Control of the reaction between 2-aminobenzothiazoles and Mannich bases. Synthesis of pyrido[2,1-*b*][1,3]benzothiazoles *versus* [1,3]benzothiazolo[2,3-*b*]quinazolines

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Reactions between 2-aminobenzothiazoles and Mannich bases are observed to be selectively controlled by the steric hindrance in the latter. Pyrido[2,1-*b*][1,3]benzothiazoles **3** are produced with non-sterically hindered Mannich bases such as 3-(dimethylamino)propiophenone hydrochlorides **2**, whilst [1,3]benzothiazolo[2,3-*b*]quinazolines are produced with bulky Mannich bases such as 2-(dimethylaminomethyl)tetralone **4**. This is shown by reactions with 2-amino-5-(ethylsulfanyl)thiadiazole, which was previously reported to follow the former reaction pathway with **2**, while the reaction with **4** follows the latter reaction pathway. The final structures are established by NMR and X-ray diffraction, thus confirming the cyclization processes.

Introduction

Benzothiazole and its fused derivatives have shown remarkable fungicidal, analgesic, anti-inflammatory, anticonvulsant, anaesthetic and pesticidal activity.[1–6]

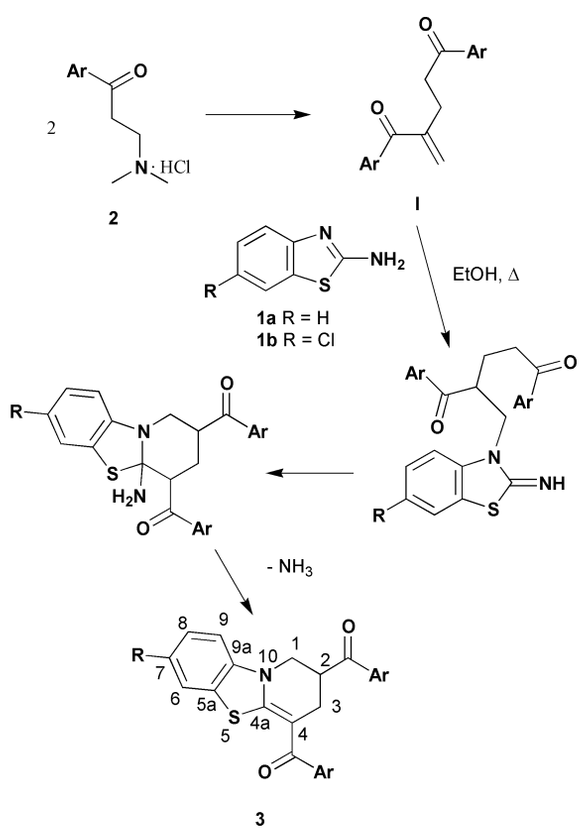
Continuing our research on the reaction of aminoazoles with β-dimethylaminopropiophenones,[7–11] we report the preparation of novel benzothiazole-fused derivatives from 2-aminobenzothiazoles **1** and Mannich bases **2**.

Results and discussion

2-Aminobenzothiazoles **1a** and **1b** were treated with two equivalents of 3-(dimethylamino)propiophenone hydrochlorides **2** in refluxing ethanol to produce pale yellow crystalline compounds **3a**–**j** (Scheme 1 and Table 1). The structures of compounds **3a**–**j** were established as 2,4-diaroyl-2,3-dihydro-1*H*-pyrido-[2,1-*b*][1,3]benzothiazoles, using analytical and spectroscopic methods. The isolation of such compounds can be explained as resulting from an annelation of benzothiazole with **I**, which is formed from **2**, producing the isolated structure following the elimination of ammonia as shown in Scheme 1. A similar process was previously reported in the case of the reaction

Table 1 Results of reaction between 2-aminobenzothiazoles **1** and (dimethylamino)propiophenone hydrochlorides **2**

Comp.	R	Ar	Mp/°C	Yield (%)
3a	H	C_6H_5	239	53
3b	H	4-$CH_3OC_6H_4$	282	50
3c	H	4-ClC_6H_4	290	62
3d	H	4-BrC_6H_4	285	66
3e	H	2-HOC_6H_4	253	50
3f	Cl	C_6H_5	287	55
3g	Cl	4-$CH_3OC_6H_4$	285	55
3h	Cl	4-ClC_6H_4	288	65
3i	Cl	4-BrC_6H_4	308	65
3j	Cl	2-HOC_6H_4	270	62



Scheme 1 Reaction between 2-aminobenzothiazoles **1** and β-(dimethylamino)propiophenone hydrochlorides **2**.

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Table 2 ^{1}H-NMR data[a] of compounds **3a**–**j** (δ/ppm)

Comp.	C(1)H–C(2)H	C(3)H	Benzo	2-Aroyl	4-Aroyl
3a	4.20–4.32	2.92	7.23–7.83	7.31–7.66	7.31–7.66
3b	4.10–4.27	2.94	7.23–7.80	7.02–8.02	6.90–7.43
3c	4.18–4.31	2.89	7.22–7.80	7.54–7.98	7.37–7.75
3d	4.18–4.32	2.89	7.25–7.84	7.72–7.94	7.32–7.54
3e	4.13–4.31	2.89	7.26–7.84	6.89–7.51	6.71–7.49
3f	4.15–4.26	2.91	7.32–7.63	7.32–7.47	7.32–7.47
3g	4.10–4.27	2.94	7.42–7.94	7.02–8.02	6.90–7.42
3h	4.11–4.29	2.90	7.39–7.79	7.76–8.01	7.39–7.46
3i	4.15–4.30	2.88	7.48–7.99	7.72–7.95	7.33–7.55
3j	4.12–4.27	2.88	7.44–7.82	6.87–7.20	6.71–6.94

[a] All signals appear as multiplets. OCH_3 at δ 3.76 and 3.83 for **3b** and δ 3.76 and 3.83 for **3g**. OH at δ 10.25 and 11.32 for **3e** and δ 10.08 and 11.36 for **3j**.

Table 3 ^{13}C-NMR selected data of compounds **3a**–**j** (δ_C/ppm)

	C-1	C-2	C-3	C-4	C-4a	C-5a	C-9a	2-CO	4-CO
3a	45.2	38.1	28.9	96.7	155.3	126.3	139.7	200.2	186.1
3b[a]	45.3	37.8	29.6	97.2	155.0	128.0	139.8	198.5	185.3
3c	45.6	39.0	28.7	96.9	155.9	126.8	139.8	199.2	185.2
3d	45.4	38.5	28.6	96.6	155.7	126.6	139.8	199.4	184.3
3e	45.2	38.6	28.1	98.6	155.1	126.6	139.6	204.5	186.1
3f	45.6	38.5	28.7	97.5	155.2	126.8	139.1	200.1	186.9
3g[b]	45.5	37.8	29.4	97.8	154.9	126.4	138.9	198.4	185.7
3h	45.5	38.3	28.5	98.8	155.6	126.5	138.8	199.1	185.1
3i	45.5	38.3	28.4	97.2	155.6	126.8	139.4	199.3	185.1
3j	45.4	38.7	27.9	99.1	155.1	126.6	138.8	204.4	186.6

[a] OCH_3 groups appear at δ_C 55.0 and 55.5. [b] OCH_3 groups appear at δ_C 55.1 and 55.5.

of (dimethylamino)propiophenones with 2-amino-5-(ethylsulfanyl)thiadiazole **6**[9] and aminothiazole.[12]

The IR spectra of compounds **3** measured in KBr pellets showed two bands for the elongation vibrations of C=O groups at 1680–1735 cm^{-1}.

NMR studies of compounds **3** revealed them to be 1 : 2 adducts (**1** : **2**) containing a (CH_2–CH–CH_2) fragment.

Tables 2 and 3 summarize the ^{1}H- and ^{13}C chemical shifts of **3a**–**j**. The assignment of the signals is supported by ^{1}H, ^{1}H COSY and NOESY techniques and ^{1}H, ^{13}C shift correlation.

In the ^{13}C-NMR spectra, the number of signals belonging to quaternary, tertiary and secondary carbon atoms for compounds **3** was determined using a DEPT experiment (see Table 3) and corresponds to the proposed structure.

NMR spectra of compounds **3** show the presence of the fragment C(1)H_2–C(2)H–C(3)H_2 in the pyridine ring; that for ^{1}H-NMR showed a typical A_2BC_2 pattern, in addition to aromatic protons at δ 6.71–8.02 (see Table 2). In the case of the ^{13}C-NMR spectra, in addition to the corresponding signals for the residues described above, it is worth mentioning the presence of two signals for C=O groups around δ_C 185 and 200 ppm.

The main pattern found from the MS spectra of compounds **3a**–**j** was the loss of aroyl residue (see Experimental section).

The proposed molecular structures for **3e** and **3f** were confirmed by X-ray analysis as shown in Fig. 1 and 2, respectively. The structure of compound **3e**[13] shows two strong intramolecular hydrogen bonds with S(6) motifs, as shown in Fig. 1. Analysis of its supramolecular structure indicated the presence of weak C–H $\cdots$ O hydrogen bonds forming primary $C(11)$, $R_2^1(7)$ and R_2^2 motifs which combine to form a complex three-dimensional network.

In compound **3f** the asymmetric unit is formed by two molecules with slightly different conformations of the pyridine-like residue (see Fig. 2a,b); both have a ring conformation between half-chair and envelope, with a slightly higher contribution of the envelope conformation.

In contrast, the reaction of 2-aminobenzothiazoles **1a** and **1b** with 2-(dimethylaminomethyl)tetralone hydrochloride **4**, under similar conditions to those described above, yielded 1 : 1-adducts, whose structures were determined as 5,7-dihydro-6*H*-benzo[*h*]-[1,3]benzothiazolo[2,3-*b*]quinazolines **5a**,**b** by analytical and spectroscopic methods (Scheme 2). In this case the higher steric hindrance of compound **4** with respect to **2** prevents the formation of the intermediate form type **I**, the α,β-unsaturated ketone of **4** undergoing a Michael addition with the nucleophilic endocyclic nitrogen. A further cyclocondensation between amino and carbonyl group leads to structures **5**.

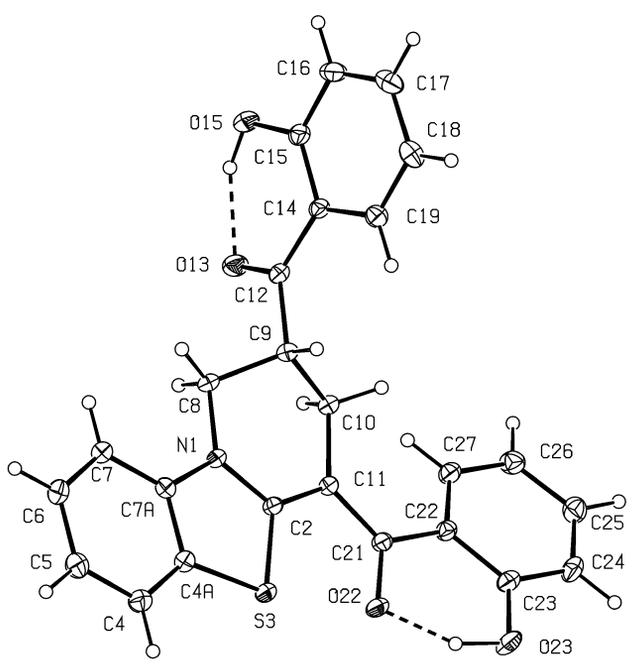


Fig. 1 The asymmetric unit of compound **3e**. Displacement ellipsoids are drawn at the 30% probability level. Numbering is not consistent with IUPAC rules but with ref. 13.

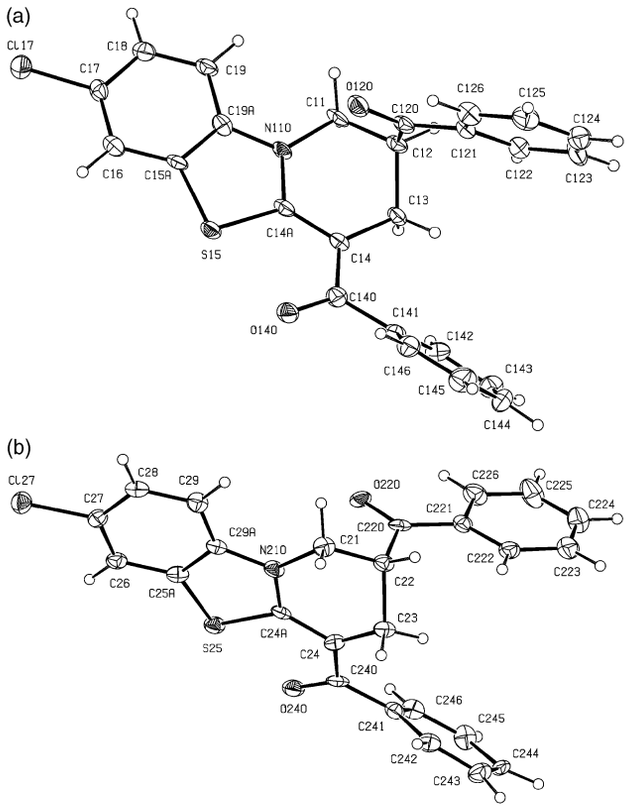
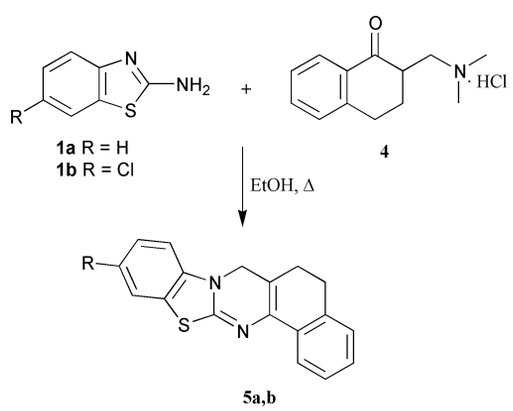


Fig. 2 The two molecules of the asymmetric unit of compound **3f**. Displacement ellipsoids are drawn at the 30% probability level. Numbering is not consistent with IUPAC rules.



Scheme 2 Reaction between 2-aminobenzothiazoles **1** and 2-(dimethylaminomethyl)tetralone hydrochloride **4**.

2-Amino-5-ethylsulfanylthiadiazole **6** similarly reacts with 2-(dimethylaminomethyl)tetralone hydrochloride **4** with formation of 1 : 1-adduct **7**, which was also completely characterized as 10-ethylsulfanyl-5,7-dihydro-6*H*-benzo[*h*][1,3,4]thiadiazolo-[2,3-*b*]quinazoline through analytical and spectroscopic methods (Scheme 3).

Fig. 3 summarizes the ^{1}H and ^{13}C chemical shifts of **5a**,**b** and **7**. The assignment of the signals is also supported by ^{1}H, ^{1}H COSY and NOESY techniques and ^{1}H, ^{13}C shift correlation.

The structures were unambiguously determined by analysis of the crystal structure of **5b** by X-ray diffraction.[14] No special features were found in its structure except for the presence of two independent molecules with differences in the conformation of the cyclohexadiene fragment, which shows much more pronounced deviations from planarity in one of the molecules than in the other (see Fig. 4a,b).

Conclusions

In conclusion, we have shown that the reaction of 2-amino-benzothiazoles **1** with Mannich bases, an annelation condensation with elimination of an ammonia molecule, yields **3**, or a cyclocondensation involving the amino group to yield **5** or **7**, can be selectively controlled by using the appropriate Mannich base. Hence the use of Mannich bases that can easily form a dimer like compound **I** (non-sterically hindered) can select the former reaction pathway, while bulky Mannich bases should lead to the latter reaction pathway.

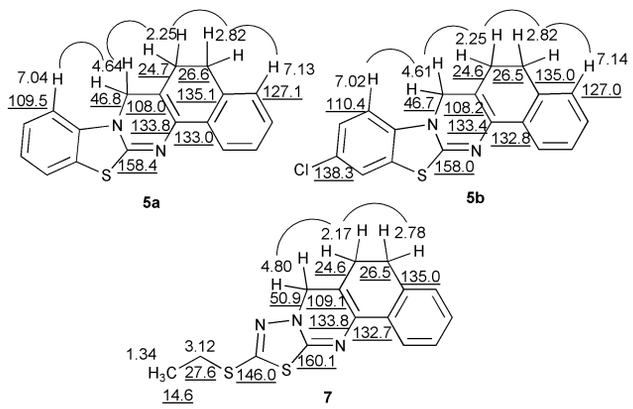
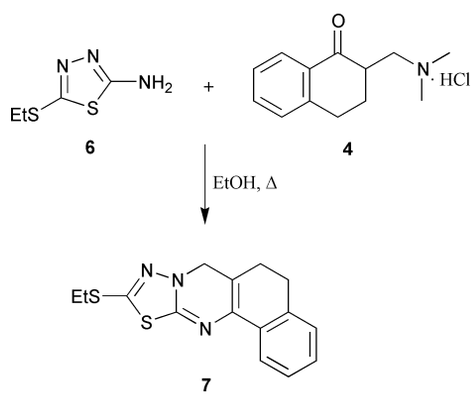


Fig. 3 ^{1}H and ^{13}C NMR data of **5a**, **5b** and **7**. Lines indicate the most important observed NOEs.



Scheme 3 Reaction between 2-amino-5-(ethylsulfanyl)thiadiazole **6** and 2-(dimethylaminomethyl)tetralone hydrochloride **4**.

Experimental

Melting points were determined in a Buchi Melting Point Apparatus and are uncorrected. ^{1}H- and ^{13}C-NMR spectra were run on a Bruker DPX 300 spectrometer operating at 300 MHz and 75 MHz respectively, using (dimethyl sulfoxide)-d_6 as solvent and tetramethylsilane as internal standard. Mass spectra were scanned on a Hewlett-Packard HP Engine-5989 spectrometer (equipped with a direct-inlet probe) and operating at 70 eV. Elemental analyses were obtained using a LECO CHNS-900 equipment.

General procedure for the synthesis of 2,4-diaroyl-2,3-dihydro-1*H*-pyrido[2,1-*b*] [1,3]benzothiazoles 3

A solution of 2-aminobenzothiazole **1a** or 2-amino-6-chlorobenzothiazole **1b** (0.5 mmol) and the corresponding β-(dimethylamino)propiophenone hydrochloride **2** (1 mmol) in 15 ml of absolute ethanol was heated to reflux for 20 minutes. Products **3** were isolated by cooling the reaction mixture, followed by filtration, washing with ethanol, drying in air, and recrystallization from ethanol. In all cases the products were isolated as yellow crystals.

2,4-Dibenzoyl-2,3-dihydro-1*H*-pyrido[2,1-*b*][1,3]benzothiazole 3a. (Found: C, 75.65; H, 4.87; N, 3.66. $C_{25}H_{19}NO_2S$ requires C, 75.54; H, 4.82; N, 3.52%); *m*/*z* (EI) 398 (12%), 397

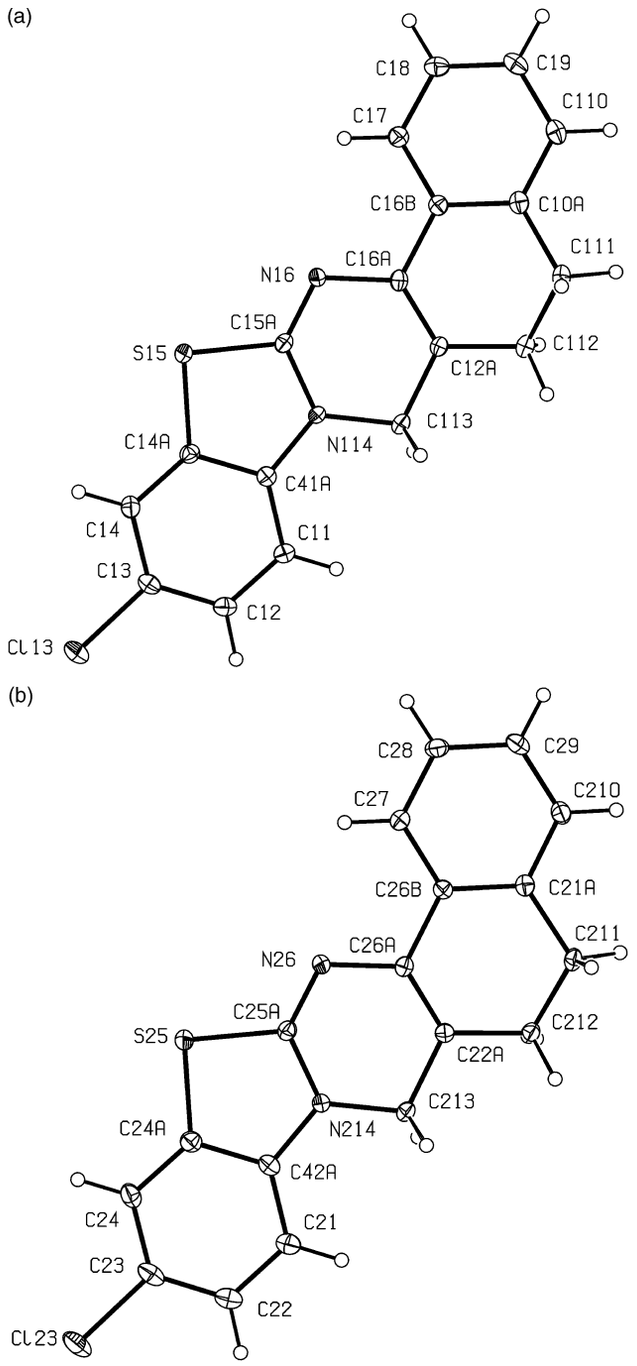


Fig. 4 The two molecules of the asymmetric unit of compound **5b**. Displacement ellipsoids are drawn at the 30% probability level. Numbering is not consistent with IUPAC rules but with ref. 14.

(37, M^+), 293 (22), 292 (100, $M^+ - C_6H_5C{=}O$), 186 (17), 105 (38, $C_6H_5C{=}O$) and 77 (36).

2,4-Bis-(4-methoxybenzoyl)-2,3-dihydro-1*H*-pyrido[2,1-*b*]-[1,3]benzothiazole 3b. (Found: C, 70.76; H, 4.98; N, 3.17. $C_{27}H_{23}NO_4S$ requires C, 70.88; H, 5.07; N, 3.06%); *m*/*z* (EI) 457 (27%, M^+), 323 (22), 322 (100, $M^+ - 4\text{-}MeOC_6H_4C{=}O$), 214 (13), 186 (14), 135 (49, $4\text{-}CH_3OC_6H_4C{=}O$), 107 (10), 92 (10) and 77 (18).

2,4-Bis-(4-chlorobenzoyl)-2,3-dihydro-1*H*-pyrido[2,1-*b*][1,3]-benzothiazole 3c. (Found: C, 64.45; H, 3.82; N, 3.06. $C_{25}H_{17}Cl_2NO_2S$ requires C, 64.38; H, 3.67; N, 3.00%); *m*/*z* (EI) 469/467/465 (4/17/20%, M^+), 328/326 (41/100, $M^+ - 4\text{-}ClC_6H_4C{=}O$), 327 (22), 187 (11), 186 (26), 141 (14), 139 (39, $4\text{-}ClC_6H_4C{=}O$), 113 (10), 111 (28), 75 (11).

2,4-Bis-(4-bromobenzoyl)-2,3-dihydro-1*H*-pyrido[2,1-*b*][1,3]-benzothiazole 3d. (Found: C, 54.15; H, 3.20; N, 2.63. $C_{25}H_{17}Br_2NO_2S$ requires C, 54.08; H, 3.09; N, 2.52%); *m*/*z* (EI) 557/555/553 (10/18/10%, M^+), 373 (21), 372/370 (100/99, $M^+ - 4\text{-}BrC_6H_4C{=}O$), 371 (20), 187 (19), 186 (41), 185 (36), 183 (34), 157 (19), 155 (21), 76 (21) and 75 (11).

2,4-Bis-(2-hydroxybenzoyl)-2,3-dihydro-1*H*-pyrido[2,1-*b*]-[1,3]benzothiazole 3e. (Found: C, 69.83; H, 4.39; N, 3.21. $C_{25}H_{19}NO_4S$ requires C, 69.91; H, 4.46; N, 3.26%); *m*/ 430 (15%), 429 (45, M^+), 309 (23), 308 (100, $M^+ - 2\text{-}HOC_6H_4C{=}O$), 188 (20), 186 (18), 121 (29, $2\text{-}HOC_6H_4C{=}O$), 93 (12) and 65 (19).

2,4-Dibenzoyl-7-chloro-2,3-dihydro-1*H*-pyrido[2,1-*b*][1,3]-benzothiazole 3f. (Found: C, 69.48; H, 4.15; N, 3.29. $C_{25}H_{18}ClNO_2S$ requires C, 69.52; H, 4.20; N, 3.24%); *m*/*z* (EI) 433/431 (6/14%, M^+), 328/326 (18/52, $M^+ - C_6H_5CO$), 270 (5), 220 (13), 105 (83, C_6H_5CO) and 77 (100, C_6H_5).

2,4-Bis-(4-methoxybenzoyl)-7-chloro-2,3-dihydro-1*H*-pyrido-[2,1-*b*][1,3]benzothiazole 3g. (Found: C, 65.86; H, 4.59; N, 2.79. $C_{27}H_{22}ClNO_4S$ requires C, 65.92; H, 4.51; N, 2.85%); *m*/*z* (EI) 493/491 (1/3%, M^+), 357 (10), 358/356 (18/45, $M^+ - 4\text{-}CH_3OC_6H_5C{=}O$), 248 (14), 220 (16), 135 (100, $4\text{-}CH_3OC_6H_4C{=}O$), 107 (21), 92 (21) and 77 (39).

2,4-Bis-(4-chlorobenzoyl)-7-chloro-2,3-dihydro-1*H*-pyrido-[2,1-*b*][1,3]benzothiazole 3h. (Found: C, 59.90; H, 3.15; N, 2.88. $C_{25}H_{16}Cl_3NO_2S$ requires C, 59.96; H, 3.22; N, 2.80%); *m*/*z* (EI) 503/501/499 (7/20/18%, M^+), 364 (13), 363 (14), 361 (20), 362/360 (59/100, $M^+ - 4\text{-}ClC_6H_4C{=}O$), 220 (22), 141/139 (22/62, $4\text{-}ClC_6H_4C{=}O$), 113 (15), 111 (44) and 75 (16).

2,4-Bis-(4-bromobenzoyl)-7-chloro-2,3-dihydro-1*H*-pyrido-[2,1-*b*][1,3]benzothiazole 3i. (Found: C, 50.96; H, 2.78; N, 2.29. $C_{25}H_{16}Br_2ClNO_2S$ requires C, 50.92; H, 2.73; N, 2.38%); *m*/*z* (EI) 591 (12%), 589 (20), 587 (10), 408 (31), 407 (25), 406 (100), 405 (20), 404 (87), 222 (15), 221 (13), 220 (36), 185 (77), 184 (11), 183 (67), 157 (41), 155 (40), 104 (10), 77 (11), 76 (38), 75 (26) and 50 (16).

2,4-Bis-(2-hydroxybenzoyl)-7-chloro-2,3-dihydro-1*H*-pyrido-[2,1-*b*][1,3]benzothiazole 3j. (Found: C, 64.79; H, 3.86; N, 3.10. $C_{25}H_{18}ClNO_4S$ requires C, 64.72; H, 3.91; N, 3.02%); *m*/*z* (EI) 465/463 (8/17%, M^+), 344/342 (21/64, $M^+ - 2\text{-}HOC_6H_4C{=}O$), 343 (15), 222 (23), 343 (15), 222 (23), 220 (22), 147 (10), 122 (11), 121 (100, $2\text{-}HOC_6H_4C{=}O$), 93 (42), 65 (78), 63 (16) and 39 (45).

General procedure for the synthesis of 5,7-dihydro-6*H*-benzo[*h*]-[1,3]benzothiazolo[2,3-*b*]quinazolines 5

A solution of 2-aminobenzothiazole **1a** or 2-amino-6-chlorobenzothiazole **1b** (0.5 mmol) and 2-(dimethylaminomethyl)-tetralone hydrochloride **4** (1 mmol) in 15 ml of absolute ethanol was heated to reflux for 30 minutes. The products **5** were isolated by cooling the reaction mixture, followed by filtration, washing with ethanol, drying in air, and recrystallization from ethanol. In both cases the products were isolated as yellow crystals.

5,7-Dihydro-6*H*-benzo[*h*][1,3]benzothiazolo[2,3-*b*]quinazoline 5a. Mp 153 °C (75% yield) (Found: C, 78.75; H, 5.13; N, 4.76. $C_{19}H_{15}NS$ requires C, 78.86; H, 5.22; N, 4.84%); *m*/*z* (EI) 291 (22%), 290 (73, M^+), 289 (100), 287 (13), 145 (5), 144 (6), 127 (5) and 109 (6).

11-Chloro-5,7-dihydro-6*H*-benzo[*h*][1,3]benzothiazolo[2,3-*b*]-quinazoline 5b. Mp 179 °C (70% yield) (Found: C, 70.36; H, 4.28; N, 4.27. $C_{19}H_{14}ClNS$ requires C, 70.47; H, 4.36; N, 4.33%); *m*/*z* (EI) 325 (52%), 326/324 (25/74, M^+), 323 (100), 321 (8) and 162 (5).

Synthesis of 10-ethylsulfanyl-5,7-dihydro-6*H*-benzo[*h*][1,3,4]-thiadiazolo[2,3-*b*]quinazoline 7

A solution of 2-amino-5-ethylsulfanyl-1,2,4-thiadiazole **6** (0.5 mmol) and 2-(dimethylaminomethyl)tetralone hydrochloride **4** (1 mmol) in 15 ml of absolute ethanol was heated to reflux for 30 minutes. The product **7** was isolated in 60% yield by cooling, followed by filtration, washing with ethanol, drying in air, and recrystallization from ethanol. Mp 180 °C (Found: C, 59.85; H, 5.09; N, 13.86. $C_{15}H_{15}N_3S_2$ requires C, 59.77; H, 5.02; N, 13.94%); *m*/*z* (EI) 302 (29%), 301 (87, M^+), 300 (100), 272 (10), 240 (13, $M^+ - C_2H_5S$), 214 (30), 213 (23), 181 (31), 154 (12), 129 (14), 128 (20), 127 (18), 115 (15), 77 (11) and 59 (10).

Selected data for crystal structure determination of 2,4-dibenzoyl-7-chloro-2,3-dihydro-1*H*-pyrido[2,1-*b*][1,3]benzothiazole 3f‡

Crystal data. $C_{25}H_{18}ClNO_2S$, M = 431.91, triclinic, a = 10.681(2), b = 14.080(3), c = 14.690(3) Å, α = 108.97(3), β = 103.67(3), γ = 90.03(3)°, V = 2022.7(7) Å^3, T = 150(1) K, space group P-1 (no. 2), Z = 4, μ(Mo-Kα) = 0.315 mm^{-1}, 24 712 reflections measured, 8480 unique (R_{int} = 0.118) which were used in all calculations. The final $R(F^2)$ was 0.191 (all data).

This structure was determined from data with an R_{int}-value of 0.118. At the conclusion of the first refinement, there were six peaks of size 1.8 to 1.3 e Å^{-3} in the difference map. These peaks were distributed in identical locations around the two molecules of the asymmetric unit. These peaks, three to each molecule, made no chemical sense.

However, it was then noted that the separation of pairs of these peaks was essentially identical to the intramolecular C ··· S separations in the two independent molecules (5.5–5.6 Å). Rerefinement of the structure with these peaks assumed to be Cl atoms indicated that in the crystal there is some minor (between 5 and 10%) disorder. Such disorder would allow the minor C and S atoms to be seen (as peaks between 1 and 2 e Å^{-3} in the difference map), but not the lighter atoms. Thus modelling of the disorder is precluded.

This explanation is also consistent with the relatively high R-factor (11%) and the general 'noise'. There is full confidence in the structure of the two independent molecules. Full anisotropic refinement of all non-H atoms led to perfectly satisfactory anisotropic displacement parameters.

‡ CCDC reference number(s) 171803. See http://www.rsc.org/suppdata/p1/b1/b109676a/ for crystallographic files in .cif other electronic format.

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References

1 M. Di Braccio, G. Roma, M. Mazzei, A. Balbi and R. Jesta, *Farmaco, Ed. Sci.*, 1986, **41**, 183.
2 D. Evans, *Br. Pat.*, 1 345 148, 1974 (*Chem. Abstr.*, 1974, **80**, 133418r).
3 J. Baetz, *Ger. Offen.*, 2 242 241, 1973 (*Chem. Abstr.*, 1973, **78**, 147990s).
4 S. C. Mehra, S. Zaman and A. A. Khan, *J. Indian Chem. Soc.*, 1980, **57**, 829.
5 A. Bartovic, D. Ilavsky, O. Simo, L. Zalibera, A. Belicova and M. Seman, *Collect. Czech. Chem. Commun.*, 1995, **60**, 583.
6 R. H. Khan and R. C. Rastogi, *J. Agric. Food Chem.*, 1991, **39**, 2300.
7 J. Quiroga, B. Insuasty, R. Rincón, M. Larrahondo, N. Hanold and H. Meier, *J. Heterocycl. Chem.*, 1994, **31**, 1333.
8 J. Quiroga, B. Insuasty, M. Marín, A. Aguirre and H. Meier, *Rev. Col. Quim.*, 1992, **21**, 29.
9 J. Quiroga, B. Insuasty, P. Hernández, R. Moreno, R. H. de Almeida and H. Meier, *Eur. J. Org. Chem.*, 1998, **6**, 1201.
10 J. Quiroga, B. Insuasty, S. Cruz, P. Hernández, A. Bolaños, R. Moreno, A. Hormaza and R. H. de Almeida, *J. Heterocycl. Chem.*, 1998, **35**, 333.
11 J. Quiroga, B. Insuasty, A. Hormaza, D. Gamenara, L. Domínguez and J. Saldaña, *J. Heterocycl. Chem.*, 1999, **36**, 11.
12 J. A. Findlay, R. F. Langler, C. Podesva and K. Vagi, *Can. J. Chem.*, 1968, **46**, 3659.
13 J. Quiroga, B. Insuasty, R. Abonía, P. Hernández, M. Nogueras, A. Sánchez, J. Cobo and J. N. Low, *Acta Crystallogr., Sect. C*, 2000, **56**, 1460.
14 J. N. Low, J. Cobo, M. Nogueras, A. Sánchez, J. Quiroga and P. Hernández, *Acta Crystallogr., Sect. E*, 2001, **57**, o937.