Synthesis of 6*H*,8*H*-Isoquino[2,3-*c*][1,3]benzothiazin-8-ones [1]

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6*H*,8*H*-Isoquino-1,3-benzothiazin-8-ones have been prepared by reaction of 6,7-dimethoxy-2*H*-1,3-benzothiazines with homophthalic anhydride and by photocyclization of 3-benzoyl-4-methylene-6,7-dimethoxy 2*H*-1,3-benzothiazine. The compounds are thia analogues of protoberberine alkaloids containing a sulfur atom at C-5 and a lactam function at C-8. The mass spectra of the title compounds are discussed.

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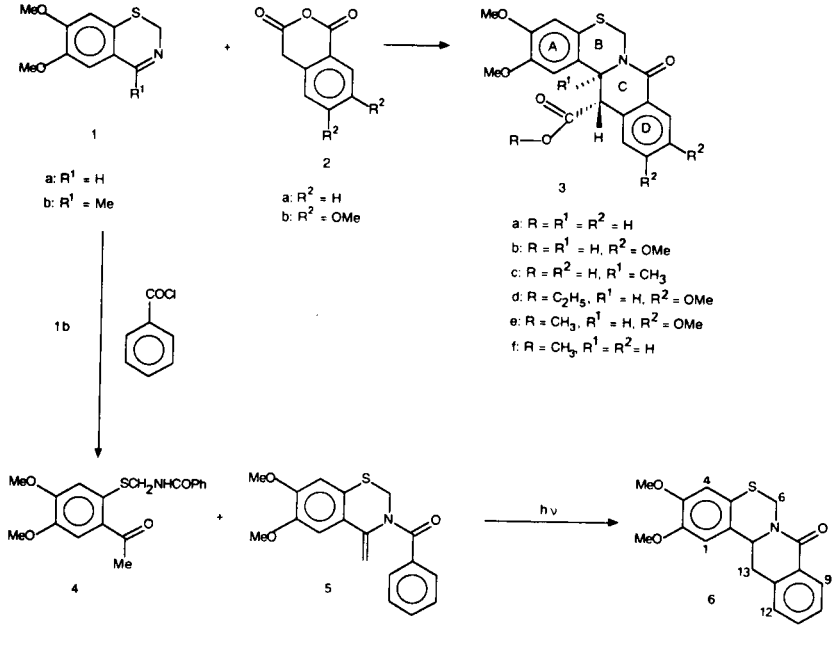
We have recently reported the synthesis of several 6*H*,8*H*-isoquino-1,3-benzothiazines [4,5]. These compounds may be considered to be thia analogues of the ring system present in the protoberberine alkaloids in which the methylene group at C-5 of the alkaloids has been replaced by a sulfur atom. Here we report the preparation of several new members of this class of compounds using 6,7-dimethoxy-2*H*-1,3-benzothiazines as starting materials, but employing different synthetic approaches from those previously used.

In the first method (Scheme 1) 6,7-dimethoxy-2*H*-1,3-benzothiazine (**1a**) was condensed with homophthalic anhydride **2a** and with 4,5-dimethoxy homophthalic anhydride **2b** to afford the condensation products **3a** and **3b**,



SCHEME 1

respectively. The condensation products were formed in high yield and their formation is strictly analogous to the condensation of 3,4-dihydroisoquinolines with homophthalic anhydrides [6-10]. A similar reaction was carried out between **1b** and **2a** to afford the tetracyclic compound **3c**. The structures assigned to the compounds are compatible with their spectroscopic properties. The reaction is diastereoselective affording a single product in which the hydrogen atoms at C-13 and C-13a are *trans* to one another in ring C. This relative stereochemistry was established from the coupling constants $J_{13,13a}$ = 5.5-6.5 Hz, between the two hydrogen atoms in compounds **3d**, **3e** and **3f** in their pmr spectra recorded in deuteriochloroform. (Compounds **3d** and **3e** are the ethyl and methyl ester, respectively, of **3b**, and **3f** is the methyl ester of **3a**). Similar values for coupling constants were observed by Cushman and co-workers [6] for the corresponding berberine derivatives in which a *trans* relationship of the protons at C-13 and C-13a was established.

The pmr spectra of **3a**, **3b**, **3e** and **3f** recorded in dimethyl sulfoxide-d_6 (**3a** and **3b** are insoluble in deuteriochloroform) gave, however, greatly different values for the coupling constants of these compounds, namely $J_{13,13a}$ = 2.0 Hz, and cast doubt on the assignments made above. These apparently contradictory results prompted a thorough examination of the pmr and cmr spectra of the compounds which is reported elsewhere [11]. As a result of that investigation it was concluded that the favoured conformation of the molecules may be represented as **A** in deuteriochloroform solution and as **B** in dimethyl sulfoxide-d_6 solution (Figure 1). The change in conformation in dimethyl sulfoxide-d_6 solution is compatible with the lower value of the coupling constant observed in that medium and also with the shift to lower field of H-13 owing to the change in anisotropy of ring A in changing the solvent from deuteriochloroform to dimethyl sulfoxide-d_6.

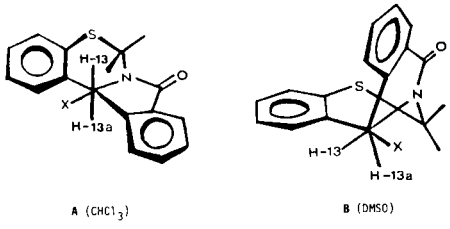


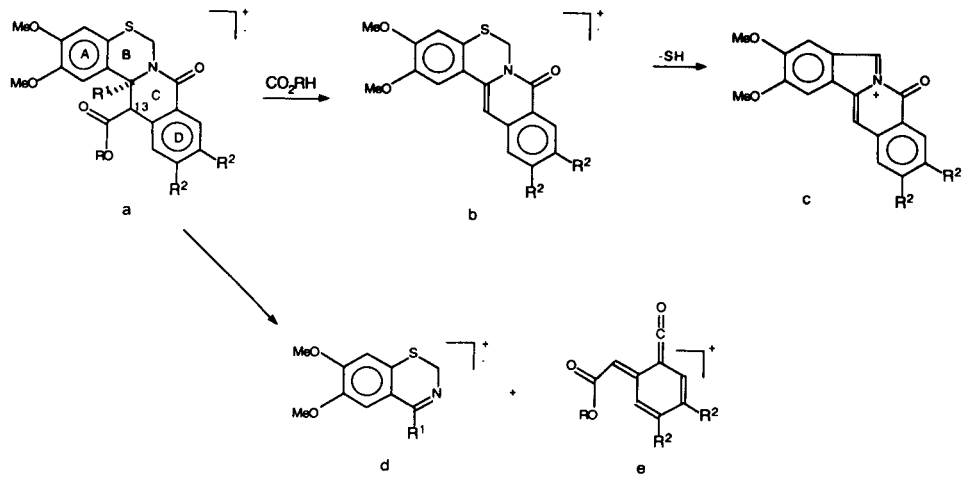
Figure 1. Favoured conformation in solution in chloroform and in dimethyl sulfoxide; X = CO_2R.

For compound **3c** the methyl group at C-13a and the hydrogen at C-13 are considered to be *trans* to one another in ring C since the development of *trans* stereochemistry at these sites is characteristic of this [6-10] and related synthetic approaches [5]. Moreover this assignment is in accord with the nmr analysis [11].

The second route to the isoquinobenzothiazines was photochemical and is analogous to the approach used by others [12,13] to synthesise the protoberberine and related skeleta. To this end compound **1b** was condensed with benzoyl chloride in the presence of triethylamine to afford a separable mixture of **4** and **5** whose structures were assigned on the basis of spectroscopic examination. Compound **5** was readily recognized by nmr spectroscopy through the presence of signals attributed to the methylene group at C-1. Compound **4** on the other hand showed a singlet of area 3 H corresponding to the acetyl group. Irradiation of enamide **5** in solution in *t*-butyl alcohol with a high pressure mercury lamp (Pyrex filter) provided a mixture of products from which **6** was isolated in *ca.* 60% yield. The spectroscopic properties of **6** are compatible with the assigned structure and comparable to those of related compounds prepared previously [5].

We have examined the mass spectra of the isoquino-[2,3-*c*][1,3]benzothiazines prepared in this study. The molecular ions **a** of the carboxylic acids, **3a** and **3b**, sequentially lose CO_2H and H leading to ions of M-46 formulated as **b** in Scheme 2; ions **b** in both cases lose SH to afford ions formulated as **c**. A similar loss of SH has been reported to be the major fragmentation of 13,13a-didehydro-6*H*,8*H*-isoquino[2,3-*c*][1,3]benzothiazin-8-ones [5]. In the case of compound **3c**, the molecular ion loses CH_3 to afford an ion at m/z 370 which eliminates CO_2 yielding an ion at m/z 326 of low intensity. An ion at m/z 325 is also observed but is less abundant in this spectrum than in the spectra of **3a** and **3b**. Ion **c** is not observed. The fragmentation processes noted above have been confirmed by mass analysed ion kinetic energy spectra (MIKES) experiments [14].

The second important fragmentation that these molecules undergo is a *retro* Diels-Alder opening of ring C affording ions formulated as **d** and **e**. Ion **d** comprises the benzothiazine moiety of rings A and B and ion **e** comprises ring D and the carbon centres of ring C not present in ion **d**. Ion **d** appears at m/z 209 in **3a** and **3b** and at m/z 223 in **3c**. In all three cases an ion at **d**-15 is observed, presumably formed through loss of CH_3 from one or the other of the methoxyl groups. Other fragmentation of **d** is not observed or, if it occurs, the fragment ions are of low intensity. Ion **d** is accompanied in all cases by ions **d** + H and **d** − H which are of low intensity for **3a** and **3c** but **d** + H is more intense than **d** in the case of **3b**. Ion **e** is of low intensity in **3a**, **3c** and **3f** but is a prominent ion in the spectrum of **3b** and **3d**. The formation of ion **d** direct from the molecular ion is supported by MIKES experiments in the case of **3a**, **3b** and **3c**; similarly, ion **e** is shown to be derived direct from the molecular ion in the case of **3d**.



3a, R = R^1 = R^2 = H; 3b, R = R^1 = H, R^2 = OMe; 3c, R = R^2 = H, R^1 = CH_3

3d, R = C_2H_5, R^1 = H, R^2 = OCH_3 ; 3f, R = CH_3, R^1 = R^2 = H

6, no substituent at C-13, R^1 = R^2 = H

SCHEME 2

The spectra of esters **3d** and **3f** differ somewhat from those of the acids **3a-c**. In both cases ion **b** is formed by consecutive loss of CO_2R and H from $M^{+\cdot}$, with both **b** and **b** + H fragmenting further to yield **c** and **c** + H, respectively. In ethyl ester **3d**, which bears two methoxyl groups in ring C, the spectrum is dominated by ion **e**, which loses 28 mass units forming a doublet, corresponding to loss of carbon monoxide in one case and ethene in the other. This fragmentation was confirmed by MIKES and by high resolution measurements. Ions **d** and **d**-15 are also present in the spectrum of **3d**. The dominance of **e** in the spectrum of **3d** may be a function of charge stabilization by the two methoxyl groups. In contrast to **3d** the spectrum of methyl ester **3f** is dominated by ion **d**. Ion **e** is of low intensity and it too shows an ion at **e**-28, which is also observed in the case of **3d**.

The spectrum of compound **6** which bears no substituent at C-13 is dominated by the molecular ion and shows relatively intense ions at M-1 and M-2. All three ions lose SH. The *retro* Diels-Alder fragmentation is observed in the spectrum of **6** but the ions are of low intensity. Ion **d**, at m/z 209, is less intense than **d**-H at m/z 208. The latter ion was present in the spectra discussed previously but was always less abundant than **d** itself. The reason for this behavior is not immediately apparent.

This research has demonstrated that isoquino[2,3-*c*]-[1,3]benzothiazines may be prepared readily by two routes previously used in the synthesis of protoberberine alkaloids. It has also provided further insight into the mass spectral fragmentation of this recently reported ring system.

EXPERIMENTAL

The ^1H and ^{13}C nmr spectra were recorded at room temperature in deuteriochloroform or dimethyl sulfoxide-d_6 solution on Bruker WM-250 (^1H and ^{13}C) and WP80-SY ^{13}C FT spectrometers using tetramethylsilane as internal standard. Chemical shifts, quoted as δ values, were measured in relation to tetramethylsilane. The symbols, s, singlet, d, doublet, t, triplet, q, quartet and m, multiplet are used in reporting spectra. The mass spectra were recorded on a VG ZAB-E mass spectrometer at 70eV using a probe inlet system. Infrared spectra were run in potassium bromide discs on a Bruker IFS-113v FT vacuum optic spectrometer equipped with an aspect 2000 computer. Melting points are uncorrected.

The following compounds were prepared by standard methods and gave satisfactory physical data, **1a** and **1b** [15,16] and **2b** [17].

(13**R***,13a**R***)-13-Carboxy-13,13a-dihydro-2,3-dimethoxy-6*H*,8*H*-isoquino[2,3-*c*][1,3]benzothiazin-8-one (**3a**).

Homophthalic anhydride (**2a**, 1.62 g, 0.01 mole) was added to a stirred solution of 6,7-dimethoxy-2*H*-1,3-benzothiazine (**1a**, 2.09 g, 0.01 mole) in chloroform (10 ml). An exothermic reaction occurred as the anhydride dissolved. The reaction mixture was allowed to stand for 2 hours and the solvent was evaporated. The residual yellow powder was recrystallized from glacial acetic acid affording **3a** (3.52 g, 95%), mp 236-238°; ir: (ν max, cm^{-1}) 1734 (CO_2H), 1651 (lactam); pmr (dimethyl sulfoxide-d_6): δ 3.60 (3H, s, OMe), 3.65 (3H, s, OMe), 4.76 (1H, d, J = 11.0 Hz, H-6$_{ax}$) 5.06 (1H, d, J = 2.0, H-13), 5.38 (1H, d, J = 2.0, H-13a), 5.52 (1H, d, J = 11.0 Hz, H-6$_{eq}$), 6.62 (1H, s, H-4), 6.90 (1H, s, H-1), 7.37 (1H, m, H-10), 7.60 (2H, m, H-11 and H-12), 7.82 (1H, m, H-9); cmr: (dimethyl sulfoxide-d_6, 20.14 MHz): δ 45.9 (C-6), 46.6 (C-13), 57.4 (OMe), 57.8 (OMe), 59.6 (C-13a), 112.8, 113.2, 129.0, 129.4, 131.2, 136.2, 136.9 (Ar methine) 126.4, 126.6, 129.0, 134.1, 147.7, 150.3 (Ar quaternary), 164.3 (C-8), 173.6 (CO_2H); ms: m/z (%) 371 (100), 326 (16), 325 (9), 292 (5), 209 (3), 162 (1).

Anal. Calcd. for $C_{19}H_{17}NO_5S$: C, 61.44; H, 4.61; N, 3.77; S, 8.63. Found: C, 61.66; H, 4.74; N, 3.81; S, 8.84.

(13**R***,13a**R***)-13-Carboxy-13,13a-dihydro-2,3,10,11-tetramethoxy-6*H*,-8*H*-isoquino[2,3-*c*][1,3]benzothiazin-8-one (**3b**).

This compound was prepared from **1a** and **2b** in the manner described for the preparation of **3a**, yield 96%, mp 223-224°; ir: (ν max, cm^{-1}) 1735

(CO_2H), 1620 (lactam); pmr (dimethyl sulfoxide-d_6, 250 MHz): δ 3.66, 3.68, 3.77, 3.87 (12H, 4s, 4 x OMe), 4.78 (1H, d, J = 11.0 Hz, H-6_{ax}), 4.95 (1H, d, J = 2.0 Hz, H-13), 5.37 (1H, d, J = 2.0 Hz, H-13a), 5.62 (1H, d, J = 11.0 Hz, H-6_{eq}), 6.64 (1H, s, H-4), 6.93 (1H, s, H-1), 7.24 (1H, s, H-12), 7.34 (1H, s, H-9); cmr (dimethyl sulfoxide-d_6, 62.89 MHz): δ 46.0 (C-6), 46.3 (C-13), 57.4, 57.5, 57.7, 58.0 (4 x OCH_3), 59.9 (C-13a), 112.3, 113.0, 113.6, 114.4 (Ar methine), 112.0, 126.8, 127.0, 130.8, 148.0, 150.3, 150.5, 154.3 (Ar quaternary), 164.4 (C-8), 173.8 (CO_2H); ms: m/z (%) 431 (53), 385 (13), 352 (4), 293 (5), 222 (35), 210 (100), 209 (96).

Anal. Calcd. for $C_{21}H_{21}NO_7S$: C, 58.46; H, 4.91; N, 3.25; S, 7.43. Found: C, 58.28; H, 4.91; N, 3.16; S, 7.42.

(13*R**,13a*R**)-13-Carboxy-13,13a-dihydro-2,3-dimethoxy-13a-methyl-6*H*,8*H*-isoquino[2,3-*c*][1,3]benzothiazin-8-one (**3c**).

This compound was prepared from **1b** and **2a** in the manner described for the preparation of **3a**, yield 94%, mp 204-205°; ir: (ν max, cm^{-1}): 1734 (CO_2H), 1618 (lactam); pmr (dimethyl sulfoxide-d_6, 250 MHz): δ 1.80 (3H, s, CH_3 at C-13a), 3.62 (3H, s, OMe), 3.63 (3H, s, OMe), 4.70 (1H, d, J = 11.0 Hz, H-6_{ax}), 4.94 (1H, s, C-13), 5.86 (1H, d, J = 11.0 Hz, H-6_{eq}), 6.58 (1H, s, H-4), 6.96 (1H, s, H-1), 7.35 (1H, m, H-10), 7.50 (2H, m, H-11 and H-12), 7.80 (1H, m, H-9); cmr (dimethyl sulfoxide-d_6, 20.14 MHz): δ 26.6 (CH_3, C-13a) 40.6 (C-6), 53.5 (C-13), 57.2, 57.7 (2 x OMe), 60.8 (C-13a), 112.5, 113.1, 129.1, 129.4, 130.3, 137.0 (Ar methine), 125.7, 129.4, 129.8, 134.1, 147.4, 147.9 (Ar quaternary) 165.1 (C-8), 172.9 (CO_2H); ms: m/z (%) 385 (58), 370 (13), 223 (100), 208 (8), 162 (1).

Anal. Calcd. for $C_{20}H_{19}NO_5S$: C, 62.32; H, 4.97; N, 3.63; S, 8.32. Found: C, 62.19; H, 5.01; N, 3.70; S, 8.44.

(13*R**,13a*R**)-13-Carboethoxy-13,13a-dihydro-2,3,10,11-tetramethoxy-6*H*,8*H*-isoquino[2,3-*c*][1,3]benzothiazin-8-one (**3d**).

Compound **3b**, (1.08 g, 0.0028 mole) was mixed with ethanol (15 ml) and ethanol saturated with hydrogen chloride (10 ml). The mixture was refluxed for 2 hours and evaporated to dryness. Recrystallization of the residue from ethanol gave colourless crystals (0.94 g, 82%), mp 160-161°; pmr (deuteriochloroform, 250 MHz): δ 1.22 (3H, t, J = 7.0 Hz, CH_2CH_3), 3.74, 3.82, 3.91, 3.93 (12H, 4s, 4 x OMe), 4.20 (2H, q, J = 7.0 Hz, CH_2CH_3), 4.32 (1H, d, J = 6.0 Hz, H-13), 4.40 (1H, d, J = 11.5 Hz, H-6_{ax}), 5.28 (1H, d, J = 6.0 Hz, H-13a), 5.76 (1H, d, J = 11.5 Hz, H-6_{eq}), 6.66 (1H, s, ArH), 6.76 (2H, apparent s, ArH), 7.56 (1H, s, H-9); cmr (deuteriochloroform, 20.14 MHz): δ: 14.0 (CH_3CH_2), 44.8 (C-6), 48.0 (C-13), 56.0 (two overlapping lines), 56.2, 56.4 (4 x OMe), 58.3 (C-13a), 61.5 (OCH_2CH_3), 110.3, 111.2, 111.3, 112.8 (Ar methine), 121.2, 125.6, 126.9, 128.1, 147.0, 149.2, 149.3, 152.8 (Ar quaternary), 163.0 (C-8), 170.8 (CO_2Et); ms: m/z (%) 459 (70), 386 (14), 385 (8), 352 (3), 250 (100), 222 (19), 209 (18).

Anal. Calcd. for $C_{23}H_{25}NO_7S$: C, 60.11; H, 5.48; N, 3.05; S, 6.98. Found: C, 60.17; H, 5.39; N, 3.11; S, 7.04.

(13*R**,13a*R**)-13-Carbomethoxy-13,13a-dihydro-2,3,10,11-tetramethoxy-6*H*,8*H*-isoquino[2,3-*c*][1,3]benzothiazin-8-one (**3e**).

Compound **3b** (1.08 g, 0.0025 mole) was mixed with methanol (10 ml) and methanol saturated with hydrogen chloride (10 ml). The mixture was refluxed for 2 hours and evaporated to dryness. Recrystallization of the residue from methanol gave colorless crystals (0.91 g, 82%) mp 205-206°; ir: (ν max, cm^{-1}) 1742 (ester), 1647 (lactam); pmr (dimethyl sulfoxide-d_6, 250 MHz): δ 3.60, 3.62, 3.65, 3.68, 3.74, (15H, 5s, 5 x OMe), 4.75 (1H, d, J = 11.0 Hz, H-6_{ax}), 5.06 (1H, d, J = 2.0 Hz, H-13), 5.32 (1H, d, J = 2.0 Hz, H-13a), 5.54 (1H, d, J = 11.0 Hz, H-6_{eq}), 6.62 (1H, s, H-4), 6.88 (1H, s, H-1), 7.20 (1H, s, H-12), 7.29 (1H, s, H-9); pmr (deuteriochloroform, 250 MHz): δ 3.73, 3.75, 3.81, 3.83, 3.90, (15H, 5s, 5 x OMe), 4.37 (1H, d, J = 6.5 Hz, H-13), 4.42 (1H, d, J = 11.0 Hz, H-6_{ax}), 5.28 (1H, d, J = 6.5 Hz, H-13a), 5.75 (1H, d, J = 11.0 Hz, H-6_{eq}), 6.65 (1H, s, H-1), 6.74 (1H, s, H-12), 6.77 (1H, s, H-4), 7.55 (1H, s, H-9); cmr (dimethyl sulfoxide-d_6, 20.14 MHz): δ 45.6 (C-6), 45.9 (C-13a), 54.2, 57.1, 57.3, 57.6, 57.7 (5 x OMe), 59.7 (C-13a), 112.2, 112.8, 114.0, 116.6 (Ar methine), 121.7, 125.9, 126.4, 129.8, 147.5, 150.1, 150.2, 154.1 (Ar quaternary), 164.3 (C-8), 173.0 (CO_2Me); cmr (deuteriochloroform, 20.14 MHz): δ 44.7 (C-6), 47.7 (C-13), 52.3, 55.9, 55.9, 56.1, 56.3 (5 x OMe), 58.2 (C-13a), 110.3, 111.0, 111.3, 112.6 (Ar methine), 121.0, 125.3, 126.7, 127.8, 146.9, 149.1, 149.3, 152.8 (Ar quaternary), 163.0 (C-8), 171.2 (CO_2Me).

Anal. Calcd. for $C_{22}H_{23}NO_7S$: C, 59.31; H, 5.20; N, 3.14; S, 7.20. Found: C, 59.42; H, 5.14; N, 3.19; S, 7.24.

(13*R**,13a*R**)-13-Carbomethoxy-13,13a-dihydro-2,3-dimethoxy-6*H*,8*H*-isoquino[2,3-*c*][1,3]benzothiazin-8-one (**3f**).

The acid **3a** (0.93 g, 0.0025 mole) was slowly added to a solution of diazomethane (1 g) in ether-ethanol (30 ml) at 0°. The reaction mixture was allowed to stand for 3 hours at 0°; the excess diazomethane was then decomposed by addition of acetic acid. The solvent was evaporated affording a crystalline product (0.89 g, 93%). Recrystallization from methanol gave colourless crystals, mp 172-173°; ir: (ν max, cm^{-1}) 1730 (ester), 1651 (lactam); pmr (dimethyl sulfoxide-d_6, 250 MHz): δ 3.60, 3.65, 3.68, (9H, 3s, 3 x OMe), 4.78 (1H, d, J = 11.0 Hz, H-6_{ax}), 5.23 (1H, d, J = 2.0 Hz, H-13), 5.40 (1H, d, J = 2.0 Hz, H-13a), 5.55 (1H, d, J = 11.0 Hz, H-6_{eq}), 6.64 (1H, s, H-4), 6.89 (1H, s, H-1), 7.39 (1H, m, H-10), 7.60 (2H, m, H-11 and H-12), 7.83 (1H, m, H-9); pmr (deuteriochloroform, 250 MHz): δ 3.71, 3.73, 3.83 (9H, 3s, 3 x OMe), 4.37 (1H, d, J = 11.0 Hz, H-6_{ax}), 4.40 (1H, d, J = 5.5 Hz, H-13), 5.32 (1H, d, J = 5.5 Hz, H-13a), 5.80 (1H, d, J = 11.0 Hz, H-6_{eq}), 6.63 (1H, s, H-1), 6.76 (1H, s, H-4), 7.20 (1H, m, H-12), 7.41 (1H, m, H-10), 7.52 (1H, m, H-11), 8.07 (1H, m, H-9); cmr (dimethyl sulfoxide-d_6, 62.89 MHz): δ 46.0 (C-6), 46.5 (C-13), 54.3, 57.4, 57.9 (3 x OMe), 59.5 (C-13a), 112.7, 113.2, 129.3, 129.9, 131.3, 136.2 (Ar methine), 126.0, 126.7, 129.2, 134.4, 147.8, 150.5 (Ar quaternary), 164.4 (C-8), 172.9 (CO_2Me); cmr (deuteriochloroform, 62.89 MHz): δ 44.8 (C-6), 48.9 (C-13), 52.5, 56.0, 56.3 (3 x OMe), 58.3 (C-13a), 111.0, 112.6, 127.5, 128.4, 129.0, 132.6 (Ar methine), 125.1, 126.7, 128.1, 134.5, 147.0, 149.0 (Ar quaternary), 163.2 (C-8), 171.3 (CO_2Me); ms: m/z (%) 385 (100), 353 (5), 326 (21), 325 (9), 292 (4), 209 (62), 176 (2).

Anal. Calcd. for $C_{20}H_{19}NO_5S$: C, 62.32; H, 4.97; N, 3.63; S, 8.32. Found: C, 62.24; H, 4.82; N, 3.58; S, 8.39.

Preparation of *N*-(2-Acetyl-4,5-dimethoxyphenylthiomethyl)benzamide (**4**) and 3-Benzoyl-6,7-dimethoxy-4-methylene-2*H*-1,3-benzothiazine (**5**).

6,7-Dimethoxy-4-methyl-2*H*-1,3-benzothiazine (2.23 g, 0.01 mole) (**1b**) was dissolved in dry benzene (70 ml). Benzoyl chloride (0.01 mole) was added followed by a solution of triethylamine (0.01 mole) in dry benzene (50 ml). The mixture was heated under reflux conditions for 1 hour. The triethylamine hydrochloride was removed, the benzene was evaporated, and the residue was crystallized from benzene (15 ml). The crystals which separated were filtered and recrystallized from ethanol affording colorless crystals of **4** (0.55 g, 16%), mp 174-175°; ir: (ν max, cm^{-1}) 3394 (NH), 1653 (overlapping bands of amide-I and ketone carbonyls); pmr (deuteriochloroform, 80 MHz): δ 2.59 (3H, s, $COCH_3$), 3.89, 3.91 (6H, 2s, 2 x OMe), 4.92 (2H, d, J = 5.6 Hz, SCH_2N), 6.85 (1H, br t, NH), 7.10, 7.20 (2H, 2s, ArH), 7.25-7.55 (3H, m, ArH), 7.65-7.90 (2H, m, ArH); ms: m/z (%) 345 (1), 212 (70), 197 (65), 105 (100).

Anal. Calcd. for $C_{18}H_{19}NO_4S$: C, 62.59; H, 5.54; N, 4.06; S, 9.28. Found: C, 62.29; H, 5.43; N, 3.98; S, 9.34.

The benzene mothers liquors, from which **4** had separated, were evaporated and the residue was crystallized from ethanol (10 ml). Yellow crystals of **5** (2.25 g, 69%) were obtained which melted at 133-134°; ir: (ν max, cm^{-1}) 1636 (amide); pmr (deuteriochloroform, 80 MHz): δ 3.86, 3.88 (6H, 2s's, 2 x OMe), 4.54 (1H, d, J = 1.5 Hz, olefinic H), 5.18 (2H, s, N-CH_2-S), 5.36 (1H, d, J = 1.5 Hz, olefinic H *syn* to carbonyl), 6.66 (1H, s, ArH), 7.04 (1H, s, ArH), 7.35 (5H, m, ArH's); cmr (deuteriochloroform, 20.14 MHz): δ 45.2 (C-2), 56.1, 56.4 (2 x OMe), 107.8 (=CH_2), 109.5, 110.8 (C-5 and C-8), 128.0 (two overlapping signals corresponding to four carbon atoms), 130.1, (Ar methine), 120.3, 124.9, 135.8, 141.5, 147.8, 150.7 (Ar quaternary and one olefinic quaternary), 169.3 (C=O); ms: m/z (%) 327 (31), 299 (81), 222 (32), 208 (25), 105 (99), 77 (100).

Anal. Calcd. for $C_{18}H_{17}NO_3S$: C, 66.03; H, 5.24; N, 4.28; S, 9.79. Found: C, 66.12; H, 5.29; N, 4.35; S, 9.68.

13,13a-Dihydro-2,3-dimethoxy-6*H*,8*H*-isoquino[2,3-*c*][1,3]benzothiazin-8-one (**6**).

The enamide **5** (3.27 g, 0.01 mole) in *t*-butyl alcohol (1000 ml) was irradiated with a high pressure mercury lamp (Pyrex filter) at 30-40° under nitrogen for 3 hours. Evaporation of the solvent left a yellow-red solid which was recrystallized from benzene to afford the photocyclized lactam **6** (1.11 g) as pale orange crystals. Column chromatography of the residue obtained from the above mother liquor on silica-gel afforded an additional crop of **6** (0.87 g), combined yield - 61%. Recrystallization from benzene gave pale yellow crystals, mp 165-166°; ir: (ν max, cm^{-1}) 1649 (lactam); pmr (deuteriochloroform, 250 MHz): δ 3.00 (1H, m, H-13), 3.09 (1H, dd, J = 11.5 and 5 Hz, H-13), 3.79, 3.84 (6H, 2s, 2 x OMe), 4.17 (1H, d, J = 12.5 Hz, H-6_{ax}), 4.86 (1H, m, H-13a), 5.70 (1H, d, J = 12.5 Hz, H-6_{eq}), 6.73, 6.75 (2H, 2s, H-1 and H-4), 7.20 (1H, d, J ≅ 8 Hz, H-12), 7.30 (1H, t, J ≅ 8 Hz, H-10), 7.40 (1H, t, J ≅ 8 Hz, H-11), 8.02 (1H, d, J ≅ 8 Hz, H-9); cmr (deuteriochloroform, 20.14 MHz): δ 36.4 (C-13), 42.9 (C-6), 55.3 (C-13a), 55.6, 56.0 (2 x OMe), 111.2, 112.2, 126.4, 126.5, 128.0, 131.6 (Ar methine), 124.9, 126.8, 127.8, 136.7, 147.5, 148.1 (Ar quaternary), 162.8 (C-8); ms: m/z (%); 327 (100), 326 (12), 325 (8), 294 (16), 293 (1), 292 (4), 209 (2), 118 (7).

Anal. Calcd. for $C_{18}H_{17}NO_3S$: C, 66.03; H, 5.24; N, 4.28; S, 9.79. Found: C, 66.12; H, 5.29; N, 4.35; S, 9.86.

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REFERENCES AND NOTES

[1] This paper may be regarded as Part **4** of the series "Thiaalkaloids", Part **3**: see ref [2], and as Part **8** of the series "Cycloaddition Reactions of 1,3-Benzothiazines", Part **7**: see ref [3].

[2] L. Fodor and D. B. MacLean, *Can. J. Chem.*, **65**, 636 (1987).

[3] L. Fodor and D. B. MacLean, *Can. J. Chem.*, **65**, 18 (1987).

[4] L. Fodor, J. Szabó, G. Bernáth and P. Sohár, *Tetrahedron Letters*, **25**, 2013 (1984).

[5] R. Marsden, D. B. MacLean and L. Fodor, *Can. J. Chem.*, **62**, 2682 (1984).

[6] M. Cushman, J. Gentry and F. W. Dekow, *J. Org. Chem.*, **42**, 1111 (1977).

[7] M. A. Haimova, N. M. Mollov, S. C. Ivanova, A. I. Dimitrova and V. I. Ognyanov, *Tetrahedron*, **33**, 331 (1977).

[8] M. Cushman and F. W. Dekow, *Tetrahedron*, **34**, 1435 (1978).

[9] M. Cushman and F. W. Dekow, *J. Org. Chem.*, **44**, 407 (1979).

[10] K. Iwasa, Y. P. Gupta and M. Cushman, *J. Org. Chem.*, **46**, 4744 (1981).

[11] P. Sohár, L. Fodor, J. Szabó and G. Bernáth, submitted for publication.

[12] I. Ninomiya and T. Naito, in "The Alkaloids", Vol **XXII**, A. Brossi, ed, Academic Press, New York, NY, 1983, p 189.

[13] G. R. Lenz, *Synthesis*, 489 (1978).

[14] J. R. Chapman, "Practical Organic Mass Spectrometry", John Wiley and Sons, Inc., New York, NY, 1985, p 146.

[15] J. Szabó, L. Fodor, I. Varga, E. Vinkler and P. Sohár, *Acta Chim. Acad. Sci. Hung.*, **92**, 317 (1977).

[16] J. Szabó, L. Fodor, I. Varga and P. Sohár, *Acta Chim. Acad. Sci. Hung.*, **88**, 149 (1976).

[17] S. N. Rastogi, J. S. Bindra and N. Anand, *Indian J. Chem.*, **9**, 1175 (1971).