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RING TRANSFORMATIONS OF 1,3-BENZOTHIAZINES, 5[1]

SYNTHESIS OF BENZISOTHIAZOLES BY THE OXIDATIVE RING CONTRACTION OF 2-ARYL-4H- AND 4-ARYL-2H-1,3-BENZOTHIAZINES

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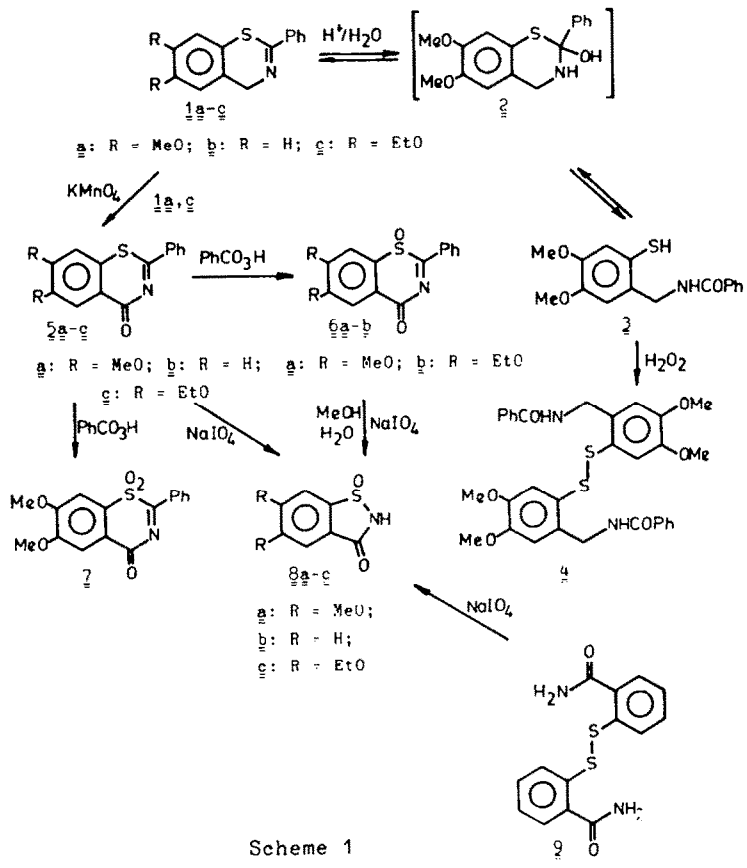
Abstract - 6,7-Dimethoxy-2-phenyl-4H-1,3-benzothiazine (1a) was oxidized with hydrogen peroxide to yield [2,2'-bis(benzoylamino-methyl)-4,4',5,5'-tetramethoxy]diphenyl disulfide (4). Potassium permanganate oxidation of 1a gave 6,7-dimethoxy-2-phenyl-4H-1,3-benzothiazin-4-one (5a), which was oxidized with the calculated amounts of perbenzoic acid to obtain the corresponding 1-oxide (6a) and 1,1-dioxide (7). Oxidation of 5a-c with sodium periodate involved ring contraction, affording 1,2-benzisothiazol-3(2H)-one 1-oxides (8a-c). A similar ring transformation was observed in the oxidation of 4-aryl-2H-1,3-benzothiazines (13a-f), resulting in the formation of 3-aryl-5,6-dialkoxy-1,2-benzisothiazoles (14a-f). The assumed mechanism of these ring transformations is discussed. The conversion of 1,3-benzothiazines to 1,2-benzisothiazoles actually represents a ring transformation reaction of 1,3-benzothiazines and a new synthesis of 1,2-benzisothiazole derivatives. The structures of the new compounds were confirmed by ir, ^{1}H and ^{13}C nmr spectroscopy.

In the course of our investigations of 1,3-benzothiazines,[2-7] we studied the oxidation reactions of 1,3-benzothiazine derivatives containing partially saturated hetero rings; we aimed at achieving syntheses of the sulfone derivatives, which hold out the promise of biological activity. Previously, only the oxidations of 3,4-dihydro-1,3-benzothiazin-4-ones and their N-substituted derivatives to sulfoxides[8,9] and sulfones[10-12] have been reported, and thus this work was also of chemical interest.

In our earlier experiments, chromic acid oxidation of 2-aryl-6,7-dialkoxy-4H-1,3-benzothiazine derivatives (1a,c) furnished the corresponding 4-oxo-4H-1,3-benzothiazines (5a,c).[13,14] Later, it was reported by other authors[8] that 2-phenyl-4H-1,3-benzothiazine (1b), containing no alkoxy groups, could not be converted to the 4-oxo derivative by oxidation with chromic acid. The latter compound (5b) was prepared by oxidation with potassium permanganate in acetone; however, further oxidation to the sulfoxide and sulfone by means of permanganate remained unsuccessful.

RESULTS AND DISCUSSION

In the present work, oxidation of 6,7-dimethoxy-2-phenyl-4*H*-1,3-benzothiazine (1a), with hydrogen peroxide in glacial acetic acid gave not the expected sulfone, but [2,2'-bis(benzoylaminomethyl)-4,4',5,5'-tetramethoxy] diphenyl disulfide (4) (Scheme 1).



Scheme 1

Under the given experimental conditions, the cyclic thioimide (1a) reacts in aqueous acid solution to add on the elements of water to give *N*-benzoyl-4,5-dimethoxy-2-mercaptobenzylamine (3) through ring cleavage of the transitory product 2;[15,16] in the presence of hydrogen peroxide, 3 is readily oxidized to the disulfide 4 (Scheme 1).

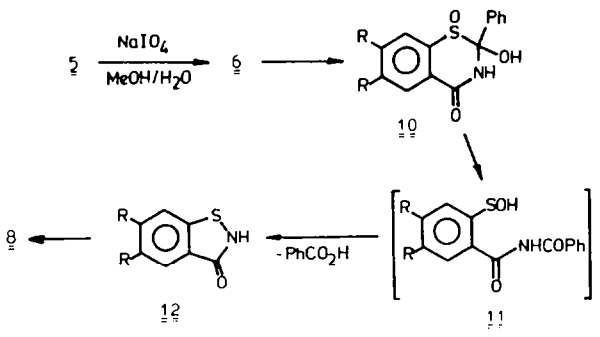
Potassium permanganate oxidation of 1a in acetone solution (similarly to chromic acid oxidation) furnished the 4-oxo derivative 5a in good yield. This product (5a) was successfully oxidized to the sulfoxide 6a and sulfone 7 by treatment with the calculated amounts of perbenzoic acid in chloroform solution (Scheme 1).

Attempted oxidation of 5a to the sulfoxide 6a by means of sodium periodate in aqueous methanol resulted in ring contraction to give 5,6-dimethoxy-1,2-benzisothiazol-3(2*H*)-one 1-oxide (8a), instead of the expected 6a (Scheme 1).

A similar reaction was observed in the sodium periodate oxidation of 2-phenyl-4*H*-1,3-benzothiazin-4-one (5b); the product was 1,2-benzisothiazol-3(2*H*)-one 1-oxide (8b). Compound 8b was also prepared through oxidation of diphenyl disulfide-2,2'-dicarboxamide 9 with sodium periodate (Scheme 1). The substances prepared by these two ways were identical with each other and with compound 8b synthesized via other routes by other authors.[17-19]

We assume that the 4-oxo-1,3-benzothiazine derivative 5 is oxidized by periodate first to the sulfoxide 6, followed by the addition of water to the C=N bond to give the transitory product 10. Ring-opening of the latter yields the sulfenic acid derivative 11, which loses benzoic acid to furnish the 1,2-benzisothiazol-3(2*H*)-one derivative 12; finally, this is oxidized to the sulfoxide 8 (Scheme 2).

The above mechanism is supported by the experiments in which the sulfoxide 6a, prepared by the perbenzoic acid oxidation of 5a, was treated with periodate under identical experimental conditions to give 1,2-benzisothiazol-3(2*H*)-one

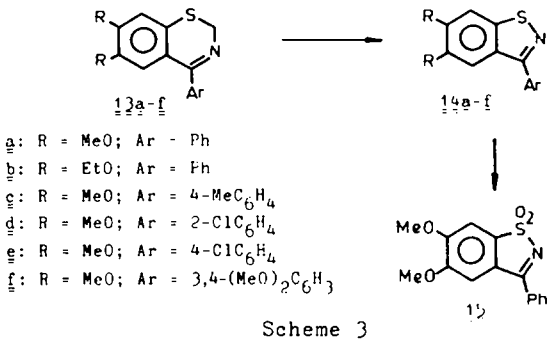


Scheme 2

1-oxide (8a). However, isolation of the 1,3-benzothiazine sulfoxide 6a from the periodate oxidation of 5a remained unsuccessful. On the other hand, during the periodate oxidation of 6,7-diethoxy-2-phenyl-4H-1,3-benzothiazin-4-one (5c), not only the end-product 8c, but also the intermediate of its formation, the 4-oxo-1,3-benzothiazine 1-oxide 6b, was isolated. When the sulfoxide 6a was stirred in aqueous methanol until complete dissolution, 5,6-dimethoxy-1,2-benzisothiazol-3(2H)-one (12) was isolated from the reaction mixture in high yield; this compound was oxidized with sodium periodate to the 1,2-benzisothiazol-3(2H)-one 1-oxide (8). These experiments support our suggestion that both 6 and 12 are intermediates of the oxidation (Schemes 1 and 2).

Further evidence seems to be provided by the observation of Morin and Spry[9] on the conversion of 2,2-dimethyl-3,4-dihydro-2H-1,3-benzothiazin-4-one 1-oxide into N-substituted 1,2-benzisothiazol-3(2H)-one.

A search of the literature did not reveal earlier data on the oxidation reactions of 2H-1,3-benzothiazines. We oxidized one representative of these compounds, 6,7-dimethoxy-4-phenyl-2H-1,3-benzothiazine (13a) with peracetic acid, when a ring transformation, similar to those described above, led to 5,6-dimethoxy-3-phenyl-1,2-benzisothiazole (14a). Peracetic acid oxidation of 14a gave the sulfone 15 (Scheme 3).



a: R = MeO; Ar = Ph
b: R = EtO; Ar = Ph
c: R = MeO; Ar = 4-MeC_6H_4
d: R = MeO; Ar = 2-ClC_6H_4
e: R = MeO; Ar = 4-ClC_6H_4
f: R = MeO; Ar = 3,4-$(MeO)_2C_6H_3$

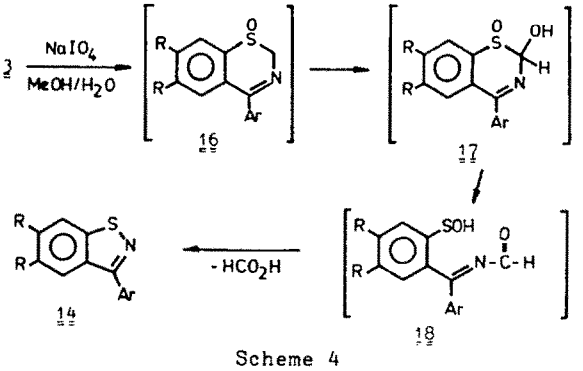
Scheme 3

By oxidation of the 2H-1,3-benzothiazine analogues 13a-f with periodate, we also obtained the 1,2-benzisothiazoles 14a-f, formed by ring contraction (Scheme 3).

It may be assumed that in the oxidations involving ring transformation, the benzothiazines 13 are first converted into the sulfoxides 16; further oxidation on the meso-carbon of 16 then gives the transitory products 17. Cleavage of the thiazine ring of 17 affords the sulfenic acid derivatives 18, which furnish the 1,2-benzisothiazoles 14 by the loss of formic acid (Scheme 4).

Although the assumed intermediate 16 could not be isolated, acidimetric titration of the reaction mixture at the end of the periodate oxidation showed the presence of about one equivalent of formic acid. The sulfur atom of the quasi-aromatic 1,2-isothiazole ring is not oxidized by periodate.

The above-described conversion of 1,3-benzothiazines into 1,2-benzisothiazoles represents a ring transformation reaction of 1,3-benzothiazines and also a new method of preparing 1,2-benzisothiazole derivatives.



Scheme 4

The assumed structures of the new compounds were confirmed by ir, ^{1}H and ^{13}C nmr spectroscopy. The spectral data proving the given constitutions are listed in Tables 1 and 2.

Table 1. ^{1}H nmr data (δ_{TMS} = 0 ppm, coupling constants in Hz) in $CDCl_3$ solution at 250 MHz and characteristic ir bands (KBr, cm^{-1}) of compounds 4, 5a, 6a,b, 7, 8a-c, 12a, 14a-f, 15

Compound	OCH_3 2xs[a]	OCH_3 (2x3H)	H-5 s(1H)	H-8 s(1H)	C-2',6' dd(2H)	C-3',5' dt(2H)	C-4' dt(1H)	Other ^{1}H nmr signals / ir bands
4	3.72	3.82	6.82	6.98	7.80	7.40	7.48	CH_2: 4.60 d (2H, J: 5.9) NH: 6.80 t (1H) / ∂NH: 3308, amide-I: 1639
5a	4.00	4.01	7.94	6.89	8.15	7.50	7.60	- / amide-I: 1641
6a[b]	3.81	3.89	7.56	7.23	7.68	7.47	7.60	- / ∂ C=O: 1705, ∂ C_{Ar}-C(=O): 1274, ∂ S=O: 1149
6b	4.10	4.20	7.29	6.89	7.72	7.45	7.55	CH_3: 1.47 t, (J: 7.0), 1.54 t (J: 7.1) / ∂C=O: 1707, ∂ C_{Ar}-C(=O): 1283, ∂S=O: 1155
7	3.99	4.06	7.36	7.38	7.79	7.48	7.62	- / ∂C=O: 1728, ∂ SO_2: 1265[c], 1105
8a	4.01	4.04	7.40	7.32	-	-	-	NH: ∿7.6 / ∂NH: 3275, ∂C=O: 1722, ∂ S=O: 1090
8b	-	-	8.03	7.92	-	-	-	NH: 8.83, H-6,7: 7.85, 7.94 2x∿t (2x1H) / ∂NH: 3130, ∂C=O: 1720, ∂S=O: 1099
8c	4.21	4.23	7.31	7.37	-	-	-	CH_3: 1.51, 1.53, 2xt (J: 7), NH: 8.84, ∂NH: ∿3500, ∂C=O: 1705, ∂S=O: 1099
12a	3.97	3.99	7.43	7.02	-	-	-	- / ∂NH: 3260, amide-I: 1650
14a	3.93	4.00	7.33	7.47	7.83	7.51	7.54	- / -
14b	4.11	4.17	7.30	7.48	7.83	7.50[d]		CH_3: 1.48, 1.52, 2xt (J: 7) / -
14c	3.92	3.99	7.31	7.46	7.75[e]	7.35[e]	-	CH_3: (4'): 2.44 s (3H) / -
14d[f]	3.86	3.98	7.33	7.05	7.4 - 7.6[d,g]			- / -
14e	3.94	4.01	7.33	7.39	7.80[e]	7.52[e]	-	- / -
14f	3.94	3.97[d]	7.33	7.50	7.41[h] 7.48	3.97[d,i] 7.03[h]	4.01[i]	- / -
15	3.96	4.05	7.20	7.47	7.94	7.64	7.70	- / ∂ SO_2: 1334, 1318 and 1164, 1146[k]

[a] Methylene signal, 2xqa (2x2H) for 6b, 8c and 14b. [b] In DMSO-d_6 solution. [c] Coalesced with the ∂C-O band of the methoxy groups. [d] Overlapping signals. [e] ∿d (2H): A or B part of an AA'BB' multiplet (J: 8.0 and 8.5 for 14c and 14e, respectively). [f] Measuring frequency: 80 MHz. [g] Intensity: 4H. [h] Doublet (J: 1.5 and 8.8 for H-2' and H-5', respectively). [i] OCH_3(veratryl), s(3H). [k] Split band-pairs.

EXPERIMENTAL

M.p.s (°C) are uncorrected.

The nmr spectra were recorded in $CDCl_3$ or DMSO-d_6 solution in 5 or 10 mm tubes at room temperature, on a Bruker WM-250 (^{1}H) or a WP-80 SY (^{13}C) FT spectrometer controlled by an Aspect 2000 computer at 250.13 (^{1}H) and 20.14 (^{13}C) MHz; the deuterium signal of the solvent was used as the lock and TMS as internal standard. The most important measurement parameters were: sweep width 5 kHz, pulse width 1 and 3.5 μs (∿20° and ∿30° flip angle), acquisition time 1.64 s, number of scans 16 or 32 (^{1}H) and 1-6 K (^{13}C), computer memory 16 K. Lorentzian exponential multiplication for signal-to-noise enhancement (line width: 0.7 and 1.0 Hz), and for ^{13}C nmr spectra proton noise decoupling (∿1.5 W) were applied.

Table 2. ^{13}C nmr chemical shifts (δ_{TMS} = 0 ppm) of compounds 4, 5a, 6a,b, 7, 8a-c, 12a, 14a-f, 15 in $CDCl_3$ or DMSO-d_6 solution[a] at 20 MHz

Compound	C-2	C-4	C-4a	C-8a	C-5	C-8	C-6	C-7	OCH_3(6,7)		C-1'	C-2',6'	C-3',5'	C-4'
4	167.3	42.3	135.1[b]	125.9	118.8	113.1	148.6	151.0	56.1[c]		134.5[b]	127.1	128.6	131.5
5a	168.7	171.8	128.8[c]	115.6	110.7	106.8	150.8	153.5	56.1	56.3	136.6	127.2[b]	128.8[b,c]	133.0
6a[d]	163.9	170.2	135.2[b]	118.0	109.2	105.3	150.3	157.1	57.5	57.9	137.2[b]	130.3[f]	129.4[f]	133.5
6b	163.0	169.0	135.8[b]	117.1	109.7	102.8	148.6	155.9	65.0[e]	65.3[e]	133.5[b]	128.0[f]	129.1[f]	132.2
7	163.8	170.7	140.3	122.2	109.3[b]	109.8[b]	155.0	157.1	58.2	58.5	135.0	130.8[f]	129.9[f]	134.5
8a	-	168.9	121.8	142.9	109.4[b]	108.1[b]	154.3[f]	155.6[f]	57.8	58.1	-	-	-	-
8b	-	169.1	128.9	149.8	127.0[b]	127.4[b]	134.8[f]	136.3[f]	-	-	-	-	-	-
8c	-	167.7	120.3	141.5	108.3[b]	108.5[b]	153.2[f]	154.7[f]	65.4[e]	65.6[e]	-	-	-	-
12a	-	166.9	142.3	119.2	106.8[b]	104.7[b]	150.1	154.7	57.6	57.8	-	-	-	-
14a	-	163.5	148.3[b]	128.0	105.1	100.7	149.2[b]	151.5[b]	56.3[c]		135.8	128.9[f]	128.5[f]	129.1
14b	-	163.3	148.3[b]	127.7	106.8	101.6	148.0[b]	150.9[b]	64.6[e]	65.0[e]	135.6	128.3[f]	128.6[f]	128.9
14c[g]	-	163.2	148.7[b]	127.7	104.9	100.4	147.9[b]	151.1[b]	56.0[c]		132.8	128.1[f]	129.3[f]	138.8
14d	-	151.6	149.0[b]	128.8	104.9	100.5	147.4[b]	151.6[b]	56.3[c]		134.6[f]	133.3[f] 131.7[h]	130.2[h] 126.9	130.4
14e	-	162.2	148.5[b]	127.8	104.7	100.8	149.3[b]	151.6[b]	56.3	56.3	134.2[f]	129.8[h]	129.1[h]	135.4[f]
14f	-	162.7	148.4[b]	128.2[f]	104.9	100.1	149.1[b]	150.7[b]	55.7[i]		127.3[f]	111.0[h] 120.5	149.7[b] 116.6[h]	147.6[b]
15	-	171.0	131.1[b]	123.7	105.8	108.4	154.2[f]	153.3[f]	56.7	56.9	135.4[b]	129.3[h]	129.4[h]	133.1

[a] Solvent DMSO-d_6 for compounds 6a, 7, 8a,b and 12a. [b,f,h] Assignments may also be reversed. [c] Two overlapping lines. [d] Measuring frequency: 63 MHz. [e] OCH_2 lines of the ethoxy groups; the methyl signals (coalesced) were found at 14.5 ppm (6b, 8b, 14b). [g] CH_3(4'): 21.1. [i] Four overlapping lines.

[2,2'-bis(Benzoylaminomethyl)-4,4'5,5'-tetramethoxy]diphenyl disulfide (4)

Compound 1a (1.43 g; 5 mmol) was dissolved in glacial acetic acid (10 ml) and 30% H_2O_2 (1 ml) was added dropwise, with cooling and stirring. The mixture was allowed to stand overnight. It was then diluted with water (5 ml); the precipitated product was filtered off and crystallized from glacial acetic acid to give 1.0 g (66%) of 4, m.p. 198-199 °C, which was in all respects identical with an authentic sample.

Ring cleavage in 4 is evidenced by the νNH and amide-I ir bands, characteristic of acid amides, and also by the triplet and doublet splittings of the NH and methylene signals, respectively, in the ^1H nmr spectra, indicative of the presence of the $-CH_2NH-$group.

6,7-Dimethoxy-2-phenyl-4H-1,3-benzothiazin-4-one (5a)

Potassium permanganate (4.24 g) was dissolved in acetone (200 ml) and a solution of 1a (2.85 g; 10 mmol) in acetone (50 ml) was added, with stirring and cooling in ice-water. Stirring was continued for 3 h. Chloroform (100 ml) was then added, and the precipitated MnO_2 was removed by filtration with suction, and washed with chloroform. The solvent was evaporated off and the residue was crystallized from ethanol (30 ml) to give light-yellow crystals (2.47 g; 83%) m.p. 195-196 °C, identical with an authentic sample.[14, 15]

The structure of 5a is proved by the presence of the amide-I band in the ir spectrum and its low frequency characteristic of acylamino compounds;[20-25] further evidence is the lack of the signal of the methylene proton in the ^1H nmr spectrum, while the H-5 line has suffered a strong paramagnetic shift (by 1.12 ppm as compared with 4), due to the anisotropic effect of the coplanar carbonyl group.[26a] Finally, the carbon resonance signal of the amide carbonyl is found in the range expected[26b] (171.8 ppm).

6,7-Dimethoxy-2-phenyl-4H-1,3-benzothiazin-4-one 1-oxide (6a)

A solution of 5a (1.5 g; 5 mmol) in chloroform (20 ml) was treated with perbenzoic acid (0.69 g; 5 mmol) dissolved in chloroform (30 ml). The mixture was allowed to stand at room temperature for 2 days. It was then washed with aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4) and evaporated. The residue was crystallized from methanol to yield 1.35 g (49%) of 6a: colorless crystals from ethanol, m.p. 227-228 °C (decompn.). (Found: C, 60.70; H, 4.43; N, 4.26. $C_{16}H_{15}NO_4S$ requires: C, 60.94; H, 4.15; N, 4.44%.)

In the ir spectra of 6a,b, the strong -I effect of the sulfoxide group gives rise to a considerable increase of the carbonyl frequency;[27] thus, this signal is not found in the range of lower frequencies, characteristic of amides due to mesomerism, but at significantly higher wavenumbers. At the same time, the characteristic νS=O band of sulfoxides can be recognized in the ir spectrum. The repression of amide mesomerism (i.e. of the limiting structure $^{\ominus}O-C=N-C^{\oplus}$) is also well shown by the upfield shift of the C-2 signal; in 6a δ is 4.8 ppm less than in the spectrum of 5a.

6,7-Dimethoxy-2-phenyl-4H-1,3-benzothiazin-4-one 1,1-dioxide (7)

Compound 5a (1.0 g; 3.3 mmol) was dissolved in chloroform (10 ml). A solution of perbenzoic acid (0.92 g; 6.6 mmol) in chloroform (40 ml) was added, and the mixture was allowed to stand for 2 days. It was then washed with $NaHCO_3$ solution and with water and next dried (Na_2SO_4), and the solvent was evaporated off. The residue was crystallized from ethanol to give colorless needles (0.32 g; 29%), m.p. 244-245 °C. (Found: C, 58.26; H, 4.25; N, 4.50. $C_{16}H_{15}NO_5S$ requires: C, 58.00; H, 3.95; N, 4.23%.)

The spectral evidence given above for structure 6a also applies to 7, with the exception that the sulfoxide band in the ir spectrum is now replaced by the pair of intense $\nu_{as}SO_2$–ν_sSO_2 bands, appearing in the expected[28] frequency range. The substituent effect of the sulfone group, causing a downfield shift as compared with the effect of the sulfoxide substituent, can be observed on the C-6 and C-8 bands.

5,6-Dimethoxy-1,2-benzisothiazol-3(2H)-one 1-oxide (8a)

A solution of sodium periodate (1.7 g; 5 mmol) in water (10 ml) was added to a methanolic solution (50 ml) of compound 5a (1.49 g; 5 mmol). The mixture was stirred for 7 days, then concentrated, and the residue was treated with water (30 ml). The precipitated crystals were recrystallized from chloroform to give 1.02 g (90.2%) of 8a. A sample was recrystallized from ethyl acetate for analysis; colorless needles, m.p. 255-256 °C. (Found: C, 47.80; H, 4.29; S, 14.06. $C_9H_9NO_4S$ requires: C, 47.56; H, 3.99; S, 14.10%.)

1,2-Benzisothiazol-3(2H)-one 1-oxide (8b)

Compound 9 (1.21 g; 5 mmol) was dissolved in methanol (50 ml), and with stirring, a solution of sodium periodate (2.14 g; 6.6 mmol) in water (20 ml) was added. The mixture was stirred for 3 days. It was then concentrated, mixed with water (25 ml) and extracted with chloroform. After drying (Na_2SO_4), the solvent was evaporated off and the residue was purified by preparative thin-layer chromatography on silica gel, using benzene–methanol (10:1) as the developing solvent mixture. The product (0.6 g; 71.8%) was recrystallized from acetone; m.p. 157-158 °C. It was identical with the compound reported in the literature.[16]

Preparation of 1,2-benzisothiazol-3(2H)-one 1-oxide (8b) by periodate oxidation of 9

A mixture of 9 (1.01 g; 3.3 mmol) in methanol (70 ml) and sodium periodate (2.14 g; 6.6 mmol) in water (15 ml) was stirred for 2 days. The solution was concentrated, water (25 ml) was added and the mixture was extracted with chloroform. The extract was dried (Na_2SO_4) and the solvent was evaporated off to obtain colorless needles, m.p. 157-158 °C (from acetone). The product was identical with that described in the literature.[16]

Preparation of 5,6-dimethoxy-1,2-benzisothiazol-3(2H)-one 1-oxide (8a) by periodate oxidation of 6a

Compound 6a (0.63 g; 2 mmol) in methanol (50 ml) was mixed with an aqueous solution (10 ml) of sodium periodate (0.43 g; 2 mmol). The mixture was stirred for 7 days. It was then concentrated and the residue was treated with water (10 ml). The crystalline product (0.32 g; 70%) was filtered off and recrystallized from ethyl acetate to give colorless crystals, m.p. 255-256 °C, identical with the substance prepared by the periodate oxidation of 5a.

6,7-Diethoxy-2-phenyl-4H-1,3-benzothiazin-4-one 1-oxide (6b) and 5,6-diethoxy-1,2-benzisothiazol-3(2H)-one 1-oxide (8c)

A mixture of 5c (0.82 g; 2.5 mmol) in methanol (50 ml) and sodium periodate (1.07 g; 5 mmol) in water (15 ml) was stirred for 7 days. The solution was concentrated, water (100 ml) was added, and the precipitated crystalline product (6b) (0.5 g; 58%) was filtered off. Recrystallization from ethyl acetate gave colorless needles, m.p. 215-216 °C. (Found: C, 62.57; H, 5.03; N, 4.41. $C_{18}H_{17}NO_4S$ requires: C, 62.95; H, 4.98; N, 4.08%.)

The aqueous mother liquor of the above procedure was concentrated to 20 ml, whereupon compound 8c (0.1 g; 15.6%) separated out as colorless needles. After recrystallization from ethyl acetate the m.p. was 188-189 °C. (Found: C, 51.44; H, 5.44; N, 5.32. $C_{11}H_{13}NO_4S$ requires: C, 51.75; H, 5.13; N, 5.49%.)

5,6-Dimethoxy-1,2-benzisothiazol-3(2H)-one (12)

In a mixture of methanol (50 ml) and water (5 ml), compound 6a (0.96 g; 3.3 mmol) was stirred until complete dissolution. The solution was evaporated to dryness. The residue was dissolved in 5% sodium hydroxide, the solution was filtered, and the product was precipitated by acidification with 10% hydrochloric acid. The crystals were washed with water on the filter and dried to obtain a colorless crystalline product (0.55 g; 85.9%), m.p. 228-229 °C (Found: C, 50.90; H, 4.62; N, 6.34; S, 15.42. $C_9H_9NO_3S$ requires: C, 51.17; H, 4.30; N, 6.63; S, 15.18%.)

Preparation of 5,6-dimethoxy-1,2-benzisothiazol-3(2H)-one 1-oxide (8a) from 12

Compound 12 (0.21 g; 1 mmol) was stirred for 2 days in a mixture of methanol (25 ml) and an aqueous solution (5 ml) of sodium periodate (0.25 g). The crystals were filtered off and washed with water; the colorless crystalline product (0.19 g; 83.7%) had m.p. 250-251 °C (from acetic acid). The product was identical with 8a prepared as described above.

In the cases of 8a-c and 12, the bands due to the phenyl ring are missing from the ir spectra, the multiplets of the aromatic protons from the ^1H nmr spectra, and the signals of the aromatic carbons and of C-2 from the ^{13}C nmr spectra. The ir spectra of both 8a-c and 12 contain the ν NH band, and for 8a-c the sulfoxide band is also present. The vicinity of the sulfoxide group causes a downfield shift of the H-8 signal. (In 8a this shift is 0.3 ppm as compared with 12a.)

Table 3. Physical and analytical data on compounds 14a-f

Compound	Yield %	M.p. °C	Formula Mol. weight	Analysis %, Calcd. Found C	H	N
14a	55	131-132	$C_{15}H_{13}NO_2S$ 271.32	66.40 66.12	4.83 4.92	5.16 4.96
14b	58	125-126	$C_{17}H_{17}NO_2S$ 299.38	68.20 68.07	5.73 5.97	4.58 4.56
14c	40	164-165	$C_{16}H_{15}NO_2S$ 285.35	67.34 67.21	5.30 5.52	4.91 4.97
14d	49	88-89	$C_{15}H_{12}ClNO_2S$ 305.78	58.91 58.81	3.96 3.54	4.58 4.31
14e	55	177-178	$C_{15}H_{12}ClNO_2S$ 305.78	58.91 59.04	3.96 3.95	4.58 4.61
14f	51.5	181-182	$C_{17}H_{17}NO_4S$ 331.38	61.61 61.33	5.17 5.47	4.23 4.20

5,6-Dimethoxy-3-phenyl-1,2-benzisothiazole (14a)

To a solution of 13a (1.42 g; 5 mmol) in glacial acetic acid (10 ml), peracetic acid (10 mmol) was added by drops over a period of 0.5 h, with stirring and cooling. The reaction mixture was allowed to stand overnight, then poured into ice-water, and the crystalline product was filtered off. Recrystallization from ethanol gave 0.88 g (65%) of 14a, m.p. 131-132 °C. (Found: C, 66.21; H, 5.13; N, 5.30; S, 12.05. $C_{15}H_{13}NO_2S$ requires: C, 66.40; H, 4.83; N, 5.16; S, 11.82%.)

5,6-Dimethoxy-3-phenyl-1,2-benzisothiazole 1,1-dioxide (15)

Compound 14a (1.36 g; 5 mmol) was dissolved in glacial acetic acid (10 ml). Peracetic acid (15 mmol) was added, and the mixture was refluxed for 1 h. It was then poured into ice-water. The product was filtered off and recrystallized from glacial acetic acid to obtain 0.88 g (53%) of 15, m.p. 258-259 °C. (Found: C, 60.14; H, 4.57; N, 4.50; S, 10.30. $C_{15}H_{13}NO_4S$ requires: C, 59.39; H, 4.32; N, 4.62; S, 10.57%.)

General procedure for preparation of 1,2-benzisothiazoles (14a-f)

Compound 13a-f (5 mmol) was dissolved in methanol (50 ml) and a solution of sodium periodate (2.14 g; 10 mmol) in water (20 ml) was added. The mixture was stirred for 2 days. The crystalline product was filtered off, washed with water and recrystallized from methanol (cf. Table 3).

The ir and ^{13}C nmr spectra of the benzisothiazole derivatives 14a-f and 15 lack the carbonyl absorption; the ^{1}H nmr signals of the C-2 methylene protons of the starting compounds (13a-f) are also absent. On the other hand, all signals characteristic of the aryl group can be identified in each spectrum. Further, in the ir spectrum of 15 the sulfone bands are present; the effect of the sulfone group, causing downfield shifts of the C-4, C-6 and C-8 signals, can also be observed in the ^{13}C nmr spectra; at the same time, owing to cessation of the quasi-aromatic character of the hetero ring, C-8a and particularly C-4a are much more shielded: by about 4 ppm and more than 13 ppm, respectively, as compared with the analogous compounds 14.

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