Synthesis and Trapping of 4*H*- and 5*H*-Thieno[3,4-*c*]pyrroles

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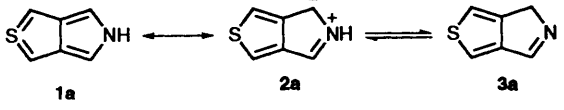
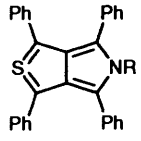
The synthesis and trapping of the parent compound and derivatives of the thieno[3,4-*c*]pyrrole ring system are reported. Intramolecular 1,3-dipolar cycloaddition of the azides **9a–d** and subsequent acid-catalysed 1,3-dipolar cycloreversion of the thienopyrrolotriazoles **10a–d** afforded the parent compound **3a** and its derivatives **3b–d**. Trapping of **3a–d** by 1,3-dipolar cycloaddition with *N*-phenylmaleimide *via* the azomethine ylide **2a–d** gave cycloadducts **14a–d** and **15a–d**. Reactions of the halides **8a**, **c**, **d** and **g** with benzylamine produced *N*-benzylazomethine ylides **18a**, **c**, **d** and **g** which were also trapped by *N*-phenylmaleimide to give the cycloadducts **19a**, **c**, **d** and **g**.

The 5*H*-thieno[3,4-*c*]pyrrole ring system, represented by resonance structures **1a** and **2a**, has long been a subject of synthetic[1] and theoretical interest.[2] The nature of the sulfur bonding in these iso-condensed thiophenes remains a matter of controversy. Klasinc and Trinajstic predicted that compound **1a** has a triplet state of lower energy than the lowest singlet



1a **2a** **3a**

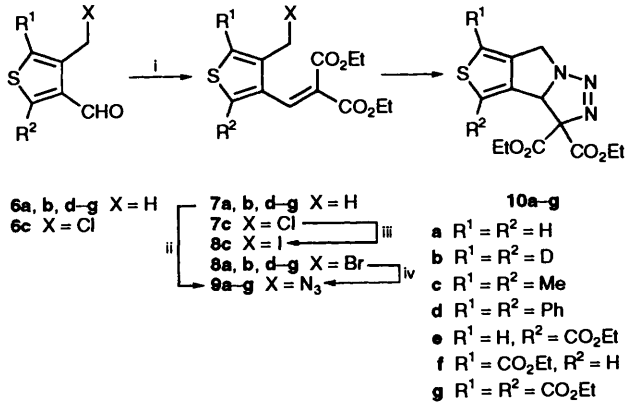


4 R = Ph
5 R = Me

state.[3] Using a semiempirical molecular-orbital method with configuration interaction, Lahti and Ichimura concluded that the azomethine ylide form **2a** is favoured energetically (10–25 kcal mol^{-1}) for the zwitterionic singlet ground state.[4] Experimentally, Cava and Potts and co-workers independently synthesized the highly substituted derivatives **4** and **5**, and assigned the sulfur atom in the thiophene rings as tetravalent.[5] In our preliminary communication, we described the first synthesis of the parent system, 4*H*-thieno[3,4-*c*]pyrrole **3a**.[6] Here we report in detail the investigation of the synthesis and trapping of the parent compound and several derivatives of the thieno[3,4-*c*]pyrrole ring system.

Results and Discussion

Knoevenagel condensation of the aldehyde **6a** with diethyl malonate gave the alkylidene malonate **7a**, which was treated with *N*-bromosuccinimide to afford the bromide **8a**. Treatment of this with sodium azide in ethanol at room temperature gave the azide **9a** smoothly (Scheme 1). However, when compound **9a** was subjected to an intramolecular 1,3-dipolar cycloaddition only 14% of the desired product **10a** was observed after 48 h at room temperature. In order to understand this process better, we investigated the 1,3-dipolar cycloaddition systematically. Thus, compounds **7c** and **8d–g**, prepared by known procedures from thiophenecarbaldehydes **6c–g**,[6] were treated with sodium azide in ethanol. The reaction conditions and yields of the cycloadducts are summarized in Table 1. Examination of Table



6a, b, d–g X = H
6c X = Cl
7a, b, d–g X = H
7c X = Cl
8c X = I
8a, b, d–g X = Br
9a–g X = N_3

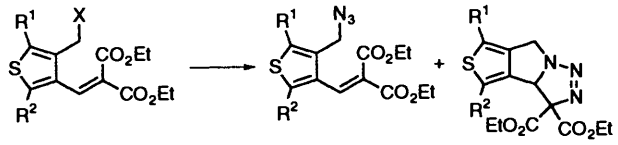
10a–g
a $R^1 = R^2 = H$
b $R^1 = R^2 = D$
c $R^1 = R^2 = Me$
d $R^1 = R^2 = Ph$
e $R^1 = H$, $R^2 = CO_2Et$
f $R^1 = CO_2Et$, $R^2 = H$
g $R^1 = R^2 = CO_2Et$

Scheme 1 *Reagents:* i, $TiCl_4$, $CH_2(CO_2Et)_2$, pyridine, THF; ii, NBS, $(PhCO_2)_2$, CCl_4; iii, NaI; iv, NaN_3, EtOH

1 clearly reveals that the rate of cycloaddition was significantly enhanced by the presence of substituents. As shown in entry 3 the dimethyl substituted thiophene **9c**, generated *in situ* from compound **7c**, was found to undergo cycloaddition more rapidly than the unsubstituted compound **9a**. Similarly, the diphenyl substituted compound **9d**, generated *in situ* from compound **8d**, cyclized even more rapidly (entry 4). In these cases, we believe that the rate enhancement was due to steric effects. The dimethyl or diphenyl substituents at C-2 and C-5 of the thiophene ring forced the azidomethyl group and alkylidenemalonate unit to approach each other more closely and thus to undergo 1,3-dipolar cycloaddition more readily. The observed rate enhancement of compounds **9e** (entry 5) and **9f** (entry 6), each possessing an electron-withdrawing group (CO_2Et), can be rationalized by taking into account an electronic effect. Compound **9e** with an electron-withdrawing group in conjugation with the alkylidenemalonate unit was found to undergo cycloaddition much more rapidly than compound **9f**, in which the ester group is not in conjugation with the alkylidenemalonate moiety. Of all cases examined, compound **9g** exhibited the greatest rate enhancement (entry 7); the cycloaddition was complete within 45 min, apparently due to one electron-withdrawing ester group at C-2 and one at C-5, which induce favourable steric and electronic effects simultaneously.

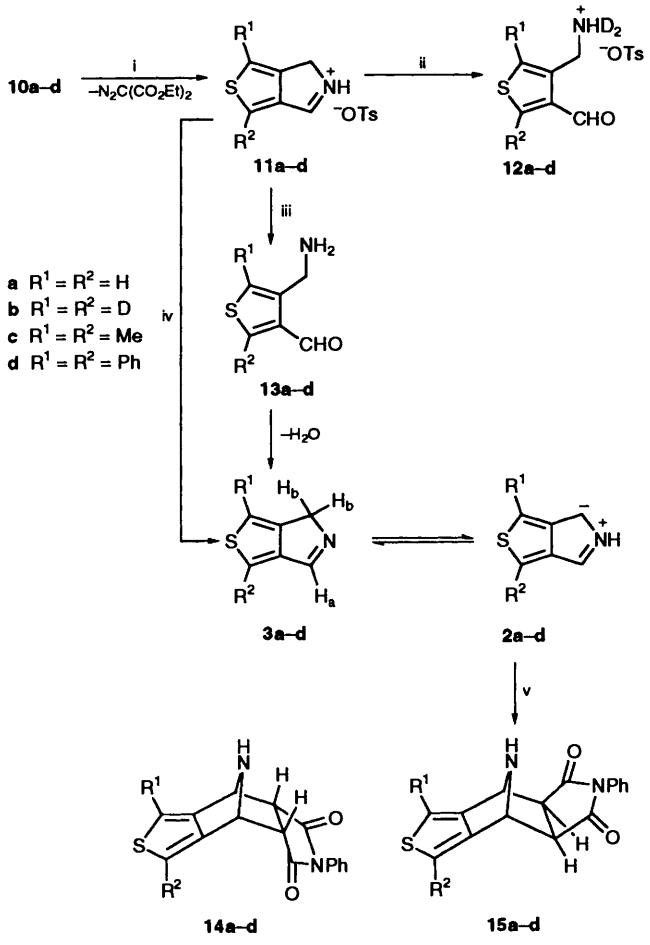
Compound **10a** was treated with toluene-*p*-sulfonic acid in an attempt to effect 1,3-dipolar cycloreversion and resulted in formation of the iminium salt **11a** and diethyl diazomalonate.[6,7] The iminium salt **11a**, which precipitated with time, was filtered off. When the ^1H NMR spectrum of **11a** was measured in D_2O,

Table 1 Intramolecular 1,3-dipolar cycloaddition of azide-alkylidenemalonate



9a–g **10a–g**

Entry	Starting material	Reaction conditions	Products (% yield)
1	**8a** $R^1 = R^2 = H$, X = Br	NaN_3, EtOH, 48 h	**9a** (85) **10a** (14)
2	**9a** $R^1 = R^2 = H$, X = N_3	Room temp., EtOH, 5 months	**9a** (trace) **10a** (88)
3	**7c** $R^1 = R^2$ = Me, X = Cl	NaN_3, EtOH, 28 h	**9c** (trace) **10c** (97)
4	**8d** $R^1 = R^2$ = Ph, X = Br	NaN_3, EtOH, 4.5 h	**9d** (trace) **10d** (93)
5	**8e** R^1 = H, $R^2 = CO_2Et$, X = Br	NaN_3, EtOH, 2 h	**9e** (trace) **10e** (88)
6	**8f** $R^1 = CO_2Et$, R^2 = H, X = Br	NaN_3, EtOH, 10 h	**9f** (trace) **10f** (89)
7	**8g** $R^1 = R^2 = CO_2Et$, X = Br	NaN_3, EtOH, 45 min	**9g** (trace) **10g** (95)



Scheme 2 *Reagents:* i, TsOH; ii, D_2O; iii, Na_2CO_3, H_2O; iv, Et_3N, Et_2O; v, *N*-phenylmaleimide

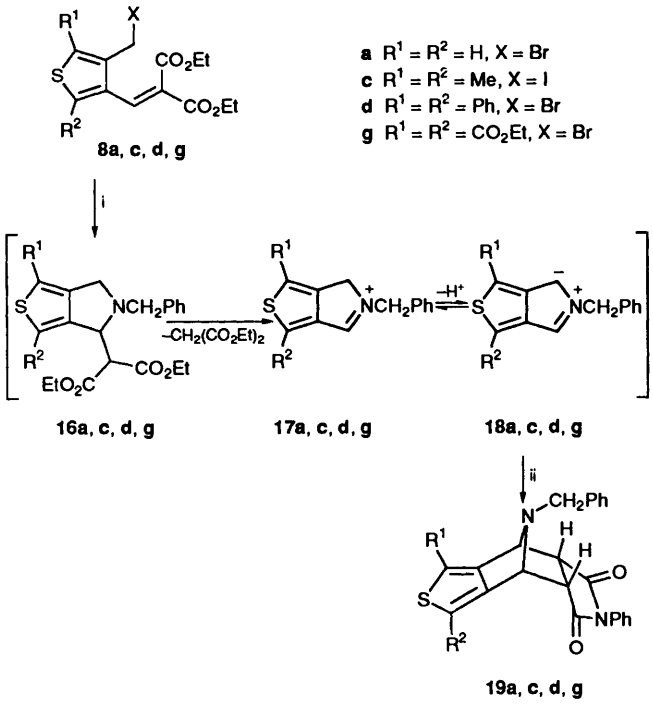
it hydrolysed to the amino aldehyde **12a** (Scheme 2). When iminium salt **11a** was neutralized with saturated aqueous sodium carbonate followed by extraction with dichloromethane, parent compound **3a** was obtained, presumably *via* **13a**. The ^1H NMR spectrum of the thienopyrrole **3a** shows a triplet at δ 8.24 (J 2.7) for H_a and a doublet of doublets at δ 4.54 (J 2.7 and 1.4) for H_b. Signals due to the protons attached to the thiophene ring appear at δ 7.05 (bs) and 7.28 (d, J 2.2). In order to confirm the ^1H NMR assignments, we prepared the deuteriated compound **3b** from **6b** by the same method.[6,7] In the ^1H NMR spectrum of **3b**, the signal of H_a (δ 8.24) appears as a triplet and that of H_b (δ 4.54) as a doublet, as expected, due to incorporation of deuterium on the thiophene ring.

Treatment of the iminium salt **11a** in dichloromethane with an excess of triethylamine in the presence of *N*-phenylmaleimide gave the *endo*-adduct **14a** (13%) and the *exo*-adduct **15a** (42%). A single crystal X-ray analysis of **15a** confirmed that cycloaddition had occurred at the pyrrole portion.[6] According to the same procedure, compounds **3c**, **d** were synthesized from **6c**, **d** *via* thienopyrrolotriazoles **10c**, **d** (Scheme 2). Compounds **3b–d** were trapped with *N*-phenylmaleimide to give the cycloadducts **14b–d** and **15b–d**. The facile formation of these cycloadducts *via* a 1,3-dipolar cycloaddition process indicates that an equilibrium between the imines **3a–d** and the tautomeric azomethine ylides **2a–d**. The latter tautomers are believed to be the reactive species undergoing cycloaddition with *N*-phenylmaleimide.

We also succeeded in preparing the *N*-substituted azomethine ylides **18a**, **c**, **d** and **g** by a retro-malonate addition approach.[8] The bromides **8a**, **d** and **g**, and the iodide **8c** that was prepared from the chloride **7c**,* were treated directly with benzylamine in the presence of *N*-phenylmaleimide to give the cycloadducts **19a**, **c**, **d** and **g** (Scheme 3). In each case, the reaction is believed to involve the replacement of the halides with benzylamine followed by intramolecular Michael addition to form the intermediates **16a**, **c**, **d** and **g**. (In one experiment, compound **16g** was isolated and characterized.) Subsequent thermolysis of the intermediates **16a**, **c**, **d** and **g** resulted in elimination of diethyl malonate to give the unisolable intermediates **17a**, **c**, **d** and **g**. These intermediates were deprotonated readily under the reaction conditions to give the azomethine ylides **18a**, **c**, **d** and **g**, which were then trapped with *N*-phenylmaleimide to give the cycloadducts **19a**, **c**, **d** and **g**.

In summary, we have synthesized the parent system **3a** of the 4*H*-thieno[3,4-*c*]pyrrole ring system and several derivatives including the compounds **3b–d** *via* tandem intramolecular 1,3-dipolar cycloaddition–cycloreversion reaction, and *N*-benzylthieno[3,4-*c*]pyrroles **18a**, **c**, **d** and **g** by retro-malonate addition approach. During the course of these experiments, we demonstrated that 4*H*-thieno[3,4-*c*]pyrroles (*e.g.* **3a**) are in equilibrium with their tautomers 5*H*-thieno[3,4-*c*]pyrroles (*e.g.* **2a**). We believe that the azomethine ylide **2a** is more important than the non-classical thiophene **1a** as a resonance contributor of the 5*H*-thieno[3,4-*c*]pyrrole ring system.

* Compound **8c** was prepared by the treatment of **7c** with sodium iodide in acetone (see Scheme 1).



Scheme 3 *Reagents:* i, $PhCH_2NH_2$, Et_3N, EtOH; ii, *N*-phenylmaleimide

Experimental

General.—^1H NMR spectra were recorded on a Varian EM-390, a JEOL HX-100 or a Bruker AM-400 spectrometer. ^{13}C NMR spectra were recorded on a Bruker AM-400 spectrometer. Mass spectra refer to electron-impact mass spectra and were recorded on a JEOL TMS-D-100 mass spectrometer. High-resolution mass spectra were recorded on a JEOL HX-110 mass spectrometer. IR spectra were recorded on a Perkin-Elmer 781 spectrometer, and UV spectra on a Perkin-Elmer Lambda 5 UV–VIS spectrometer. Melting points were determined with a Büchi 530 melting-point apparatus and are uncorrected. Flash column chromatography was performed as follows: silica gel, Merck No. 7736 Kieselgel 60H, was placed in a sintered-glass column packed dry. Solvent was flushed through the silica gel under reduced pressure using a water-aspirator. The compound was then deposited with a mimimal amount of solvent and eluted with solvent under reduced pressure. Diethyl ether and tetrahydrofuran (THF) were distilled from potassium/sodium metal under a nitrogen atmosphere with benzophenone ketyl as the indicator. All reactions were conducted under a nitrogen atmosphere.

Diethyl [(4-*Methyl*-3-*thienyl*)*methylidene*]*propanedioate* **7a** *and the Deuterium-labelled Derivative* **7b**.—To a solution of 4-methylthiophene-3-carbaldehyde **6a** (1.26 g, 10.0 mmol) in benzene (70 cm^3) was added diethyl malonate (3.20 g, 20.0 mmol), piperidine (70 mg) and acetic acid (40 mg). The reaction mixture was refluxed for 20 h with a Dean–Stark water separator attached. After cooling, the solution was washed with water, aqueous sodium carbonate and brine. Concentration and flash column chromatography (hexane–ethyl acetate, 6:1) gave the title compound **7a** (2.36 g, 88%) as a yellow oil (Found: M^+, 268.0745. $C_{13}H_{16}O_4S$ requires *M*, 268.0769); ν_{max}(neat)/cm^{-1} 3020, 1725 and 1630; δ_H(90 MHz; $CDCl_3$) 7.59 (1 H, s), 7.57 (1 H, d, *J* 3), 6.91 (1 H, m), 4.30 (2 H, q, *J* 7.5), 4.26 (2 H, q, *J* 7.5), 2.27 (3 H, s), 1.28 (3 H, t, *J* 7.5) and 1.26 (3 H, t, *J* 7.5); δ_C(100.6 MHz; $CDCl_3$) 166.58 (s), 163.92 (s), 137.89 (s), 133.75 (d), 133.34 (s), 127.17 (d), 125.49 (s), 121.56 (d), 61.41 (t), 61.25 (t), 14.24 (q), 13.73 (q) and 13.69 (q); *m/z* 268 (M^+, 35%), 223 (100), 178 (30) and 150 (45).

Data for compound **7b**, a yellow oil: ν_{max}(neat)/cm^{-1} 2985, 1730 and 1630; δ_H(90 MHz; $CDCl_3$) 7.59 (1 H, s), 4.30 (2 H, q, *J* 7.5), 4.26 (2 H, q, *J* 7.5), 2.27 (3 H, s), 1.28 (3 H, t, *J* 7.5) and 1.26 (3 H, t, *J* 7.5); *m/z* 270 (M^+, 20%), 225 (100), 180 (25) and 152 (20).

General Procedure for the Synthesis of Compounds **7c–g**.—*Diethyl* [(4-*chloromethyl*-2,5-*dimethyl*-3-*thienyl*)*methylidene*]*propanedioate* **7c**. A solution of titanium tetrachloride (0.3 cm^3, 2.2 mmol) in dry carbon tetrachloride (1 cm^3) was added dropwise to dry tetrahydrofuran (5 cm^3) at 0 °C over 1 h. To the resulting bright yellow suspension was added dropwise a solution of diethyl malonate (160 mg, 1.0 mmol) and the aldehyde **6c** (190 mg, 1.0 mmol) in dry tetrahydrofuran (4 cm^3). The reaction mixture was stirred for 1 h, after which a solution of dry pyridine (0.3 cm^3, 4.0 mmol) in tetrahydofuran (2 cm^3) was added to it over 1 h at 0 °C. The resulting mixture was stirred at 0 °C for an additional 12 h and then at room temperature for 12 h. The reaction mixture was quenched with water and extracted with diethyl ether. The combined organic layers were washed (0.5 mol dm^3 HCl) and brine, and then dried ($MgSO_4$). Concentration and flash column chromatography (hexane–ethyl acetate, 6:1) gave compound **7c** (295 mg, 89%) as a pale yellow oil (Found: M^+, 330.0672. $C_{15}H_{19}ClO_4S$ requires *M*, 330.0692); ν_{max}(neat)/cm^{-1} 2980, 2925, 2870, 1730 and 1635; δ_H(400 MHz; $CDCl_3$) 7.73 (1 H, s), 4.42 (2 H, s), 4.32 (2 H, q, *J* 6.9), 4.13 (2 H, q, *J* 6.9), 2.40 (3 H, s), 2.25 (3 H, s), 1.35 (3 H, t, *J* 7.0) and 1.10 (3 H, t, *J* 6.9); δ_C(100.6 MHz; $CDCl_3$) 164.86 (s), 163.37 (s), 138.97 (d), 135.75 (s), 134.11 (s), 131.98 (s, 2 C), 131.19 (s), 61.47 (t), 61.03 (t), 37.69 (t), 13.93 (q), 13.76 (q), 13.60 (q) and 12.54 (q); *m/z* 332 (M^+ + 2, 25%), 330 (M^+, 53), 286 (45), 285 (45), 284 (100) and 212 (70).

Diethyl [(4-*methyl*-2,5-*diphenyl*-3-*thienyl*)*methylidene*]*propanedioate* **7d**. Compound **6d** (352 mg, 1.27 mmol) was converted into **7d** (469 mg, 93%) as a yellow oil (Found: M^+, 420.1396. $C_{25}H_{24}O_4S$ requires *M*, 420.1395); ν_{max}(neat)/cm^{-1} 3060, 2980, 2940, 2900, 2870, 1735–1710, 1620 and 1593; δ_H(400 MHz; $CDCl_3$) 7.77 (1 H, s), 7.46–7.31 (10 H, m), 4.27 (2 H, q, *J* 7.0), 3.96 (2 H, q, *J* 7.0), 2.18 (3 H, s), 1.30 (3 H, t, *J* 7.0) and 1.03 (3 H, t, *J* 7.0); *m/z* 420 (M^+, 100%), 347 (45) and 264 (38).

Diethyl [(2-*ethoxycarbonyl*-4-*methyl*-3-*thienyl*)*methylidene*]*propanedioate* **7e**. Compound **6e** (88.0 mg, 0.44 mmol) was converted into **7e** (140.0 mg, 94%) as a yellow oil (Found: M^+, 340.0991. $C_{16}H_{20}O_6S$ requires *M*, 340.0980); ν_{max}(neat)/cm^{-1} 3095, 1743–1707 and 1642; δ_H(400 MHz; $CDCl_3$) 7.92 (1 H, s), 7.12 (1 H, s), 4.29 (2 H, q, *J* 7.2), 4.28 (2 H, q, *J* 7.3), 4.04 (2 H, q, *J* 7.3), 2.10 (3 H, s), 1.34–1.28 (2 × t, 6 H) and 1.01 (3 H, t, *J* 7.3); *m/z* 340 (M^+, 35%), 295 (33), 267 (100) and 239 (47).

Diethyl [(5-*ethoxycarbonyl*-4-*methyl*-3-*thienyl*)*methylidene*]*propanedioate* **7f**. Compound **6f** (23.0 mg, 0.12 mmol) was converted into **7f** (36.7 mg, 90%) as colourless crystals, m.p. 62.0–64.0 °C (Found: M^+, 340.0991. $C_{16}H_{20}O_6S$ requires *M*, 340.0980); ν_{max}(KBr)/cm^{-1} 3110, 2985, 2950, 1735–1710, 1623 and 1540; δ_H(90 MHz; $CDCl_3$) 7.68 (1 H, s), 7.60 (1 H, s), 4.40–4.13 (6 H, m), 2.55 (3 H, s) and 1.40–1.17 (9 H, m); *m/z* 340 (M^+, 100%) and 295 (86).

Diethyl {[(2,5-*bis*(*ethoxycarbonyl*)-4-*methyl*-3-*thienyl*]*methylidene*}*propanedioate* **7g**. Compound **6g** (270 mg, 1.0 mmol) was converted into **7g** (379 mg, 92%) as a yellow oil (Found: M^+, 412.1193. $C_{19}H_{24}O_8S$ requires *M*, 412.1192); ν_{max}(neat)/cm^{-1} 2992, 2943, 2910, 2880, 1740–1708 and 1648; δ_H(90 MHz; $CDCl_3$) 7.82 (1 H, s), 4.45–4.18 (6 H, m), 4.05 (2 H, q, *J* 7.2), 2.43 (3 H, s), 1.44–1.24 (9 H, m) and 1.03 (3 H, t, *J* 7.2); *m/z* 412 (M^+, 40%), 367 (30) and 339 (100).

Diethyl [(4-*Bromomethyl*-3-*thienyl*)*methylidene*]*propanedioate* **8a** *and the Deuterium-labelled Derivative* **8b**.—To a solution of compound **7a** (1.34 g, 5.00 mmol) in carbon tetrachloride (50 cm^3) was added *N*-bromosuccinimide (0.89 g, 5.00 mmol) and dibenzoyl peroxide (0.02 g). The reaction mixture was stirred and heated at reflux for 2 h, and then cooled in an ice bath. The solid was filtered off and washed with carbon tetrachloride. The combined filtrate and washings were concentrated to give an oily residue, flash column chromatography (hexane–ethyl acetate, 7:1) of which gave **8a** (1.21 g, 70%) as a yellow oil [and unchanged **7a** (0.24 g)] (Found: M^+, 345.9868. $C_{13}H_{15}BrO_4S$ requires *M*, 345.9874); $\nu_{max}(CHCl_3)/cm^{-1}$ 3008, 1720 and 1623; δ_H(90 MHz; $CDCl_3$) 7.72 (1 H, s), 7.60 (1 H, d, *J* 3.5), 7.30 (1 H, d, *J* 3.5), 4.45 (2 H, s), 4.25 (4 H, 2 × q, *J* 7.5), 1.30 (3 H, t, *J* 7.5) and 1.23 (3 H, t, *J* 7.5); δ_C(100.6 MHz; $CDCl_3$) 168.33 (s), 163.65 (s), 137.50 (s), 132.66 (d + s), 128.31 (d), 126.91 (s), 125.96 (d), 61.49 (t), 61.40 (t), 24.97 (t), 13.84 (q) and 13.68 (q), *m/z* 348 (M^+ + 2, 30%), 346 (M^+, 36), 267 (100), 221 (60), 195 (20) and 193 (20).

Data for compound **8b**, a yellow oil: $\nu_{max}(CHCl_3)/cm^{-1}$ 2982, 1725 and 1625; δ_H(90 MHz; $CDCl_3$) 7.60 (1 H, s), 4.45 (2 H, s), 4.26, 4.21 (4 H, 2 × q, *J* 7.5) and 1.30 (6 H, t, *J* 7.5); δ_C(25.1 MHz; $CDCl_3$) 166.95 (s), 163.42 (s), 137.17 (s), 132.54 (s + d), 126.74 (s), 61.57 (2 × t), 25.88 (t), 14.86 (q) and 13.95 (q); *m/z* 350 (M^+ + 2, 10%), 348 (M^+, 10), 269 (98), 223 (100) and 195 (53).

Diethyl [(4-*Azidomethyl*-3-*thienyl*)*methylidene*]*propanedioate* **9a** *and the Deuterium-labelled Derivative* **9b**.—To a solution of compound **8a** (174 mg, 0.50 mmol) in 95% ethanol (10 cm^3) was added sodium azide (65 mg, 2 mmol). The reaction mixture was stirred at room temperature for 2 h after which concentration and flash column chromatography (hexane–ethyl acetate, 5:1) gave the title compound **9a** (151 mg, 98%) as a yellow oil, ν_{max}(neat)/cm^{-1} 3120, 3000–2895, 2120, 1760–1710 and 1635; δ_H(90 MHz; CCl_4) 7.63 (1 H, d, *J* 3.0), 7.45 (1 H, s), 7.20 (1 H, d, *J* 3.0), 4.35 (2 H, s), 4.23 (2 H, q, *J* 7.5), 4.19 (2 H, q, *J* 7.5), 1.31 (3 H, t, *J* 7.5) and 1.23 (3 H, t, *J* 7.5); *m/z* 309 (M^+, 3%), 281 (12), 267 (6), 235 (15), 208 (100) and 162 (85).

Data for compound **9b**, a yellow oil: $\nu_{max}(CHCl_3)/cm^{-1}$ 3000, 2120, 1730 and 1635; δ_H(90 MHz; $CDCl_3$) 7.44 (1 H, s), 4.35 (2 H, s), 4.23 (2 H, q, *J* 7), 4.19 (2 H, q, *J* 7) and 1.30 and 1.22(6 H, 2 × t); *m/z* 283 (M^+ − 28, 7%), 210 (100), 164 (68).

Diethyl 1,8b-*Dihydro*-5H-*thieno*[3′,4′:3,4]*pyrrolo*[1,2-c][1,2,3]*triazole*-1,1-*dicarboxylate* **10a** *and its Deuterium-labelled Derivative* **10b**.—A solution of compound **9a** (309 mg, 1.00 mmol) in diethyl ether (20 cm^3) was allowed to stand at room temperature for 5 months after which concentration of the reaction mixture and silica gel flash column chromatography (hexane–ethyl acetate, 4:1) of the residue gave the title compound **10a** (272 mg, 88%) as a colourless oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 3020 and 1745; δ_H(90 MHz; CCl_4) 6.77 (2 H, m), 5.30 (1 H, s), 5.00 (1 H, d, *J* 15), 4.42 (1 H, d, *J* 15), 4.37–4.00 (4 H, 2 × q), 1.31 (3 H, t, *J* 7) and 1.17 (3 H, t, *J* 7); *m/z* 310 (M^+ + 1, 5%), 281 (M^+ − 28, 63), 236 (31), 208 (78), 180 (88), 162 (57), 137 (100) and 123 (15).

Data for compound **10b**, a colourless oil: $\nu_{max}(CHCl_3)/cm^{-1}$ 2990 and 1745; δ_H(90 MHz; CCl_4) 5.30 (1 H, s), 5.02 (1 H, d, *J* 15), 4.43 (1 H, d, *J* 15), 4.54–3.97 (4 H, 2 × q), 1.30 (3 H, t, *J* 7) and 1.18 (3 H, t, *J* 7); *m/z* 312 (M^+ + 1, 8), 283 (M^+ − 28, 28), 211 (85), 182 (100), 164 (49) and 139 (46).

Diethyl 6,8-*Dimethyl*-1,8b-*dihydro*-5H-*thieno*[3′,4′:3,4]*pyrrolo*[1,2-c][1,2,3]*triazole*-1,1-*dicarboxylate* **10c**.—A solution of compound **7c** (109 mg, 0.33 mmol), sodium azide (65 mg, 1.0 mmol) and 95% ethanol (10 cm^3) was stirred at room temperature for 28 h after which concentration of the reaction mixture and flash column chromatography (hexane–ethyl acetate, 4:1) of the residue gave the title compound **10c** (108 mg, 97%) as colourless crystals, m.p. 98.5–99.0 °C (Found: M^+, 337.1084. $C_{15}H_{19}N_3O_4S$ requires *M*, 337.1096); ν_{max}(KBr)/cm^{-1} 2990, 2940, 2925, 2880 and 1735; δ_H(400 MHz; $CDCl_3$) 5.48 (1 H, s), 4.82 (1 H, d, *J* 14.6), 4.38 (1 H, d, *J* 14.6), 4.45–4.40 and 4.33–4.25 (2 H, ABq of q), 4.19–4.11 and 4.04–3.96 (2 H, ABq of q), 2.22 (3 H, s), 2.17 (3 H, s), 1.35 (3 H, t, *J* 6.9) and 1.06 (3 H, t, *J* 6.9); δ_C(100.6 MHz; $CDCl_3$) 165.57 (s), 165.05 (s), 137.45 (s), 135.60 (s), 129.35 (s), 126.14 (s), 94.02 (s), 63.76 (d), 63.09 (t), 62.59 (t), 49.99 (t), 13.91 (q), 13.52 (q), 13.38 (q) and 13.19 (q); *m/z* 337 (M^+, 25%), 309 (M^+ − 28, 17), 264 (31), 236 (100), 208 (50), 190 (44) and 151 (42).

General Procedure for the Syntheses of the Bromides **8d–g** *and the Triazoles* **10d–g**.—*Tetraethyl* 1,8b-*Dihydro*-5H-*thieno*[3′,4′:3,4]*pyrrolo*[1,2-c][1,2,3]*triazole*-1,1,6,8-*tetracarboxylate* **10g**. To a solution of compound **7g** (202 mg, 0.49 mmol) in carbon tetrachloride (25 cm^3) was added *N*-bromosuccinimide (93.0 mg, 0.52 mmol) and dibenzoyl peroxide (1 mg). The reaction mixture was stirred and heated at reflux for 5 h. After the mixture had been cooled in an ice bath, the solid was filtered off and the filtrate concentrated to give the crude bromide **8g** (236 mg) as a yellow oil (Found: M^+, 490.0287. $C_{19}H_{23}BrO_8S$ requires *M*, 490.0297); ν_{max}(neat)/cm^{-1} 2992, 2935, 2905 and 1730–1712; δ_H(90 MHz; $CDCl_3$) 7.81 (1 H, s), 4.79 (2 H, s), 4.48–4.17 (6 H, m), 4.05 (2 H, q, *J* 7.2), 1.47–1.24 (9 H, m) and 1.04 (3 H, t, *J* 7.2); *m/z* 492 (M^+ + 2, 23%), 490 (M^+, 23), 419 (100), 417 (94) and 339 (52).

To crude **8g** was added sodium azide (96.0 mg, 1.48 mmol) and 95% ethanol (10 cm^3) and the mixture was stirred at room temperature for 45 min. Concentration and flash column chromatography (hexane–ethyl acetate, 5:1) gave the title compound **10g** (184 mg, 95%) as colourless crystals [and unchanged starting material **7g** (12.0 mg)], m.p. 71.0–73.0 °C; ν_{max}(neat)/cm^{-1} 2980, 2940, 2903, 2870, 1755–1710 and 1583; δ_H(400 MHz; $CDCl_3$) 5.67 (1 H, s), 5.23 (1 H, d, *J* 16.9), 4.55 (1 H, d, *J* 16.1), 4.43–4.34 and 4.13–4.04 (4 H, ABq of q, *J* 10.7, 72), 4.30–4.18 (4 H, m), 1.30–1.23 (9 H, m) and 1.01 (3 H, t, *J* 7.2); δ_C(100.6 MHz; $CDCl_3$) 165.05 (s), 163.81 (s), 160.62 (s), 160.43 (s), 147.94 (s), 146.60 (s), 130.02 (s), 127.30 (s), 90.45 (s), 65.79 (d), 62.89 (t), 62.53 (t), 61.94 (t), 61.74 (t), 52.07 (t), 13.95 (q), 13.72 (2 × q) and 13.30 (q); *m/z* 425 (M^+ − 28, 61%), 398 (39), 380 (24), 353 (100), 352 (95), 324 (72) and 222 (89).

Diethyl 6,8-*diphenyl*-1,8b-*dihydro*-5H-*thieno*[3′,4′:3,4]*pyrrolo*[1,2-c][1,2,3]*triazole*-1,1-*dicarboxylate* **10d**. Compound **7d** (65.8 mg, 0.16 mmol) was treated with *N*-bromosuccinimide (28.5 mg, 0.16 mmol) for 4 h to give compound **8d** (75.0 mg, 96%) as a yellow oil (Found: M^+, 498.0473. $C_{25}H_{23}BrO_4S$ requires *M*, 498.0501); ν_{max}(neat)/cm^{-1} 3160, 3020, 2980, 2930, 2900, 2865, 1745–1708, 1642 and 1597; δ_H(400 MHz; $CDCl_3$) 7.94 (1 H, s), 7.59–7.57 (2 H, m), 7.49–7.33 (8 H, m), 4.44 (2 H, s), 4.28 (2 H, q, *J* 7.2), 3.84 (2 H, q, *J* 7.3), 1.30 (3 H, t, *J* 7.0) and 0.96 (3 H, t, *J* 7.2); *m/z* 500 (M^+ + 2, 100%), 498 (M^+, 98), 419 (98) and 373 (35).

The crude bromide **8d** was treated with sodium azide (30.1 mg, 0.46 mmol) for 4.5 h for give compound **10d** (66.1 mg, 93%) as colourless crystals, m.p. 138–140 °C (decomp.) (Found: M^+, 461.1388. $C_{25}H_{23}N_3O_4S$ requires *M*, 461.1409); ν_{max}(KBr)/cm^{-1} 3200–2980, 1732 and 1585; δ_H(400 MHz; $CDCl_3$) 7.45 (2 H, d, *J* 7.2), 7.44–7.36 (6 H, m), 7.32–7.29 (2 H, m), 6.03 (1 H, s), 5.30 (1 H, d, *J* 15.0), 4.75 (1 H, d, *J* 15.0), 4.46 (1 H, dq, *J* 10.8, 7.1), 4.30 (1 H, dq, *J* 10.7, 7.1), 3.65 (1 H, dq, *J* 10.9, 7.2), 3.03 (1 H, dq, *J* 10.5, 7.2), 1.34 (3 H, t, *J* 7.1) and 0.87 (3 H, t, *J* 7.2); *m/z* 461 (M^+, 31%), 433 (M^+ − 28, 22) and 275 (100).

Triethyl 1,8b-*dihydro*-5H-*thieno*[3′,4′:3,4]*pyrrolo*[1,2-c][1,2,3]*triazole*-1,1,8-*tricarboxylate* **10e**. Compound **7e** (77.0 mg, 0.23 mmol) was treated with *N*-bromosuccinimide (41.1 mg,

0.23 mmol) for 5 h to give the crude bromide **8e**, which was treated with sodium azide (22.0 mg, 0.34 mmol) for 2 h to give the title compound **10e** (34 mg, 89%) as a yellow oil [and some unchanged starting material **7e** (43.1 mg)], $\nu_{max}(CHCl_3)/cm^{-1}$ 2980, 2937, 1738 and 1710; δ_H(400 MHz; $CDCl_3$) 7.13 (1 H, s), 5.80 (1 H, s), 5.09 (1 H, dd, *J* 15.3, 1.2), 4.49 (1 H, d, *J* 14.8), 4.49–4.43 and 4.18–4.09 (2 H, m), 4.40–4.26 (2 H, m), 4.08–3.92 (2 H, m), 1.38–1.30 (6 H, m) and 1.04 (3 H, t, *J* 7.1); δ_C(100.6 MHz; $CDCl_3$) 170.09 (s), 163.98 (s), 161.05 (s), 148.69 (s), 142.33 (s), 125.92 (s), 121.14 (d), 94.74 (s), 65.83 (d), 62.95 (t), 62.49 (t), 61.47 (t), 50.66 (t), 13.93 (q), 13.85 (q) and 13.34 (q); *m/z* 353 (M^+ − 28, 27%), 327 (15), 308 (23), 281 (50), 280 (5), 234 (53), 209 (62), 208 (50), 207, (43), 206 (43), 205 (53) and 150 (100).

Triethyl 1,8b-*dihydro*-5H-*thieno*[3′,4′:3,4]*pyrrolo*[1,2-c]-[1,2,3]*triazole*-1,1,6-*tricarboxylate* **10f**. Compound **7f** (31.7 mg, 0.09 mmol) was treated with *N*-bromosuccinimide (16.6 mg, 0.09 mmol) for 3 h to give the crude bromide **8f**, which was treated with sodium azide (20.0 mg, 0.31 mmol) for 10 h to give the title compound **10f** (12.3 mg, 88%) as a yellow oil [and some unchanged starting material **7f** (19.3 mg)], $\nu_{max}(CHCl_3)/cm^{-1}$ 2990, 2942, 2903, 1745, 1713 and 1585; δ_H(400 MHz; $CDCl_3$) 7.09 (1 H, s), 5.50 (1 H, s), 5.37 (1 H, d, *J* 17.1), 4.67 (1 H, d, *J* 17.2), 4.42–4.26 (6 H, m), 1.39–1.33 (6 H, m) and 1.27 (3 H, t, *J* 7.2); *m/z* 382 (M^+ + 1, 15%), 353 (M^+ − 28, 41), 280 (100) and 252 (83).

4H-*Thieno*[3,4-c]*pyrrolium Toluene*-p-*sulfonate* **11a** *and the Deuterium-labelled Derivative* **11b**.—To a solution of compound **10a** (60.2 mg, 0.19 mmol) in dry diethy ether (6 cm^3) was added toluene-*p*-sulfonic acid (50.0 mg, 0.26 mmol) in dry diethyl ether–tetrahydrofuran (5:1; 2.5 cm^3). The reaction mixture was stirred at room temperature for 30 min, during which time the product precipitated out as a white solid. It was filtered and washed with dry diethyl ether (3 × 3 cm^3) to give the title compound **11a** (55.0 mg, 96%), which was unstable in air, ν_{max}(KBr)/cm^{-1} 3450, 3100–2920, 1680 and 1600; *m/z* 172 (M^+ − 123, 100%). When compound **11a** was dissolved in D_2O for the NMR measurements, the spectrum indicated its hydrolysis to compound **12a**, δ_H(400 MHz; dioxane; δ 3.54 as an internal standard) 9.62 (1 H, s), 8.37 (1 H, d, *J* 2.8), 7.45 (2 H, d, *J* 8.0), 7.41 (1 H, d, *J* 2.5), 7.11 (2 H, d, *J* 8.0), 4.11 (2 H, s) and 2.16 (3 H, s); δ_C(100.6 MHz; dioxane; δ 67.4 as an internal standard) 191.80 (d), 145.99 (d), 143.15 (s), 140.47 (s), 139.87 (s), 131.88 (s), 130.72 (d), 130.23 (d), 126.20 (d), 38.26 (t) and 21.30 (q).

The same method was used for preparation of compound **11b**, ν_{max}(KBr)/cm^{-1} 3450, 3100–3030, 1690, 1681 and 1496; *m/z* 172 (M^+ − 125, 100%) and 125 (M^+ − 172, 17). When compound **11b** was dissolved in D_2O for NMR measurements, the spectrum indicated its hydrolysis to compound **12b**, δ_H(400 MHz; HOD; δ 4.60 as an internal standard) 9.65 (1 H, s), 7.46 (2 H, d, *J* 8.2), 7.14 (2 H, d, *J* 8.1), 4.13 (2 H, s) and 2.17 (3 H, s).

1,3-*Dimethyl*-4H-*thieno*[3,4-c]*pyrrolium Toluene*-p-*sulfonate* **11c** *and its Hydrolysis to* **12c**.—To a solution of compound **10c** (63.5 mg, 0.19 mmol) in dry diethyl ether (4 cm^3) was added toluene-*p*-sulfonic acid (39.0 mg, 0.21 mmol) in dry diethyl ether (1.5 cm^3). The reaction mixture was stirred at room temperature for 1 h during which time the resulting product had coated the flask as an oil. The mother liquid was removed and the oil washed with dry diethyl ether (3 × 3 cm^3) under nitrogen to give the crude product **11c** (64.0 mg, 100%), which was unstable in air, ν_{max}(KBr)/cm^{-1} 3100–2750, 1615 and 1565; *m/z* 172 (M^+ − 151, 55%) and 151 (M^+ − 172, 100).

When compound **11c** was dissolved in D_2O for NMR measurements, the spectrum indicated its hydrolysis to compound **12c**, δ_H(400 MHz) 9.64 (1 H, s), 7.42 (2 H, d, *J* 7.7), 7.09 (2 H, d, *J* 8.1), 3.92 (2 H, s), 2.48 (3 H, s), 2.15 (3 H, s) and 2.13 (3 H, s).

4H-*Thieno*[3,4-c]*pyrrole* **3a** *and its Deuterium-labelled Derivative* **3b**.—A solution of compound **11a** (15.0 mg, 0.05 mmol) in water (5 cm^3) was treated with saturated aqueous sodium carbonate (0.5 cm^3), and the mixture then extracted with chloroform (2 × 3 cm^3). The organic layer was dried ($MgSO_4$) and concentrated to give the parent compound **3a** (5.8 mg, 93%) as colourless crystals, m.p. 145–147 °C (decomp.) (Found: M^+, 123.0137. C_6H_5NS requires *M*, 123.0144); $\nu_{max}(CHCl_3)/cm^{-1}$ 3110, 3000–2980, 1680, 1640, 1575, 1540 and 1490; $\lambda_{max}(CHCl_3)$/nm 254 (ε/dm^3 mol^{-1} cm^{-1} 7.4 × 10^3); δ_H(400 MHz; $CDCl_3$) 8.24 (1 H, t, *J* 2.7), 7.28 (1 H, d, *J* 2.2), 7.05 (1 H, br s) and 4.54 (2 H, dd, *J* 2.7, 1.4); δ_C(100.6 MHz; $CDCl_3$) 157.89 (d), 151.71 (s), 149.29 (s), 114.44 (d), 113.53 (d) and 58.59 (t); *m/z* 123 (M^+, 100%).

Data for compound **3b**: ν_{max}(KBr)/cm^{-1} 1682 and 1645; δ_H(400 MHz; CD_2Cl_2) 8.24 (1 H, t, *J* 2.6) and 4.54 (2 H, d, *J* 2.6); *m/z* 125 (M^+, 100%).

1,3-*Dimethyl*-4H-*thieno*[3,4-c]*pyrrole* **3c**.—A solution of the crude product **11c** (64.0 mg, 0.19 mmol) in water (3 cm^3) was treated with saturated aqueous sodium carbonate (0.3 cm^3) and then extracted with dichloromethane (3 × 2 cm^3). The organic layer was concentrated to give the title compound **3c** (26.0 mg, 91%) as colourless crystals (Found: M^+, 151.0451. C_8H_9NS requires *M*, 151.0456); m.p. 92–95 °C (decomp.); ν_{max}(KBr)/cm^{-1} 2920, 2860 and 1633; δ_H(400 MHz; $CDCl_3$) 8.12 (1 H, br s), 4.40 (2 H, s), 2.47 (3 H, s) and 2.31 (3 H, s); *m/z* 151 (M^+, 100%).

endo- *and* exo-4,8-*Epimino*-2-*phenyl*-2,3,3a,4,8,8a-*hexahydro*-1H-*thieno*[3,4-f]*isoindole*-1,3-*dione* **14a** *and* **15a** *and the Deuterium-labelled Derivatives* **14b** *and* **15b**.—To a solution of compound **10a** (49.1 mg, 0.16 mmol) in dry diethyl ether (10 cm^3) was added toluene-*p*-sulfonic acid (39.5 mg, 0.21 mmol) in tetrahydrofuran (2 cm^3) under nitrogen. The reaction mixture was stirred at room temperature for 30 min, after which *N*-phenylmaleimide (83.0 mg, 0.48 mmol) and triethylamine (0.1 cm^3) in tetrahydrofuran (2 cm^3) were added to it. The mixture was stirred for a further 24 h and then concentrated. The residue was dissolved in dichloromethane and the solution washed with water and then concentrated. Flash column chromatography (ethyl acetate–hexane, 1:3) of the residue gave compounds **14a** (6.1 mg, 13%) and **15a** (19.6 mg, 42%).

Data for compound **14a**, colourless crystals: m.p. 238–240 °C; ν_{max}(KBr)/cm^{-1} 3290, 3240, 1776, 1715 and 1502; δ_H(400 MHz; $CDCl_3$) 7.35–7.28 (3 H, m), 6.98–6.91 (2 H, br s), 6.68 (2 H, br d, *J* 7.8), 4.88–4.87 (2 H, m), 3.85–3.84 (2 H, m) and 2.54 (1 H, br s, NH); δ_C(100.6 MHz; $CDCl_3$) 174.61 (s), 147.90 (s), 131.30 (s), 129.10 (d), 128.83 (d), 126.60 (d), 114.62 (d), 60.33 (d) and 49.19 (d); *m/z* 296 (M^+, 7%), 173 (16), 123 (100).

Data for compound **15a**, colourless crystals: m.p. 238–240 °C (Found: M^+, 296.0616. $C_{16}H_{12}N_2O_2S$ requires *M*, 296.0619); ν_{max}(KBr)/cm^{-1} 3300, 3115, 3080, 1770, 1708 and 1502; δ_H(400 MHz; [$^2H_6$]DMSO) 7.50–7.47 (2 H, m), 7.43–7.40 (1 H, m), 7.20 (2 H, br d, *J* 8.7), 7.11 (2 H, s), 4.56 (2 H, s) and 3.04 (2 H, s); *m/z* 296 (M^+, 19%), 173 (11), 123 (100) (Found: C, 64.8; H, 4.0; N, 9.45. Calc. for $C_{16}H_{12}N_2O_2S$: C, 64.85; H, 4.08; N, 9.45%).

Data for compound **14b**, a yellow oil: ν_{max}(KBr)/cm^{-1} 1770 and 1710; δ_H(400 MHz; $CDCl_3$) 7.35–7.31 (3 H, m), 6.69 (2 H, d, *J* 6.7), 4.90–4.89 (2 H, m), 3.87–3.86 (2 H, m) and 1.26 (1 H, s, NH); *m/z* 298 (M^+, 29), 173 (29) and 125 (100).

Data for compound **15b**: ν_{max}(KBr)/cm^{-1} 3300, 1768 and 1705; δ_H(400 MHz; $CDCl_3$–[$^2H_6$]DMSO) 7.40–7.30 (3 H, m), 7.20 (2 H, d, *J* 7.3), 4.69 (2 H, s) and 3.00 (2 H, s); *m/z* 298 (M^+, 19%), 173 (22) and 125 (100).

exo-4,8-*Epimino*-5,7-*dimethyl*-2-*phenyl*-2,3,3a,4,8,8a-*hexahydro*-1H-*thieno*[3,4-f]*isoindole*-1,3-*dione* **15c**.—Compound **3c** (20.0 mg, 0.13 mmol), *N*-phenylmaleimide (30.2 mg, 0.17 mmol) and benzene (2.6 cm^3) were mixed and stirred at 65 °C for 40 h. Concentration of the mixture and flash column chromatography (hexane–ethyl acetate, 3:1) of the residue gave the title compound **15c** (18.0 mg, 41%) as colourless crystals, m.p. 209–211 °C (Found: M^+, 324.0921. $C_{18}H_{16}N_2O_2S$ requires *M*, 324.0932); ν_{max}(KBr)/cm^{-1} 3320, 2995, 2915, 1770, 1703 and 1502; δ_H(400 MHz; $CDCl_3$) 7.50–7.47 (2 H, t), 7.42–7.39 (1 H, t), 7.31 (2 H, dd, *J* 7.5, 1.2), 4.64 (2 H, s), 3.09 (2 H, s), 3.00–2.67 (1 H, br s, NH) and 2.32 (6 H, s); *m*/*z* 324 (M^+, 4%), 173 (M^+ − 151, 4) and 151 (100).

endo- *and* exo-4,8-*Epimino*-2,5,7-*triphenyl*-2,3,3a,4,8,8a-*hexahydro*-1H-*thieno*[3,4-f]*isoindole*-1,3-*dione* **14d** *and* **15d**.—To a solution of toluene-*p*-sulfonic acid (9.40 mg, 0.05 mmol) in dry diethyl ether (3 cm^3) was added rapidly compound **10d** (21.0 mg, 0.05 mmol) at 0 °C under a nitrogen atmosphere. The mixture was stirred at 0 °C for 20 min, after which *N*-phenylmaleimide (11.0 mg, 0.06 mmol) and triethylamine (14.0 mg, 0.14 mmol) in diethyl ether (1 cm^3) were added to it. The reaction mixture was stirred for 12 h at room temperature after which the product was filtered off, washed with dry diethyl ether (2 × 2 cm^3), and dissolved in dichloromethane (4 cm^3). The solution was washed with water and concentrated to give compounds **14d** and **15d** (1:1) (6.7 mg, 16%) as colourless crystals; ν_{max}(KBr)/cm^{-1} 3046, 3020 and 1711; δ_H(300 MHz; $CDCl_3$) 7.64 (2 H, d, *J* 7.6), 7.54 (2 H, d, *J* 7.5), 7.56–7.17 (10 H, m), 6.75 (1 H, dd, *J* 8.6, 1.9), 5.03–5.02 (1 H, m), 5.01 (1 H, s), 4.03–4.02 (1 H, m) and 3.78 (1 H, s); *m*/*z* 448 (M^+, 5%), 275 (M^+ − 173, 100) and 173 (M^+ − 273, 55).

Diethyl 5-*Benzyl*-4-*bis*(*ethoxycarbonyl*)*methyl*-5,6-*dihydro*-4H-*thieno*[3,4-c]*pyrrole*-1,3-*dicarboxylate* **16g**.—To a solution of the bromide **8g** (87.0 mg, 0.15 mmol) in chloroform (5 cm^3) was added benzylamine (48.2 mg, 0.45 mmol). The reaction mixture was stirred at room temperature for 1 h after which it was concentrated. Flash column chromatography (hexane–ethyl acetate, 6:1) of the residue gave the title compound **16g** as a yellow oil, ν_{max}(neat)/cm^{-1} 3063, 2990, 2940, 2910, 2890, 2815, 1750–1690 and 1590; λ_{max}(EtOH)/nm 278 (ε/dm^3 mol^{-1} cm^{-1} 2.38 × 10^4) and 216 (1.72 × 10^4); δ_H(400 MHz; $CDCl_3$) 7.35–7.21 (5 H, m), 5.02 (1 H, br d, *J* 2.2), 4.43 (1 H, d, *J* 13.5), 4.37–4.31 (4 H, q + s), 4.28 (2 H, q, *J* 7.1), 4.23–4.01 (4 H, 2 × AB q), 3.85 (1 H, d, *J* 13.5), 3.66 and 3.63 (1 H, 2 × s, 1.3:1), 1.37 (3 H, t, *J* 7.2), 1.30–1.27 (6 H, 2 × t) and 1.10 (3 H, t, *J* 7.2); *m*/*z* 357 (M^+ − 160, 100%).

endo-4,8-*Benzylepimino*-2-*phenyl*-2,3,3a,4,8,8a-*hexahydro*-1H-*thieno*[3,4-f]*isoindole*-1,3-*dione* **19a**.—To a solution of compound **8a** (30.0 mg, 0.09 mmol) was added benzylamine (10.0 mg, 0.09 mmol) and triethylamine (14.0 mg, 0.14 mmol) in chloroform (1 cm^3). The reaction mixture was stirred at room temperature for 12 h after which *N*-phenylmaleimide (19.1 mg, 0.11 mmol) in chloroform (1 cm^3) was added to it, the mixture was stirred at room temperature for a further 24 h and then diluted with dichloromethane (5 cm^3), washed with water (3 cm^3) and concentrated. Flash column chromatography (hexane–ethyl acetate, 2:1) of the residue gave the product **19a** (22.3 mg, 80%) as a colourless oil (Found: M^+, 386.1058. $C_{23}H_{18}N_2O_2S$ requires *M*, 386.1089); ν_{max}($CHCl_3$)/cm^{-1} 3100, 3017, 2906, 2870, 2828, 1769 and 1699; δ_H(400 MHz; $CDCl_3$) 7.41–7.05 (8 H, m), 7.04 (2 H, s), 6.83 (2 H, dd, *J* 5.7, 1.2), 4.51–4.49 (2 H, m), 3.86–3.85 (2 H, m) and 3.48 (2 H, s); *m*/*z* 386 (M^+, 33%), 213 (M^+ − 173, 100) and 173 (M^+ − 213, 33).

endo-4,8-*Benzylepimino*-5,6-*dimethyl*-2-*phenyl*-2,3,3a,4,8,8a-*hexahydro*-1H-*thieno*[3,4-f]-*isoindole*-1,3-*dione* **19c**.—To a solution of compound **8c** (40.0 mg, 0.14 mmol) in chloroform (1.4 cm^3) was added benzylamine (38.3 mg, 0.42 mmol). The reaction mixture was stirred at room temperature for 15 min, after which *N*-phenylmaleimide (31.0 mg, 0.18 mmol) in chloroform (0.5 cm^3) was added to it, the mixture was stirred for a further 30 min and then concentrated. Flash column chromatography (hexane–ethyl acetate, 2:1) of the residue gave the product **19c** (21.1 mg, 37%) as colourless crystals, m.p. 159–161 °C (Found: M^+, 414.1375. $C_{25}H_{22}N_2O_2S$ requires *M*, 414.1402); ν_{max}(KBr)/cm^{-1} 1711; δ_H(400 MHz; $CDCl_3$) 7.38–7.22 (8 H, m), 6.77 (2 H, dd, *J* 7.4, 1.5), 4.35–4.33 (2 H, m), 3.80–3.78 (2 H, m), 3.51 (2 H, s) and 2.23 (6 H, s); *m*/*z* 414 (M^+, 9%), 214 (M^+ − 173, 100), 173 (M^+ − 241.6).

endo-4,8-*Benzylepimino*-2,5,6-*triphenyl*-2,3,3a,4,8,8a-*hexahydro*-1H-*thieno*[3,4-f]*isoindole*-1,3-*dione* **19d**.—To a solution of compound **8d** (47.0 mg, 0.09 mmol) in chloroform (1 cm^3) was added benzylamine (9.6 mg, 0.09 mmol) and triethylamine (11.4 mg, 0.11 mmol). The reaction mixture was stirred at room temperature for 25 min, after which *N*-phenylmaleimide (23.0 mg, 0.13 mmol) was added to it. The mixture was stirred for a further 18 h and then concentrated. Flash column chromatography (hexane–ethyl acetate, 2:1) of the residue gave the title compound **19d** (22.5 mg, 44%) as colourless crystals, m.p. 166–168 °C (Found: M^+, 538.1752. $C_{35}H_{26}O_2N_2S$ requires *M*, 538.1715); ν_{max}(KBr)/cm^{-1} 3064, 3029, 2941, 2841 and 1709; δ_H(400 MHz; $CDCl_3$) 7.64 (4 H, d, *J* 7.2), 7.41–7.37 (4 H, m), 7.32–7.10 (8 H, m), 7.12–7.10 (2 H, m), 6.77 (2 H, dd, *J* 7.9, 1.3), 4.68–4.67 (2 H, m), 4.04–4.02 (2 H, m) and 3.49 (2 H, s); *m*/*z* 538 (M^+, 8%), 365 (M^+ − 173, 100), 274 (22) and 173 (M^+ − 365, 38).

endo-4,8-*Benzylepimino*-5,6-*bis*(*ethoxycarbonyl*)-2-*phenyl*-2,3,3a,4,8,8a-*hexahydro*-1H-*thieno*[3,4-f]*isoindole*-1,3-*dione* **19g**.—To a solution of compound **16g** (25.5 mg, 0.05 mmol) in ethanol (1 cm^3) was added *N*-phenylmaleimide (11.0 mg, 0.06 mmol). The mixture was stirred at room temperature for 2 days after which it was concentrated. Flash column chromatography (hexane–ethyl acetate, 3:1) of the residue gave the title compound **19g** (15.8 mg, 61%) as colourless crystals, m.p. 127–129 °C (Found: M^+, 530.1503. $C_{29}H_{26}N_2O_6S$ requires *M*, 530.1511); ν_{max}(KBr)/cm^{-1} 1714; δ_H(400 MHz; $CDCl_3$) 7.41–7.27 (6 H, m), 7.22 (2 H, br d, *J* 7.3), 6.68 (2 H, dd, *J* 8.1, 1.3), 4.89–4.88 (2 H, m), 4.34 (4 H, q, *J* 7.1), 3.95–3.92 (2 H, m), 3.51 (2 H, s) and 1.35 (6 H, t, *J* 7.1); *m*/*z* 530 (M^+, 5%), 357 (M^+ − 173, 100) and 173 (M^+ − 357, 35).

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