Reactions of 1,3-diethyl-2-thiobarbituric acid with aldehydes: formation of arylbis(1,3-diethyl-2-thiobarbitur-5-yl)methanes † and crystallographic evidence for ground state polarisation in 1,3-diethyl-5-[4-(dimethylamino)benzylidene]-2-thiobarbituric acid

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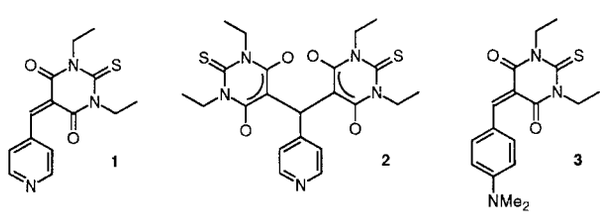
The reactions of 1,3-diethyl-2-thiobarbituric acid (detba) in ethanol at room temperature with 4-(dimethylamino)-benzaldehyde (dmabza) or cinnamaldehyde afford the Knoevenagel products **3** and **4**, respectively. Under identical conditions, pyridine-4-carbaldehyde, 4-methoxybenzaldehyde, benzaldehyde, 4-cyanobenzaldehyde, 4-nitrobenz-aldehyde and 4-ferrocenylbenzaldehyde yield exclusively the arylbis(1,3-diethyl-2-thiobarbitur-5-yl)methane Michael adducts **2**, **5**, **6**, **7**, **8** and **9**, respectively. Although **3** can be forced to react further by treatment with excess detba in refluxing ethanol, the product **10** is unstable in solution and readily reverts to **3**. The stability of **4** is attributed to extended conjugation, and it is likely that the pronounced difference in reactivity between dmabza and the other arylaldehydes arises primarily from electronic factors, *i.e.* the strongly electron donating effect of the -NMe_2 substituent. Single crystal X-ray structures have been determined for the products **3** and **6**. The structure of **6** confirms the formation of the Michael adduct and shows that both of the detba rings are present in mixed keto–enol forms, although the oxygens differ slightly in their degree of enolic character. The bond distances in **3** provide clear evidence for extensive ground state polarisation, in accord with the marked molecular nonlinear optical properties of the analogous -$N(^nBu)_2$ compound.

Introduction

It is well established that barbituric acid (ba) and 2-thio-barbituric acid (tba) undergo Knoevenagel condensations with aldehydes to give 5-substituted derivatives.[1,2] Such reactions have attracted interest recently for the preparation of compounds which have potential utility in two disparate fields of research. In the realm of biological chemistry, work involving artificial, hydrogen-bonding receptors for barbiturate drugs[3] has inspired the preparation of barbiturate derivatives possessing specific host–guest recognition properties.[4] Barbiturate groups are strongly electron-withdrawing because they gain aromatic stabilisation upon reduction.[5] This property has been exploited in the preparation of molecules which possess very pronounced quadratic non-linear optical (NLO) properties, of interest for potential applications in opto-electronic and photonic technologies.[6]

The 1 : 1 reaction of 4′-methyl-2,2′-bipyridyl-4-carbaldehyde with ba in refluxing ethanol affords the Knoevenagel product in high yield.[4] As part of an ongoing investigation into the NLO properties of organotransition metal complexes,[7] we hence sought to prepare the potential ligand 1,3-diethyl-5-(4-picolylidene)-2-thiobarbituric acid (**1**) *via* reaction of 1,3-diethyl-2-thiobarbituric acid (detba) with pyridine-4-carbalde-hyde. However, using standard conditions,[6b] we instead isolated the compound 4-pyridylbis(1,3-diethyl-2-thiobarbitur-5-yl)-methane (**2**). This unexpected outcome stimulated us to engage in further studies of the reactions of detba with aldehydes, and the results of these investigations are reported herein, including crystallographic characterisations of two of the products.



5 R = OMe **8** R = NO_2
6 R = H **9** R = (η^5-C_5H_5)Fe(η^5-C_5H_4)
7 R = CN **10** R = NMe_2

Results and discussion

Syntheses

It is clear that compound **2** results from the Michael addition of a second molecule of detba across the vinyl group of **1**. Variation of the reaction stoichiometry and/or temperature

† IUPAC name for arylbis(1,3-diethyl-2-thiobarbitur-5-yl)methane is arylbis(1,3-diethyl-2-thio-4,6-dioxohexahydro-5-pyrimidyl)methane.

Table 1 Crystallographic data and refinement details for compounds **3** and **6**

	3	**6**
Formula	$C_{17}H_{21}N_3O_2S$	$C_{23}H_{28}N_4O_4S_2$
M	331.43	488.61
Crystal system	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P2_1/c$
a/Å	7.913(5)	8.920(2)
b/Å	10.040(3)	9.845(2)
c/Å	10.363(5)	26.878(3)
α/°	88.87(4)	
β/°	79.58(4)	92.23(2)
γ/°	85.40(4)	
U/Å^3	807.1(6)	2358.6(4)
Z	2	4
D_c/Mg m^{-3}	1.364	1.376
T/K	173(2)	293(2)
λ/Å	0.710 73 (Mo-Kα)	0.710 73 (Mo-Kα)
F(000)	352	1032
μ/mm^{-1}	0.214	0.264
Scan type	ϕ and ω	ϕ and ω
θ range/°	2.00–27.48	5.11–23.24
h, k, l ranges	−10/10, −12/13, −13/12	−9/9, −10/10, −29/29
Reflections collected	8147	22873
Independent reflections (R_{int})	3650 (0.0349)	3233 (0.0549)
Data/restraints/parameters	3650/0/212	3233/0/310
Final R indices [$I > 2\sigma(I)$] [a,b]	$R_1 = 0.0443$, $wR_2 = 0.1086$	$R_1 = 0.0420$, $wR_2 = 0.1305$
Final R indices (all data)	$R_1 = 0.0623$, $wR_2 = 0.1127$	$R_1 = 0.0525$, $wR_2 = 0.1399$
Weighting factors (x, y) [b]	0.0616, 0	0, 0
Goodness of fit, S	0.909	1.111
Peak and hole, e Å^{-3}	0.532, −0.302	0.161, −0.250

[a] Structures were refined on F_o^2 using all data; the value of R_1 is given for comparison with older refinements based on F_o with a typical threshold of $F_o > 4\sigma(F_o)$. [b] $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$; $S = [\Sigma w(F_o^2 - F_c^2)^2/(M - N)]^{1/2}$, where M = number of reflections and N = number of parameters; $w^{-1} = [\sigma^2(F_o^2) + (xP)^2 + yP]$ and $P = [\max(F_o^2, 0) + 2F_c^2]/3$.

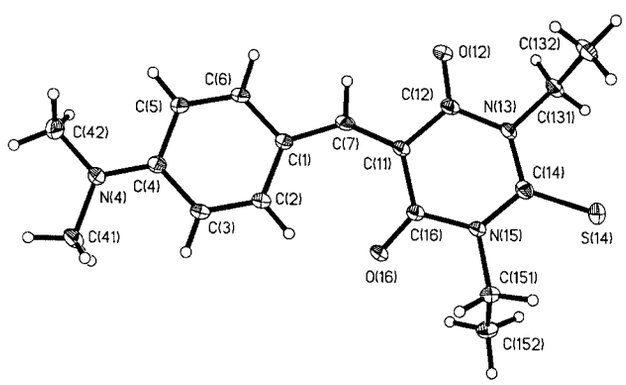


Fig. 1 Structural representation of compound **3** (50% probability ellipsoids).

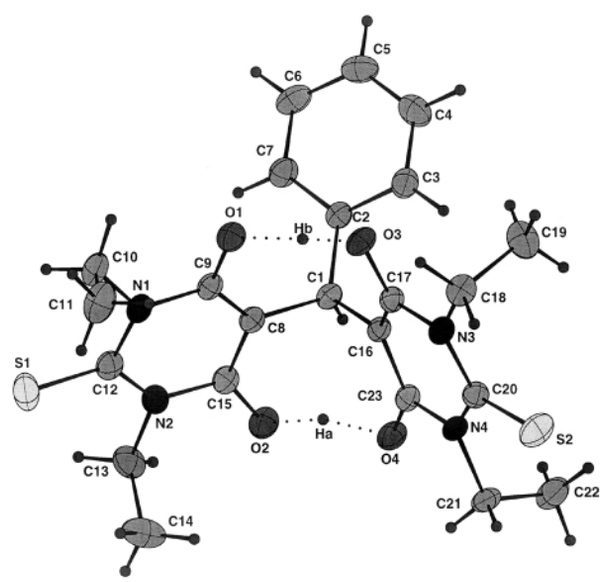


Fig. 2 Structural representation of compound **6** (50% probability ellipsoids).

affect the yield of **2**, but we have not detected any traces of **1**. The formation of Michael adducts often follows Knoevenagel condensations,[1] but this has not been observed previously with tba or its *N*-alkyl derivatives. Furthermore, reactions of ba with arylaldehydes also typically afford Knoevenagel products, the only reported exception being salicylaldehyde.[8] However, no explanation was offered for the production of the Michael adduct in the latter case.[8]

The Knoevenagel product derived from detba and 4-(dimethylamino)benzaldehyde (dmabza), 1,3-diethyl-5-[4-(dimethylamino)benzylidene]-2-thiobarbituric acid (**3**), was first prepared as part of an investigation into merocyanine dyes.[9] Compound **3** was obtained in 80% crude yield from a 1 : 1 reaction in refluxing ethanol with piperidine as a base catalyst. Other workers have since prepared similar derivatives of ba or 1,3-dimethylbarbituric acid by reaction with benzaldehydes in refluxing water or ethanol,[10] and related derivatives of detba have been synthesised in benzene with morpholine as catalyst.[2] We have found that detba condenses with dmabza at room temperature in ethanol with no additional catalyst to precipitate pure **3** in high yield, and a similar reaction occurs with cinnamaldehyde to afford **4**. However, reactions with benzaldehyde or 4-substituted benzaldehydes under identical conditions precipitate the new arylbis(1,3-diethyl-2-thiobarbitur-5-yl)-methanes **5**–**9** in good yields. Concentration of the filtrates affords further quantities of **5**–**9**, but no traces of the Knoevenagel products have been detected, irrespective of the reaction stoichiometries. The compound **9** is unstable when dissolved in various common solvents, rapid colour changes from golden to olive green suggesting air oxidation of the ferrocenyl moiety.

The isolation of a Knoevenagel product **4** from the reaction of detba with cinnamaldehyde is consistent with previous reports involving other vinylaldehydes.[6] Presumably these 1 : 1

Table 2 Selected interatomic distances (Å) and angles (°) for compounds **3** and **6**

3			
C(1)–C(2)	1.422(3)	C(11)–C(16)	1.459(2)
C(1)–C(6)	1.419(3)	C(12)–N(13)	1.414(2)
C(1)–C(7)	1.430(3)	C(12)–O(12)	1.225(2)
C(2)–C(3)	1.369(3)	C(14)–N(15)	1.384(2)
C(3)–C(4)	1.419(3)	C(14)–S(14)	1.667(2)
C(4)–C(5)	1.421(3)	C(16)–O(16)	1.221(2)
C(4)–N(4)	1.355(2)	N(4)–C(41)	1.466(2)
C(5)–C(6)	1.366(3)	N(4)–C(42)	1.463(2)
C(7)–C(11)	1.377(3)	N(13)–C(14)	1.378(2)
C(11)–C(12)	1.464(3)	N(15)–C(16)	1.411(2)
C(2)–C(1)–C(7)	128.5(2)	C(14)–N(15)–C(16)	124.6(2)
C(2)–C(3)–C(4)	122.0(2)	C(16)–C(11)–C(12)	118.1(2)
C(3)–C(2)–C(1)	121.6(2)	C(42)–N(4)–C(41)	117.8(2)
C(4)–N(4)–C(41)	120.9(2)	N(4)–C(4)–C(3)	121.6(2)
C(4)–N(4)–C(42)	121.1(2)	N(4)–C(4)–C(5)	121.4(2)
C(5)–C(4)–C(3)	117.0(2)	N(13)–C(12)–C(11)	117.4(2)
C(5)–C(6)–C(1)	123.4(2)	N(13)–C(14)–N(15)	116.6(2)
C(6)–C(1)–C(2)	115.6(2)	N(13)–C(14)–S(14)	122.08(14)
C(6)–C(1)–C(7)	115.8(2)	N(15)–C(14)–S(14)	121.3(2)
C(6)–C(5)–C(4)	120.3(2)	N(15)–C(16)–C(11)	117.2(2)
C(7)–C(11)–C(12)	115.6(2)	O(12)–C(12)–C(11)	123.9(2)
C(7)–C(11)–C(16)	126.2(2)	O(12)–C(12)–N(13)	118.7(2)
C(11)–C(7)–C(1)	138.5(2)	O(16)–C(16)–C(11)	125.1(2)
C(14)–N(13)–C(12)	124.7(2)	O(16)–C(16)–N(15)	117.7(2)
6			
C(1)–C(2)	1.537(3)	N(2)–C(15)	1.383(3)
C(1)–C(8)	1.518(3)	N(3)–C(17)	1.388(3)
C(1)–C(16)	1.515(3)	N(3)–C(18)	1.482(3)
C(2)–C(3)	1.383(3)	N(3)–C(20)	1.381(3)
C(2)–C(7)	1.381(3)	N(4)–C(20)	1.372(3)
C(3)–C(4)	1.383(4)	N(4)–C(23)	1.385(3)
C(4)–C(5)	1.362(4)	O(1)–C(9)	1.272(3)
C(5)–C(6)	1.370(4)	O(2)–C(15)	1.301(3)
C(6)–C(7)	1.386(3)	O(3)–C(17)	1.296(3)
C(8)–C(9)	1.391(3)	O(4)–C(23)	1.278(3)
C(8)–C(15)	1.378(3)	S(1)–C(12)	1.661(3)
C(16)–C(17)	1.378(3)	S(2)–C(20)	1.665(2)
C(16)–C(23)	1.405(3)	O(1)–Hb	1.346(6)
N(1)–C(9)	1.390(3)	O(2)–Ha	1.104(5)
N(1)–C(12)	1.386(3)	O(3)–Hb	1.209(5)
N(2)–C(12)	1.379(3)	O(4)–Ha	1.470(7)
C(2)–C(3)–C(4)	120.7(2)	C(17)–C(16)–C(23)	117.6(2)
C(2)–C(7)–C(6)	121.1(2)	C(20)–N(3)–C(17)	122.26(19)
C(3)–C(2)–C(1)	120.45(19)	C(20)–N(4)–C(23)	123.22(18)
C(3)–C(2)–C(7)	117.7(2)	C(23)–C(16)–C(1)	118.27(19)
C(4)–C(5)–C(6)	118.9(2)	N(1)–C(12)–N(2)	115.4(2)
C(5)–C(4)–C(3)	121.2(3)	N(1)–C(12)–S(1)	121.87(18)
C(5)–C(6)–C(7)	120.5(2)	N(2)–C(12)–S(1)	122.76(19)
C(7)–C(2)–C(1)	121.72(19)	N(3)–C(20)–S(2)	121.50(18)
C(8)–C(1)–C(2)	114.63(16)	N(4)–C(20)–N(3)	116.12(19)
C(8)–C(9)–N(1)	119.2(2)	N(4)–C(20)–S(2)	122.36(16)
C(8)–C(15)–N(2)	120.7(2)	N(4)–C(23)–C(16)	119.3(2)
C(9)–C(8)–C(1)	121.5(2)	O(1)–C(9)–C(8)	124.4(2)
C(12)–N(1)–C(9)	123.4(2)	O(1)–C(9)–N(1)	116.46(19)
C(12)–N(2)–C(15)	122.6(2)	O(2)–C(15)–C(8)	124.1(2)
C(15)–C(8)–C(1)	120.19(19)	O(2)–C(15)–N(2)	115.2(2)
C(15)–C(8)–C(9)	117.8(2)	O(3)–C(17)–C(16)	123.9(2)
C(16)–C(1)–C(2)	115.58(18)	O(3)–C(17)–N(3)	115.7(2)
C(16)–C(1)–C(8)	111.54(17)	O(4)–C(23)–C(16)	123.9(2)
C(16)–C(17)–N(3)	120.46(19)	O(4)–C(23)–N(4)	116.81(19)
C(17)–C(16)–C(1)	123.63(18)		

products are stabilised by extended conjugation. It is likely that the pronounced difference in reactivity between dmabza and the other arylaldehydes arises primarily from electronic factors. It has been shown that the Lewis acidity of Knoevenagel products, and hence reactivity towards Michael addition, increases either as electron-withdrawing substituents are added or as the molecule becomes more planar.[11] The strongly basic 4-NMe_2 substituent in **3** will stabilise the vinyl group and render it less susceptible to nucleophilic attack. By contrast, the electron-withdrawing pyridyl group will enhance the Lewis acidity of **1**, and a similar situation pertains to the analogues of **3** bearing -H, -CN or -NO_2 4-substituents, leading to the formation of **6**, **7** or **8**, respectively. Although the methoxy or ferrocenyl groups are moderately electron-donating, they clearly do not stabilise the Knoevenagel products sufficiently to prevent further reaction. Compound **3** can be forced to react further by treatment with excess detba in refluxing ethanol, but the Michael adduct **10** is unstable in solution and readily reverts to **3**, as shown by proton NMR and UV-visible spectra. The observed reactivity differences are hence not simply due to the poor solubility of **3** in ethanol.

Crystallographic and spectroscopic studies

Many X-ray crystal structures of ba derivatives have been reported,[3,10,12] but the only ones of tba derivatives are those of 1,3-diethyl-5-[5-(*N*,*N*-diethylamino)penta-2,4-dienylidene]-2-thiobarbituric acid (**11**),[13] and 1,3-diethyl-5-(hydroxyimino)-2-thiobarbituric acid.[14] We have undertaken single crystal X-ray diffraction studies of **3** and **6**, and representations of the molecular structures are shown in Fig. 1 and 2, respectively.

The structure of **6** confirms the formation of the Michael adduct and shows that both of the detba rings are present in mixed keto–enol forms. The enolic protons (Ha and Hb) were located from the difference Fourier map and freely refined. Investigation of the bond lengths (Table 2) around these hydrogens shows that the oxygens differ slightly in their degree of enolic character. The bond distances O(2)–Ha and O(3)–Hb are significantly shorter than O(4)–Ha and O(1)–Hb, respectively, showing that O(2) and O(3) possess greater enolic properties than O(4) and O(1), respectively. Furthermore, C(9)–O(1) and C(23)–O(4) are shorter than C(17)–O(3) and C(15)–O(2), respectively, with all four of these separations being of intermediate length between the ideal values for the keto and enol forms. Indeed, their average value (1.287(6) Å) is *ca*. 0.06 Å longer than the average C=O bond distance (1.223(3) Å) in **3**. In addition, evidence for partial C=C double bonding in the detba rings in **6** is given by the average C–C distance of 1.388(6) Å which is *ca*. 0.07 Å shorter than the average of C(11)–C(12) and C(11)–C(16) in **3** (1.462(4) Å). The structure of **6** exhibits no noteworthy intermolecular contacts.

Evidence that the other Michael adducts also adopt mixed keto–enol structures in the solid state is provided by the infrared spectra of **2** and **5**–**10** which show ν(CO) absorptions in the region 1618–1607 cm^{-1}. As expected, the Knoevenagel products **3** and **4** show keto stretching bands at higher energies. The absence of clear signals for the enolic protons in the NMR spectra of **2** and **5**–**10** is consistent with excessive broadening due to rapid exchange in solution. Indeed, very broad signals in the region *ca*. 9–10 ppm can be observed in some of these spectra. Complex splitting of the proton NMR ethyl signals for **2** and **5**–**10** is also in keeping with the presence of mixed keto–enol structures in solution.

The structure of **3** is especially interesting because the molecular dimensions can be correlated with NLO properties. Although **3** itself has not been subjected to NLO investigations, its -$N(^nBu)_2$ analogue (**3**-Bu) is known to possess marked molecular quadratic NLO properties, *i.e.* a large first hyperpolarisability, β.[6b] This observation, together with dipole moment measurements,[6b] is indicative of a significant contribution by the charge-separated (zwitterionic) resonance form to the ground state structure (Fig. 3). Recent theoretical and experimental studies with donor–acceptor polyenes have clarified understanding of structure–property relationships for molecular NLO properties. Hence, a relationship between β and the "bond length alternation" (BLA, defined as the difference between the average "C–C" and "C=C" bond distances) has been established.[13] If the neutral form prevails in the ground

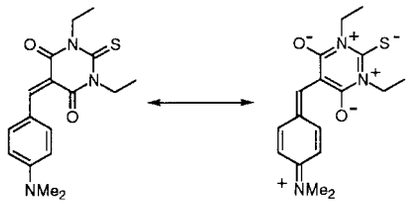
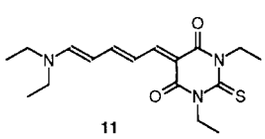


Fig. 3 Limiting canonical resonance forms for compound **3**.

state, then $0 < BLA/Å < 0.11$, whilst predominance of the zwitterionic form leads to $-0.11 > BLA/Å > 0$. Equal mixing of the two limiting resonance forms gives BLA and β values of 0, whilst β is maximised at intermediate BLA values [$\pm(0.05 \pm 0.01)$ Å].[6b]

Our crystallographic study confirms that extensive polarisation occurs in the ground state of **3**. The bond distance C(1)–C(7) is *ca.* 0.05 Å shorter than a typical C(Ar)–C(sp^2) distance, whilst C(7)–C(11) is *ca.* 0.04 Å longer than a typical C(sp^2)=C(sp^2) distance in a C=C–C=O fragment.[15] Furthermore, the phenyl ring shows a partial quinoidal structure, the average of C(5)–C(6) and C(2)–C(3) being *ca.* 0.05 Å shorter than the average of the other four intra-ring bonds. However, comparison of the bond distances within the detba ring with those in **6** provides no evidence for the adoption of an aromatic structure. The difference C(1)–C(7) − C(7)–C(11) for **3** is *ca.* 0.05 Å, and if taken as a BLA value then this structure is optimised with regard to a NLO response. This is only an approximation because **3** contains only a single methine unit, but nevertheless the structural data are clearly consistent with the pronounced NLO properties of **3**-Bu. By contrast, **11** has a BLA of *ca.* −0.01 Å, indicating a slight predominance of the charge-separated form in the ground state.[13] The marked difference in the extent of ground state charge-separation between **3** and **11** can be ascribed to more effective donor–acceptor π-conjugation *via* the *trans*-buta-1,4-dienyl unit when compared to the phenylene bridge in **3**.



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As expected for a highly conjugated structure, the phenyl and detba rings in **3** are almost perfectly coplanar, with torsion angles as follows: C(2)–C(1)–C(7)–C(11) = 1.4°, C(6)–C(1)–C(7)–C(11) = 178.9°, C(1)–C(7)–C(11)–C(16) = 2.9°, C(1)–C(7)–C(11)–C(12) = −179.2°. There is evidence for opening out of the bond angles in the methine bridge to accommodate this planar structure, with the angle C(11)–C(7)–C(1) of 138.5(2)° being particularly large for a trigonal centre. Although the molecular structure of **3** is clearly highly favourable for quadratic NLO properties, the adoption of a centrosymmetric space group precludes the observation of any macroscopic NLO effects with this particular crystalline form.[16] As with **6**, the structure of **3** exhibits no interesting intermolecular contacts.

Conclusions

We have shown that novel arylbis(1,3-diethyl-2-thiobarbitur-5-yl)methanes can be readily prepared from various arylaldehydes in high yields. The sp^3 methine unit in these compounds renders them unlikely to exhibit marked NLO properties, but they can be expected to possess interesting host–guest recognition behaviour and biological activity. X-Ray crystallography provides clear evidence for extensive polarisation in the ground state molecular structure of 1,3-diethyl-5-[4-(dimethylamino)-benzylidene]-2-thiobarbituric acid (**3**), consistent with the pronounced molecular NLO properties of the analogous -N(^{n}Bu)$_2$ compound.

Experimental

Materials and procedures

4-Ferrocenylbenzaldehyde was prepared according to a published procedure[17] and all other reagents were obtained commercially and used as supplied. Products were dried overnight at room temperature in a vacuum desiccator ($CaSO_4$) prior to characterisation.

Physical measurements

Proton NMR spectra were recorded on a Varian Gemini 200 spectrometer and all shifts are referenced to TMS. Chemical shifts are given in ppm; *J* values are given in Hz; cm = complex multiplet. Any fine splitting of pyridyl or phenyl ring AA′BB′ patterns is ignored and the signals are reported as simple doublets. Elemental analyses were performed by the Microanalytical Laboratory, University of Manchester. Melting points were recorded by using a Gallenkamp melting point apparatus. IR spectra were obtained as KBr discs with an ATI Mattson Genesis Series FTIR instrument, and UV-visible spectra were recorded using a Hewlett-Packard 8452A diode array spectrophotometer. Mass spectra were recorded by using +/− electrospray on a Micromass Platform spectrometer (cone voltage 80 V) (for **2** and **5**–**10**) or using NH_3 chemical ionisation on a VG Trio 2000 spectrometer (for **3** and **4**).

Syntheses

4-Pyridylbis(1,3-diethyl-2-thio-4,6-dioxohexahydro-5-pyrimidyl)methane 2. To a stirring solution of pyridine-4-carbaldehyde (pyca, 69 mg, 0.644 mmol) in ethanol (50 mL) was added a solution of 1,3-diethyl-2-thiobarbituric acid (detba, 513 mg, 2.56 mmol) in ethanol (45 mL). A white precipitate began to form within minutes. After stirring at room temperature for 8 h, the precipitate was filtered off, washed with ethanol and dried. The white solid obtained was found to contain residual ethanol by proton NMR, so was reprecipitated from DMF–water: yield 285 mg, 88%; $\delta_H(CD_3SOCD_3)$ 8.69 (2 H, d, *J* 6.6, C_5H_4N), 7.75 (2 H, d, *J* 6.8, C_5H_4N), 6.51 (1 H, s, CH), 4.56–4.38 (8 H, cm, 4CH_2-Me), 1.20 (12 H, t, *J* 6.8, 4CH_2-*Me*). ν(C=O) 1607 cm^{-1}. Mp 245–248 (decomp.) °C. Found: C, 52.49; H, 5.60; N, 13.78; S, 12.74. Calc. for $C_{22}H_{27}N_5O_4S_2 \cdot 0.75H_2O$: C, 52.52; H, 5.71; N, 13.92; S, 12.75%. *m*/*z*: 489 (M^+).

1,3-Diethyl-5-[4-(dimethylamino)benzylidene]-2-thiobarbituric acid 3. This was prepared in a similar manner to **2** by using 4-(dimethylamino)benzaldehyde (dmabza, 96 mg, 0.643 mmol) in place of pyca, and detba (258 mg, 1.29 mmol) in ethanol (30 mL). The solution turned orange immediately and a red precipitate began to form within minutes. A red solid was obtained: yield 185 mg, 87%; $\delta_H(CDCl_3)$ 8.42 (2 H, d, *J* 9.3, C_6H_4), 8.42 (1 H, s, CH), 6.71 (2 H, d, *J* 9.4, C_6H_4), 4.59 (2 H, q, *J* 6.9, CH_2-Me), 4.58 (2 H, q, *J* 7.0, CH_2-Me), 3.17 (6 H, s, NMe_2), 1.33 (3 H, t, *J* 6.9, CH_2-*Me*), 1.31 (3 H, t, *J* 7.0, CH_2-*Me*). λ_{max}(MeCN)/nm (ε/dm^3 mol^{-1} cm^{-1}) 244 (15 100), 284 (12 200), 314 (11 600), 492 (87 100). ν(C=O) 1653 cm^{-1}. Mp 204–208 °C (lit.[9] 212–214 °C). Found: C, 61.51; H, 6.32; N, 12.57; S, 9.80. Calc. for $C_{17}H_{21}N_3O_2S$: C, 61.61; H, 6.39; N, 12.68; S, 9.67%. *m*/*z*: 332 (M^+).

1,3-Diethyl-5-[3-phenylprop-2-enylidene]-2-thiobarbituric acid 4. This was prepared in a similar manner to **3** by using cinnamaldehyde (100 mg, 0.757 mmol) in place of dmabza, and detba (303 mg, 1.51 mmol). The reaction turned yellow within minutes, and precipitation commenced after *ca.* 1.5 h. A bright yellow solid was obtained: yield 82 mg, 34%; $\delta_H(CDCl_3)$ 8.63 (1 H, dd, *J* 12.1, 15.3, CH), 8.22 (1 H, d, *J* 12.1, CH), 7.72–7.68 (2 H, C_6H_5), 7.51–7.43 (4 H, CH and C_6H_5), 4.55 (4 H, cm, 2CH_2-Me), 1.31 (6 H, cm, 2CH_2-*Me*). λ_{max}(MeCN)/nm (ε/dm^3 mol^{-1} cm^{-1}) 240 (13 900), 266 (9800), 398 (56 300). ν(C=O) 1665

cm^{-1}. Mp 179–180 °C. Found: C, 65.16; H, 5.78; N, 8.85; S, 10.44. Calc. for $C_{17}H_{18}N_2O_2S$: C, 64.94; H, 5.77; N, 8.91; S, 10.20%. *m*/*z*: 315 (M^+).

4-Methoxyphenylbis(1,3-diethyl-2-thio-4,6-dioxohexahydro-5-pyrimidyl)methane 5. This was prepared in an identical manner to **2** by using 4-methoxybenzaldehyde (83 mg, 0.644 mmol) in place of pyca. The reaction turned yellow within minutes, and precipitation commenced after *ca*. 5 h. A bright yellow solid was obtained: yield 216 mg, 65%; $\delta_H(CDCl_3)$ 7.04 (2 H, d, *J* 8.9, C_6H_4), 6.85 (2 H, d, *J* 8.9, C_6H_4), 5.63 (1 H, s, CH), 4.72–4.54 (8 H, cm, 4CH_2-Me), 3.81 (3 H, s, OMe), 1.42–1.27 (12 H, cm, 4CH_2-*Me*). λ_{max}(MeCN)/nm (ε/dm^3 mol^{-1} cm^{-1}) 288 (26 900), 400 (16 200). ν(C=O) 1618 cm^{-1}. Mp 133–136 °C. Found: C, 55.80; H, 5.95; N, 10.89; S, 12.24. Calc. for $C_{24}H_{30}N_4O_5S_2$: C, 55.58; H, 5.83; N, 10.80; S, 12.36%. *m*/*z*: 519 (M^+). Concentration of the filtrate produced a further 64 mg of pure product (total yield 84%).

Phenylbis(1,3-diethyl-2-thio-4,6-dioxohexahydro-5-pyrimidyl)methane 6. This was prepared in an identical manner to **2** by using benzaldehyde (68 mg, 0.641 mmol) in place of pyca. Precipitation commenced after *ca*. 2.5 h and a white solid was obtained: yield 132 mg, 42%; $\delta_H(CDCl_3)$ 7.34–7.26 (3 H, $H^{3,4,5}$), 7.14 (2 H, d, *J* 8.1, $H^{2,6}$), 5.69 (1 H, s, CH), 4.73–4.54 (8 H, cm, 4CH_2-Me), 1.39 (6 H, t, *J* 7.0, 2CH_2-*Me*), 1.30 (6 H, t, *J* 7.0, 2CH_2-*Me*). ν(C=O) 1617 cm^{-1}. Mp 174–176 °C. Found: C, 56.70; H, 5.77; N, 11.39; S, 13.12. Calc. for $C_{23}H_{28}N_4O_4S_2$: C, 56.54; H, 5.78; N, 11.47; S, 13.12%. *m*/*z*: 489 (M^+). Concentration of the filtrate produced a further 150 mg of pure product (total yield 90%).

4-Cyanophenylbis(1,3-diethyl-2-thio-4,6-dioxohexahydro-5-pyrimidyl)methane 7. This was prepared in an identical manner to **2** by using 4-cyanobenzaldehyde (84 mg, 0.641 mmol) in place of pyca. Precipitation commenced after *ca*. 2 h and a white solid was obtained: yield 175 mg, 53%; $\delta_H(CDCl_3)$ 7.63 (2 H, d, *J* 8.4, C_6H_4), 7.28 (2 H, d, *J* 8.1, C_6H_4), 5.67 (1 H, s, CH), 4.71–4.52 (8 H, cm, 4CH_2-Me), 1.41–1.26 (12 H, cm, 4CH_2-*Me*). ν(C=O) 1618 cm^{-1}. Mp 195–196 °C. Found: C, 56.59; H, 5.13; N, 13.55; S, 12.49. Calc. for $C_{24}H_{27}N_5O_4S_2$: C, 56.12; H, 5.30; N, 13.63; S, 12.49%. *m*/*z*: 513 (M^+). Concentration of the filtrate produced a further 41 mg of pure product (total yield 66%).

4-Nitrophenylbis(1,3-diethyl-2-thio-4,6-dioxohexahydro-5-pyrimidyl)methane 8. This was prepared in an identical manner to **2** by using 4-nitrobenzaldehyde (97 mg, 0.642 mmol) in place of pyca. Precipitation commenced after *ca*. 2 h and a white solid was obtained: yield 176 mg, 51%; $\delta_H(CDCl_3)$ 8.19 (2 H, d, *J* 8.9, C_6H_4), 7.33 (2 H, d, *J* 9.0, C_6H_4), 5.70 (1 H, s, CH), 4.75–4.56 (8 H, cm, 4CH_2-Me), 1.39 (6 H, t, *J* 7.0, 2CH_2-*Me*), 1.30 (6 H, t, *J* 7.0, 2CH_2-*Me*). ν(C=O) 1618 cm^{-1}. Mp 198–199 °C. Found: C, 51.89; H, 5.20; N, 12.98; S, 11.86. Calc. for $C_{23}H_{27}N_5O_6S_2$: C, 51.77; H, 5.10; N, 13.12; S, 12.02%. *m*/*z*: 534 (M^+). Concentration of the filtrate produced a further 44 mg of pure product (total yield 64%).

4-Ferrocenylphenylbis(1,3-diethyl-2-thio-4,6-dioxohexahydro-5-pyrimidyl)methane 9. This was prepared in an identical manner to **3** by using 4-ferrocenylbenzaldehyde (93 mg, 0.321 mmol) in place of dmabza. The reaction turned brown followed by olive green within 1 h, but no precipitation occurred. After 8 h the solution was concentrated to *ca*. 10 mL and upon standing overnight at room temperature, the product crystallized out as a brown solid: yield 188 mg, 87%; $\delta_H(CDCl_3)$ 7.42 (2 H, d, *J* 8.4, C_6H_4), 7.04 (2 H, d, *J* 8.1, C_6H_4), 5.65 (1 H, s, CH), 4.72–4.56 (10 H, cm, 4CH_2-Me and C_5H_4), 4.32 (2 H, s, C_5H_4), 4.04 (5 H, s, C_5H_5), 1.43–1.29 (12 H, cm, 4CH_2-*Me*). $\lambda_{max}(CH_2Cl_2)$/nm (ε/dm^3 mol^{-1} cm^{-1}) 294 (38 100), 434 (630). ν(C=O) 1619 cm^{-1}. Mp 147–151 °C (decomp.). Found: C, 59.04; H, 5.48; N, 8.50; S, 9.70. Calc. for $C_{33}H_{36}FeN_4O_4S_2$: C, 58.93; H, 5.39; N, 8.33; S, 9.53%. *m*/*z*: 671 (M^+).

4-Dimethylaminophenylbis(1,3-diethyl-2-thio-4,6-dioxohexahydro-5-pyrimidyl)methane 10. A solution of **3** (100 mg, 0.302 mmol) and detba (181 mg, 0.904 mmol) in ethanol (40 mL) was heated at reflux for 8 h. The reaction solution was allowed to cool to room temperature overnight, and the precipitate was filtered off, washed with ethanol to remove detba, then $CHCl_3$ to remove unreacted **3** and dried: yield 31 mg, 19%; $\delta_H(CD_3SOCD_3)$ 7.48 (2 H, d, *J* 8.4, C_6H_4), 7.16 (2 H, d, *J* 8.3, C_6H_4), 6.32 (1 H, s, CH), 4.55–4.38 (8 H, cm, 4CH_2-Me), 1.19 (12 H, t, *J* 6.6, 4CH_2-*Me*). ν(C=O) 1613(1638sh) cm^{-1}. Mp 158–161 °C (decomp.). Found: C, 56.16; H, 6.45; N, 13.05; S, 12.12. Calc. for $C_{25}H_{33}N_5O_4S_2$: C, 56.47; H, 6.26; N, 13.17; S, 12.06%. *m*/*z*: 529 (M^-).

X-Ray structural determinations

Crystals were obtained from $CHCl_3$ solutions, those of **3** by slow evaporation and those of **6** by inward diffusion of diethyl ether vapour. An orange crystal of **3** of approximate dimensions 0.4 × 0.3 × 0.3 mm and a pale yellow crystal of **6** with dimensions 0.6 × 0.2 × 0.2 mm were chosen for diffraction studies.

Data collection details are as follows: for **3**, data were collected on a Siemens SMART CCD area-detector diffractometer. For three settings of ϕ, narrow data frames were collected for 0.3° increments in ω to afford a sphere of data. At the end of data collection the first 50 frames were recollected to confirm that crystal decay had not taken place. An empirical absorption correction was applied by using multiple measurements of equivalent reflections, and the data frames were integrated using SAINT.[18] For **6**, data were collected on a Nonius Kappa CCD area-detector diffractometer at the window of a rotating anode FR591 generator (50 kV, 20 mA) and controlled by the Collect software package.[19] Images of 2° thickness and 10 s exposure were taken in a 360° ϕ scan, followed by five shorter ω scans, with a detector-to-crystal distance of 30 mm (θ offsets between 3.3° and 9.95°) and processed by Denzo[20] to give 99.4% coverage of the unique data set. Data were corrected for absorption by using the empirical method employed in Sortav[21] from within the MaXus suite of programs.[22]

The structure of **3** was solved by direct methods and refined by full-matrix least-squares on all F_0^2 data using Siemens SHELXTL 5.03.[18] The same approach was used for **6**, but using SHELXS-97[23] and SHELXL-97.[24] In both cases, all non-hydrogen atoms were refined anisotropically with hydrogen atoms included in idealised positions (C–H distance = 0.97 Å) with thermal parameters riding on those of the parent atom.

Representations of **3** and **6** are given in Fig. 1 and 2. Crystallographic data and refinement details are presented in Table 1, and selected bond distances and angles in Table 2. Additional material available from the CCDC comprises final atomic fractional coordinates, thermal parameters, and complete tables of bond lengths and angles. CCDC reference number 207/253. See http://www.rsc.org/suppdata/p1/1999/2483 for crystallographic files in .cif format.

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