stirred reaction mixture was heated at reflux for 5 hours and thereafter at 25-30° for 18 hours. After the mixture was stirred at 0-10° for 30 minutes, the solid was collected by filtration and air-dried at 25-30°. Crude **2**, mp 173-174°, was obtained in 67% yield. After recrystallization from ethyl acetate **2** melted at 184-185°; ir (potassium bromide): 3420 (NH and OH), 3151 and 3095 (ArCH), 2992-2808 (aliphatic CH), 1733 (chloroform solution) and 1694 (solid) (ArNH (C=O)O-), 1613 and 1511 (Ar ring modes), 1539 (CNH deform), 1475 (asym CH_3 deform), 1448 (CH_2 deform), 1218 (ArCF), 1075 (C-O of *t*-alcohol), 835 (H wag on *p* subst Ar), and 734 (H wag on *o*-subst Ar) cm^{-1}; electron impact ms: m/e (relative intensity) 387 (8) M$^+$, 219 (16), 189 (28), 177 (19), 164 (16), 150 (67), 137 (17), 122 (22), 118 (12), 110 (24) and 43 (100); isobutane chemical ionization ms: m/e 388 (M + 1)$^+$.

Anal. Calcd. for $C_{19}H_{18}FN_3O_3S$: C, 58.89; H, 4.68; F, 4.90; N, 10.84, S, 8.27. Found: C, 58.90; H, 4.77; F, 5.03; N, 10.56; S, 8.26.

4-Methyl-5-(β-acetoxyethyl)-2-thiazolinethione (3).

To a stirred slurry containing 88 g (0.80 mole) of ammonium dithiocarbamate in 400 ml of methanol, 134 g (0.75 mole) of 3-acetyl-3-chloropropyl acetate [11] was added in one portion. An exothermic reaction set in causing a temperature rise from 22° to 64° over a 3 minute period. The reaction mixture was stirred for 24 hours. After the addition of 2 ℓ of water stirring was continued at 25-30° for 30 minutes. The solid was collected by filtration, washed with 500 ml of water and air-dried at 25-30°. Crude **3**, mp 95-96°, was obtained in 71% yield. After recrystallization from ethyl alcohol the melting point remained unchanged; nmr (deuteriochloroform): δ 2.09 (s, 3, $CH_3C=C$), 2.19 (s, 3, $-COCH_3$), 2.84 (t, 2, $-C=CCH_2$), 4.20 (t, 2, $-CH_2O$), 12.30 (br s, 1, NH).

Anal. Calcd. for $C_8H_{11}NO_2S_2$: C, 44.21; H, 5.10; N, 6.45; O, 14.73; S, 29.51. Found: C, 44.02; H, 5.22; N, 6.24; O, 14.56; S, 29.65.

Crystal Data for 2.

Single crystals of **2** suitable for use in X-ray diffraction studies were obtained from slow evaporation of an ethanol solution at 20°. A rectangular tabloid shaped crystal with dimensions 0.54 x 0.35 x 0.25 mm was mounted on a thin glass fiber and optically aligned on a Syntex (Nicolet) P2$_1$ autodiffractometer. Crystals of **2** are monoclinic, space group P2$_1$/n an alternative setting of P2$_1$/c-C$_{2h}^5$, No. 14 [14] with a = 5.395(2)Å, b = 10.916(3)Å, C = 30.812(7)Å, β = 91.28°, and Z = 4.

Intensity measurements were collected for 3343 independent reflections with 2 θ < 50.70° (the equivalent of 0.70 limiting CuKα spheres), using the theta-two theta scanning technique and a variable scan rate (3.0 deg/min to 9.0 deg/min). Background counts were accumulated 1.0 degree above and below the calculated Kα doublet value for each reflection. The total background count time used was half the total peak accumulation time. Three standard reflections were measured every 100 reflections as a monitor for crystal deterioration and/or disalignment and gave no indication of either. No absorption correction was applied to the intensity data which were reduced to a set of relative structure factors after corrections for Lorentz and polarization effects.

All computer programs utilized for data reduction, structure solution and refinement were those contained in the "Structure Determination Package" [15]. The atomic coordinates for all twenty-seven non-hydrogen atoms were deduced from the E-map calculated from the initial trial phase set output from MULTAN. The atomic fractional coordinates and isotropic thermal parameters for these twenty-seven atoms were refined in initial cycles of unit-weighted full-matrix least-squares and converged at conventional residuals (R$_1$ = 0.145 and R$_w$ = 0.153 for the 1426 reflections with 2θ < 50.70 degrees and I > 3.0 (sigma (I)). Further cycles of least-squares utilized anisotropic thermal factors for all non-hydrogen atoms and reached convergence at R$_1$ = 0.086 and R$_w$ = 0.098 for the 1426 reflection data set. Coordinates for the eighteen hydrogen atoms contained in the asymmetric unit were deduced from successive difference Fourier syntheses. Final cycles of least-squares employed a non-Poisson weight scheme, a least-squares refinable extinction correction, and isotropic refinement of all hydrogen atoms and converged at R$_1$ = 0.057 and R$_w$ = 0.061 for 1426 reflections. The highest residual peak in a difference Fourier map calculated at this point had an electron density of 0.25 electrons/Å^3. No residual peaks could be attributed to ethanol solvate.

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