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SYNTHESIS OF THE 5-THIA-1,3,6-TRIAZACYCL[3.2.3]AZINE AND 4-THIA-1,3,6-TRIAZACYCL[3.2.3]AZINE SYSTEMS

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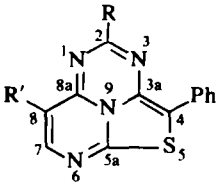
Abstract—The syntheses, structural proofs, and chemical and spectral properties of four members of the 5-thia-1,3,6-triazacycl[3.2.3]azine system and of two members of the 4-thia-1,3,6-triazacycl[3.2.3]azine system are described. Electrophilic substitution is predicted and found to occur in the 8-position in both systems.

At present, about twenty cyclazine[1] systems are known, and so far, the syntheses of two principal types, one with a carbocyclic[1-4] and another with a C–N periphery,[3-9] have been described. All of these, with the notable exception of cycl[3.3.3[azine,[3,10] exhibit aromatic properties. It therefore seemed of interest to attempt the preparation of similar systems containing additional heteroatoms, e.g. S[11] and Se,[12] in the periphery. The present communication reports synthesis, structural determination, and spectral and chemical properties of the phenyl derivatives **1–6** of the isomeric 5 - thia - 1,3,6 - triaza - and 4 - thia - 1,3,6 - triazacycl[3.2.3]azine systems.

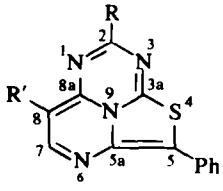
We anticipated employing the synthetic route which was successfully used to prepare tri- and tetraazacycl[3.3.3]azines.[6-8] For the present purpose, 2,4-diaminothiazole[13] and ethyl 2 - cyano - 3 - ethoxyacrylate, **7**,[14] would be appropriate starting compounds. In a preceding communication[15] on the tautomeric equilibria and some substitution reactions in a few 2,4-diaminothiazoles, we concluded that the parent compound could not be used on account of the reactive C-5 atom. We presumed that instead the 5-phenyl derivative, **8**,[13] where this position is blocked, would be more suitable.

Condensation of 5 - phenyl - 2,4 - diaminothiazole, **8**,[13] with ethyl 2 - cyano - 3 - ethoxyacrylate, **7**,[14] gives the isomers **9** and **10** in a 4:1 mixture from which the major product, but not **10**, could be isolated in pure form. Treatment of **9** with acetic anhydride gave **11**, while the isomeric N-acetate, **12**, was isolated from the acetylated mixture of **9** and **11**. Ring closure to **3** and **5** was achieved by heating **11** and **12** respectively in diphenyl ether. Decarbethoxylation of **3** and **5** to **4** and **6** respectively was finally performed in the above-mentioned solvent containing *p*-toluenesulphonic acid.

Spectral and other pertinent data supporting the gross structures **1–6** are summarized in Table 1 and in Experimental. Very little information on the difference in reactivity of the two amino groups in **8** is available.[13] On this basis, therefore, no distinction can be made between structures **9** and **10** and, consequently, not between **4** and **6** either. The spectral data are too similar to be used for structural assignment. The structural proof was therefore performed in the following way. Monoacetylation of thiourea with acetyl chloride yields **13**,[16] which with α-bromobenzyl cyanide forms **14**. On reaction with **7**, this acetamidoaminothiazole, in which the 2-amino group is acetylated, gives a product which is identical with **12**. Hence all structures in Chart 1 are secured.



1: R = H R′ = COOEt
2: R = H R′ = H
3: R = CH_3 R′ = COOEt
4: R = CH_3 R′ = H



5: R = CH_3 R′ = COOEt
6: R = CH_3 R′ = H

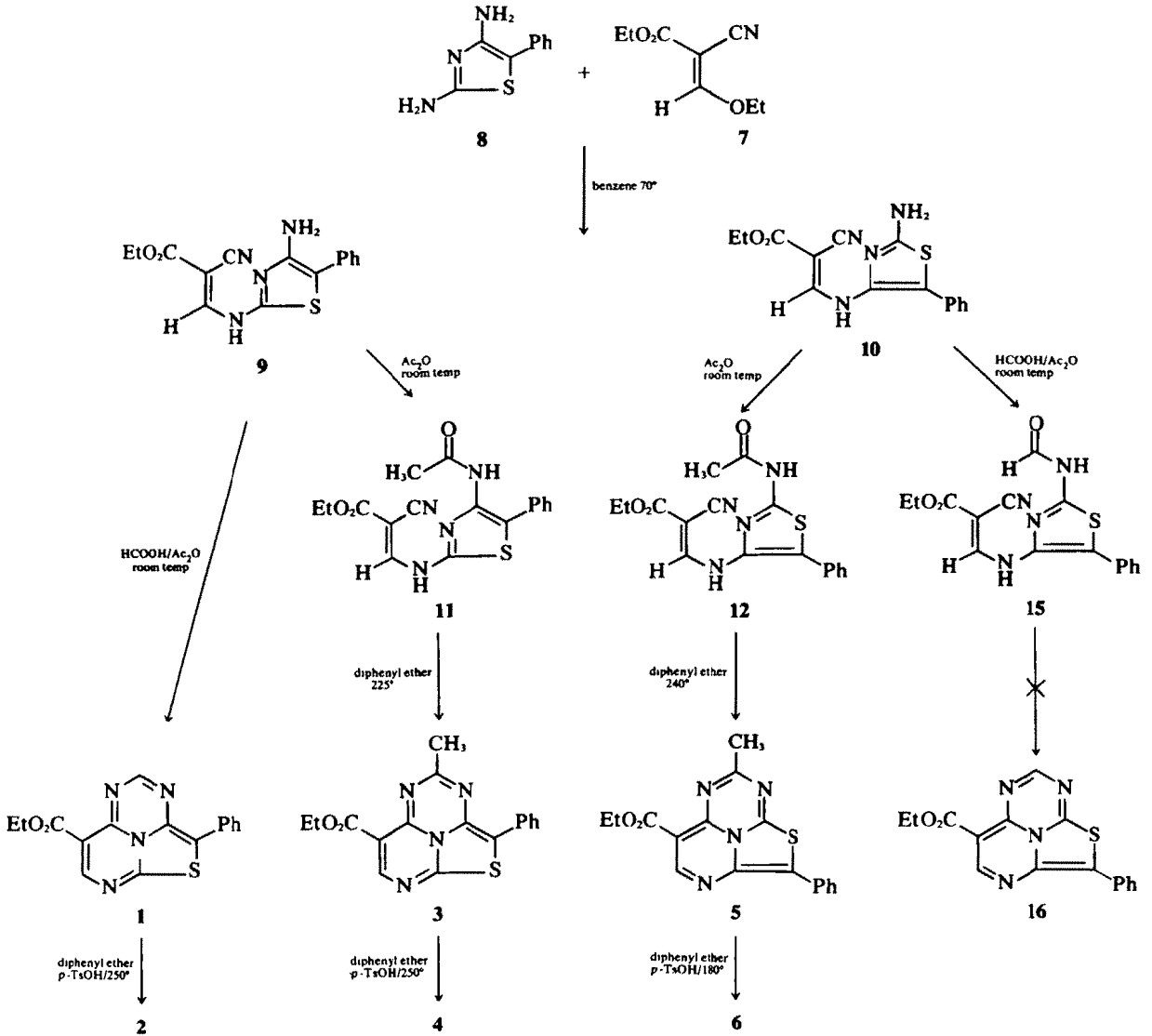
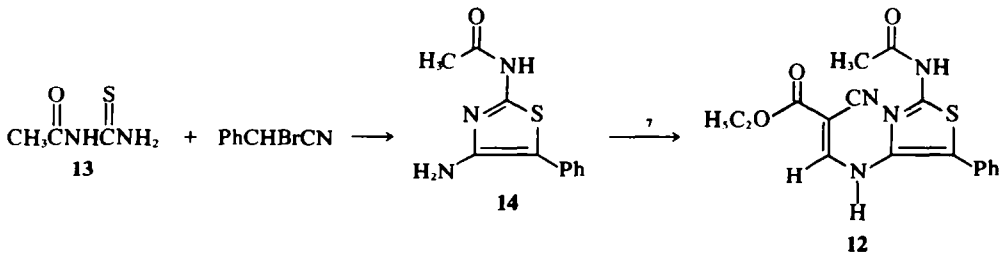

8
7
benzene 70°
9
10
Ac2O room temp
HCOOH/Ac2O room temp
11
12
15
diphenyl ether 225°
diphenyl ether 240°
1
3
5
16
diphenyl ether p-TsOH/250°
diphenyl ether p-TsOH/250°
diphenyl ether p-TsOH/180°
2
4
6

CHART 1

Table 1. NMR spectral data for **1–6** and **19**

Cpd. (solvent)	H-2	H-7	H-8	Phenyl	CH_3	Ester	$J_{7,8}$(Hz)
1: ($CDCl_3$)	7·21	8·02		7·15–7·67		1·30, 4·27	
2: ($CDCl_3$)	6·97	7·33	5·49	7·15–7·67			6
2: (CF_3COOH)	7·25	8·37	6·53	7·37–7·77			6
3: ($CDCl_3$)		8·05		7·19–7·72	2·07	1·30, 4·26	
4: ($CDCl_3$)		7·48	5·61	7·00–7·70	1·97		6
4: (CF_3COOH)		8·40	6·54	7·33–7·90	2·20		6
5: ($CDCl_3$)		7·88		7·19–7·72	2·13	1·27, 4·20	
6: ($CDCl_3$)		7·27	4·64	7·20–7·65	1·92		6
19: (CF_3COOH)	7·21	8·45		7·56			



Formylation of **9** with acetic-formic anhydride at room temperature yielded directly the cyclazine **1**, which was decarbethoxylated to **2** at 250° in diphenyl ether containing *p*-toluenesulphonic acid. The structure of **9**, and consequently the structures of **1** and **2**, follow from the argument just presented for **12**. Acetylation of **9** gives **11**, which is isomeric, but not identical, with **12**; the latter compound was prepared from the monoacetyl derivative **14**. Formylation of **10** yielded **15**, which, however, could not be ring-closed to **16** by a number of methods (diphenyl ether at 250° with and without *p*-toluenesulphonic acid, sublimation etc; *cf* Ref 6).

The thiaazacyclazines **1–6** are stable and coloured (**1–5**, dark-brown and **6**, green), crystalline (m.p. 150–220°) compounds, soluble in organic solvents and in weak and strong acids. Their mass spectra (*cf* Experimental) are characteristic of aromatic compounds: large molecular ion peaks and an abundance of doubly charged ions. The fragmentation patterns for the isomers **4** and **6** differ very little. The UV spectra of **1–6** display a pattern of five to six bands of medium to high intensity between 220 and 340 nm (*cf* Experimental), similar to that observed in the spectra of the tri- and tetraazacycl[3.3.3]azines.[6,7]

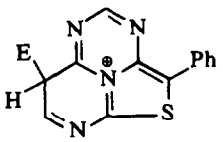
The presence of the S- atom in the periphery in a formal sense locks the double bonds and only one Kekulé-type structure can be drawn for each of **1–4** and for **5** and **6**. As a consequence, the C-7–C-8 bond would be expected to have more single-bond character in **5** and **6** than in **1–4**. The NMR chemical shift values (in $CDCl_3$) for the ring protons, which are all in the aromatic region, illustrate the differences: H-8 appears at a considerably higher field, *ca* 1 ppm, in **6** than in **2** and **4**. It seems that the 5-thiaazacyclazine system is more stable than the 4-thia homologue; the ring closure and decarbethoxylation steps to form **1–4** are easily performed, whereas the same procedure to prepare the isomeric ring system requires great care to avoid excessive decomposition of **5** and **6**.

When the solvent is changed from chloroform to trifluoroacetic acid, the NMR chemical shift values for H-7 and H-8 in **2** and **4** are displaced about 1 ppm towards lower field. This indicates protonation on the peripheral N atoms, and the shift change is of the same magnitude as earlier observed for the azacycl[3.3.3]azines.[17,18]

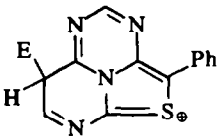
The spectral properties displayed by the thiaazacyclazines **1–6** thus indicate that the systems are "aromatic"[19] and would undergo substitution rather than addition when they were allowed to react with electrophiles. In **2** and **4**, electrophilic substitution would be expected to occur at C-8 since C-7, and in **2** also C-2, are adjacent to N atoms and since good resonance structures, **17** and **18** (all atoms surrounded by full octets), can be written for the 8-intermediate. Structures like **18** are not decisive, however, because such structures can also be written for the 7- and 2-intermediates. Similar arguments predict an electrophile to enter at C-8 also in the isomeric system **6**.

Bromine in glacial acetic acid converts **2** to the 8-bromo derivative **19**. Its structure follows from the mass spectrum (M^+ = 329·956 and 331·945) and the NMR spectrum, where H-7 appears as a singlet and the H-8 signal is lacking.

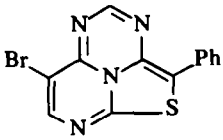
Nitration of **2** with $Cu[NO_3]_2 \cdot 3H_2O$ analogously yielded a mononitro compound (MS). We assume it



17



18



19

to be the 8-nitro derivative, although the position of substitution has not been determined.

Treatment of **6** with bromine in glacial acetic acid yields a disubstituted product (MS), which we believe to be the 8 - bromo - 2 - bromomethyl derivative. Amounts sufficient for NMR measurements could not be conveniently prepared.

EXPERIMENTAL

General. IR spectra were determined in KBr with a Perkin-Elmer 337 spectrophotometer. NMR spectra were recorded with a Varian Model A-60, a Jeol Model MH-60, or a Jeol Model MH-100 spectrometer using TMS as internal reference. Chemical shifts are given in δ-values. UV and visible spectra were measured in EtOH with a Cary Model 15 spectrophotometer. The mass spectra have been obtained from the Department of Medical Biochemistry, University of Göteborg, and they were recorded with a GEC-AEI 902 instrument at an ionizing potential of 70 eV. The elemental analyses were carried out at the Microanalytical Laboratory, Institute of Physical Chemistry, University of Vienna. TLC was performed on Silica Gel GF_{254} (Merck) plates with ethyl acetate as the developing solvent, and the spots were visualized with short-wave UV light and with iodine vapour. Ethyl 2 - cyano - 3 - ethoxy acrylate was obtained from Fluka AG and recrystallized from ethanol.

Condensation of 2,4 - *diamino* - 5 - *phenylthiazole*, **8**, *with ethyl* 2 - *cyano* - 3 - *ethoxy* - *acrylate*, **7**, *to* **9** *and* **10**. To a stirred soln of **8** (10·69 g; 56·0 mmol) in 25 ml benzene **7** (9·46 g; 56·0 mmol) dissolved in 100 ml benzene was added dropwise under anhyd conditions under N_2 at 70°. After 48 h at 70°, the hot mixture was filtered, and the bright-yellow solid was washed with hot benzene, yield 7·55 g (43%) of **9** giving only one spot on TLC; m.p. 184–186°. (Found: C, 57·29; H, 4·49; N, 17·55; S, 10·31. $C_{15}H_{14}N_4O_2S$ requires: C, 57·31; H, 4·49; N, 17·82; S, 10·20%). MS: $M^+ = 314$; IR: 2210 (C≡N) and 1710 cm^{-1} (C=O); UV: λ_{max} at 238 (ϵ = 7100), 283 (ϵ = 12,700), and 389 nm (ϵ = 19,500); NMR (DMSO-d_6) signals from: ethyl ester protons at 1·30 (3H) and 4·24 (2H), NH_2 (broad) at 5·65 (2H), phenyl protons at 7·41 (5H), and olefinic proton at 8·71 ppm. (1H). From the filtrate, 5·25 g of a yellow solid was precipitated with 100 ml of hexane. TLC showed it to be a *ca* 1:1 mixture of **9** and **10**.

Acetylation of **9** *and* **11**. A suspension of 300 ml freshly distilled Ac_2O and **9** (6·10 g) was stirred at room temp. After 10 days, a pale-yellow solid had formed. It was filtered off and washed with ether, yield: 4·30 g (63%) of **11**. Recrystallization from anhyd EtOH gave pale-yellow needles, m.p. 214–215° (dec). (Found: C, 57·14; H, 4·66; N, 15·58; S, 8·92. $C_{17}H_{16}N_4O_3S$ requires: C, 57·29; H, 4·53; N, 15·72; S, 9·00%); MS: $M^+ = 356$; IR: 2220 (C≡N) and 1720 cm^{-1} (C=O); UV: λ_{max} at 220 sh. (ϵ = 15,700), 288 (ϵ = 5300), and 373 nm (ϵ = 26,000); NMR (DMSO-d_6) signals from: ethyl ester protons at 1·24 (3H) and 4·22 (2H), acetyl protons at 1·98 (3H), phenyl protons at 7·38 (5H), olefinic proton at 8·63 (1H), NH proton at 9·88 (1H), and broad amide proton at 12·10 ppm (1H).

Preparation of **12** *from the mixture* **9** *and* **10**. A suspension of *ca* 1:1 mixture of **9** and **10** (2 g) in 75 ml freshly distilled Ac_2O was stirred at room temp. After 3 days, TLC showed that all starting material had been consumed and that **11** and **12** had formed. The solid was filtered off and chromatographed on 100 g of Al_2O_3. Eluation with EtOH gave **12** (0·83 g) , which was recrystallized from EtOH to give pale-yellow needles, m.p. 233–235°. (Found: C, 57·38; H, 4·55; N, 15·75; S, 8·51. $C_{17}H_{16}N_4O_3S$ requires: C, 57·29; H, 4·53; N, 15·72; S, 9·00); MS: $M^+ = 356$, IR: 2235 (C≡N) and 1695 cm^{-1} (C=O). UV: λ_{max} at 260 (ϵ = 14,900) and 335 nm (ϵ = 26,000); NMR (DMSO-d_6) signals from: ethyl ester protons at 1·24 (3H) and 4·22 (2H), acetyl protons at 2·20 (3H), phenyl protons at 7·46 (5H), olefinic proton at 8·33 (1H), NH proton at 10·95 (1H), and amide proton at 12·36 ppm (1H).

Preparation of **15** *from a mixture of* **9** *and* **10**. To 35 ml of formic acid containing *ca* 1:1 mixture of **9** and **10** (0·8 g) kept at 5°, 15 ml Ac_2O was added dropwise. The resulting soln was stirred at room temp for 16 h, poured into 100 ml ice water, and then extracted with 3 × 25 ml of CH_2Cl_2. The combined extracts were washed in the following order, with 25 ml water, 25 ml 10% $NaHCO_3$ aq, 25 ml water, and then dried ($MgSO_4$). The solvent was evaporated and the residue was chromatographed on silica gel (60 g). CH_2Cl_2–EtOAc (10:1) eluted 310 mg of **15**. Recrystallization from anhyd EtOH gave pale-yellow prisms of m.p. 193–194°. (Found: C, 56·08; H, 4·12; N, 16·33; S, 10·01. $C_{16}H_{14}N_4O_3S$ requires: C, 56·13; H, 4·12; N, 16·36; S, 9·37%); MS: M' = 342. IR: 2220 (C≡N) and 1685 cm^{-1} (C=O); UV: λ_{max} at 258 (ϵ = 13,600) and 332 nm (ϵ = 25,000); NMR (DMSO-d_6) signals from: ethyl ester protons at 1·24 (3H) and 4·20 (2H), phenyl protons at 7·49 (5H), olefinic proton at 8·25 (1H), formyl proton at 8·61 (1H), NH proton at 11·03 (1H), and broad amide proton at 12·57 ppm (1H).

2 - *Acetamido* - 4 - *amido* - 5 - *phenylthiazole*, **14**. To a stirred soln of α-bromobenzyl cyanide (19·6 g; 0·10 mol) in 25 ml anhyd EtOH thiourea (9·0 g; 0·10 mol) in 150 ml anhyd EtOH was added dropwise at room temp. After 16 h, the mixture was filtered and the EtOH was removed at reduced pressure. The remaining oil was diluted with 150 ml acetone and left for 3 days; 6·5 g of a white solid had then separated. Column chromatography on silica gel (200 g) using EtOAc as the eluant gave further 2·2 g of **14** as a white solid, which slowly became brown in the air, m.p. 175–177° (dec) MS: M^+ found 233·062 ± 0·003. $C_{11}H_{11}N_3O^{32}S$ requires 233·062. $(M+2)^+$ found 235·058 ± 0·003. $C_{11}H_{11}N_3O^{34}S$ requires: 235·058; UV: λ_{max} at 221 sh (ϵ = 11,200), 284 sh (ϵ = 4600), and 333 nm sh (ϵ = 10,500); NMR (DMSO-d_6) signals from: acetyl protons at 2·16 (3H). NH_2 protons at 5·33 (2H), phenyl protons at 7·10–7·50 (5H), and amide proton at 11·95 ppm (1H).

Preparation of **12** *by condensation of* 2 - *acetamido*-4 - *amino* - 5 - *phenylthiazole*, **14**, *with ethyl* 2 - *cyano* - 3 - *ethoxyacrylate*, **7**. A soln of **7** (150 mg; 0·90 mmol) in 10 ml

benzene was added dropwise and with stirring to **14** (150 mg; 0·65 mmol) in 10 ml benzene at 70° under anhyd conditions in a N_2 atmosphere. After 48 h at 70° TLC showed, apart from starting material, the presence of a component with the same R_f value (0·58) as **12**. The mixture was chromatographed on silica gel (10 g). CH_2Cl_2–EtOAc (10:1) eluted 90 mg (39%) of a pale-yellow solid, m.p. 233–235°; IR spectra and MS proved this product to be identical with **12**.

Ring closure of **11** *to* **3**. Compound **11** (500 mg) was added to 50 ml diphenyl ether at room temp. This mixture was heated to and kept at 225° for 15 min. The resulting dark soln was rapidly cooled, diluted with 50 ml CH_2Cl_2, and passed over silica gel (50 g). The diphenyl ether was eluted with CH_2Cl_2 and elution with CH_2Cl_2–EtOAc (5:1) yielded 150 mg (32%) of **3**, which was recrystallized from anhyd MeOH to give brown needles, m.p. 200–201°. (Found: C, 60·05; H, 4·04; N, 16·54; S, 9·48. $C_{17}H_{14}N_4O_2S$ requires: C, 60·34; H, 4·17; N, 16·55; S, 9·48%); IR: 1715 cm^{-1} (C=O); UV: λ_{max} at 230 (ϵ = 26,000), 305 (ϵ = 8050), 318 (ϵ = 10,100), 333 (ϵ = 10,800), 407 (ϵ = 13,800), 500 sh (ϵ = 1240), 540 sh (ϵ = 850), and 600 nm sh (ϵ = 330); MS: *m/e* (Rel int) 340 (5) 339 (13), 338 (M^+, 62), 310 (6), 293 (4), 267 (20), 266 (100), 225 (4), 198 (6), 147 (23), 146 (16), 121 (24), 120 (13), 115 (8), 103 (7), 89 (7), 77 (27). Doubly charged ions: *m/2e* (Rel int) 146·5 (2·0), 132·5 (2·0), 119·5 (0·6), 113·5 (0·6), 112·5 (0·6), 103·5 (2·0), 79·5 (0·6), 60·5 (1·5).

Ring closure of **12** *to* **5**. Compound **12** (300 mg) was added to 30 ml diphenyl ether at room temp. This mixture was heated to and kept at 240° for 25 min. The resulting dark soln was rapidly cooled, diluted with 30 ml CH_2Cl_2 and passed over silica gel (50 g). The diphenyl ether was eluted with CH_2Cl_2 and elution with CH_2Cl_2–EtOAc (6:1) yielded 85 mg (30%) of brown, crystalline **5**, m.p. 174–176°; MS: M^+ found 338·083 ± 0·003. $C_{17}H_{14}N_4O_2{}^{32}S$ requires: 388·084. $(M+2)^+$ found 340·082 ± 0·003. $C_{17}H_{14}N_4O_2{}^{34}S$ requires: 340·080; IR: 1710 cm^{-1} (C=O). UV: λ_{max} at 232 (ϵ = 25,700), 278 sh (ϵ = 7500), 347 (ϵ = 29,200), 361 (ϵ = 27,300), 410 (ϵ = 13,300), 510 sh (ϵ = 900), 550 sh (ϵ = 700), and 597 nm sh (ϵ = 400). MS: *m/e* (Rel int) 340 (5), 339 (21), 338 (M^+, 100), 310 (15), 293 (18), 267 (17), 266 (92), 225 (16), 198 (5), 147 (12), 146 (13), 121 (78), 115 (13), 103 (7), 89 (14), 77 (38). Doubly charged ions: *m/2e* (Rel int) 169·5 (0·7), 146·5 (3·2), 132·5 (1·2), 119·5 (1·0), 113·5 (0·5), 112·5 (0·5), 107·5 (0·7), 98·5 (1·0), 86·5 (1·7), 85·5 (0·5), 83·5 (0·7), 72·5 (0·5).

Formylation of **9** *with acetic-formic anhydride*[20] *and direct ring closure to form* **1**. To a stirred soln of **9** (4·23 g) in 300 ml formic acid 100 ml Ac_2O was added dropwise at 5°. After 16 h at room temp, the brown soln was poured into 300 ml sat NaCl aq and the mixture eas extracted with 5 × 150 ml CH_2Cl_2. The combined extracts were washed in the following order, with 300 ml water, 2 × 300 ml 10% $NaHCO_3$ aq, 300 ml water, and the dried ($MgSO_4$). The solvent was evaporated and the brown, solid residue was recrystallized from anhyd MeOH, yield: 2·57 g (59%) of **1** as brown needles, m.p. 200–201°. (Found: C, 59·26; H, 3·79; N, 17·37; S, 10·39. $C_{16}H_{12}N_4O_2S$ requires: C, 59·25; H, 3·73; N, 17·27; S, 9·89%); IR: 1700 cm^{-1} (C=O); UV: λ_{max} at 233 (ϵ = 26,800), 292 (ϵ = 6800), 304 (ϵ = 7700), 318 (ϵ = 9700), 334 (ϵ = 9900), 410 (ϵ = 14,400), 510 sh (ϵ = 940), 550 sh (ϵ = 650), and 603 nm sh (ϵ = 260). MS: *m/e* (Rel int) 326 (5), 325 (20), 324 (M^+, 100), 295 (13), 267 (7), 256 (16), 252 (70), 251 (20), 224 (5), 198 (3), 147 (18), 146 (12), 121 (32), 120 (8), 115 (9), 103 (5), 89 (6), 77 (22). Doubly charged ions: *m/2e* (Rel int) 162·5 (0·5), 139·5 (4·3), 126·5 (0·5), 125·5 (4·5), 112·5 (0·8), 106·5 (0·4), 98·5 (1·1), 96·5 (0·8), 79·5 (0·4), 60·5 (2·0).

Decarbethoxylation of **3** *to* **4**. A suspension of **3** (100 mg) in 10 ml diphenyl ether was heated to 250°. At that temp, 100 mg *p*-toluenesulphonic acid was added, the soln was left for 50 min, and then allowed to cool to room temp. The dark soln was passed over a column of alumina (20 g) and the diphenyl ether was then washed out with light petroleum (b.p. 60–85°). The coloured material was eluted with $CHCl_3$–MeOH (95:5). From these fractions, 20 mg (25%) of **4** (R_f = 0·16) was isolated by preparative TLC. Sublimation of **4** at 170°/1 Torr gave material with m.p. 220–223°. (Found: C, 62·75; H, 3·85; N, 20·59; S, 11·90. $C_{14}H_{10}N_4S$ requires: C, 63·14; H, 3·78; N, 21·00; S, 12·00%); UV: λ_{max} at 230 (ϵ = 21,800), 297 (ϵ = 6800), 306 (ϵ = 6600), 319 (ϵ = 9700), 334 (ϵ = 12,400), 379 (ϵ = 13,700), 473 (ϵ = 790), 500 (ϵ = 800). 540 sh (ϵ = 650), and 600 nm sh (ϵ = 270); MS: *m/e* (Rel int) 268 (6), 267 (18), 266 (M^+, 100), 225 (2), 198 (2), 147 (32), 146 (11), 121 (12), 120 (8), 115 (6), 103 (5), 77 (6). Doubly charged ions: *m/2e* (Rel int) 133·5 (1·1), 132·5 (0·5), 113·5 (0·4), 112·5 (4·5), 99·5 (0·4), 85·5 (0·4).

Decarbethoxylation of **5** *to* **6**. A suspension of **5** (20 mg) in 4 ml diphenyl ether was heated to 180°. At that temp 10 mg *p*-toluenesulphonic acid was added, the soln was left for 15 min, and then allowed to cool to room temp. The dark soln was passed over a column of silica gel (15 g) and the diphenyl ether was washed out with light petroleum (b.p. 60–85°). The coloured material was then eluted with EtOAc. From these fractions, 2 mg (13%) of green **6** (R_f = 0·28) was isolated by preparative TLC, m.p. 149–150°; UV: λ_{max} at 223 (ϵ = 18,700), 273 (ϵ = 5950), 314 (ϵ = 6500), 326 (ϵ = 9800), 342 (ϵ = 11,200), 436 (ϵ = 11,600), 541 (ϵ = 630), 582 (ϵ = 510), and 640 nm sh (ϵ = 250); MS: M^+ found 266·063 ± 0·003. $C_{14}H_{10}N_4{}^{32}S$ requires: 266·063. $(M+2)^+$ found 268·059 ± 0·003. $C_{14}H_{10}N_4{}^{34}S$ requires: 268·058. *m/e* (Rel int) 268 (6), 267 (17), 266 (M^+, 100), 225 (9), 198 (3), 147 (12), 121 (26), 104 (8), 77 (5). Doubly charged ions: *m/2e* (Rel int) 133·5 (0·7), 120·5 (0·6), 119·5 (8·3), 112·5 (0·5), 104·5 (1·3), 103·5 (0·8), 99·5 (0·5), 83·5 (1·3).

Decarbethoxylation of **1** *to* **2**. A suspension of **1** (100 mg) in 10 ml diphenyl ether was heated to 250°. At this temp, 100 mg *p*-toluenesulphonic acid was added, the soln was left for 30 min, and then allowed to cool to room temp. The dark soln was passed over a column of silica gel (20 g) and the diphenyl ether washed out with light petroleum (b.p. 60–85°). The coloured material was then eluted with EtOAc–MeOH (10:1). From these fractions, 25 mg (32%) of **2** (R_f = 0·16) was isolated by preparative TLC. Sublimation of **2** at 170°/1 Torr gave material with m.p. 195–199°. (Found: C, 61·50; H, 3·29; N, 22·13; S, 13·48. $C_{13}H_8N_4S$ requires: C, 61·89; H, 3·20; N, 22·21; S, 12·71%); UV: λ_{max} at 228 (ϵ = 23,700), 281 (ϵ = 6180), 305 (ϵ = 6700). 318 (ϵ = 9650), 334 (ϵ = 12,400), 381 (ϵ = 15,400), 480 (ϵ = 670), 514 (ϵ = 730), 553 (ϵ = 610), and 606 nm sh (ϵ = 320); MS: *m/e* (Rel int) 254 (5), 253 (12), 252 (M^+, 100), 225 (4), 198 (3), 147 (31), 146 (13), 121 (15), 120 (9), 115 (6), 103 (6), 77 (9). Doubly charged ions: *m/2e* (Rel int) 126·5 (1·2), 112·5 (3·5), 99·5 (0·6), 85·5 (0·9), 83·5 (0·6).

8 - *Bromo* - 4 - *phenyl* - 5 - *thia* - 1,3,6 - *triazacycl*[3.2.3]*azine*, **19**. To a stirred soln of **2** (50 mg; 0·20 mmol) in 10 ml glacial AcOH Br_2 (70 mg; 0·44 mmol) in 2 ml glacial AcOH was added dropwise at room temp. After 16 h, the solvent was evaporated under reduced pressure and the remaining brownish-red solid was

purified by preparative TLC; yield: 32 mg (49%) of brown, solid **19**, homogeneous on TLC, m.p. 250–251°; UV: λ_{max} at 235 (ϵ = 22,500), 293 (ϵ = 6850), 307 (ϵ = 6920), 323 (ϵ = 7850), 337 (ϵ = 9370), 388 (ϵ = 16,550), 488 (ϵ = 560), 524 (ϵ = 640), 568 (ϵ = 500), and 620 nm (ϵ = 270); MS: M^+ found 329·956 ± 0·003. $C_{13}H_7N_4{}^{32}S^{79}Br$ requires: 329·958. $(M+2)^+$ found 331·954 ± 0·003. $C_{13}H_7N_4{}^{32}S^{81}Br$ requires: 331·956. *m/e* (Rel int) 334 (6), 333 (18), 332 (^{81}Br M^+, 100), 331 (14), 330 (^{79}Br M^+, 98), 225 (6), 167 (5), 165 (5), 147 (45), 146 (15), 121 (26), 120 (12), 115 (11), 103 (7), 77 (17). Doubly charged ions: *m/2e* (Rel int) 166·5 (0·7), 165·5 (1·1), 164·5 (0·5), 126·5 (0·5), 125·5 (4·6), 112·5 (0·5), 111·5 (0·5), 60·5 (0·9).

8 - *Nitro* - 4 - *phenyl* - 5 - *thia* - 1,3,6 - *triazacycl* - [3.2.3]*azine*, **20**. To a stirred soln of $Cu(NO_3)_2 \cdot 3H_2O$ (60 mg; 0·25 mmol) in 4 ml freshly distilled Ac_2O, **2** (50 mg; 0·20 mmol) was added at room temp. After 1 h, the mixture was poured into 10% $NaHCO_3$ aq and the mixture was extracted with 3 × 25 ml CH_2Cl_2. The combined extracts were washed with 25 ml 10% $NaHCO_3$ aq and with 25 ml water, dried ($MgSO_4$) and evaporated to dryness. Purification of the brown residue by preparative TLC gave **20** (7 mg; 11%) as brown needles, m.p. 290–300° (dec); UV: λ_{max} at 238 (ϵ = 13,600), 270 sh (ϵ = 10,300), 426 (ϵ = 21,700), 540 sh (ϵ = 1140), 586 sh (ϵ = 510), and 650 nm sh (ϵ = 110). MS: M^+ found 297·030 ± 0·003. $C_{13}H_7N_5O_2{}^{32}S$ requires: 297·032. $(M+2)^+$ found 299·028 ± 0·003. $C_{13}H_7N_5O_2{}^{34}S$ requires: 299·028. *m/e* (Rel int) 299 (6), 298 (19), 297 (M^+, 100), 267 (11), 224 (13), 146 (51), 102 (7). Doubly charged ions: *m/2e* (Rel int) 148·5 (0·6), 125·5 (2·2), 112·5 (0·4), 100·5 (0·4), 98·5 (1·0), 86·5 (0·6).

Bromination of **6**. To a soln of **6** (1 mg) in 0·5 ml AcOH of bromine (8 mg) in 1 ml AcOH was added. The soln was left at room temp for 3 h and the solvent was then evaporated under reduced pressure. TLC showed a green product, R_f = 0·56, and starting material, R_f = 0·30. The bromination product was isolated by preparative TLC to give a green solid; UV: λ_{max} at 225, 289 sh, 325 sh, 337, 354, 440, and low-intensity absorptions between 500 and 650 nm. MS: *m/e* (Rel int) 426 (M^+, 9), 424 (M^+, 18), 422 (M^+, 9) 346 (16), 344 (16), 279 (14), 229 (13), 228 (57), 201 (7), 167 (28), 149 (100), 113 (19), 77 (20). Doubly charged ions: *m/2e* (Rel int) 172·5 (0·6), 171·5 (0·6), 159·5 (1·2), 158·5 (1·2), 114·5 (0·8), 113·5 (1), 101·5 (0·6), 100·5 (3·5), 99·5 (0·6), 87·5 (1), 86·5 (1).

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