Thieno[3',2':4,5][1]benzothieno[2,3-*d*]pyrimidine Derivatives: Synthesis and Conformation

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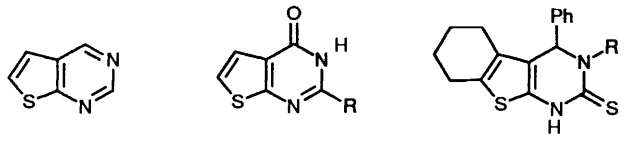
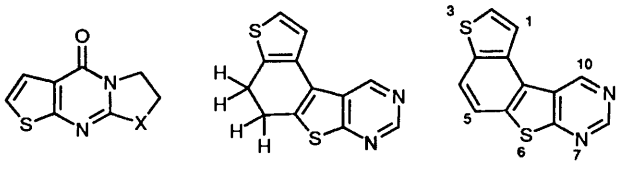
An efficient route is reported for the synthesis of derivatives of the thieno[3',2':4,5][1]benzothieno[2,3-*d*]pyrimidine system **6** with a substituent (oxygen atom or amino group) in the bay region. These molecules are shown by extensive MM calculations to show a significant degree of helical distortion.

Thieno[2,3-*d*]pyrimidine **1** has attracted increasing attention in recent years as a heterocyclic system which supports a wide spectrum of biological activity through a range of derivatives. For example, derivatives of thieno[2,3-*d*]pyrimidin-4(3*H*)-one **2** have been found to have significant analgesic and anti-inflammatory activity[1,2] and antihyperlipaemic activity.[3] Some derivatives of the partially hydrogenated [1]benzothieno[2,3-*d*]pyrimidine system **3** are active in a similar way showing both analgesic and antipyretic activity, exceeding that of ibuprofen.[4] Some derivatives of the tricyclic systems **4** (X = O, S, CH_2) demonstrate useful gastric antisecretory properties[5] and compounds derived from compound **1** have also been examined, and in some cases patented, for their anticoagulant, diuretic and antihypertensive activity.[6,7] Furthermore, antimicrobial,[8] antifungal[9] and some herbicidal activity[10] are also reported for compounds incorporating the thieno[2,3-*d*]pyrimidine structure.



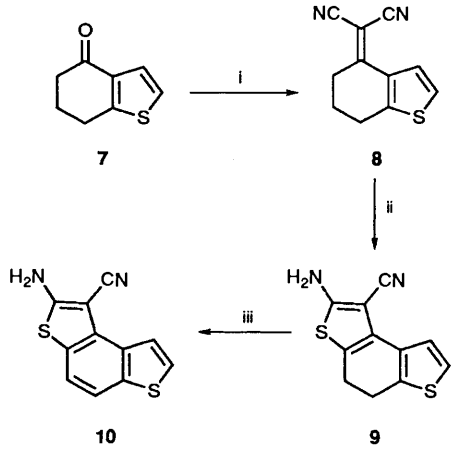
1 **2** **3**



4 **5** **6**

Such a wide range of activity suggests that structural elaboration of compound **1** may have great potential, since the core system itself has a high chemotherapeutic index. We have been exploring routes to larger ring systems related to compound **1** to examine both the effect of extending the size of the aromatic π-system and of introducing nonplanarity. It is also of value to increase the number of positions suitable for functionalisation and with the potential for interaction with a biological substrate. We report a novel approach to the formation of the 4,5-dihydrothieno[3',2':4,5][1]benzothieno-[2,3-*d*]pyrimidine system **5** and the corresponding fully aromatic compound **6**, a tetracyclic analogue of compound **1**.

The strategy has been to start with a benzo[*b*]thiophene compound (rings three and four of the target system) and to construct rings two and one sequentially by suitable annelation reactions. The key intermediate is 2-amino-1-cyano-4,5-dihydrothieno[3',2':4,5]benzo[*b*]thiophene **9**, which is obtained[11] from 6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one **7** *via* a condensation with malononitrile to give the dicyano compound **8**, followed by thianation (see Scheme 1).

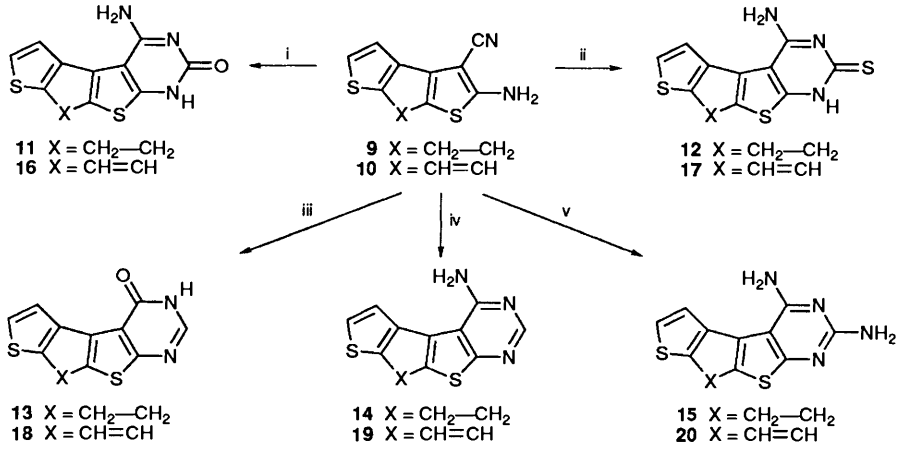


7 **8** **10** **9**

Scheme 1 *Reagents:* i, $CH_2(CN)_2$, base; ii, sulfur, morpholine; iii, DDQ or Pd/C

Compound **7** is readily prepared from inexpensive starting materials and has been used extensively in the synthesis of benzo[*b*]thiophene and related polynuclear systems containing fused thiophene rings.[12] Aromatisation of compound **9** is accomplished by treatment with DDQ or palladium-on-carbon[11] to afford 2-amino-1-cyanothieno[3',2':4,5]benzo[*b*]-thiophene **10**. Compound **9** was subjected to a variety of annelation reactions (Scheme 2) to give derivatives **11**–**15**. Compound **10** has a similar reactivity to that of compound **9** and forms the corresponding fully aromatic compounds **16**–**20**. The reactions were selected to demonstrate the annelation to the thiophene ring of pyrimidin-8(7*H*)-one ring (compounds **11** and **16**), pyrimidine-8(7*H*)-thione ring (compounds **12** and **17**) and pyrimidin-10(9H)-one ring (compounds **13** and **18**) and the formation of 10-aminothieno[3',2':4,5][1]benzothieno[2,3-*d*]-pyrimidine **19**, its dihydro analogue **14** and the corresponding 2,4-diamino derivatives **20** and **15**. In these latter compounds, the aminated terminal ring is structurally similar to the pyrimidine ring in the purine nucleotides and provides the potential for a biochemical interaction.

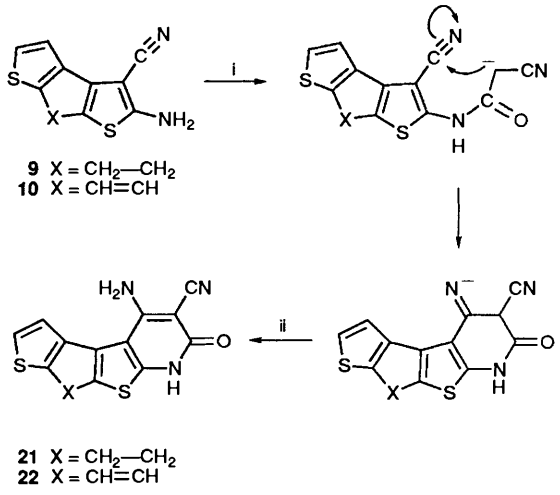
Formation of a thieno[2,3-*d*]pyrimidine derivative from a corresponding 2-amino-1-cyanothiophene has been reported only rarely[13] perhaps reflecting the relative inaccessibility of these precursors by available methods.[14] The present route is convenient and reasonably efficient, with yields usually in the range 40–80%. The yields of the dihydro derivatives were generally higher than those of the aromatic compounds.



Scheme 2 *Reagents:* i, NH_2CONH_2, EtONa; ii, NH_2CSNH_2, EtONa; iii, HCO_2H, $MeCO_2Na$; iv, $HCONH_2$, HCO_2H; v, $HNC(NH)_2)_2$, EtONa

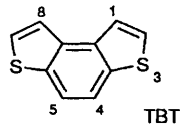
Treatment of the dihydro derivative **9** with ethyl cyanoacetate (ECA) in presence of base gave the compound **21** by the mechanism shown in Scheme 3. The aromatic compound **10** correspondingly gave compound **22** when refluxed with ECA in the presence of ammonium acetate–acetic acid, with continuous removal of the water. The products of this reaction are functionalised in the same way as their precursors and hence may undergo further annelation reactions. These reactions are under investigation.

It is likely that all of the reactions shown in Scheme 2 are subject to steric inhibition, due to the interaction which develops between the substituent atom or group in the 10-position and the opposed thiophene ring proton. This interaction would be relieved by distortion of the molecule in a helical fashion. In order to investigate the extent of this distortion and to obtain an estimate of the energy barrier between the two helical configurations, the structure of selected compounds has been studied theoretically by molecular mechanics and molecular orbital methods.



Scheme 3 *Reagents:* i, ECA, NaOEt; ii, H^+

The starting point was the planar tricyclic system thieno[2,3-*e*]benzo[*b*]thiophene **23** (TBT). The separation between the bay hydrogen atoms 1-H and 8-H in TBT is 2.68 Å, as determined from the optimised geometry of the molecule in its minimum energy state (MM). The same value was found for this H···H distance by MO calculation. The analogous species with a $-CH_2-CH_2-$ bridge between the thiophene rings (*i.e.* notional hydrogenation and hence lengthening of the C-4–C-5 bond) has a more closed bay region and the separation of the bay hydrogens is 2.20 Å (MM). Annelation of a second benzene ring onto TBT gives TBTB, a compound of the [4]heterohelicene type, which should be similar to compound **6** in terms of the dimensions of the bay region and the magnitude of the repulsive interaction and is hence a good model for the core ring system in the derivatives shown in Scheme 2. Substitution of a thiophene ring for a benzene ring in a helicene opens the bay region slightly,[15] and hence the TBTB type of [4]heterohelicene is expected to be planar and this has been confirmed by MM calculation. The separation of the bay hydrogen atoms is 1.92 Å and the sum of the inter-ring exocyclic angles in the bay is 392° (compared to a theoretical value of 360° in all-benzenoid [4]helicene). The MO optimised geometry indicated a H···H separation of 1.90 Å and a very small helical distortion. No torsion angle was greater than 0.5°.



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The core ring system having been confirmed as essentially planar, the effect of introducing a substituent into the bay region was investigated. The presence of a substituent group within the bay region (such as the 10-amino group in compound **16**) is expected to produce a similar degree of repulsive interaction as is found in a [5]helicene. Thus, the barrier associated with helical inversion will be similar in magnitude in the new compounds described in this work to that found in analogous [5]heterohelicenes. The fully benzenoid pentahelicene has an inversion barrier ($\Delta G^{\ddagger}$) of 100.9 kJ mol^{-1} which is high enough to allow optical resolution.[16] However the steric relief produced by a thiophene ring reduces the bay contacts to the extent that neither BTBTB[15] nor TBTBT[17] are resolvable by chiral chromatography, suggesting that the corresponding energy barriers are low enough to allow rapid thermal isomerisation. No rates of isomerisation, however have been measured. Another illustration of the expected $\Delta G^{\ddagger}$ value for inversion in compound **16** comes from a study of the analogous inversion in the 4,5-dimethylphenanthrene system. The transition state in this case must involve the crossing of two methyl groups, and $\Delta G^{\ddagger}$ ranges from 67 kJ mol^{-1} (no other substituents) through 78 kJ mol^{-1} (additional 1,8-substitution) to 90.2 kJ mol^{-1} (9,10-dione).[18]

The series of compounds synthesised in this work are on the borderline of stable chirality and the extent of nonplanarity has been evaluated for the four compounds **11**, **13**, **16** and **18**, to determine the effect of carbonyl and amino groups in the bay

Table 1 Geometry parameters for helically twisted compounds **11**, **13**, **16** and **18**

Compound	d(H···O)[a]	T(C-4,C-6a)[b]	T(S-3,C-8)	T(2-H,9-H)	T(1-H,10-O)
18	2.09	1°	3°	4°	3°
13	2.07	12°	14°	20°	22°
Compound	d(H···H)	T(C-4,C-6a)	T(S-3,C-8)	T(2-H,N-9)	T(1-H,NH)
16	1.92	4°	14°	14°	23°
11	2.03	12°	21°	25°	29°

[a] Distance between closest atoms in the bay region, in Å. [b] Spatial torsion between the indicated atoms with respect to the line joining C-9 and S-10.

region and the effect of changing the nature of the bridge between the thiophene rings. To provide a simple characterisation of the nonplanarity of the energy-minimised structures in terms of helical twisting, the notional spatial torsion was determined for selected pairs of atoms with respect to the line between C-5 and S-6 (see structure **6** for numbering). Thus, T(2-H, C-8) is the torsion apparent along the pathway (2-H, C-5, S-6, C-8). This permits easy comparison of different structures and the values of four selected torsion angles derived from the MM calculations, are given in Table 1 for compounds **11**, **13**, **16** and **18**.

As expected, the 10-oxo group in compound **18** does not give rise to a severe repulsive interaction with the opposed thiophene hydrogen atom and the degree of helical distortion is very small. The separation between 10-O and 1-H atoms is 2.09 Å (2.4 Å from a partially optimised MO structure) which is similar to the closest H···H approach in the heteropentahelicene TBTBT (2.11 Å by X-Ray diffraction[17]). Compound **18** is most unlikely to exhibit chirality. In contrast, the data for the other three compounds (Table 1) indicate substantial helical distortion in all cases. The increase in the length of the two-carbon bridge between the thiophene rings in the 4,5-dihydro-10-oxo compound **13** leads to an increase in the steric interaction in the bay region. The loss of aromatic character in the central dihydrobenzene ring allows greater relaxation of this interaction by helical distortion, such that the 10-O, 1-H separation is almost the same as that for compound **18** (Table 1). It is notable that the twisting of the ring system in compound **13** is developed progressively, the angular torsion being about twice as great in the bay region as on the opposite edge of the molecule. The greater flexibility which follows from the loss of aromatic character in one ring means that the transition state for helical inversion is unlikely to be planar.

Replacement of the carbonyl oxygen with an amino substituent, as in compound **16**, increases the steric congestion in the bay region, resulting in a 14° twist of the molecule at the periphery of the terminal rings (Table 1). The MM calculations also show that a substantial part of the repulsive interaction is actually taken up by distortion of the 10-amino group. The NH_2 plane is bent by 15° (with respect to the notional plane of the pyrimidine ring) and rotated by 12°, both these deviations being complementary to the general helical distortion in reducing the 1-H, NH contact. In the dihydro analogue **11** the helical distortion is more smoothly developed although the bending of the plane of the amino group is similar (17°).

These results suggest that stable chirality may be observable in compounds **11** and **16** and other similar compounds, or at least the rate of isomerisation will be measurable. It is not possible to estimate the inversion barrier in the compounds with a hydrogenated bridge since the transition state cannot be taken as planar. However, for compound **16**, the more rigid ring system is probably close to planarity in the transition state. Allowing the amino group to become orthogonal to that plane, gave a calculated energy barrier of 200 kJ mol^{-1}, relative to the energy minimised form discussed above. This must be an overestimate but, nonetheless, it does point to the interesting possibility that some of the new compounds reported in this work could have therapeutic activity based on chemical reactivity and stereoselectivity. Further studies of potential chirality of these compounds is underway.

Experimental

Melting points (uncorrected) were recorded on a Reichert hot stage melting point apparatus. IR spectra (KBr) were recorded on a Perkin-Elmer PE-298 spectrometer. ^1H NMR spectra were recorded on JEOL FX-100 and Bruker WP-200 instruments, using [$^2H_6$]dimethyl sulfoxide as solvent unless otherwise stated, with tetramethylsilane as internal standard. Commercially available solvents were distilled prior to use.

Molecular mechanics calculations were carried out using the Desktop Molecular Modelling program (DTMM) which uses the Cosmic force field.[19] The published parameterisation does not include data for an aromatic sulfur atom as required for thiophene and appropriate additions were made to the program as follows. Atom-type labels 25 and 26 were assigned in the DTMM program to a thiophene carbon (C_T) and a thiophene sulfur (S_T) respectively. The inclusion of a C_T type atom improved the calculation for the C=C bond in the non-annelated thiophene ring. Because the DTMM program requires every type of bond, bond angle and torsion angle to be specifically associated with its own parameter set, the introduction of the two new atom types necessitated the inclusion of twenty new parameter sets to deal with the compounds involved in this work. These are given in the form (geometry type, parameter 1, parameter 2) where geometry type refers to a bond (two atoms with C_A indicating an aromatic carbon), a bond angle (three atoms) or a torsion interaction (two atoms), and parameters 1 and 2 are the numerical values required by the program: C_T–S_T, 190, 1.74; C_A–S_T, 190, 1.74; C_A–C_T, 700, 1.44; C_T–C_T, 670, 1.34; H–C_T, 346, 1.089; C_T–C_T–S_T, 0.031, 94; H–C_T–S_T, 0.01, 125; C_A–C_A–S_T, 0.031, 112; CH_2–C_A–S_T, 0.012, 130; N–C_A–S_T, 0.02, 128; C_T–S_T–C_A, 0.031, 94; C_A–S_T–C_A; 0.031, 94; C_T–C_T–C_A, 0.031, 112; H–C_T–C_A, 0.01, 125; C_T–C_A–C_A, 0.012, 112; H–C_T–C_T, 0.01, 125; C_A–S_T, 3.0, −2.0; C_T–S_T, 3.0, −2.0; C_A–C_T 3.0, −2.0; C_T–C_T, 6.0, −2.0. Finally a hydrogen atom attached to a nitrogen atom was given a normal Van der Waal radius (1.20) and parameter (0.042).

Molecular orbital calculations were carried out at the MINDO3 level. Full geometry optimisation by this method was only possible for selected molecules due to the large number of atoms and geometry variables involved. Where comparisons were possible the MM and MO methods were in excellent agreement.

10-*Aminothieno*[3′,2′:4,5][1]*benzothieno*[2,3-d]*pyrimidin*-8(7*H*)-*one* **16** *and* 10-*Amino*-4,5-*dihydrothieno*[3′,2′:4,5][1]-*benzothieno*[2,3-d]*pyrimidin*-8(7H)-*one* **11**.—Urea (0.02 g) and the thienobenzothiophene **10** (0.05 g) were dissolved in dry ethanol (10 cm^3) and added to freshly prepared sodium

ethoxide (prepared from 0.01 g of sodium). After the mixture had been heated to reflux for 45 min, the solvent was removed under reduced pressure and the residue triturated with water to give a solid which was recrystallised from aqueous formic acid to afford *compound* **16** (0.03 g, 51%) m.p. 298–300 °C (Found: C, 52.65; H 2.4; N, 15.0. $C_{12}H_7N_3OS_2$ requires C, 52.75; H, 2.6; N, 15.4%); ν_{max}/cm^{-1} 3300 (NH_2) and 1640 (CO); δ 12.40 (1 H, br s, NH), 12.00 (2 H, br s, NH_2) and 8.64–8.00 (ArH).

Similarly, urea (0.025 g) and the dihydrothienobenzothiophene **9** (0.1 g) on treatment for 2 h in the presence of sodium ethoxide (prepared from 0.012 g Na) afforded *compound* **11** (42%), m.p. > 300 °C (Found: C, 52.3; H, 3.4; N, 15.4. $C_{12}H_9N_3OS_2$ requires C, 52.3; H, 3.3; N, 15.3%); ν_{max}/cm^{-1} 3300 (NH_2) and 1630 (CO); $\delta(CDCl_3)$ 7.5 (1 H, d, 1-H), 7.0 (1 H, d, 2-H), 4.6 (3 H, br s, NH_2 and NH) and 3.2–2.6 (4 H, m, CH_2CH_2).

10-*Aminothieno*[3′,2′:4,5][1]*benzothieno*[2,3-d]*pyrimidine*-8(7H)-*thione* **17** *and* 10-*Amino*-4,5-*dihydrothieno*[3′,2′:4,5][1]*benzothieno*[2,3-d]*pyrimidine*-8(7H)-*thione* **12**.—Thiourea (0.02 g) and the thienobenzothiophene **10** were refluxed in dry ethanol (10 cm^3) in the presence of sodium ethoxide (prepared from 0.005 g of sodium) for 45 min. Work up and crystallisation from aqueous formic acid gave *compound* **17** (67%), m.p. 294 °C (Found: C, 49.5; H, 2.4; N, 14.5. $C_{12}H_7N_3S_3$ requires C, 49.85; H, 2.4; N, 14.4%); ν_{max}/cm^{-1} 3300 (NH_2); δ 8.4–7.65 (ArH).

Similarly, thiourea (0.03 g) and the dihydrothienobenzothiophene **9** (0.1 g) heated under reflux for 2 h in dry ethanol (10 cm^3), in the presence of sodium ethoxide, gave *compound* **12** (47%) which was crystallised from aqueous formic acid; m.p. 300 °C (Found: 49.8; H, 3.3; N, 14.2 $C_{12}H_9N_3S_3$ requires C, 49.4; H, 3.1; N, 14.4%); ν_{max}/cm^{-1} 3420 (NH_2); $\delta(CDCl_3)$ 7.50 (1 H, d, 1-H), 7.10 (1 H, d, 2-H), 4.70 (3 H, br s, NH_2 and NH) and 3.2–2.6 (4 H, m, CH_2CH_2).

Thieno[3′,2′:4,5][1]*benzothieno*[2,3-d]*pyrimidin*-10(9H)-*one* **18** *and* 4,5-*Dihydrothieno*[3′,2′:4,5][1]*benzothieno*[2,3-d]*pyrimidin*-10(9H)-*one* **13**.—The thienobenzothiophene **10** (0.1 g) in formic acid (10 cm^3) was refluxed for 13 h in the presence of sodium acetate (0.05 g). The greyish crystalline material which separated upon cooling was washed (H_2O, 10 cm^3), dried under reduced pressure and recrystallised from aqueous formic acid to give *compound* **18** (0.7 g, 63%), m.p. > 300 °C (Found: C, 55.9; H, 2.4; N, 10.8. $C_{12}H_6NOS_2$ requires C, 55.8; H, 2.3; N, 10.85%); ν_{max}/cm^{-1} 3400 (NH) and 1640 (CO); δ 13.00 (1 H, br s, NH), 9.36 (1 H, d, 1-H), 8.64 (1 H, s, 8-H), 8.50 (1 H, d, 2-H) and 8.3 and 8.2 (2 H, 2 d, 4-H and 5-H).

Similarly, the dihydro compound **9** gave a yellow crystalline material which was crystallised from aqueous formic acid to afford *compound* **13**, (80%), m.p. > 300 °C (Found: C, 55.2; H, 3.0; N, 11.6. $C_{12}H_8NOS_2$ requires C, 55.4; H, 3.1; N, 11.6%); ν_{max}/cm^{-1} 3410 (NH) and 1655 (CO); δ 7.92 (1 H, d, 1-H), 7.51 (1 H, s, 8-H), 7.20 (1 H, d, 2-H), 5.51 (1 H, br s, NH) and 2.6–3.2 (4 H, m, CH_2CH_2).

10-*Aminothieno*[3′,2′:4,5][1]*benzothieno*[2,3-d]*pyrimidine* **19** *and* 10-*Amino*-4,5-*dihydrothieno*[3′,2′:4,5][1]*benzothieno*[2,3-d]*pyrimidine* **14**.—The thienobenzothiophene **10** (0.1 g) was heated to reflux with formamide (10 cm^3) and formic acid (2 cm^3) for 3 h. The crystalline material which separated upon cooling was recrystallised from ethanol to give *compound* **19** (0.06 g, 54%), m.p. 296–298 °C (Found; C, 56.0; H, 3.5; N, 16.0. $C_{12}H_7N_3S_2$ requires C, 56.0; H, 3.9; N, 16.3%); ν_{max}/cm^{-1} 3300 (NH_2); δ 8.57 (1 H, s, 8-H) and 8.22–7.79 (ArH).

Similar treatment of the dihydro compound **9** with formamide and formic acid for 13 h afforded *compound* **14** (77%), m.p. 224–225 °C (Found: C, 55.55; H, 3.5; N, 16.2. $C_{12}H_9N_3S_2$ requires C, 55.6; H, 3.5; N, 16.2%); ν_{max}/cm^{-1} 3420 (NH_2); δ 8.02 (1 H, d, 1-H), 7.80 (1 H, s, 8-H), 7.40 (1 H, d, 2-H), 4.8 (2 H, br s, NH_2) and 3.02–2.27 (4 H, m, CH_2CH_2).

8,10-*Diaminothieno*[3′,2′:4,5][1]*benzothieno*[2,3-d]*pyrimidine* **20** *and* 8,10-*Diamino*-4,5-*dihydrothieno*[3′,2′:4,5][1]*benzothieno*[2,3-d]*pyrimidine* **15**.—Guanidine (0.02 g) and the thienobenzothiophene **10** (0.05 g) were refluxed in ethanol (10 cm^3) in the presence of sodium ethoxide (prepared from 0.01 g sodium). Removal of the solvent and work-up gave *compound* **20** which was recrystallised from aqueous formic acid (0.02 g, 34%), m.p. 299–300 °C (Found: C, 52.8; H, 3.0; N, 20.5. $C_{12}H_8N_4S_2$ requires C, 52.9; H, 3.0; N, 20.6%); ν_{max}/cm^{-1} 3400 (NH_2); δ 12.48 (2H, br s, NH_2), 12.06 (2 H, br s, NH_2), 8.36 (1 H, d, 8-H) and 8.19–7.92 (3 H, m, 2-H, 4-H, 5-H).

Similarly, *compound* **15** was obtained from guanidine (0.03 g) and the dihydro compound **9**, (0.1 g, 43%), m.p. > 300 °C (Found: C, 52.5; H, 3.7; N, 20.0. $C_{12}H_{10}N_4S_2$ requires C, 52.55; H, 3.7; N, 20.4%); ν_{max}/cm^{-1} 3420 (NH_2); $\delta(CDCl_3)$ 7.5 (1 H, d, 1-H), 7.1 (1 H, d, 2-H), 5.1 (4 H, br s, NH_2) and 3.2–2.6 (4 H, m, CH_2CH_2).

10-*Amino*-9-*cyanothieno*[3′,2′:4,5][1]*benzothieno*[2,3-d]*pyridin*-8(7H)-*one* **22** *and* 10-*Amino*-9-*cyano*-4,5-*dihydrothieno*[3′,2′:4,5][1]*benzothieno*[2,3-d]*pyridin*-8(7H)-*one* **21**.—The thienobenzothiophene **10** (0.2 g) and ethyl cyanoacetate (0.098 g) were refluxed for 24 h in dry benzene (25 cm^3) in the presence of ammonium acetate (0.02 g) and acetic acid (0.1 cm^3) with continuous removal of water (Dean–Stark method). Ammonium acetate was added every 6 h during this period, after which the reaction mixture was cooled, washed (H_2O, 10 cm^3) and dried (Na_2SO_4) and the solvent removed under reduced pressure. The residue was recrystallised from benzene–light petroleum (60–80 °C) to give *compound* **22** (50%), m.p. 298–300 °C (Found: C, 56.35; H, 2.6; N, 14.0. $C_{12}H_7N_3S_2$ requires C, 56.6; H, 2.35; N, 14.1%); ν_{max}/cm^{-1} 3420 (NH_2), 2205 (CN) and 1660 (CO); δ 8.59 (1 H, br s, NH) and 8.19–7.92 (ArH).

Similarly, ethyl cyanoacetate (1.0 g) and the dihydrothienobenzothiophene **9** (1.8 g) were refluxed for 3 h in dry ethanol (10 cm^3) in the presence of sodium ethoxide (prepared from 0.18 g Na). The solvent was removed under reduced pressure and the residue crystallised from aqueous ethanol to afford *compound* **21** (87%), m.p. 182–184 °C (Found: C, 56.2; H, 3.0; N, 14.0. $C_{12}H_9N_3S_2$ requires C, 56.3; H, 3.0; N, 14.0%); ν_{max}/cm^{-1} 2200 (CN) and 1630 (CO); $\delta(CDCl_3)$ 7.60 (1 H, d, 1-H), 7.16 (1 H, d, 2-H) and 4.72 (3 H, br s, NH, NH_2).

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