Preparation of Potentially Bioactive Aza and Thiaza Polycyclic Compounds Containing a Bridgehead Nitrogen Atom. Synthesis of Pyrrolo[1,2,3-*de*]-1,4-benzothiazine Derivatives

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The synthesis of some pyrrolo[1,2,3-*de*]-1,4-benzothiazine derivatives by using a modified Bischler type cyclization of *N*-(2,2-diethoxyethyl)-2*H*-1,4-benzothiazines as a crucial step is described. The alternative approach based on Friedel-Crafts alkylation of the *N*-(2-chloroethyl)-2*H*-1,4-benzothiazines is shown to be impractical due to the low yield obtained.

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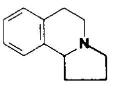
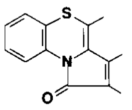
We have previously synthesized polycyclic compounds containing bridgehead nitrogen atom such as the benzopyrrocoline **A** [1] and the pyrrolo[2,1-*c*]-1,4-benzothiazine **B** [2]. As part of our research program to construct systems with a bridgehead nitrogen atom, considering also that several thiaza polycyclic compounds have some biological activity [3], we now report the synthesis of pyrrolo[1,2,3-*de*]-1,4-benzothiazine derivatives **C**. So far, there are no reports about the preparation of these compounds even though a number of analogs of the phenothiazine ring system **D** appeared in the recent literature [4].


A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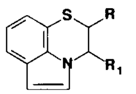
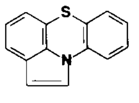


C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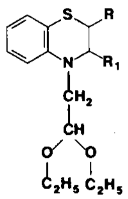
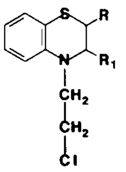


E



F

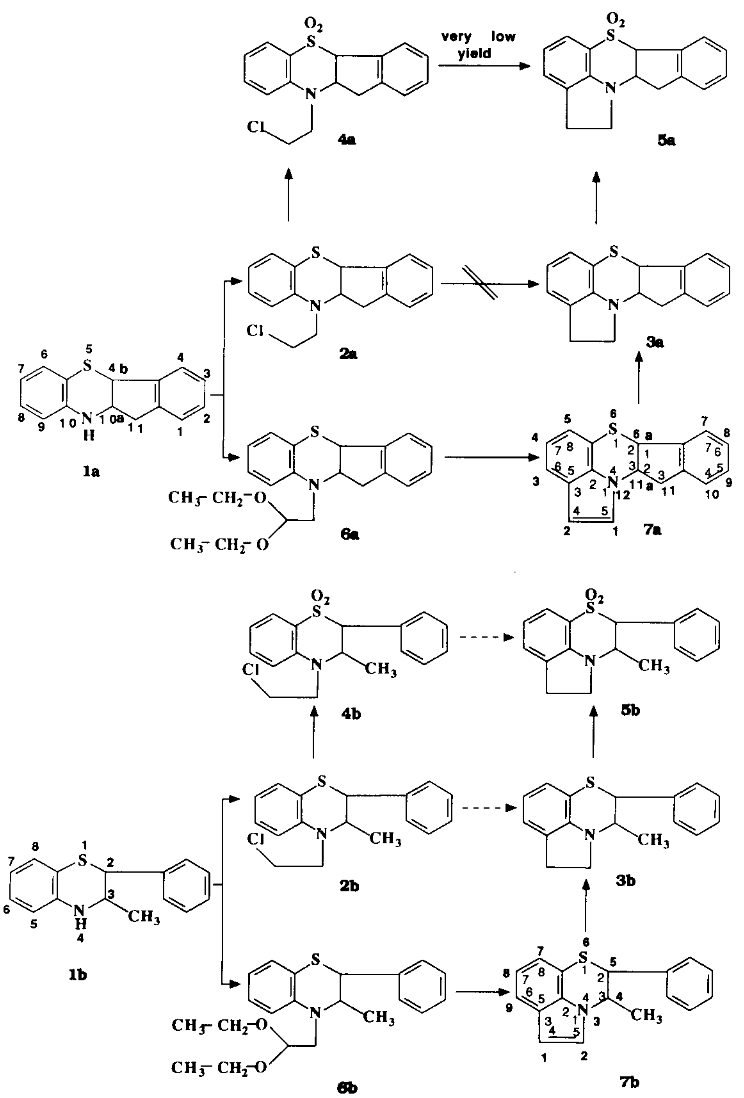
From a synthetic view point two approaches were considered for our goal. Thus, we planned to prepare systems of type **C** *via* an acid catalyzed cyclization of the acetals **E** according to a modification of the well known Bischler indole synthesis [5]. Alternatively, an intramolecular Friedel-Crafts alkylation of the intermediate **F** was also evaluated. However, we found that this last approach was unsatisfactory due to the very low yields obtained in the Friedel-Crafts alkylation of the 2-chloroethyl derivative **F**. In fact, when 4b,10,10a,11-tetrahydroindeno[1,2-*b*]-1,4-benzothiazine **1a** [6] (Scheme 1) was treated with the system chloroacetic acid-sodium borohydride according to a literature method [7] the alkylation at nitrogen atom occurred in 60% yield leading to compound **2a**. The cyclization of **2a** was attempted with aluminium trichloride in decaline following a published procedure [8]. However, the starting tetracyclic compound underwent ring cleavage and 3,4-dihydro-2*H*-1,4-benzothiazine [9] was recovered in 20% yield.

With the aim to minimize the observed ring opening of the starting material, we investigated the alkylation reaction of the sulfone **4a** first with aluminium trichloride in decaline and next with an aluminium trichloride/ammonium chloride mixture. In both cases only traces of compound **5a** were obtained according to gc/ms and ^{1}H-nmr analyses of the crude reaction products.

Taking into account these results, attention was focused on the Bischler method. Treatment of **1a** with bromoacetaldehyde diethyl acetal in refluxing toluene gave the *N*-alkylated derivative **6a** in 32% yield. Hydrolytic cleavage of the acetal with *p*-toluenesulfonic acid in dioxane afforded the required compound **7a** in 38% yield. Sodium borohydride in acetic acid reduction of this compound yielded **3a** (31%) which was oxidized by *m*-chloroperbenzoic acid to **5a** in 31% yield. As shown in Scheme 1 similar results were obtained starting from the 2-phenyl-3-methyl-3,4-dihydro-2*H*-1,4-benzothiazine **1b** [10]. Repetition of the reaction sequences outlined above afforded **2b** (58%), **4b** (57%), **6b** (62%), **7b** (25%), **3b** (53%) and **5b** (42%). Due to the poor yield obtained by Friedel-Crafts alkylation of **4a** as well as to the unsatisfactory results reported in the literature [11] concerning similar Friedel-Crafts ring closures, attempts to cyclize **2b** or **4b** in this way were not made.

The structures of the new compounds were confirmed by ^{1}H-nmr spectroscopy, mass spectra and microanalytical data. In particular, interesting feature of the ^{1}H-nmr spectra of **7a,b** was the presence of two doublets: the first well separated at δ *ca* 6.5 and the second one masked by the signals of the aromatic protons at δ *ca* 7.1. These doublets are attributed to the vinyl protons at positions β and α to the nitrogen, respectively. Irradiation of the proton at higher field (corresponding to that at the β-position) allow-

Scheme 1



ed the determination of the exact chemical shift of the proton at the α-position (CH = C*H*-N) superimposed on the phenyl signals.

As for some stereochemical features, it is interesting to point out that the ^{1}H-nmr spectroscopy and thin-layer chromatography showed that the parent compounds of the two series, **1a** and **1b**, respectively, are single geometrical isomers.

Taking into account that it is reported in the literature [12] - (i) the 2,3-diphenyl-2,3-dihydro-1,4-benzothiazines show a coupling constant between C_2H and C_3H of 9 and 3 Hz, for *trans* and *cis* isomer, respectively (ii) the 2-trimethylsilyl-3-phenyl-2,3-dihydro-1,4-benzothiazine, obtained as single isomer with coupling constant of 8.8 Hz, is regarded as a *trans* isomer - our compounds **1a** and **1b** should be regarded as *cis* isomers. In fact, both compounds possess a small value (J = 3 Hz) of the coupling constants relative to the $C_{4b}H$ of **1a** and to the C_2H of **1b**. On this basis, also the other synthesized compounds should be regarded as *cis* isomers. However, ^{1}H-nmr data do not allow a conclusive stereochemical assignment particularly for the compounds which show coupling constant of 6 Hz. Further informations, at present unavailable, are necessary to specify unambiguously the stereochemistry.

In summary, the present work [13] demonstrates that the route outlined in Scheme 1 involving the Bischler type approach is successfully applicable to prepare the pyrrolo[1,2,3-*de*]-1,4-benzothiazine system so far unknown in the literature. The alternative approach based on Friedel-Crafts type alkylation was concluded to be impractical since only very low yields of the required compounds were obtained.

EXPERIMENTAL

Melting points were determined on a Tottoli apparatus and are uncorrected. The ir spectra were taken on a Perkin-Elmer 257 instrument; all compounds exhibit absorption bands between 1605-1570 cm^{-1} (C=C vibrations) and 1360-1330 cm^{-1} (C–N vibrations due to tertiary aromatic amines); the absorptions due to other groups are reported below. The ^{1}H-nmr spectra were recorded on a Varian EM-390 instrument operating at 90 MHz. Chemical shifts are given in δ (ppm) from tetramethylsilane as the internal standard. Gas-mass analysis has been carried out on a Hewlett-Packard 5995 C-CG/MS instrument. Column chromatography of the crude residue of reaction mixtures on silica gel (Merck 70-325 mesh) (ratio 1:35) were carried out using light petroleum ether (bp 40-70°) - ethyl acetate (9:1 v/v) as eluant, unless otherwise stated. Preparative tlc on silica gel Carlo Erba Stratocrom SIF$_{254}$ were carried out using petroleum ether (bp 40-70°) - ethyl acetate (8:2 v/v) as eluant.

N-(2-Chloroethyl)-4b,10,10a,11-tetrahydroindeno[1,2-*b*]-1,4-benzothiazine **2a**.

To a solution of **1a** [6] (1.5 g, 6.3 mmoles) in dry benzene (50 ml), 8.9 g (94.2 mmoles) of chloroacetic acid and 1.2 g of sodium borohydride were added. The mixture was refluxed under stirring for 2 hours. After cooling, the mixture was made alkaline with aqueous sodium hydroxide solution. The aqueous phase was extracted with benzene, which was dried over sodium sulfate and evaporated. The residue was purified by column chromatography to give **2a** (60%), mp 111-112°; ^{1}H-nmr (deuteriochloroform): δ [2.9-3.5 (m, 2H), 3.5-4.0 (m, 4H), 4.1-4.5 (m, 2H): $\text{Cl-C}H_2\text{-C}H_2\text{-N(C}_{11}H_2\text{)-C}_{10a}H\text{-C}_{4b}H\text{-S}$], 6.5-6.85 (m, 2H, aromatic-H *ortho* and *para* to N), 6.95-7.5 (m, 6H, aromatic protons); ms: m/e 303 and 301 (M$^+$), 252, 136 (base peak), 117, 115.

Anal. Calcd. for $C_{17}H_{16}ClNS$: C, 67.65; H, 5.34; N, 4.64. Found: C, 67.35; H, 5.15; N, 4.63.

N-(2-Chloroethyl)-4b,10,10a,11-tetrahydroindeno[1,2-*b*]-1,4-benzothiazine *S,S*-Dioxide **4a**.

To a solution of **2a** (2.78 g, 9.2 mmoles) in chloroform (104 ml), 4.74 g, (27.5 mmoles) of 3-chloroperbenzoic acid was added and the mixture was refluxed with stirring for 1 hour. After cooling, the mixture was made alkaline with aqueous sodium carbonate. The aqueous phase was extracted with chloroform, which was dried over sodium sulfate and evaporated. The residue was recrystallized from 2-propanol to give **4a** (67%), mp 177-179°; ir (Nujol mull): 1340, 1300, 1165 and 1145 cm^{-1} (SO$_2$); ^{1}H-nmr (deuteriochloroform): δ [3.2-3.6 (m, 2H), 3.6-4.2 (m, 4H), 4.5-4.9 (m, 2H): $\text{Cl-C}H_2\text{-C}H_2\text{-N(C}_{11}H_2\text{)-C}_{10a}H\text{-C}_{4b}H\text{-SO}_2$], 6.7-7.0 (m, 2H, aromatic-H *ortho* and *para* to N), 7.2-7.65 (m, 5H, aromatic protons), 7.7-8.0 (m, 1H, aromatic-H *ortho* to SO$_2$; ms: m/e 335 and 333 (M$^+$), 284 (base peak), 220 and 218, 204, 115.

Anal. Calcd. for $C_{17}H_{16}ClNO_2S$: C, 61.16; H, 4.83; N, 4.20. Found: C, 61.21; H, 5.04; N, 4.27.

N-(2,2-Diethoxyethyl)-4b,10,10a,11-tetrahydroindeno[1,2-*b*]-1,4-benzothiazine **6a**.

To a solution of **1a** [6] (1.5 g, 6.3 mmoles) in dry toluene (20 ml), 0.7 g of sodium hydride were added with stirring under nitrogen. The mixture was refluxed for 5 hours. Then, 2-bromoacetaldehyde diethylacetal (5.7 g, 28.9 mmoles) was slowly added and the reflux was prolonged for 72 hours. After cooling, the reaction mixture was diluted cautiously with water and the aqueous phase extracted with toluene, which was dried over sodium sulfate and evaporated. The residue was purified by column chromatography to give **6a** (32%) as a yellow oil; ir (Neat): 1150-1060 cm^{-1} (C-O-C, series of bands); ^{1}H-nmr (deuteriochloroform): δ 1.15 and 1.20 (2 t, J = 6.0 Hz, (3+3)H, $(\text{C}H_3)_2$), [2.9-4.0 (m, 8H), 4.3-4.6 (m, 1H): $(\text{C}H_2)_4 + \text{N-C}_{10a}H$], 4.15 (d, J = 6.0 Hz, 1H, $\text{S-C}_{4b}H$), 4.75 (t, J = 6.0 Hz, 1H, $\text{O-C}H\text{-O}$), 6.5-7.5 (m, 8H, aromatic protons); ms: m/e 355 (M$^+$), 252, 136, 115, 103 (base peak).

Anal. Calcd. for $C_{21}H_{25}NO_2S$: C, 70.95; H, 7.09; N, 3.94. Found: C, 71.24; H, 7.08; N, 4.04.

6a,11a-Dihydro-11*H*-indeno[1,2-*b*]pyrrolo[1,2,3-*de*]-1,4-benzothiazine **7a**.

To a solution of **6a** (3g, 8.4 mmoles) in dioxane (15 ml) 0.15 g of *p*-toluenesulfonic acid in 1 ml of water was added. The reaction mixture was allowed to stir at room temperature for 72 hours. Then the mixture was diluted with toluene-water (3:1 v/v) and the aqueous phase extracted with toluene, which was dried over sodium sulfate and evaporated. The residue was purified by column chromatography (toluene as eluant) to give **7a** (38%) as a pale yellow oil, ir (potassium bromide): 800, 775 and 735 cm^{-1} (free H adjacent deformation, CH=CH *cis*); ^{1}H-nmr (deuteriochloroform): δ [3.0-3.6 (m, 2H), 4.9-5.2 (m, 1H): $\text{Ar-C}_{11}H_2\text{-C}_{11a}H\text{-N}$], 4.57 (d, J = 6.0 Hz, 1H, $\text{S-C}_{6a}H$), 6.56 (d, J = 3.0 Hz, 1H, $\text{C}_2H\text{=C}_1\text{H-N}$), 7.0-7.6 (m, 7H, aromatic protons + 1H superimposed at δ 7.20), 7.20 (d, J = 3.0 Hz, 1H, $\text{C}_2\text{H=C}_1H\text{-N}$); this last signal on irradiation at 6.56 zone, becomes s; ms: m/e 263 (M$^+$, base peak), 262, 230, 115.

Anal. Calcd. for $C_{17}H_{13}NS$: C, 77.53; H, 4.98; N, 5.32. Found: C, 77.86; H, 5.00; N, 5.22.

1,2,6a,11a-Tetrahydro-11*H*-indeno[1,2-*b*]pyrrolo[1,2,3-*de*]-1,4-benzothiazine **3a**.

To a solution of **7a** (1.25 g, 4.7 mmoles) in glacial acetic acid (100 ml), 9.0 g of sodium borohydride was added in small portions with stirring at room temperature. Then, mixture was stirred for 24 hours. After evaporation of the solvent under reduced pressure, the mixture was made alkaline by potassium hydroxide and extracted with chloroform. The organic phase was dried over sodium sulfate and evaporated. The residue was purified by column chromatography (light petroleum ether-toluene 1:1 v/v as eluant) to give **3a** (31%) as oil; ir (Nujol mull): 740 cm^{-1} (free H adjacent deformation): ^{1}H-nmr (deuteriochloroform): δ [2.8-3.5 (m, 5H), 3.7-4.2 (m, 3H): $\text{C}_2H_2\text{-C}_1H_2\text{-N-C}_{11a}H\text{-(C}_{11}H_2\text{)-C}_{6a}H\text{-S}$], 6.4-6.65 (m, 1H, aromatic-H *para* to N), 6.75-7.0 (m, 2H, aromatic-H *meta* to N), 7.05-7.4 (m, 4H, aromatic protons); ms: m/e 265 (M$^+$, base peak), 232, 150, 115.

Anal. Calcd. for $C_{17}H_{15}NS$: C, 76.94; H, 5.70; N, 5.28. Found: C, 77.01; H, 5.81; N, 5.10.

1,2,6a,11a-Tetrahydro-11*H*-indeno[1,2-*b*]pyrrolo[1,2,3-*de*]-1,4-benzothiazine *S,S*-Dioxide **5a**.

To a solution of **3a** (0.35 g, 1.3 mmoles) in chloroform (14 ml), 0.7 g (4.1 mmoles) of 3-chloroperbenzoic acid was added and the mixture was refluxed with stirring for 1 hour. After cooling, the mixture was made alkaline with aqueous sodium carbonate. The aqueous phase was extracted with chloroform, which was dried over sodium sulfate and evaporated. The residue was purified by column chromatography (elution mixture 7:3 v/v) to give **5a** (31%), mp 222-225°; ir (Nujol mull): 1340, 1300, 1160 and 1120

cm^{-1} (SO_2); ^1H-nmr (deuteriochloroform): δ [3.0-3.7 (m, 5H), 3.9-4.4 (m, 2H): C_2H_2-C_1H_2-N-$C_{11a}H$-$C_{11}H_2$-Ar], 4.55 (d, J = 6.0 Hz, 1H, $C_{6a}H$-SO_2), 6.6-6.8 (m, 1H, aromatic-H *para* to N), 7.1-7.4 (m, 4H, aromatic protons), 7.45-7.55 (m, 1H, aromatic-H *meta* to N), 7.6-7.7 (m, 1H, aromatic-H *ortho* to SO_2); ms: m/e 297 (M^+, base peak), 232, 115.

Anal. Calcd. for $C_{17}H_{15}NO_2S$: C, 68.66; H, 5.08; N, 4.71. Found: C, 68.36; H, 5.02; N, 4.47.

N-(2-Chloroethyl)-2-phenyl-3-methyl-3,4-dihydro-2*H*-1,4-benzothiazine **2b**.

To a solution of **1b** [10] (3.0 g, 12.4 mmoles) in dry benzene (14 ml), 20 g (211.6 mmoles) of chloroacetic acid and 2.6 g of sodium borohydride were added. The mixture was refluxed with stirring for 4 hours. After cooling, the mixture was made alkaline with aqueous sodium hydroxide solution. The aqueous phase was extracted with benzene, which was dried over sodium sulfate and evaporated. The residue was purified by column chromatography to give **2b** (58%) as a brown oil; ^1H-nmr (deuteriochloroform): δ 1.05 (d, J = 6.0 Hz, 3H, CH_3), 2.5-3.9 (m, 5H, Cl-CH_2-CH_2-N-C_3H), 4.63 (d, J = 3.0 Hz, 1H, S-C_2H), 6.5-6.8 (m, 2H, aromatic-H *ortho* and *para* to N), 6.9-7.5 (m, 7H, aromatic protons); ms: m/e 305 and 303 (M^+), 288, 254, 214, 212 (base peak).

Anal. Calcd. for $C_{17}H_{18}ClNS$: C, 67.20; H, 5.97; N, 4.61. Found: C, 67.36; H, 6.01; N, 4.75.

N-(2-Chloroethyl)-2-phenyl-3-methyl-3,4-dihydro-2*H*-1,4-benzothiazine *S,S*-Dioxide **4b**.

To a solution of **2b** (1.5 g, 4.9 mmoles) in chloroform (60 ml), 2.5 g (14.5 mmoles) of 3-chloroperbenzoic acid was added and the mixture was refluxed with stirring for 1 hour. After cooling, the mixture was made alkaline with aqueous sodium carbonate. The aqueous phase was extracted with chloroform, which was dried over sodium sulfate and evaporated. The residue was purified by column chromatography (elution mixture 8:2 v/v) to give **4b** (57%) as white solid, mp 165-167°; ir (Nujol mull): 1320, 1300, 1140, 1120 cm^{-1} (SO_2); ^1H-nmr (deuteriochloroform): δ 1.50 (d, J = 6.0 Hz, 3H, CH_3), 3.2-4.4 (m, 5H, Cl-CH_2-CH_2-N-C_3H), 4.62 (d, J = 3.0 Hz, 1H, C_2H-SO_2), 6.6-7.0 (m, 2H, aromatic-H *ortho* and *para* to N), 7.1-7.6 (m, 6H, aromatic protons), 7.7-7.9 (m, 1H, aromatic-H *ortho* to SO_2); ms: m/e 337 and 335 (M^+), 300 (base peak), 286, 268, 208, 193, 180, 117, 91.

Anal. Calcd. for $C_{17}H_{18}ClNO_2S$: C, 60.80; H, 5.40; N, 4.17. Found: C, 61.03; H, 5.15; N, 4.10.

N-(2,2-Diethoxyethyl)-2-phenyl-3-methyl-3,4-dihydro-2*H*-1,4-benzothiazine **6b**.

To a solution of **1b** [10] (1.5 g, 6.2 mmoles) in dry toluene (20 ml), 1.12 g of sodium hydride were added with stirring under nitrogen. The mixture was refluxed for 4 hours. Then, 2-bromoacetaldehyde diethylacetal (6.6 g, 33.5 mmoles) was slowly added and the reflux was prolonged for 48 hours. After cooling the reaction mixture, with caution, was diluted with water and the aqueous layer extracted with toluene, which was dried over sodium sulfate and evaporated. The residue was purified by column chromatography to give **6b** (62%), as a yellow oil; ir (neat): 1120-1060 cm^{-1} (C-O-C, series of bands); ^1H-nmr deuteriochloroform): δ 1.02 (d, J = 6.0 Hz, 3H, N-C_3H-CH_3), 1.22 and 1.26 (2t, J = 6.0 Hz, (3+3)H, (CH_2-CH_3)$_2$), 3.1-4.0 (m, 7H, C_3H-N-CH_2-CH=(O-CH_2-CH_3)$_2$), 4.55 (d, J = 3.0 Hz, 1H, S-C_2H), 4.6-4.8 (m, 1H, O-CH-O), 6.5-7.18 (m, 4H, phenylene-H), 7.18-7.6 (m, 5H, phenyl protons); ms: m/e 357 (M^+), 254, 136, 103 (base peak), 91.

Anal. Calcd. for $C_{21}H_{27}NO_2S$: C, 70.55; H, 7.61; N, 3.92. Found: C, 70.7; H, 7.91; N, 3.83.

5-Phenyl-4-methyl-4,5-dihydropyrrolo[1,2,3-*de*]-1,4-benzothiazine **7b**.

To a solution of **6b** (1.0 g, 2.8 mmoles) in dioxane (4 ml), 0.05 g of *p*-toluenesulfonic acid in 0.3 ml of water was added. The reaction mixture was allowed to stir at room temperature for 48 hours. Then the mixture was diluted with toluene-water (3:1 v/v) and the mixture extracted with toluene, which was dried over sodium sulfate and evaporated. The residue was purified by column chromatography (light petroleum ether-toluene 7:3 v/v as eluant) to give **7b** (25%) as a pale yellow oil: ir (neat): 780, 750, 710, 695 cm^{-1} (free H adjacent deformation, CH=CH *cis*); ^1H-nmr (deuteriochloroform): δ 1.32 (d, J = 6.0 Hz, 3H, CH_3), 4.4-4.8 (m, 2H, S-C_5H-C_4H-N), 6.47 (d, J = 3.0 Hz, 1H, C_1H=C_2H-N), 6.8-7.1 (m, 3H, aromatic-H *ortho*, *meta* and *para* to S + 1H superimposed at δ 7.02), 7.02 (d, J = 3.0 Hz, 1H, C_1H=C_2H-N) (this last signal on irradiation at 6.47 zone, becomes s), 7.1-7.5 (m, 5H, phenyl protons); ms: m/e 265 (M^+, base peak), 250, 205, 174 (base).

Anal. Calcd. for $C_{17}H_{15}NS$: C, 76.94; H, 5.70; N, 5.28. Found: C, 77.0; H, 5.77; N, 5.18.

5-Phenyl-4-methyl-1,2,4,5-tetrahydropyrrolo[1,2,3-*de*]-1,4-benzothiazine **3b**.

To a solution of **7b** (1.0 g, 3.8 mmoles) in glacial acetic acid (80 ml), 7.8 g of sodium borohydride was added in small portions with stirring at room temperature. Then, the mixture was allowed to stir for 24 hours. Following evaporation of the solvent under reduced pressure, the mixture was made alkaline by potassium hydroxide solution. The mixture was extracted with chloroform, which was dried over sodium sulfate and evaporated. The residue was purified by column chromatography (light petroleum ether-toluene 7:3 v/v as eluant) to give **3b** (53%) as a white solid, mp 90-93°; ir (Nujol mull): 755, 745 cm^{-1} (free H adjacent deformation); ^1H-nmr (deuteriochloroform): δ 1.03 (d, J = 6.0 Hz, 3H, CH_3), [2.8-3.5 (m, 4H), 3.5-3.7 (m, 1H): C_1H_2-C_2H_2-N-C_4H], 4.46 (d, J = 3.0 Hz, 1H, S-C_5H), 6.5-7.3 (m, 8H, aromatic protons); on irradiation at 1.03 zone, the signal m in zone 3.5-3.7 is modified but the d which appears is superimposed on other signals; on irradiation at 2.8-3.7 zone, the signal d at δ 1.03 becomes s and d at δ 4.46 becomes s; ms: m/e 267 (M^+), 252 (base peak), 206, 176, 144, 117.

Anal. Calcd. for $C_{17}H_{17}NS$: C, 76.36; H, 6.41; N, 5.24. Found: C, 76.59; H, 6.60; N, 5.11.

5-Phenyl-4-methyl-1,2,4,5-tetrahydropyrrolo[1,2,3-*de*]-1,4-benzothiazine *S,S*-Dioxide **5b**.

To a solution of **3b** (0.65 g, 2.4 mmoles) in chloroform (26 ml), 1.26 g (7.3 mmoles) of 3-chloroperbenzoic acid was added and the mixture was refluxed with stirring for 30 minutes. After cooling, the mixture was made alkaline with aqueous sodium carbonate. The aqueous phase was extracted with chloroform, which was dried over sodium sulfate and evaporated. The residue was purified by column chromatography (elution mixture 7:3 v/v) to give **5b** (42%), mp 231-233°; ir (Nujol mull): 1340, 1300, 1160, 1120 cm^{-1} (SO_2); ^1H-nmr (deuteriochloroform): δ 1.20 (d, J = 6.0 Hz, 3H, CH_3), 2.9-4.5 (m, 5H, C_1H_2-C_2H_2-N-C_4H + 1H superimposed at δ 4.09), 4.09 (d, J = 3.0 Hz, 1H, C_5H-SO_2), 6.6-6.82 (m, 1H, aromatic-H *para* to N), 6.9-7.6 (m, 7H, aromatic protons); ms: m/e 299

(M^+), 284, 235, 234 (base peak), 219, 117.

Anal. Calcd. for $C_{17}H_{17}NO_2S$: C, 68.20; H, 5.72; N, 4.68. Found: C, 67.85; H, 5.61; N, 4.49.

Attempts to Prepare Compounds **3a** and **5a** by Friedel-Crafts Alkylation.

To a solution of **2a** (0.4 g, 1.3 mmoles) in dry decaline (14 ml), aluminium trichloride (0.53 g, 4.0 mmoles) freshly sublimed was added. The mixture was heated at 145-150° for 3 hours. After cooling to room temperature, the mixture was acidified with aqueous hydrochloric acid (1:1 v/v) and neutralized with sodium hydroxide. The aqueous phase was extracted with diethyl ether, which was dried over sodium sulfate and evaporated. Preparative tlc of the residue gave 20% yield of 3,4-dihydro-2*H*-1,4-benzothiazine, identified by comparison with an authentic sample [9].

To a mixture of **4a** (0.50 g, 1.5 mmoles) and ammonium chloride (0.08 g, 1.5 mmoles) heated at 160°, aluminium trichloride (0.99 g, 7.42 mmoles) was added and the heating was prolonged for 30 minutes. After cooling to room temperature hydrochloric acid 3 *N* (5 ml) was added. The mixture was neutralized with sodium hydroxide and the aqueous phase was extracted with diethyl ether, which was dried over sodium sulfate and evaporated. Preparative tlc of the residue gave a crude fraction containing only traces of compound **5a** according to gc/ms and ^{1}H-nmr analyses.

REFERENCES AND NOTES

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[13] Biological assays on the new compounds are in progress: particularly to test for the presumable properties mentioned in note [3].