

SYNTHESIS OF 1,2-BENZISOTHIAZOLES BY THE OXIDATIVE RING
 CONTRACTION OF 2-ARYL- AND 4-ARYL-3,4-DIHYDRO-2H-1,3-
 BENZOTHIAZINES¹

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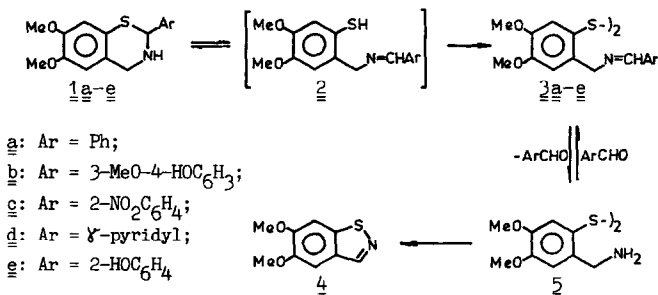
Abstract - Sodium periodate oxidation of 6,7-dimethoxy-2-aryl-3,4-dihydro-2H-1,3-benzothiazines (1a-e) gave 5,6-dimethoxy-1,2-benzisothiazole (4). The N-substituted analogues (6a-c) and the 4-aryl isomers of the latter (11a,b) furnished 2-substituted 1,2-benzisothiazolidine 1-oxides (7a-c) and their 3-aryl analogues (12a,b), respectively. The observed conversions of the 1,3-benzothiazines to 1,2-benzisothiazole and to 1,2-benzisothiazolidines are new ring transformation reactions of 3,4-dihydro-1,3-benzothiazines, representing a new route for the synthesis of 1,2-benzisothiazoles and their hydrogenated derivatives.

We earlier described the oxidative ring contraction of 2-aryl-4H- and 4-aryl-2H-1,3-benzothiazines to give 1,2-benzisothiazole derivatives as the final products.¹

The present communication reports on the very similar oxidation reactions of 2-aryl- and 4-aryl-3,4-dihydro-2H-1,3-benzothiazines. In the literature we found accounts only of the oxidation of 3,4-dihydro-1,3-benzothiazin-4-ones and their N-substituted derivatives;²⁻⁵ in these reactions ring contraction was not observed.

When 2-aryl-6,7-dimethoxy-3,4-dihydro-2H-1,3-benzothiazines (1a-e) (of these compounds, 1a⁶ and 1e⁷ have been described in our earlier communications) are oxidized with sodium periodate in aqueous methanolic solution, the product is 5,6-dimethoxy-1,2-benzisothiazole (4), formed in a yield of 45-66% (Scheme 1).

It could be assumed that the oxidative ring transformation takes place in several steps; therefore, the course of the oxidation process was studied. It was found that when a methanolic solution of compound 1a⁶ was allowed to stand exposed to air, it was slowly transformed into the disulfide 3a. The latter



- a: Ar = Ph;
- b: Ar = 3-MeO-4-HOC₆H₃;
- c: Ar = 2-NO₂-C₆H₄;
- d: Ar = 8-pyridyl;
- e: Ar = 2-HOC₆H₄

Scheme 1

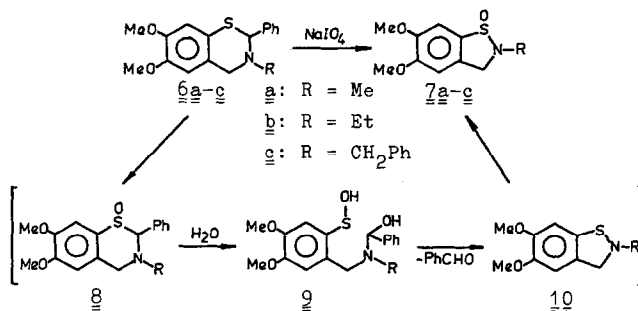
compound was also formed if 1a was reacted with an equivalent amount of iodine or sodium periodate. Accordingly, we concluded that the open-ring tautomeric form (2) of 1a is first oxidized to the disulfide derivative 3a, and that this compound is the intermediate in the oxidation. In accordance with this assumption when compound 3a was further oxidized with more sodium periodate in aqueous methanol, it gave the benzisothiazole derivative 4.

It is known that 2-mercaptobenzylamines can be oxidized to 1,2-benzisothiazole derivatives.^{8,9} Analogously, the disulfide 5 also gave the 1,2-benzisothiazole 4. The disulfide 5 can be formed from compounds 3 by hydrolysis; thus, it can be the next intermediate in the oxidation.

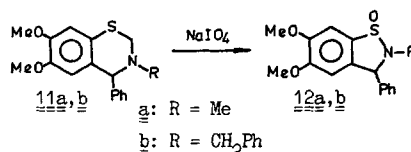
Compound 5 was condensed with the appropriate aldehydes to prepare the Schiff bases 3b-e; similarly to the analogous compound 3a, these latter were oxidized by periodate to the benzisothiazole 4. The quasi-aromatic 1,2-benzisothiazole 4 is not oxidized further to sulfoxide by periodate.

Periodate oxidation of the *N*-substituted analogues of 1 (6a,¹⁰ 6b,⁶ 6c) in aqueous methanol led to the 1,2-benzisothiazolidine 1-oxide derivatives 7a-c. We suggest that compounds 6a-c are first oxidized to the sulfoxides 8 from which benzaldehyde is eliminated *via* 9

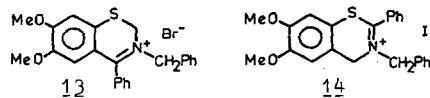
to furnish the 1,2-benzisothiazole intermediates 10. In the final step, the latter are oxidized to the sulfoxides 7a-c. Attempted isolation of intermediates in this reaction proved unsuccessful. When the oxidation was effected with less than the stoichiometric amount of periodate, only the sulfoxides 7 were obtained, in addition to unchanged starting compounds (Scheme 2).



A ring contraction reaction similar to those described above was also observed in the periodate oxidation of the isomeric *N*-substituted 4-phenyl-3,4-dihydro-2*H*-1,3-benzothiazine derivatives 11a¹⁰ and 11b; the products were the 2-substituted 3-phenyl-1,2-benzisothiazoline 1-oxides 12a,b (Scheme 3). The starting materials 11b and 6c, which have not been described hitherto, were prepared by reduction of the quaternary salts 13 and 14 with zinc and acid.



The structures of the new compounds were confirmed by ir, ¹H and ¹³C nmr spectroscopy (Tables 1 and 2).



The spectral data are self explanatory; it need only be added that, as evidence of the asymmetrically substituted heterocyclic structure, the C-4 methylene protons in 1c, 1d, 6c and 7a-c, and the 2-methylene hydrogens in 11b, are not equivalent in the ¹H nmr spectrum: they give an AB-type spectrum. The H-4 protons in 1b in DMSO-*d*₆ are equivalent accidentally.

The spectra of compounds 4, 7a-c and 12a,b unequivocally prove the ring contraction. The evidence includes the lack of the signals due to the C-2 substituents present in the starting materials, and the absence of the H-2 and C-2 signals in the ¹H and ¹³C nmr spectra, respectively.

Compounds 12a,b may exist in two isomeric forms. Indeed, in the crude product two components were detected; in the preparation of 12a and 12b, the ratios of these components were about 10:1 and 10:3, respectively. The latter mixture allowed the determination of some of the ¹H and ¹³C nmr chemical shifts for the by-

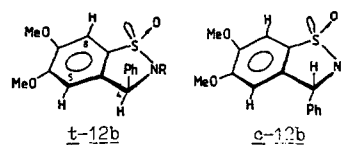


Table 1. Ir^a and ¹H nmr data (chemical shifts, $\delta_{\text{TMS}} = 0$ ppm and coupling constants, Hz) of compounds 1b-d, 3a-g, 4, 6c, 7a-c, 11b and 12a,b in CDCl₃ solutions^b at 250 MHz

Com- pound	H-2 $\delta(1\text{H})^c$	H-4 $\delta(2\text{H})^d$	H-5 $\delta(1\text{H})$	H-8 $\delta(1\text{H})$	MeO (6,7) $\delta(2\text{s})$ ($2 \times 3\text{H}$)	Further signals
<u>1b</u>	5.58	4.07	6.55	6.75	3.73 3.80	ArH: 6.77 ^e , 6.90 ^f , 7.15 ^g
<u>1c</u>	6.30	3.98 4.14	6.56	6.60	3.83 ^h	ArH: 7.84 ^e , 7.46 ⁱ , 7.61 ⁱ , 7.78 ^e
<u>1d</u>	5.61	4.05 4.15	6.55	6.58	3.82 8.83	ArH: 7.40 ^e , 8.61 ^e
<u>3a</u>	8.25	4.82	6.96	6.97	3.76 3.86	ArH: 7.3-7.5 ^j , 7.75 ^f
<u>3b</u>	8.12	4.78		6.94	3.77 3.81	ArH: 6.85 ^e , 7.05 ^f , 7.40 ^g
<u>3c</u>	8.66	4.88	6.93	6.97	3.77 3.88	ArH: 7.60 ⁱ , 7.70 ⁱ , 7.98 ^{e,h}
<u>3d</u>	8.19	4.84	6.93	6.97	3.77 3.86	ArH: 7.57 ^e , 8.67 ^e
<u>3e</u>	8.29	4.76		6.95	3.76 3.85	ArH: 6.90 ^e , 6.95 ⁱ , 7.2-7.4 ^j
<u>4</u> [*]	-	8.71	7.30	7.37	3.96 3.98	-
<u>6c</u> [*]	5.70	3.78 ^h	6.42	6.70	3.78 ^h 3.89	CH ₂ : 3.8 ^{h,i,l} , ArH: 7.2-7.4 ^j , 7.60 ^f
<u>7a</u> [*]	-	4.34 4.72	6.91	7.21	3.91 3.92	NCH ₃ : 3.09 δ (3H)
<u>7b</u> [*]	-	4.36 4.75	6.91	7.22	3.91 3.92	CH ₃ : 1.40 δ (7.1), CH ₂ : δ 3.36 ^k
<u>7c</u> [*]	-	4.42 4.72	6.83	7.23	3.88 3.92	CH ₂ : 4.23, 4.66 ^l , ArH: 7.3-7.5 ^j
<u>11b</u>	3.89 ^h 4.48	4.83	6.43	6.69	3.73 3.90 ^h	CH ₂ : 3.83, 4.00 ^l , ArH: 7.1-7.5 ^j
<u>12a</u> [*]	-	5.65	6.42	7.30	3.73 3.93	NCH ₃ : 2.84 δ (3H), ArH: 7.2-7.5 ^j
<u>t-12b</u> [*]	-	5.74	6.46	7.52	3.63 3.82	CH ₂ : 4.12, 4.25 ^l , ArH: 7.2-7.45 ^j
<u>c-12b</u> [*]	-	5.38	6.64	7.48	3.66 3.88	CH ₂ : 3.92, 4.56 ^l , ArH: 7.2-7.45 ^j

* The numbering of the hydrogen and carbon atoms (see text and Tables) is not identical with that of the compounds numbered according to the IUPAC nomenclature. This was necessary for ease of comparison of spectroscopically analogous atoms in benzothiazine and benzisothiazole derivatives, respectively. Characteristic ir-bands (in KBr, cm⁻¹): ν_{OH} : 3150-2300 (1b), 3600-3300 (3b,e); ν_{NH} : 3275 (1b), 3315 (1c), 3235 (1d); ν_{NO_2} : 1520, 1350 and 850 (1c), 1521, 1508, 1350 and 860 (3c); $\nu_{\text{C=N}}$: 1640 (3a), 1630 (3b,c), 1645 and 1625 (3d), 1625 (3e); $\nu_{\text{S=O}}$: 1055 (7a,c), 1060 (7b), 1075 (12a), 1070 (12b). Further ¹H nmr signals: OH: 9.10 (1b), δ 5.95 (3b), δ Me (Pos. 3⁷): 3.72 δ (3H) for 1b and 3b. ^bIn DMSO-d for 1b and 12b. ^cAB-type spectrum for 11b: 2d(2x1H), J(A,B) 12.5 Hz. ^d δ (1H) for 4, 11b and 12a,b; AB-type doublet pair (2x1H) for 1c,d and 7a-c, J(A,B) 16.7 (1c,d), 14.2 (7a,b) and 14.5 (7c). ^ed (J 8 Hz, for 1d and 3d 5.8 Hz). ^fdd (J 2 and 8 Hz), intensity: 1H (1b, 3b) and 2H (3a, 6c). ^g δ (J 2 Hz). ^hOverlapping signals. ⁱ(J 8 Hz). ^jm, intensity: 3H (3a), 8H (6c), 5H (7c, 12a), 10H (11b, 12b). ^kN-ethyl group, AB part of an ABX₃-type multiplet (2H). ^lAB-type spectrum (2d, 2x1H) of the benzyl group, J(A,B) 14.3 (7c), 13.2 (11b), 14.0 (t-12b), and 17.0 Hz (c-12b).

product; in this way, the isomeric structures containing the sulfoxide oxygen and the phenyl group in the trans and cis positions could be assigned to the main product (t-12b) and the by-product (c-12b), respectively.

As the chemical shift of the H-8 singlet is practically the same (7.52 and 7.48 ppm) for the two isomers, the identical arrangement of the sulfoxide bond in t-12b and c-12b is obvious: it is nearly coplanar (quasi-equatorial) with the benzene ring. In the by-product C-4 and C-4a are considerably more shielded, indicating a strong steric hindrance. The steric compression¹¹ caused by the crowded structure results in upfield shifts of the C-4 and C-4a signals by 8.5 and 11.9 ppm, respectively, in the ¹³C nmr spectrum. It can be concluded, therefore, that the main product is the trans isomer, which contains a quasi-axial phenyl group in the preferred conformation. In accordance with this, the H-4 singlet in the spectrum of the main product is shifted downfield (by 0.36 ppm, as compared with the by-product), for in the quasi-equatorial position this atom is nearly coplanar with the benzene ring, whose anisotropic effect¹² reduced the shielding of H-4. As a consequence of the more crowded steric structure, the difference between the chemical

Table 2. ^{13}C nmr chemical shifts ($\delta_{\text{TMS}} = 0$ ppm) of compounds 1b-d, 3a-e, 4, 6c, 7a-c, 11b, 12a, t-12b and c-12b in CDCl_3 solution^a at 20 MHz^b

Compound	C-2	C-4	C-4a	C-5	C-6	C-7	C-8	C-8a	OMe(6,7)
<u>1b</u>	67.2	50.4	127.3	112.7 ^c	147.9 ^d	149.2 ^d	113.7 ^c	121.1	57.5 ^{e,f}
<u>1c</u>	60.3	48.7	134.4	111.4 ^f	147.3	148.8	111.4 ^f	123.0 ^c	56.2 56.3
<u>1d</u>	63.8	48.8	124.0	111.4 ^f	147.4	148.8 ^g	111.4 ^f	122.9	56.3 56.4
<u>3a</u>	162.6	62.5	135.9 ^c	118.7	148.6	151.0	112.9	126.6	56.4 56.5
<u>3b</u>	162.0	61.8	135.3	117.8	148.8 ^c	150.4	112.6	126.4	55.9 ^h
<u>3c</u>	158.1	62.4	134.6	118.2	148.5	150.8	112.7	126.6	56.2 ^f
<u>3d</u>	160.1	62.3	134.7	118.6	148.8	150.9	113.1	126.7	56.2 56.3
<u>3e</u>	165.9	60.7	134.3	118.6	148.6	150.9	112.4	126.3	56.1 56.2
<u>4</u> ^x	-	153.3	129.6	103.2	148.3	150.8	99.7	145.6	55.4
<u>6c</u> ^x	69.6	49.9	123.7	112.5	146.8	148.5	110.8	119.8	56.0 56.1
<u>7a</u> ^x	-	59.3	133.4	106.8 ^c	152.3	149.8	105.7 ^c	139.2	56.3 ^f
<u>7b</u> ^x	-	55.5 ^c	132.1	105.1 ^d	151.2	148.7	105.8 ^d	137.5	55.3 ^{c,f}
<u>7c</u> ^x	-	56.6	133.1	106.9 ^c	152.3	149.9	105.9 ^c	136.9	56.4 ^f
<u>11b</u> ^x	49.3	63.8	119.7	110.5	146.5	148.8	114.5	124.7	55.8 ^c 56.0 ^c
<u>12a</u> ^x	-	73.6	137.9 ^c	106.8 ^d	152.6	150.2	107.4 ^d	138.0 ^c	56.3 56.5
<u>t-12b</u> ^x	-	72.0	137.7 ^c	106.5 ^d	152.3	150.1	107.1 ^d	138.1 ^c	56.3 56.4
<u>c-12b</u> ^x	-	63.5	125.8		153.7	150.8			

Further signals: CH_2 (ethyl): 13.3 (7b); NCH_3 : 34.2 (7a), 31.5 (12a); NCH_2 : 54.6 (6c), 41.5 (7b), 52.2 (7c), 56.6 (11b), 48.9 (t-12b), 44.5 (c-12b); OCH_3 : 57.6 (11b), 55.9^h (3b); aromatic carbons, $\text{C}-1'$: 133.4 (11b), 123.9^c (1c), 148.8^g (1d), 136.8^c (3a), 128.2 (3b), 131.3 (3c), 143.1ⁱ (3d), 119.0 (3e), 138.4ⁱ, 140.3 (6c), 138.5 (7c), 138.2^j and 142.7 (11b), 138.2^c (12a), 131.2 (c-12b), 135.0 (c-12b), 136.6^c (t-12b), 137.3^c (t-12b); $\text{C}-2'$: 113.1^c (11b), 149.1 (1c), 109.4 (3b), 149.1 (3c), 161.2 (3e); $\text{C}-2',3',5',6'$: 128.6, 128.9 (3a), 128.2^h, 128.9 (6c), 128.5, 128.8 (7c), 128.1, 128.2, 128.9, 129.1 (11b), 128.4, 129.0 (12a), 128.5^f, 128.8, 129.0, 129.3 (12b), $\text{C}-2',6'$: 121.6^k (1d), 121.9^k (3d); $\text{C}-3'$: 149.7^d (1b), 124.7 (1c), 148.2^d (3b), 124.2 (3c), 117.1 (3e), $\text{C}-3',5'$: 150.3^l (1d), 150.5^l (3d), $\text{C}-4'$: 148.1^d (11b), 131.0 (3a), 147.2 (3b), 130.0^c (3c), 131.5 (3e), 127.1, 127.7 (6c), 127.9 (7c), 127.0, 127.3 (11b), 128.8 (12a), 127.8, 128.5^f (12b), $\text{C}-4',6'$: 129.1^g (1c), $\text{C}-5'$: 116.9 (1b), 132.9 (1c), 114.3 (3b), 133.2 (3c), 118.3 (3e), $\text{C}-6'$: 124.3 (1b), 123.8 (3b), 130.7^c (3c), 132.4 (3e).

^aSolvent: $\text{DMSO}-d_6$ for 1b. ^bMeasuring frequency was 63 MHz for 3d and 12a.

^{c,4,e}Reversed assignments may also be possible. ^{f,g}Two overlapping lines. ^hThree overlapping lines. ^{i,k,l} C_α , C_β and C_γ lines of the pyridine ring. ^j4-phenyl group.

shifts of the methylene hydrogens is much greater in the cis isomer (0.64 ppm, whereas for the trans isomer it is 0.13 ppm); in the latter structure the N-benzyl group can rotate more freely, and therefore the chemical environments are largely averaged.

The steric structures proposed above are in accordance with the results of our earlier nmr and X-ray examinations,¹⁰ which led to the conclusion that the preferred conformer of 11a has the phenyl and N-methyl groups in the axial positions, whereas in 6a the phenyl group is equatorial and the N-methyl group is axial.

EXPERIMENTAL

M.p.s. are uncorrected.

Ir spectra were run in KBr discs on a Bruker IFS-113v vacuum optic FT spectrometer controlled by an Aspect 2000 computer.

¹H and ¹³C nmr spectra were recorded at room temperature in CDCl_3 solution in 5 or 10 mm tubes, on a Bruker WM-250 (¹H) and a WP-80-SY (¹³C) FT spectrometer, controlled by an Aspect 2000 computer, at 250.13 (¹H) and 20.14 (¹³C) MHz, respectively, using the deuterium signal of the solvent as the lock and TMS as internal standard.

General procedure for the preparation of compounds 1b-d

4,5-Dimethoxy-2-mercaptobenzylammonium chloride (2.35 g; 10 mmol) was dissolved in water (10 ml), and a solution of the appropriate aldehyde (10 mmol) in ethanol (15 ml) was added, together with potassium carbonate (0.5 g). The reaction mixture was heated nearly to the boiling point and then allowed to stand for 1 h. The crystals which separated out were filtered off and washed with water and a small amount of ethanol (cf. Table 3).

Table 3. Physical and analytical data of compounds 1b-d, 3a-e, 7a-c and 12a,b

Com- pound	Yield %	M.p. °C	Formula	M.w.	Analysis %, Calcd./Found		
					C	H	N
1b	66	198-199 ^a	C ₁₇ H ₁₉ NO ₄ S	333.39	61.24/60.99	5.74/5.95	4.20/4.17
1c	77	153-154 ^b	C ₁₆ H ₁₆ N ₂ O ₄ S	332.38	57.81/58.03	4.85/5.04	8.43/8.74
1d	50	165-166 ^b	C ₁₅ H ₁₆ N ₂ O ₂ S	288.37	62.47/62.48	5.59/5.90	9.72/9.53
3a	72	119-120 ^a	C ₃₂ H ₃₂ N ₂ O ₄ S ₂	572.73	67.10/66.90	5.63/5.73	4.89/5.10
3b	31	173-174 ^b	C ₃₄ H ₃₆ N ₂ O ₈ S ₂	664.78	61.43/61.70	5.46/5.22	4.22/4.03
3c	62	105-107 ^a	C ₃₂ H ₃₀ N ₄ O ₈ S ₂	662.73	57.99/57.70	4.56/4.70	8.45/8.17
3d	58	158-159 ^a	C ₃₀ H ₃₀ N ₄ O ₄ S ₂	574.70	62.69/62.40	5.26/5.01	9.75/10.01
3e	65	146-147 ^a	C ₃₂ H ₃₂ N ₂ O ₆ S ₂	604.73	63.55/63.70	5.34/5.61	4.63/4.88
7a	44	138-139 ^a	C ₁₀ H ₄ NO ₃ S	227.27	52.84/53.01	5.76/6.00	6.16/6.31
7b	55	116-117 ^c	C ₁₁ H ₁₅ NO ₃ S	241.30	54.75/55.03	6.27/6.44	5.81/5.62
7c	56	176-177 ^a	C ₁₆ H ₁₇ NO ₃ S	303.37	63.34/63.60	5.64/5.87	4.62/4.56
12a	47	125-126 ^a	C ₁₆ H ₁₇ NO ₃ S	303.37	63.34/63.31	5.64/5.70	4.62/4.35
12b	68	166-168 ^a	C ₁₂ H ₂₁ NO ₃ S	379.46	69.63/69.86	5.58/5.68	3.69/3.43

Solvent: ^a ethanol, ^b benzene, ^c acetone. Anal. S % (Calcd./Found): 14.10/14.00 (7a), 13.29/13.40 (7b), 10.57/10.53 (7c), 10.57/10.40 (12a).

5,6-Dimethoxy-1,2-benzisothiazole (4)

(A) Compounds 1a-e (5 mmol) in methanol (40 ml) was stirred for 3 days with a solution of sodium periodate (15 mmol) in water (15 ml). The mixture was then diluted with water, neutralized with sodium carbonate and extracted with benzene. Drying of the extract (Na₂SO₄), evaporation of the solvent and recrystallization of the product from ethanol gave 4 in 45-66% yield, m.p. 104-105 °C. (Found: C, 55.70; H, 4.90; N, 6.95; S, 16.10. Calcd. for C₉H₉NO₂S (195.24); C, 55.36; H, 4.65; N, 7.18; S, 16.42%.)

(B) Compound 5 (0.47 g; 1 mmol) was dissolved in methanol (30 ml) and a solution of sodium periodate (0.43 g; 2 mmol) and sodium carbonate (0.11 g) in water (10 ml) was added. The mixture was stirred for 1 h and then concentrated. Water was added and the mixture was extracted with benzene. The extract was dried, the solvent was evaporated off and the residue was crystallized from ethanol to give 0.29 g (74%) of 4, m.p. 104-105 °C, identical in all respects with the product prepared according to (A).

[2,2'-Bis(benzalaminomethyl)-4,4',5,5'-tetramethoxy-diphenyl]disulfide (3a)

(A) Compound 1a (0.29 g; 1 mmol) was dissolved in methanol (50 ml) and allowed to stand for one week exposed to the air. The solution was then evaporated to dryness and the residue crystallized from a small amount of ethanol to give colourless needles (0.21 g, 74%), m.p. 118.5-120 °C. (Found: C, 56.95; H, 5.74; N, 5.10. C₃₂H₃₂N₂O₄S₂ (572.73) requires: C, 67.10; H, 5.63; N, 4.89%.)

(B) Compound 1a (1.45 g; 4 mmol) was stirred in ethanol (100 ml) and a solution of iodine (0.64 g; 2.5 mmol) in ethanol (20 ml) was added. The mixture was neutralized with a solution of sodium carbonate and extracted with benzene. Drying (Na₂SO₄) and evaporation of the extract left a residue that was crystallized from ethanol to give the product (1 g; 70%), m.p. 119-120 °C, identical in all respects with 3a prepared by route (A).

General procedure for the preparation of compounds 3a-e

2,2'-Bis(aminomethyl)-4,4',5,5'-tetramethoxydiphenyl disulfide dihydrochloride (5.2 HCl) (2.35 g; 5 mmol) and the appropriate aldehyde (5 mmol) were dissolved in ethanol (3 ml), and a solution of potassium carbonate (1 g) in water (8 ml) was added. The mixture was heated almost to the boiling point and then allowed to stand. The crystalline product was filtered off and washed with water and ethanol (cf. Table 3).

General procedure for the preparation of 7a-c and 12a,b

Compound 6a-c or 11a,b (5 mmol) was dissolved in methanol (30 ml) and a solution of sodium periodate (0.32 g; 1.5 mmol) in water (10 ml) was added. After stirring for 1 h, the mixture was evaporated to dryness. The residue was taken up in water (10 ml) and extracted with chloroform. The extract was dried (Na_2SO_4), the solvent was evaporated off and the product was recrystallized (*cf.* Table 3).

3-Benzyl-6,7-dimethoxy-4-phenyl-2H-1,3-benzothiazinium bromide (13)

6,7-Dimethoxy-4-phenyl-2H-1,3-benzothiazine (1.43 g; 5 mmol) was dissolved in acetonitrile (10 ml). Benzyl bromide (0.86 g; 5 mmol) was added and the mixture was refluxed for 1 h. After evaporation to dryness, the residue was dissolved in chloroform (3 ml). On the addition of ether, yellow crystals (1.64 g; 72%) separated out, m.p. 158-160 °C (decomp.). (Found: C, 60.10; H, 4.75; N, 3.28. $\text{C}_{23}\text{H}_{22}\text{BrNO}_2\text{S}$ (456.41) requires: C, 60.53; H, 4.86; N, 3.07%.) ^1H nmr (CDCl_3 , δ ppm): OCH_3 : 3.57, 4.02 (2s, each 3H, OCH_3); 5.48, 5.50 (2s, each 2H, ring and benzyl CH_2); 6.43 (s, 1H, H-8); 6.97 (s, 1H, H-5); 7.35 (m, 5H, ArH-benzyl); 7.7 (m, 3H, ArH-3',4',5'); 7.93 (dd, 2H, ArH-2',6').

3-Benzyl-6,7-dimethoxy-4-phenyl-3,4-dihydro-2H-benzothiazine (11b)

Compound 13 (4.56 g; 10 mmol) was dissolved in ethanol (50 ml). With stirring, zinc powder (2 g) and then 10% hydrochloric acid (20 ml) were added, and stirring was continued until the mixture became colourless. It was then immediately poured into an excess of sodium carbonate solution and extracted with benzene. The extract was dried (Na_2SO_4) and the solvent was evaporated off. The residue was crystallized from ethanol to give 2.2 g (58%) of the product. A sample was recrystallized from ethanol for analysis, m.p. 139-140 °C. (Found: C, 73.35; H, 6.40; N, 3.44. $\text{C}_{22}\text{H}_{23}\text{NO}_2\text{S}$ (377.48) requires: C, 73.18; H, 6.14; N, 3.71%.)

3-Benzyl-6,7-dimethoxy-2-phenyl-4H-1,3-benzothiazinium iodide (14)

6,7-Dimethoxy-2-phenyl-4H-1,3-benzothiazine (1.43 g; 5 mmol) was dissolved in acetonitrile (10 ml). Benzyl iodide (1.09 g; 5 mmol) was added and the mixture was refluxed for 4 h. After evaporation, the residue was dissolved in chloroform (3 ml) and the product (1.97 g; 78%) was precipitated out with ether. A sample was purified for analysis by dissolving it in chloroform and precipitating it by adding ether; the yellow crystals had m.p. 161-162 °C. (Found: C, 54.52; H, 4.38; N, 2.90. $\text{C}_{23}\text{H}_{22}\text{INO}_2\text{S}$ (503.39) requires: C, 54.88; H, 4.40; N, 2.78%.) ^1H nmr (CDCl_3 , δ ppm): OCH_3 : 3.73, 3.93 (2s, each 3H, OCH_3); 5.34 (s, 2H, CH_2 -benzyl); 5.75 (s, 2H, CH_2 -ring); 6.35 (s, 1H, H-5); 6.99 (s, 1H, H-8); 7.15 (dd, 2H, ArH-benzyl 2',6'); 7.3 (m, 3H, ArH-benzyl 3',4',5'); 8.26 (m, 3H, ArH-phenyl 2',6'); 8.7 (dd, 2H, phenyl 3',4',5').

3-Benzyl-6,7-dimethoxy-2-phenyl-3,4-dihydro-2H-1,3-benzothiazine (6c)

Compound 14 (5.03 g; 10 mmol) was reacted in the same way as described for the preparation of 11b, to give 6c (2.60 g; 70%). Colourless needles from methanol, m.p. 141-142 °C. (Found: C, 73.10; H, 6.38; N, 3.90. $\text{C}_{23}\text{H}_{23}\text{NO}_2\text{S}$ (377.48) requires: C, 73.18; H, 6.14; N, 3.71%.)

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