2,1-Benzisothiazoline 2,2-Dioxide and Derivatives

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Synthesis of new 2,1-benzisothiazoline 2,2-dioxides **1** and some of its benzene ring substitution derivatives was accomplished by two different methods of cyclisation. Also a number of new *N*-substituted derivatives, obtained by treatment of **1** and analogues with aliphatic and aromatic acid chlorides are described.

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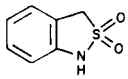
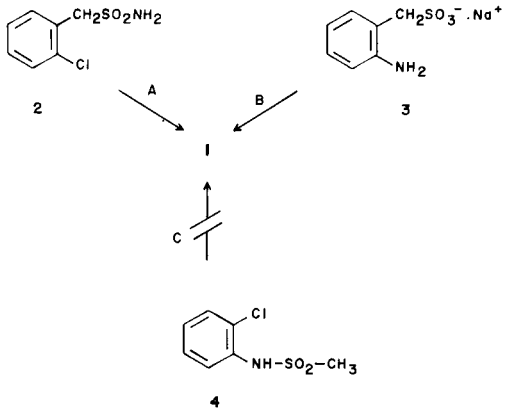
Several derivatives of 1,3-dihydro-2,1-benzisothiazole 2,2-dioxide (**1**) were previously described [1-5], however *N*-unsubstituted and *n*-acylated compounds listed in Tables I and II are new.



1

We were able to obtain **1** by cyclisation of 2-chlorobenzylsulfonamide **2** or the 2-aminobenzylsulfonic acid sodium salt **3**, whereas previous attempts to ring close 2'-chloromethanesulfonanilide **4** with potassium amide in liquid ammonia failed [1,4].

Scheme 1



The synthetic route A (Scheme 1) was carried out by heating a mixture of **2**, potassium carbonate and copper-bronze powder in 2,3-dimethylaniline as the solvent. The reaction B was accomplished warming **3** and phosphorus oxychloride at reflux.

Cyclisation of **2** bearing alkyl- and halo-groups on the benzene ring gave the corresponding substituted derivatives of **1**, while direct halogenation of **1** by chlorine and *N*-bromosuccinimide afforded respectively 5-chloro and 5-bromo compounds **6** and **8** (Table I).

Nitration of **1** under different conditions gave 5,7-dinitro derivative or a mixture of mono and dinitro compounds. The 5-nitro isomer **10** was obtained by nitration of 1-ethoxycarbonyl derivatives of **1** followed by hydrolysis with ammonia in ethanol.

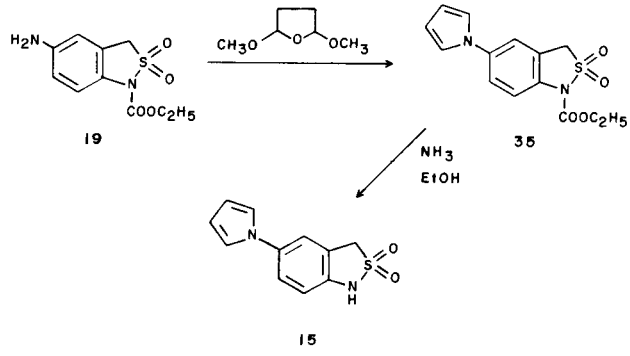
The sodium salt of **1** was treated with alkyl halides to give the corresponding *N*-alkyl compounds, in particular *N*-methyl and *N*-(2-dimethylaminoethyl) derivatives **41** and **42** (Table II) appear to be identical to samples prepared as previously described [1,4].

The *N*-acyl, *N*-aroyl and *N*-sulfonyl compounds were prepared from *N*-unsubstituted derivative by reaction with a carboxylic or sulfonic acid chloride in pyridine.

By catalytic reduction with palladium on carbon of the nitro derivatives the corresponding amines were obtained, which have been characterized as hydrochlorides and transformed into acetamides.

Reaction of 5-amino derivative **22** with 2,5-dimethoxy-2,3,4,5-tetrahydrofurane in acetic acid and successive hydrolysis with ammonia in ethanol gave the 5-pyrrol-1-yl derivatives **18** (Scheme 2).

Scheme 2

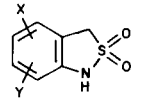


EXPERIMENTAL

Melting points, measured by means of a Büchi SMP20 capillary apparatus, are uncorrected. Infrared spectra were obtained by means of a Pye-Unicam SP-3200 spectrophotometer and ultraviolet spectra by a Pye Unicam SP 1750 spectrophotometer. Proton nuclear magnetic resonance spectra were recorded on a Varian EM-360L spectrometer with tetramethylsilane as internal standard. The purity of each derivative was verified by means of elemental analysis for C, H, N, S and Cl or Br.

Table I

1-Unsubstituted 1,3-Dihydro-2,1-benzisothiazole 2,2-Dioxides



No.	X	Y	Yield %	Mp °C (Solvent)	Formula	Calcd./(Found) C	H	N	S	Cl
1	H	H	62 [b]	128-130 (A)	$C_7H_7NO_2S$	49.69 (49.19)	4.17 (4.13)	6.28 (6.27)	18.95 (19.03)	
5	4-Cl	H	56	176-178 (A)	$C_7H_6ClNO_2S$	41.28 (41.39)	2.97 (3.10)	6.88 (6.79)	15.75 (15.66)	17.41 (17.26)
6	5-Cl	H	63	144-146 (D)	$C_7H_6ClNO_2S$	41.28 (40.93)	2.97 (3.01)	6.88 (6.83)	15.75 (15.71)	17.41 (17.33)
7	6-Cl	H	46	153-155 (A)	$C_7H_6ClNO_2S$	41.28 (41.36)	2.97 (3.09)	6.88 (6.78)	15.75 (15.67)	17.41 (17.21)
8	Br	H	54	165-167 (E)	$C_7H_6BrNO_2S$	33.89 (33.96)	2.44 (2.45)	5.65 (5.67)	12.92 (12.92)	
9	4-Cl	6-Cl	25	120-122 (C)	$C_7H_5Cl_2NO_2S$	35.31 (35.32)	2.12 (2.12)	5.88 (5.92)	13.47 (13.40)	29.78 (29.62)
10	5-NO_2	H	69	231-235 (B)	$C_7H_6N_2O_4S$	39.25 (39.20)	2.82 (2.81)	13.08 (12.97)	14.97 (14.96)	
11	7-NO_2	H	3	237-240 (B)	$C_7H_6N_2O_4S$	39.25 (39.61)	2.82 (2.81)	13.08 (13.12)	14.97 (14.92)	
12	5-NO_2	7-NO_2	63	273-275 (B)	$C_7H_5N_3O_6S$	32.44 (32.96)	1.94 (2.00)	16.21 (16.02)	12.37 (12.32)	
13	5-NH_2·HCl	H	53	>300 dec (A)	$C_7H_9ClN_2O_2S$	38.09 (37.98)	4.11 (4.18)	12.70 (12.85)	14.53 (14.44)	16.07 (15.98)
14	7-NH_2·HCl	H	66	>300 dec (A)	$C_7H_9ClN_2O_2S$	38.09 (37.96)	4.11 (4.20)	12.70 (12.83)	14.53 (14.30)	16.07 (16.01)
15	5-CH_3CONH	H	41	210-212 (B)	$C_9H_{10}N_2O_3S$	47.78 (48.02)	4.46 (5.57)	12.38 (12.52)	14.17 (13.97)	
16	5-CH_3	H	36	112-114 (A)	$C_8H_9NO_2S$	52.44 (52.26)	4.95 (4.93)	7.65 (7.67)	17.50 (17.30)	
17	4-CH_3	H	58	143-145 (A)	$C_8H_9NO_2S$	52.44 (52.86)	4.95 (4.85)	7.65 (7.74)	17.50 (17.24)	
18	5-(pirrol-1-yl)	H	50	221-222 (E)	$C_{11}H_{10}N_2O_2S$	56.39 (56.83)	4.30 (4.38)	11.96 (12.05)	13.96 (13.53)	

[a] Recrystallization solvents: A = water, B = acetic acid, O = ethanol-water (1:4), D = 1,2-dichloroethane, E = ethanol. [b] Method B, yield 36%.

1,3-Dihydro-2,1-benzisothiazoline 2,2-Dioxide (**1**).

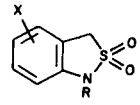
Method A.

To a stirred mixture of 30.25 g (0.22 mole) of potassium carbonate and 4 g of copper-bronze powder in 66 ml of 2,3-dimethylaniline were added portionwise 45 g (0.22 mole) of 2-chlorobenzylsulfonamide (**6**). The suspension was gradually heated to 180° distilling off a mixture of water and xylidine. Stirring was continued for 3 hours while the reaction mixture became rather thick. This was cooled, taken up in boiling ethanol and quickly filtered. The filtrate was evaporated, the residue was dissolved in boiling water and the aqueous solution was cooled and cautiously acidified with concentrated hydrochloric acid. After cooling to 4° the precipitate was filtered, washed with cold water and dried. The crude product was recrystallized from water to give 23 g (62%) of pure **1**, mp 128-130°; uv (methanol): λ max 283 mμ (ε 1,549) and 230 mμ (ε 6,702); ir (1% potassium bromide): 1330, 1140 cm^{-1} (SO_2); nmr (DMSO-d_6): δ 4.53 (s, 2H, CH_2), 7.53 (m, 4H, Ar).

Anal. Calcd. for $C_7H_4NO_2S$: C, 49.69; H, 4.17; N, 8.28; S, 18.95. Found: C, 49.49; H, 4.13; N, 8.27; S, 19.03.

Table II

1-Substituted 1,3-dihydro-2,1-benzisothiazole 2,2-Dioxide



No.	X	R	Yield %	Mp °C (Solvent) [a]	Formula	Calcd./(Found) C	H	N	S
19	H	COOEt	63	94-96 (A)	$C_{10}H_{11}NO_4S$	49.78	4.60	5.81	13.29
						(49.39)	(4.53)	(5.79)	(13.26)
20	6-Cl	COOEt	59	122-124 (A)	$C_{10}H_{10}ClNO_4S$	43.56	3.66	5.08	11.63
						(43.41)	(3.62)	(5.06)	(12.83)
21	5-NO_2	COOEt	86	127-129 (B)	$C_{10}H_{10}N_2O_6S$	41.96	3.52	9.76	11.20
						(41.94)	(3.57)	(9.84)	(11.11)
22	5-NH_2·HCl	COOEt	86	223-225 (E)	$C_{10}H_{13}ClN_2O_4S$	41.03	4.48	9.57	10.95
						(41.20)	(4.52)	(9.44)	(10.94)
23	5-CH_3CONH	COOEt	81	197-199 (B)	$C_{12}H_{14}N_2O_5S$	48.31	4.73	9.39	10.75
						(48.27)	(4.61)	(9.19)	(10.47)
24	H	$COCH_3$	72	115-117 (B)	$C_9H_9NO_3S$	51.18	4.29	6.63	15.18
						(51.07)	(4.37)	(6.59)	(15.09)
25	H	$COCH_2Cl$	41	132-134 (B)	$C_9H_8ClNO_3S$	44.00	3.28	5.70	13.05
						(44.03)	(3.26)	(5.70)	(12.95)
26	H	$COCH(CH_3)Ph$	76	140-142 (B)	$C_{16}H_{15}NO_3S$	63.77	5.01	4.65	10.64
						(63.56)	(5.00)	(4.66)	(10.53)
27	H	COPh	76	143-145 (B)	$C_{14}H_{11}NO_3S$	61.52	4.06	5.13	11.73
						(61.75)	(4.10)	(5.12)	(11.56)
28	H	CO-(2-Cl)Ph	75	155-157 (B)	$C_{14}H_{10}ClNO_3S$	54.64	3.27	4.55	10.42
						(54.28)	(3.27)	(4.52)	(10.42)
29	H	CO-(4-Cl)Ph	85	144-145 (B)	$C_{14}H_{10}ClNO_3S$	54.64	3.27	4.55	10.42
						(54.28)	(3.21)	(4.52)	(10.42)
30	4-Cl	CO-(4-Cl)Ph	73	158-160 (C)	$C_{14}H_9Cl_2NO_3S$	49.14	2.65	4.09	9.37
						(48.99)	(2.68)	(4.07)	(9.32)
31	5-Cl	CO-(4-Cl)Ph	78	153-155 (B)	$C_{14}H_9Cl_2NO_3S$	49.14	2.65	4.09	9.37
						(49.31)	(2.75)	(4.10)	(9.40)
32	6-Cl	CO-(4-Cl)Ph	64	136-138 (B)	$C_{14}H_9Cl_2NO_3S$	49.14	2.65	4.09	9.37
						(49.34)	(2.71)	(4.15)	(9.24)
33	5-Br	CO-(4-Cl)Ph	59	179-181 (C)	$C_{14}H_9ClBrNO_3S$	43.49	2.35	3.62	8.29
						(43.84)	(2.40)	(3.60)	(8.21)
34	5-NO_2	CO-(4-Cl)Ph	74	186-188 (C)	$C_{14}H_9ClN_2O_5S$	47.67	2.57	7.94	9.09
						(47.76)	(2.58)	(7.89)	(9.05)
35	7-NO_2	CO-(4-Cl)Ph	64	218-220 (C)	$C_{14}H_9ClN_2O_5S$	47.67	2.57	7.94	9.09
						(47.87)	(2.62)	(7.92)	(8.99)
36	5-CH_3	CO-(4-Cl)Ph	82	152-154 (B)	$C_{15}H_{12}ClNO_3S$	55.99	3.76	4.35	9.96
						(56.22)	(3.70)	(4.32)	(9.92)
37	H	SO_2-(4-CH_3)Ph	64	155-157 (B)	$C_{14}H_{13}NO_4S_2$	52.00	4.05	4.33	19.83
						(52.45)	(4.04)	(4.40)	(19.79)
38	5-pyrrolyl	COOEt	40	178-180 (D)	$C_{14}H_{14}N_2O_4S$	54.89	4.61	9.14	10.47
						(54.82)	(4.55)	(9.24)	(10.38)
39	H	CH_2COOEt	50	90-92 (A)	$C_{12}H_{13}NO_4S$	51.75	5.13	5.49	12.56
						(51.67)	(5.05)	(5.51)	(12.52)
40	H	CH_2COOH	67	128-130 (B)	$C_9H_9NO_4S$	47.57	3.99	6.16	14.11
						(47.82)	(4.00)	(6.12)	(13.96)
41	H	CH_3	58	91-92 [b] (A)	$C_8H_9NO_2S$	52.44	4.95	7.65	17.50
						(52.48)	(4.94)	(7.60)	(17.46)
42	H	$CH_2CH_2N(CH_3)_2$	62	44-46 [c] (F)	$C_{11}H_{16}N_2O_2S$	54.98	6.71	11.66	13.34
						(54.55)	(6.75)	(11.60)	(13.25)

[a]Recrystallization solvents: A = isopropylether, B = ethanol, C = acetonitrile, D = ethylacetate, E = water, F = isopropyl ether and exane. - (b) Lit (1) mp 89-91°. (c) Lit [4] mp 44-46.5°.

The same procedure was used for the preparation of derivatives **5**, **7**, **9**, **16**, and **17**. Yields, melting points and elemental analyses are reported in Table I.

Method B.

A stirred mixture of 10.5 g (0.05 mole) of 2-aminobenzylsulfonic acid sodium salt (**7**) and 60 ml of phosphorus oxychloride was refluxed for 3 hours at 170°. Excess of phosphorus oxychloride was distilled off under vacuum and 100 ml of water and ice mixture was added to the residue. The mixture was made alkaline with 20% sodium hydroxide, heated at 70° for a short time and filtered. The filtrate was acidified to *p*H 2.5 with concentrated hydrochloric acid and cooled to 4°. The precipitate was filtered, washed with cold water and dried. The crude product was recrystallized from water to give 3 g (36%) of **1**, mp 128-130°.

5-Chloro-1,3-dihydro-2,1-benzisothiazole 2,2-Dioxide (**6**).

To a stirred solution of 17 g (0.1 mole) of **1** in 70 ml of dimethylformamide was added portionwise at 0° 14 g (0.105 mole) of *N*-chlorosuccinimide. After having completed the addition, the cooling was discontinued and the temperature raised spontaneously to 30°. After 30 minutes the mixture was poured into 500 ml of ice water. The insoluble gum was taken up with ether and the solvent was evaporated. The residue was dissolved in 300 ml of warm aqueous 3.5% sodium bicarbonate, treated with activated carbon and filtered. The filtrate was cooled and acidified with concentrated hydrochloric acid. The precipitate was extracted with ether and the organic extracts were evaporated to dryness. The residue was crystallized from 1,2-dichloroethane and dried under vacuum, at 60° to give 12.75 g (63%) of **6**, mp 144-146°; uv (methanol): λ max, 293 mμ (ε 554) and 237 mμ (ε 10,555); ir (1% potassium bromide): 1305, 1140 cm^{-1} (SO_2); nmr (deuterioacetone): δ 4.43 (s, 2H, CH_2), 6.79-7.49 (m, 3H, ArH).

Anal. Calcd. for $C_7H_6ClNO_2S$: C, 41.28; H, 2.97; Cl, 17.41; N, 6.88; S, 15.75. Found: C, 40.93; H, 3.01; Cl, 17.33; N, 6.83; S, 15.71.

5-Bromo-1,3-dihydro-2,1-benzisothiazole 2,2-Dioxide (**8**).

To a stirred solution of 17 g (0.1 mole) of **1** in 230 ml of acetic acid was added dropwise at 20-25° a solution of 16 g (0.1 mole) of bromine in 100 ml of acetic acid. Stirring was continued for 30 minutes, then 8.5 g (0.1 mole) of anhydrous sodium acetate were added and the solution was concentrated to residue. This was dissolved in 600 ml of warm aqueous 1.7% sodium bicarbonate treated with activated carbon and filtered. The filtrate was acidified with concentrated hydrochloric acid and extracted with 600 ml of ether. The organic layers were washed twice with 100 ml of water, dried and evaporated. The crude crystalline residue (16 g) was recrystallized from 60 ml of ethanol and dried *in vacuo* to give 13.3 g (54%) of **8**, mp 165-167°; uv (methanol): λ max, 293 mμ (ε 1,516) and 237,5 mμ (ε 11,013); ir (1% potassium bromide): 1310, 1140 cm^{-1} (SO_2); nmr (deuterioacetone): δ 4.44 (s, 2H, CH_2), 6.74-7.60 (m, 3H, ArH).

Anal. Calcd. for $C_7H_6BrNO_2S$: C, 33.6; H, 2.44; Br, 32.21; N, 5.65; S, 12.92. Found: C, 33.96; H, 2.45; Br, 32.61; N, 5.67; S, 12.92.

1-(4-Chlorobenzoyl)-1,3-dihydro-2,1-benzisothiazole 2,2-Dioxide (**29**).

To a stirred solution of 17 g (0.1 mole) of **1** in 82 ml of anhydrous pyridine 18.4 g (0.15 mole) of 4-chlorobenzoylchloride were added dropwise at 0°. The suspension was stirred for 3 hours and poured into a mixture of 76 ml of concentrated hydrochloric acid and 400 ml of ice water. The precipitate was extracted with 300 ml of chloroform, and the extracts were washed with 300 ml of 1% hydrochloric acid, then with 200 ml of 1% sodium hydroxide and at last with water to neutral *p*H. The organic layers were dried and evaporated. The residue of 30 g of crude product was crystallized from 500 ml of ethanol to give 26.5 g (86%) of pure **29**, mp 144-146°; uv (methanol): λ max 247 mμ (ε 14,986) and 209 mμ (ε 18,172); ir (1% potassium bromide): 1320, 1150 cm^{-1} (SO_2); nmr (deuteriochloroform): δ 4.48 (s, 2H, CH_2), 6.95-8.35 (m, 8H, ArH).

Anal. Calcd. for $C_{14}H_{10}ClNO_3S$: C, 54.64; H, 3.27; Cl, 11.52; N, 4.55; S, 10.42. Found: C, 54.28; H, 3.27; Cl, 11.59; N, 4.52; S, 10.42.

The same procedure was used for the preparation of derivatives **19**, **20**, **24**, **26**, **27**, **28**, **30** to **37**. Yield, melting points and elemental analysis are reported in Table II.

1-Chloroacetyl-1,3-dihydro-2,1-benzisothiazole 2,2-Dioxide (**25**).

To a stirred suspension of 8.50 g (0.05 mole) of **1** and 12.4 g (1.055 moles) of anhydrous pyridine in 100 ml of anhydrous benzene was added dropwise a solution of 6.2 g (0.055 mole) of chloroacetylchloride in 15 ml of anhydrous benzene. The mixture was warmed at 60° for 3 hours to give an almost complete solution and poured into 300 ml of water. The organic layers were separated, washed thoroughly with 1% sodium hydroxide and with water, dried and evaporated. The residue (9.5 g) was recrystallized from 125 ml of ethanol to give 5 g (41%) of **25** mp 132-134°.

Anal. Calcd. for $C_9H_8ClNO_3S$: C, 44.00; H, 3.28; Cl, 14.43; N, 5.70; S, 13.05. Found: C, 44.03; H, 3.26; Cl, 14.33; N, 5.70; S, 12.95.

1-Ethoxycarbonyl-1,3-dihydro-5-nitro-2,1-benzisothiazole 2,2-Dioxide (**21**).

To 84 ml of 99% nitric acid cooled at 5° and kept under vigorous stirring, 20 g (0.083 mole) of 1-ethoxycarbonyl-1,3-dihydro-2,1-benzisothiazole 2,2-dioxide (**19**) was added over a 20 minutes period. The mixture was poured into 300 ml of ice water and the precipitate was extracted with ethyl acetate. The extracts were washed with water to neutral *p*H, dried and evaporated. The residue was recrystallized from ethanol to give 20.5 g (86%) of **21**, mp 136-138°.

Anal. Calcd. for $C_{10}H_{10}N_2O_6S$: C, 41.96; H, 3.52; N, 9.79; S, 11.20. Found: C, 41.94; H, 3.63; N, 9.84; S, 11.20.

5-Amino-1-ethoxycarbonyl-1,3-dihydro-2,1-benzisothiazole 2,2-Dioxide Hydrochloride (**22**).

A suspension of 27 g (0.095 mole) of **21** and 5.4 g of 10% palladium on carbon in 1000 ml of ethyl acetate was hydrogenated at 25° and 400 lbs/sq in pressure. After 5 hours the catalyst was filtered off and the filtrate was concentrated. The crystalline residue was dissolved in 300 ml of warm ethanol, filtered and acidified with a 10% hydrochloric acid ethanolic solution. After cooling, the precipitate was filtered and dried to yield 24 g (86%) of **22**, mp 223-225°; uv (methanol): λ max 310 mμ (ε 1,229) and 255 mμ (ε 16,142) ir (1% potassium bromide): 1375, 1152 cm^{-1} (SO_2).

Anal. Calcd. for $C_{10}H_{13}ClN_2O_4S$: C, 41.03; H, 4.48; N, 9.57; Cl, 12.11; S, 10.95. Found: C, 41.20; H, 4.52; N, 9.44; Cl, 12.03; S, 10.94.

5-Acetylamino-1-ethoxycarbonyl-1,3-dihydro-2,1-benzisothiazole 2,2-Dioxide (**23**).

To a stirred solution of 24 g (0.082 mole) of **22** and 16.4 g (0.162 mole) of triethylamine in 820 ml of benzene under argon was added portionwise 24 g (0.098 mole) of acetylchloride in 80 ml of benzene. The mixture was refluxed for 8 hours and the solvent was evaporated. The residue was stirred with 150 ml of 5% hydrochloric acid for 15 minutes, filtered, washed on the filter with water to neutral *p*H of the filtrate and dried. Recrystallisation from ethanol gave 19.8 g (81%) of **23**, mp 197-199°; uv (methanol): λ max, 258 mμ (ε 22,646); ir (1% potassium bromide): 1295, 1150 cm^{-1} (SO_2).

Anal. Calcd. for $C_{12}H_{14}N_2O_5S$: C, 48.31; H, 4.73; N, 9.39; S, 10.75. Found: C, 48.27; H, 4.61; N, 9.19; S, 10.47.

Ethyl 1,3-Dihydro-2,1-benzisothiazole-1-acetate 2,2-Dioxide (**39**), and 1,3-Dihydro-2,1-benzisothiazole-1-acetic Acid 2,2-Dioxide (**40**).

To a stirred solution of 1.6 g (0.04 mole) of sodium hydroxide in 10 ml of water and 1000 ml of ethanol were added 6.8 g (0.04 mole) of **1** and 5.4 g (0.04 mole) of ethyl chloroacetate. After refluxing for 18 hours, the solvent was distilled off, 10 ml of water were added and the mixture was extracted with ether. The organic layers were evaporated and the residue was crystallized from 300 ml of isopropyl ether to give 5.10 g of **39**, mp 90-92°; nmr (DMSO-d_6): δ 1.20 (t, 3H, CH_3), 4.15 (q, 2H, CH_2O), 4.53 (s, 2H, CH_2N), 4.72 (s, 2H, CH_2S), 7.7-6.8 (m, 4H, ArH).

Anal. Calcd. for $C_{12}H_{13}NO_4S$: C, 51.75; H, 5.13; N, 5.49; S, 12.56. Found: C, 51.67; H, 5.05; S, 12.52.

Hydrolysis of **39** with 1.5 equivalents of sodium hydroxide in water-ethanol solution gave **40**, mp 128-130°.

For the preparation of previously described derivatives **41** and **42**

(Table II) [1,4] the same procedure was adopted using methyl iodide and 2-dimethylaminoethyl chloride as the alkylating agents respectively.

1,3-Dihydro-5-nitro-2,1-benzisothiazoline 2,2-Dioxide (**10**).

Into a solution of 3.86 g (0.013 mole) of **21** in 75 ml of 96% ethanol stirred at reflux a stream of ammonia was bubbled. After two hours the mixture was concentrated and the residue was dissolved in 20 ml of 5% sodium idroxide. The solution was filtered and the filtrate was acidified with 10% hydrochloride acid. After cooling at 4°, the precipitate was filtered off washed with water and recrystallized from acetic acid giving 2 g (69%) of **10**, as yellow crystalline powder mp 233-235°; uv (methanol): λ max, 318 mμ (ε 10.015) and 207 mμ (ε 11.650); ir (1% potassium bromide): 1307, 1140 cm^{-1} (SO_2); nmr (DMSO-d_6): 4.70 (s, 2H, CH_2), 6.60-7.45 (m, 1H, ArH-4), 7.80-8.62 (m, 2H, ArH-6.7).

Anal. Calcd. for $C_7H_6N_2O_4S$: C, 39.25; H, 2.82; N, 13.08; S, 14.97. Found: C, 39.20; H, 2.82; N, 12.97; S, 14.96.

The same procedure was used for the preparation of derivatives **12** and **18** (Table I) from compounds **23** and **38** respectively.

1,3-Dihydro-5,7-dinitro-2,1-benzisothiazole 2,2-Dioxide (**12**).

To 200 ml of 65% nitric acid (d = 1.40) stirred and cooled below 10% were added portionwise 34 g (0.2 mole) of **1**. Stirring was continued for 30 minutes, then the mixture was poured into 1000 ml of ice water. A yellow precipitate was filtered, washed with water and dried to give 46 g of crude product which was recrystallized from 2000 ml of acetic acid to yield 32.5 g (63%) of **12** as yellow crystalline powder mp 273-275°; uv (methanol): λ max 363, 316, 256, 223 mμ; ir (1% potassium bromide): 1333, 1151 cm^{-1} (SO_2).

Anal. Calcd. for $C_7H_5N_3O_6S$: C, 32.44; H, 1.94; N, 16.21; S, 12.37. Found: C, 32.96; H, 2.00; N, 16.02; S, 12.32.

1,3-Dihydro-7-nitro-2,1-benzisothiazole 2,2-Dioxide (**11**).

To 200 ml of 65% nitric acid (d = 1.40) stirred and cooled below −6° were added portionwise 34 g (0.2 mole) of **1**. The solution was poured into 1000 ml of ice water and the resulting precipitate was filtered, washed with water and dried to give 36.5 g of 5,7-dinitro-, 5-nitro- and 7-nitro-derivative mixture. The mixture was refluxed for 2 hours in 750 ml of 1,2-dichloromethane and still hot filtered. The residue containing an enriched mixture of 5-nitro- and 5,7-dinitro-derivatives was discarded while the filtrate was evaporated to obtain 6.5 g of crude product which was recrystallized from 70 ml of acetic acid to give 1.3 g of **11**, mp 237-240°; uv (methanol): λ max 355 mμ (ε 3.961), 270 mμ (ε 6.948), 226 mμ (ε 12,446); ir (1% potassium bromide): 1330, 1132 cm^{-1} (SO_2); nmr (DMSO-d_6): δ 4.53 (s, 2H, CH_2), 6.7-7.5 (m, 4H, ArH).

Anal. Calcd. for $C_7H_6N_2O_4S$: C, 39.25; H, 2.82; N, 13.08; S, 14.97. Found: C, 39.61; H, 2.81; N, 13.12; S, 14.92.

5-Amino-1,3-dihydro-2,1-benzisothiazole 2,2-Dioxide Hydrochloride (**13**).

To a solution of 6.5 g (0.03 mole) of **10** in 750 ml of methanol containing 1.8 g (0.05 mole) of hydrochloride acid, was added 0.5 g of 10% palladium on carbon. The mixture was hydrogenated at room temperature and pressure until the absorption stopped (1 hour). The catalyst was filtered off and the solvent was evaporated. The residue was washed with ethanol and recrystallized from water to yield 4.7 g of **13**, crystalline powder which slowly decomposes by heating above 300°; ir (1% potassium bromide): 1320, 1150 cm^{-1} (SO_2).

Anal. Calcd. for $C_7H_9ClN_2O_2S$: N, 12.70; S, 14.53. Found: N, 12.85; S, 14.44.

The 7-amino-derivative **14** listed in Table I was prepared in the same manner.

Anal. Calcd. for $C_7H_9ClN_2O_2S$: N, 12.70; S, 14.53. Found: N, 12.83; S, 14.30.

1,3-Dihydro-1-ethoxycarbonyl-5-pyrrolyl-2,1-benzisothiazole 2,2-Dioxide (**38**).

To a stirred solution of 13.2 g (0.05 mole) of 5-amino-1,3-dihydro-1-ethoxycarbonyl-2,1-benzisothiazole 2,2-dioxide (**13**) in 70 ml of acetic acid was added dropwise 6.8 g (0.05 mole) of 2,6-dimethoxytetrahydrofuran. The mixture was refluxed for 30 minutes, cooled and filtered. The crystalline residue was washed with ether and crystallized from ethyl acetate to give 6.2 g (40%), mp 178-180°; uv (methanol): λ max 265 mμ (ε 22.079); ir (1% potassium bromide): 1315, 1142 cm^{-1} (SO_2).

Anal. Calcd. for $C_{14}H_{14}N_2O_4S$: C, 54.89; H, 4.61; N, 9.14; S, 10.47. Found: C, 54.82; H, 4.55; N, 9.24; S, 10.38.

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