Preparation of thiazolocarbazoles *via* the Fischer indole synthesis

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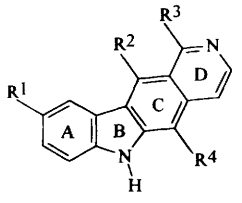
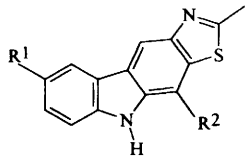
Treatment under Fischer acidic conditions, of tetrahydrobenzo[*d*]thiazolones and/or arylhydrazonobenzo-[*d*]thiazole derivatives has given a variety of thiazolocarbazoles.

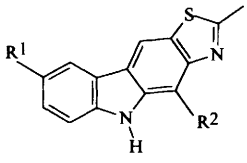
The 6*H*-pyrido[4,3-*b*]carbazoles ellipticine **1a**, 9-methoxyellipticine **1b** and olivacine **1c** are well known for their anti-mitotic properties.[1]



1a $R^1 = R^3 = H$, $R^2 = R^4 = Me$
1b $R^1 = OMe$, $R^2 = R^4 = Me$, $R^3 = H$
1c $R^1 = R^2 = H$, $R^3 = R^4 = Me$



2a $R^1 = R^3 = H$
2b $R^1 = OMe$, $R^2 = H$
2c $R^1 = H$, $R^2 = CO_2Et$
2d $R^1 = OMe$, $R^2 = CO_2Et$

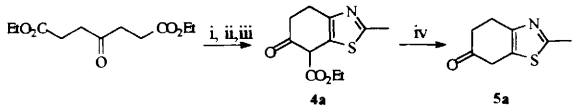


2e $R^1 = R^2 = H$
2f $R^1 = OMe$, $R^2 = H$
2g $R^1 = H$, $R^2 = CO_2Et$
2h $R^1 = OMe$, $R^2 = CO_2Et$

In order to obtain new derivatives and analogues for pharmacological evaluation, we decided to replace the pyridine ring D by a thiazole ring to form compounds **2**.

Results and discussion

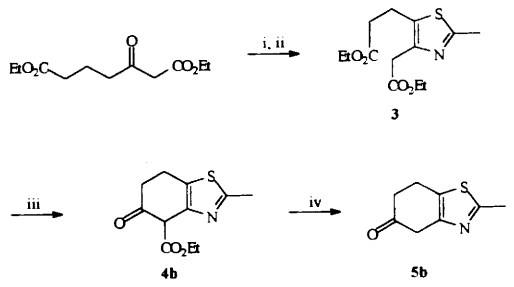
The simplest method to obtain **2** appeared to be by a Fischer indole synthesis[2] with 2-methyl-4,5,6,7-tetrahydrobenzo-[*d*]thiazol-6-one **5a**, itself prepared by a literature procedure[3] from diethyl 4-oxoheptanedioate *via* the ethoxycarbonyl derivative **4a** (Scheme 1).



Scheme 1 *Reagents and conditions:* i, Br_2, Et_2O; ii, $MeC(=S)NH_2$, EtOH; iii. EtONa, Et_2O; iv, HCl 1 mol dm^{-3}, reflux

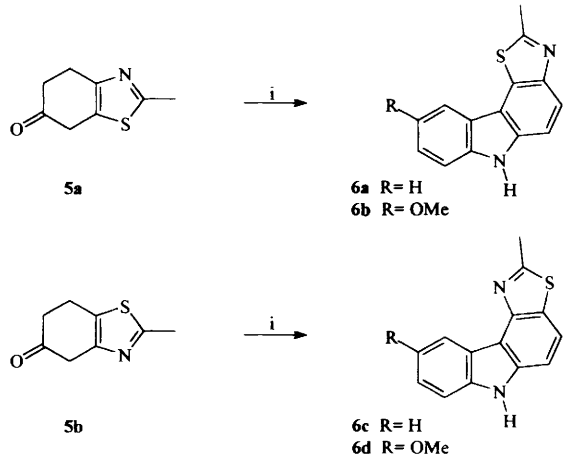
Application of the same reaction conditions to diethyl 3-oxoheptanedioate, surprisingly gave the new compound 2-methyl-4,5,6,7-tetrahydrobenzo[*d*]thiazol-5-one **5b**, *via* the ethoxycarbonyl the derivative **4b** obtained as a keto enol mixture. The bromination of diethyl 3-oxoheptanedioate had occurred at position 4 and not position 2 as expected (Scheme 2).

The Fischer indole synthesis, as a one-step procedure applied



Scheme 2 *Reagents and conditions:* i, Br_2, Et_2O; ii, $MeC(=S)NH_2$, EtOH; iii, EtONa, Et_2O; iv, HCl 1 mol dm^{-3}, reflux

to the thiazoles **5a** and **5b**, failed to give the desired compound **2a–b** and **2e–f**, but, instead, led to the isomeric angular compounds **6a–d** (Scheme 3).



5a
6a R = H
6b R = OMe

5b
6c R = H
6d R = OMe

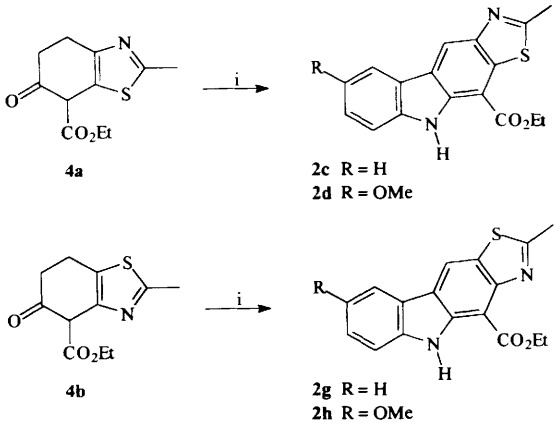
Scheme 3 *Reagents and conditions:* i, $RC_6H_4NHNH_2$·HCl, $MeCO_2H$, reflux

Under the same reaction conditions (one-step procedure, method A) the ethoxycarbonyl derivatives **4a–b**, gave the linear compounds **2c–d** and **2g–h** in good yield (60% isolated) (Scheme 4).

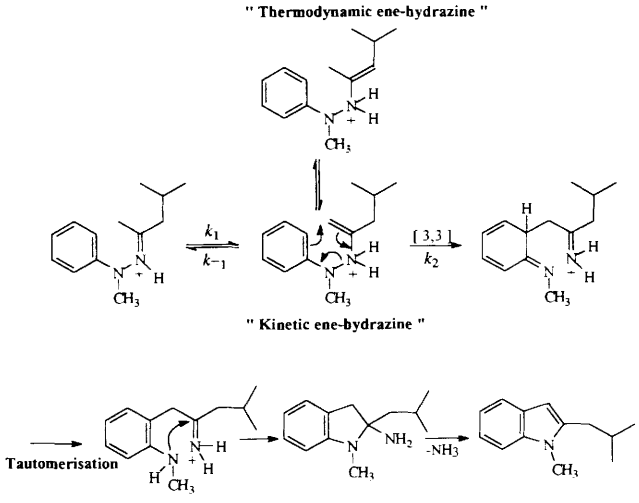
At this stage of the synthesis, which involved unsymmetrical ketones, one starting material could have generated two regioisomers. Hughes and Zhao[4] have found that under dilute acidic conditions, k_1 (Scheme 5) is no longer rate determining. Thus, since there is sufficient time for the ene–hydrazines to equilibrate, the thermodynamically more stable (most substituted) ene–hydrazine is preferentially formed and cyclisation from this intermediate predominates.

However, with our use of acetic acid, the reaction conditions were insufficiently acidic and so the sole isomer isolated resulted from the cyclisation of the less substituted ene–hydrazine.

In order to investigate whether the reaction conditions (one

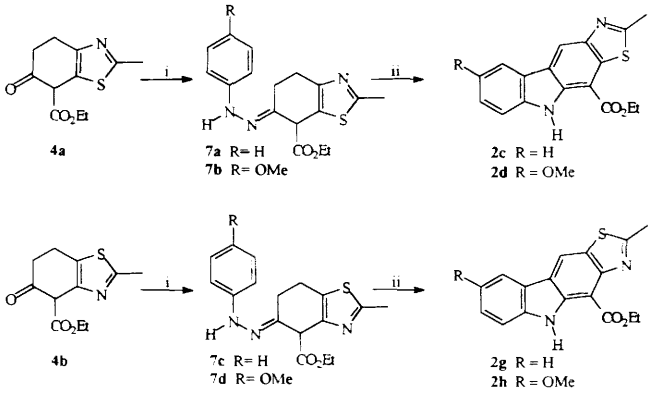


Scheme 4 *Reagents and conditions:* i, $RC_6H_4NHNH_2$·HCl, $MeCO_2H$, reflux



Scheme 5

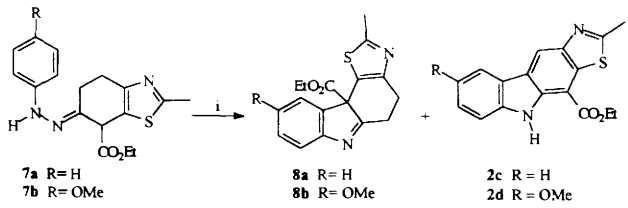
or two steps) have an influence on the regioselectivity of the cyclisation, we have isolated the corresponding hydrazones and cyclised them in a second step (method B) (Scheme 6). The same derivatives as in the one-step procedure were obtained.



Scheme 6 *Reagents and conditions:* i, $RC_6H_4NHNH_2$·HCl, $MeCO_2Na$, reflux; ii, $MeCO_2H$, reflux

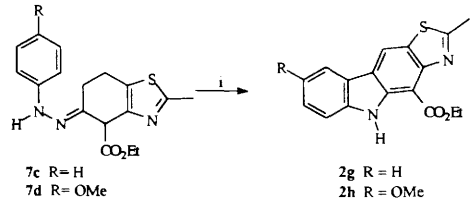
However, use of Amberlyst 15 as the acidic catalyst[5] to cyclise the hydrazones **7a** and **7b**, gave a mixture of the isomers **2** and **8** (Scheme 7)

Only compounds **8** could be isolated (40%) from the mixture, as compounds **2** were present in only small amounts (< 5%) and **8a** and **8b** result from the cyclisation of the thermodynamic ene–hydrazine. Changing the cyclisation conditions seems to change the ratio of carbazoles to indolenines formed, starting from



Scheme 7 *Reagents and conditions:* i, Amberlyst 15, toluene, 50 °C

hydrazones **7a** and **7b**. When compounds **7c** and **7d** were treated with Amberlyst 15, we isolated only the compounds **2g** and **2h**, the same as those obtained by the one-step procedure (Scheme 8).



Scheme 8 *Reagents and conditions:* i, Amberlyst 15, toluene, 50 °C

Factors which seemed to govern the regioselectivity in this indole Fischer synthesis were not only the cyclisation conditions, but also the electronic effects of the heterocycle. An examination of these cyclisation conditions will be extended to other α-cycloketone carboxylates condensed onto heterocycles.

Experimental

^1H NMR and ^{13}C NMR spectra were recorded using a 250 MHz Bruker spectrometer for solutions in $CDCl_3$ unless otherwise stated. δ Values quoted are relative to internal $CDCl_3$ and *J* values are given in Hz. Mps were determined on a Kofler hot-state apparatus and are uncorrected. Elemental analyses were performed on a Carlo Erba elemental analyser.

Ethyl 3-(4-ethoxycarbonylmethyl-2-methyl-1,3-thiazol-5-yl)-propanoate 3

Bromine (8 g, 50 mmol) was added dropwise to a stirred solution of diethyl 3-oxoheptanedioate (11.5 g, 50 mmol) in anhydrous diethyl ether (15 cm^3) at room temperature. The mixture was stirred for 1 h, after which it was washed with water and brine, dried (Na_2SO_4) and evaporated to give an oil. This was then stirred for 72 h with thiacetamide (3.75 g, 50 mmol) in anhydrous ethanol (15 cm^3) at room temperature. Evaporation of the mixture gave an oil, which was dissolved in a mixture of diethyl ether (100 cm^3) and water (100 cm^3). The two layers were separated and the aqueous layer was extracted with diethyl ether (3 × 50 cm^3). The combined extracts were washed with aq. HCl (2 mol dm^{-3}). The combined aqueous layers were neutralised with aq. NaOH (0.1 mol dm^{-3}) and extracted with diethyl ether (3 × 50 cm^3). The extract was washed with water, dried (Na_2SO_4) and evaporated to give an oil which was purified by distillation (6 g, 42%), bp 145–150 °C (3 mbar) (Found: C, 54.8; H, 6.7; N, 4.8. $C_{13}H_{19}NO_4S$ requires C, 54.73; H, 6.67; N, 4.91%); δ_H 1.24 (6 H, m), 2.59 (2 H, t, *J* 7.4), 2.60 (3 H, s), 3.02 (2 H, t, *J* 7.4), 3.70 (2 H, s) and 4.13 (4 H, m).

Ethyl 2-methyl-5-oxo-4,5,6,7-tetrahydrobenzothiazole-4-carboxylate 4b

To a stirred suspension of EtONa (35 mmol) in anhydrous diethyl ether (20 cm^3) at room temperature, was added dropwise a solution of **3** (35 mmol) in anhydrous diethyl ether (5 cm^3). The mixture was stirred for 12 h and then treated with glacial acetic acid (2.1 g) and evaporated to give an oil. This was

purified by column chromatography on silica gel with CH_2Cl_2–MeOH (100:2) as eluent to give **4b** (5.4 g, 65%) (Found: C, 55.25; H, 5.5; N, 5.8. $C_{11}H_{13}NO_3S$ requires C, 55.22; H, 5.44; N, 5.86%): keto form δ_H 1.28 (3 H, t, *J* 7.2), 2.66 (3 H, s), 3.00 (4 H, m), 4.22 (2 H, q, *J*, 7.2) and 4.57 (1 H, s); enol form δ_H 1.41 (3 H, t, *J* 7.1), 2.66 (3 H, s), 3.00 (4 H, m), 4.40 (2 H, q, *J* 7.1) and 10.69 (1 H, s).

2-Methyl-4,5,6,7-tetrahydrobenzothiazol-5-one 5b

A mixture of **4b** (2.1 mmol) and aq. HCl (1 mol dm^{-3} 50 cm^3) was heated at reflux for 20 h. After cooling, the solution was neutralised with aq. NaOH (1 mol dm^{-3}) and extracted with ethyl acetate (3 × 50 cm^3). The combined extracts were washed with water, dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography on silica gel with CH_2Cl_2–MeOH (100:2) as eluent to give **5b** (2.1 g, 60%), mp 97 °C (EtOAc) (Found: C, 57.6; H, 5.4; N, 8.3. C_8H_9NOS requires C, 57.48; H, 5.39; N, 8.37%); δ_H 2.66 (3 H, s), 2.72 (2 H, t, *J* 6.8), 3.07 (2 H, t, *J* 6.8) and 3.63 (2 H, s); δ_C 207.50, 165.42, 146.85, 126.66, 41.77, 39.04, 21.28 and 19.19.

General procedure for preparation of compounds 6a–d, 2c, 2d, 2g and 2h (method A)

To a stirred suspension of phenylhydrazine hydrochloride (4.6 mmol) in glacial acetic acid (15 cm^3) at 80 °C was added dropwise a solution of the appropriate ketone (4.2 mmol) in glacial acetic acid (5 cm^3). The mixture was heated at reflux for 3 h and, after cooling, added in small portions to cold water (20 cm^3) with stirring. The solid was collected and recrystallized.

2-Methyl-6*H*-thiazolo[4,5-*c*]carbazole 6a

The reaction of compound **5a** with phenylhydrazine hydrochloride gave **6a** (40%), mp 152 °C (MeOH) (Found: C, 70.56; H, 4.2; N, 11.75; S, 13.4. $C_{14}H_{10}N_2S$ requires C, 70.56; H, 4.20; N, 11.75; S, 13.44%); δ_H 2.94 (3 H, s), 7.36 (1 H, td, *J* 8, 7 and 1.8), 7.48 (1 H, td, *J* 8, 7 and 1), 7.54 (2 H, d, *J* 8.7), 8.03 (1 H, d, *J* 8.7), 8.06 (1 H, d, *J* 8, 7) and 8.50 (1 H, s); δ_C 163.06, 147.91, 139.39, 136.81, 127.88, 125.67, 122.07, 120.88, 119.98, 119.93, 115.95, 110.93, 109.72 and 19.89.

9-Methoxy-2-methyl-6*H*-thiazolo[4,5-*c*]carbazole 6b

The reaction of compound **5a** with 4-methoxyphenylhydrazine hydrochloride gave **6b** (45%), mp 222 °C (MeOH) (Found: C, 67.7; H, 4.5; N, 10.5; S, 12.0. $C_{15}H_{12}N_2OS$ requires C, 67.71; H, 4.48; N, 10.45; S, 11.94%); δ_H 2.95 (3 H, s), 3.99 (3 H, s), 7.13 (1 H, dd, *J* 8.8 and 2.4), 7.44 (1 H, d, *J* 8.8), 7.51 (1 H, d, *J* 2.4), 7.52 (1 H, d, *J* 8.7), 8.01 (1 H, d, *J* 8.7) and 8.27 (1 H, s); δ_C 163.21, 154.36, 137.57, 134.31, 128.15, 123.27, 117.02, 120.01, 114.92, 111.67, 110.92, 109.90, 103.75, 56.12 and 19.88.

2-Methyl-6*H*-thiazolo[5,4-*c*]carbazole 6c. The reaction of compound **5b** with phenylhydrazine hydrochloride gave **6c** (40%), mp 191 °C (MeOH) (Found: C, 70.6; H, 4.2; N, 11.75; S, 13.4. $C_{14}H_{10}N_2S$ requires C, 70.56; H, 4.20; N, 11.75; S, 13.44%); δ_H 2.93 (3 H, s), 7.29 (1 H, m), 7.41 (3 H, m), 7.76 (1 H, d, *J* 8.5), 8.25 (1 H, s) and 8.65 (1 H, d, *J* 7.6); δ_C 167.75, 148.07, 138.78, 138.03, 127.21, 125.56, 123.15, 122.33, 119.99, 118.13, 116.18, 110.40, 108.84 and 20.41.

9-Methoxy-2-methyl-6*H*-thiazolo[4,5-*c*]carbazole 6d. The reaction of compound **5b** with 4-methoxyphenylhydrazine hydrochloride gave **6d** (45%), mp 173 °C (MeOH) (Found: C, 67.8; H, 4.4; N, 10.4; S, 11.9. $C_{15}H_{12}N_2OS$ requires C, 67.71; H, 4.48; N, 10.45; S, 11.94%); δ_H 2.93 (3 H, s), 3.93 (3 H, s) 7.06 (1 H, dd, *J* 8.8 and 2.4), 7.33 (1 H, d, *J* 9), 7.38 (1 H, d, *J* 8.8), 7.73 (1 H, d, *J* 9), 8.14 (1 H, d, *J* 2.4) and 8.21 (1 H, s); δ_C 167.66, 154.27, 139.01, 133.75, 126.78, 122.70, 118.00, 116.19, 115.62, 113.37, 111.22, 109.04, 105.06, 56.14 and 20.36.

Ethyl 2-methyl-5*H*-thiazolo[5,4-*b*]carbazole-4-carboxylate 2c. The reaction of compound **4a** with phenylhydrazine hydrochloride gave **2c** (60%), mp 237 °C (MeOH) (Found: C, 65.8; H, 4.5; N, 9.0; S, 10.4. $C_{17}H_{14}N_2O_2S$ requires C, 65.80; H, 4.51; N, 9.05; S, 10.29%); δ_H 1.58 (3 H, t, *J* 7.1), 2.87 (3 H, s), 4.61 (2 H, q, *J* 7.7), 7.31 (1 H, m), 7.51 (2 H, m), 8.17 (1 H, d, *J* 7.7), 8.76 (1 H, s) and 9.94 (1 H, s); δ_C 166.20, 166.17, 147.46, 140.25, 139.47, 135.23, 126.94, 124.40, 122.46, 120.54, 120.15, 118.73, 111.02, 104.07, 61.74, 19.70 and 14.57.

Ethyl 8-methoxy-2-methyl-5*H*-thiazolo[5,4-*b*]carbazole-4-carboxylate 2d. The reaction of compound **4a** with 4-methoxyphenylhydrazine hydrochloride gave **2d** (60%), mp 234 °C (MeOH) (Found: C, 63.6; H, 4.6; N, 8.3; S, 9.4. $C_{18}H_{16}N_2O_3S$ requires C, 63.52; H, 4.70; N, 8.23; S, 9.41%); δ_H 1.58 (3 H, t, *J* 7.1), 2.87 (3 H, s), 3.96 (3 H, t), 4.61 (2 H, q, *J* 7.1), 7.14 (1 H, dd, *J* 8.8 and 2), 7.41 (1 H, d, *J* 8.8), 7.63 (1 H, d, *J* 2), 8.71 (1 H, s) and 8.80 (1 H, s); δ_C 166.14, 166.05, 154.31, 147.11, 140.01, 134.98, 124.37, 122.37, 122.96, 118.66, 115.86, 111.67, 103.99, 103.57, 61.68, 56.06, 19.68 and 14.57.

Ethyl 2-methyl-5*H*-thiazolo[4,5-*b*]carbazole-4-carboxylate 2g. The reaction of compound **4b** with phenylhydrazine hydrochloride gave **2g** (60%), mp 154 °C (MeOH) (Found: C, 65.8; H, 4.5; N, 9.15; S, 10.2. $C_{17}H_{14}N_2O_2S$ requires C, 65.80; H, 4.51; N, 9.05; S, 10.29%); δ_H 1.59 (3 H, t, *J* 7.1), 2.97 (3 H, s), 4.67 (2 H, q, *J* 7.1), 7.31 (1 H, m), 7.50 (1 H, m), 8.10 (1 H, d, *J* 7.7), 8.65 (1 H, s) and 10.19 (1 H, s); δ_C 169.05, 167.31, 150.69, 141.09, 140.61, 128.66, 126.95, 123.33, 121.59, 120.26, 120.06, 117.35, 110.94, 105.12, 61.55, 21.04 and 14.53.

Ethyl 8-methoxy-2-methyl-5*H*-thiazolo[4,5-*b*]carbazole-4-carboxylate 2h. The reaction of compound **4b** with 4-methoxyphenylhydrazine hydrochloride gave **2h** (60%), mp 167 °C (MeOH) (Found: C, 63.5; H, 4.7; N, 8.2; S, 9.35. $C_{18}H_{16}N_2O_3S$ requires C, 63.52; H, 4.70; N, 8.23; S, 9.41%); δ_H 1.58 (3 H, t, *J* 7.2), 2.97 (3 H, s), 3.94 (3 H, s), 4.66 (2 H, q, *J* 7.2), 7.12 (1 H, dd, *J* 8.8 and 2.2), 7.42 (1 H, d, *J* 8.8), 7.57 (1 H, d, *J* 2.2), 8.62 (1 H, s) and 10.05 (1 H, s); δ_C 169.08, 167.26, 154.25, 151.98, 141.97, 135.42, 128.37, 123.35, 122.05, 117.33, 115.86, 111.62, 104.93, 103.35, 61.50, 56.03, 21.03 and 14.53.

General procedure for preparation of compounds 2c, 2d, 2g, 2h, 8a and 8b via hydrazones 7a–d (method B)

Preparation of hydrazones 7a–d. A mixture of the appropriate ketone (4.2 mmol), phenylhydrazine hydrochloride (4.6 mmol) and sodium acetate (8.4 mmol) in ethanol (30 cm^3) was refluxed for 2 h. The reaction mixture was poured into water (200 cm^3). The precipitate was collected and recrystallised.

Cyclisation of 7 with acetic acid to give 2c–d and 2g–h. A solution of the hydrazone **7** (4 mmol) in glacial acetic acid (15 cm^3) was heated at reflux for 2 h. After cooling, the solution was added in small portions to cold water (200 cm^3) with stirring. The solid was collected and recrystallised.

Cyclisation of 7 with Amberlyst 15 to give 8a–b. A mixture of the hydrazone **7** (1 mmol) and Amberlyst 15 (2 g) in toluene (15 cm^3) was heated at 50 °C for 2 h and then allowed to cool. The residue was filtered off and washed with toluene (20 cm^3). The organic solution was washed successively with aq. $NaHCO_3$ (10%) and brine. Evaporation of the toluene gave a residue, which was purified by column chromatography on silica gel with CH_2Cl_2–MeOH (100:2) as eluent.

Ethyl 6-(*p*-methoxyphenyl)-2-methylhydrazono-4,5,6,7-tetrahydrobenzothiazole-7-carboxylate 7a. The reaction of compound **4a** with phenylhydrazine hydrochloride gave **7a** (90%), mp 174 °C (MeOH) (stable only if stored in a freezer) (Found: C, 62.1; H, 5.75; N, 12.8; S, 9.8. $C_{17}H_{19}N_3O_2S$ requires C, 62.00; H, 5.77; N, 12.76; S, 9.72%); δ_H 1.41 (3 H, t, *J* 7.05), 2.63 (3 H, s), 2.92 (4 H, m), 4.29 (2 H, q, *J* 7.05), 5.81 (1 H, s), 6.79 (2 H, d, *J* 7.9), 6.92 (1 H, t, *J* 7.3), 7.26 (2 H, m) and 10.51 (1 H, s).

Ethyl 6-(*p*-methoxyphenyl)-2-methylhydrazono-4,5,6,7-tetrahydrobenzothiazole-7-carboxylate 7b. The reaction of compound **4a** with 4-methoxyphenylhydrazine hydrochloride gave

7b (60%), mp 180 °C (MeOH) (stable only if stored in a freezer) (Found: C, 66.3; H, 5.6; N, 11.6; S, 8.9. $C_{18}H_{20}N_3O_3S$ requires C, 62.33; H, 5.58; N, 11.73; S, 8.94%); δ_H[$(CD_3)_2SO$] 1.41 (3 H, t, *J* 7), 2.61 (3 H, s), 2.92 (4 H, m), 3.85 (3 H, s), 4.29 (2 H, q, *J* 7), 5.83 (1 H, s), 6.90 (2 H, d, *J* 9.2), 7.21 (2 H, d, *J* 9.2) and 13.5 (1 H, s).

Ethyl 2-methyl-5-phenylhydrazono-4,5,6,7-tetrahydrobenzothiazole-4-carboxylate 7c. The reaction of compound **4b** with phenylhydrazine hydrochloride gave **7c** (70%), mp 115 °C (MeOH) (stable only if stored in a freezer) (Found: C, 61.9; H, 5.8; N, 12.7; S, 9.8. $C_{17}H_{19}N_3O_2S$ requires C, 62.00; H, 5.77; N, 12.76; S, 9.72%); δ_H 1.29 (3 H, t, *J* 7), 2.67 (3 H, s), 2.87 (4 H, m), 4.25 (2 H, m), 4.99 (1 H, s), 6.88 (1 H, t, *J* 7.3), 7.08 (2 H, d, *J* 7.9), 7.27 (2 H, m) and 8.32 (1 H, s).

Ethyl 5-(*p*-methoxyphenyl)-2-methylhydrazono-4,5,6,7-tetrahydrobenzothiazole-4-carboxylate 7d. The reaction of compound **4b** with 4-methoxyphenylhydrazine hydrochloride gave **7d** (60%), mp 128 °C (MeOH) (stable only if stored in a freezer) (Found: C, 66.25; H, 5.7; N, 11.7; S, 8.8. $C_{18}H_{20}N_3O_3S$ requires C, 62.33; H, 5.58; N, 11.73; S, 8.94%); δ_H[$(CD_3)_2SO$] 1.30 (3 H, t, *J* 7), 2.68 (3 H, s), 2.83 (4 H, m), 3.87 (3 H, s), 4.25 (2 H, m), 5.02 (1 H, s), 6.88 (2 H, d, *J* 9.1), 7.24 (2 H, d, *J* 9.1) and 13.73 (1 H, s).

Ethyl 2-methyl-4,5-dihydro-10b*H*-thiazolo[4,5-*c*]carbazole-10b-carboxylate 8a. The reaction of compound **7a** with Amberlyst 15 gave **2c** and **8a** (40%), mp 132 °C (CH_2Cl_2–MeOH) (Found: C, 62.0; H, 4.85; N, 8.6; S, 9.8. $C_{17}H_{16}N_2O_2S$ requires C, 62.20; H, 4.87; N, 8.53; S, 9.75%); δ_H 1.20 (3 H, t, *J* 7.05), 2.66 (3 H, s), 3.25 (4 H, m), 4.15 (2 H, m), 7.28 (1 H, td, *J* 7.4 and 0.9), 7.41 (1 H, td, *J* 7.6 and 1.2), 7.59 (1 H, d, *J* 7.6) and 7.66 (1 H, d, *J* 7.4); δ_C 180.94, 166.93, 155.55, 150.79, 147.23, 137.07, 129.57, 129.03, 126.17, 125.02, 123.35, 120.83, 62.58, 29.59, 26.79, 19.44 and 13.86.

Ethyl 9-methoxy-2-methyl-4,5-dihydro-10b*H*-thiazolo[4,5-*c*]-carbazole-10b-carboxylate 8b. The reaction of compound **7b** with Amberlyst 15 gave **2d** and **8b** (40%), mp 137 °C (CH_2Cl_2–MeOH) (Found: C, 63.1; H, 5.3; N, 8.15; S, 9.4. $C_{18}H_{18}N_2O_3S$ requires C, 63.15; H, 5.26; N, 8.18; S, 9.35%); δ_H 1.20 (3 H, t, *J* 7.05), 2.66 (3 H, s), 3.34 (4 H, m), 3.95 (3 H, s), 4.13 (2 H, m), 7.15 (1 H, dd, *J* 8.7 and 2), 7.43 (1 H, d, *J* 8.7) and 7.52 (1 H, d, *J* 2); δ_C 180.37, 164.82, 155.65, 151.02, 147.23, 146.83, 135.02, 129.87, 128.98, 125.95, 124.37, 123.07, 62.56, 56.10, 29.58, 26.83, 18.98 and 13.76.

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