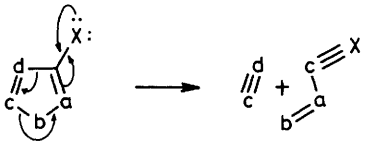
# Ring Cleavage of a 3-Azidothiophene: Novel Extrusion of Acetylene[1]

**Christopher J. Moody, Charles W. Rees, and Siu Chung Tsoi**
*Department of Chemistry, Imperial College of Science and Technology, London SW7 2AY*

Mild thermal decomposition of ethyl 2-azido-3-(3-azido-2-thienyl)propenote (**8**) results in the cleavage of the thiophene ring with extrusion of acetylene and formation of ethyl 5-cyanoisothiazole-3-carboxylate (**10**), together with ethyl thieno[3,2-*c*]pyridazine-3-carboxylate (**9**). The former reaction represents the first fragmentation of a five-membered heteroaromatic β-nitrene to extrude an acetylene, and the latter reaction is a rare example of formal intramolecular coupling of nitrenes in solution thermolysis. The vinyl azide group is necessary for this cleavage of the thiophene ring and a mechanism is proposed in which the derived nitrene co-ordinates with the thiophene sulphur atom to faciliate ring fragmentation. The analogous furan does not fragment similarly. Diels–Alder cycloadditions of 4-phenyl-1,2,4-triazole-3,5-dione to 2-vinylthiophenes were investigated as an independent approach to the thieno[3,2-*c*]pyridazine system, but the fused 4-phenyl-1,2,4-triazoline-3,5-dione ring proved resistant to hydrolytic cleavage.

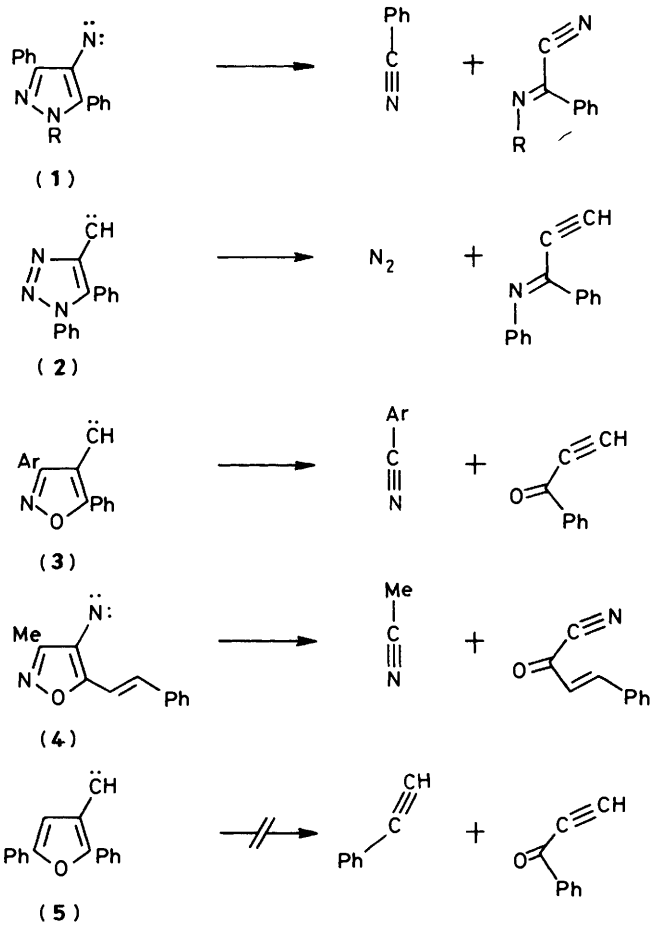
The generation of carbenes or nitrenes at the β-position of aromatic five-membered ring heterocyclic systems can lead to ring fragmentation. Although much less common than the ring-opening fragmentation of the corresponding α-carbenes and nitrenes,[2] several examples of this process which is shown in general in Scheme 1 are known. However they all involve the



Scheme 1.

extrusion of a stable fragment c≡d containing nitrogen, either molecular nitrogen or a nitrile. Thus, for example the pyrazol-4-yl nitrene (**1**),[3] the triazol-4-yl carbene (**2**),[4] and the isoxazol-4-yl carbene (**3**)[5] and nitrene (**4**)[6] fragment as shown. Fragmentation to give an acetylene has not been observed, and, for example, in the generation of the 3-furylcarbene (**5**) there was no evidence for any fragmentation into phenylacetylene and benzoylacetylene.[5] In contrast, 2-furylcarbenes readily undergo ring-opening.[7] This difference is also reflected in the relative stabilities of 5-azidofuran-2-carbaldehyde and 3-azidofuran-2-carbaldehyde. Whereas the 5-azide is thermally very labile,[8] the 3-azide (**6a**) is reported to be remarkably stable,[9] and on heating gives a very poor yield of the furoisoxazole (**7a**). Similarly the corresponding azidothiophene (**6b**) gives the thienoisoxazole (**7b**) with no mention of any ring fragmentation products.[10]

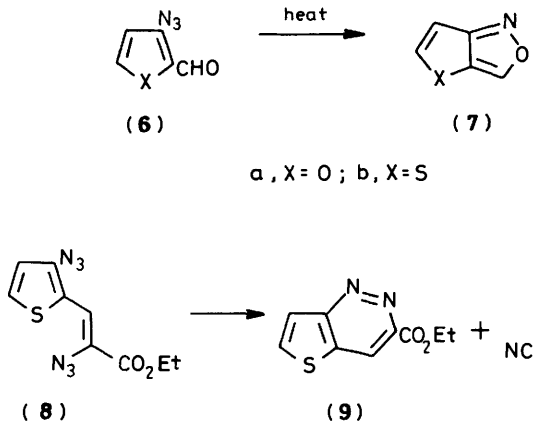
We now report full details of the decomposition of the vinyl azide (**8**), derived from (**6b**), which involves the first example of extrusion of an acetylene from a five-membered heteroaromatic ring.

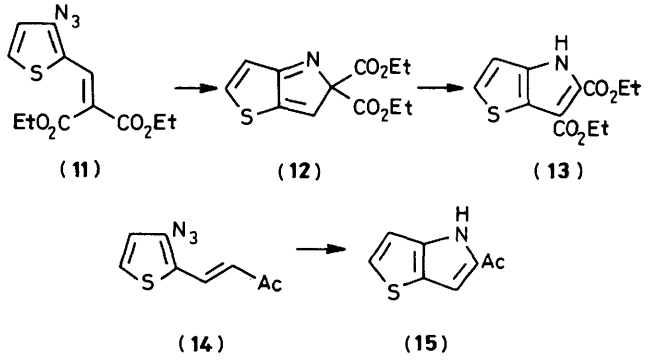


## Results and Discussion

3-Azidothiophene-2-carbaldehyde (**6b**) was prepared from the corresponding bromothiophene. The best yield (75%) was obtained using sodium azide in hexamethylphosphoramide, and represents an improvement on the literature procedure (45% yield in dimethyl sulphoxide as solvent).[9] Condensation of the aldehyde (**6b**) with ethyl azidoacetate in ethanolic sodium ethoxide at −15 °C gave the bis-azide (**8**) (63%). The bis-azide (**8**) was decomposed by heating in refluxing toluene for 0.5 h to give ethyl thieno[3,2-*c*]pyridazine-3-carboxylate (**9**) (17%) and ethyl 5-cyanoisothiazole-3-carboxylate (**10**) (19%) as the major products. When the decomposition was carried out in refluxing xylene, the yields of (**9**) and (**10**) increased to 26 and 27% respectively.

The structure of the thienopyridazine (**9**) was assigned on the basis of its n.m.r. spectrum which showed the expected long-range coupling between 4-H and 7-H (*J* 0.8 Hz). It is interesting that the spectrum, in deuteriochloroform, exhibits a marked



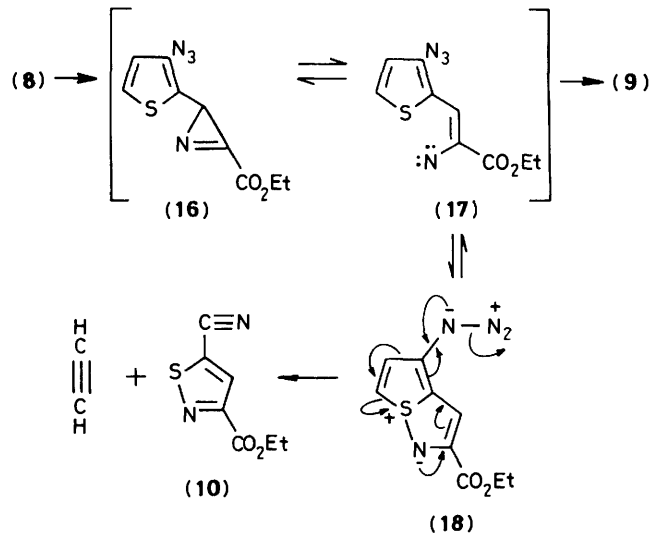




concentration dependence, and the characteristic pattern for the thiophene protons 6-H (doublet, $J_{6,7}$ 5.5 Hz) and 7-H (dd, $J_{6,7}$ 5.5 Hz, $J_{4,7}$ 0.8 Hz) could be clearly seen only when concentrated solutions were used. The structure of (**9**) was confirmed by hydrolysis and decarboxylation to give the known[11] thieno[3,2-*c*]pyridazine. [An independent synthesis of (**9**) was also attempted, and the results of this are described later.] The formation of the thienopyridazine (**9**) is envisaged to involve coupling of the two azide groups with loss of nitrogen, although the exact timing of the steps is not known. Possible intermediates include a dinitrene or the azidonitrene formed by initial decomposition of the vinyl azide. The alternative azidonitrene, formed by initial decomposition of the 3-azido group was considered unlikely since vinyl azides are generally less thermally stable than aryl nitrenes. Despite its apparent simplicity coupling of 'nitrenes' to give N=N compounds is uncommon, and although azoarene formation is observed in photochemical decomposition of aryl azides the intramolecular version is rare. For example 2,2′-diazidobiphenyl only gives useful yields of the coupled product, benzo[*c*]cinnoline, when photolysed in a matrix at 77 K;[12] no coupling occurred on thermolysis of the bisazide. Similarly photolysis of 1,8-diazidonaphthalene in a rigid matrix at 77 K gave benz[*cd*]indazole which, although it could not be isolated, was characterised by $^{15}N$ n.m.r. spectroscopy.[13] Thus the formation of (**9**) may represent the first example of intramolecular coupling of 'nitrenes' under normal solution thermolysis conditions.

The structure of the isothiazole (**10**) was confirmed by hydrolysis and decarboxylation to give the known[14] isothiazole-5-carboxamide. The stoicheiometry for the formation of (**10**) requires the loss of nitrogen (2 mol) and acetylene (1 mol). The formation of acetylene was confirmed by the production of a red-brown precipitate of copper acetylide when the exit gases from the azide thermolysis were bubbled through ammoniacal copper(I) chloride. The yield of acetylene (15 and 21% in the toluene and xylene thermolysis respectively) was determined by the silver nitrate method.[15]

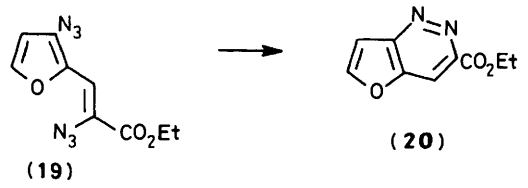
Since no ring cleavage reactions of 3-azidothiophenes have been previously reported, it seemed likely that the other azide group was playing a key role in this fragmentation of the very stable thiophene ring. Evidence for the importance of the vinyl azide was obtained from the decomposition of the mono-azide (**11**). This compound, prepared by condensation of the aldehyde (**6b**) with diethyl malonate, gave no acetylene and no ring cleavage products on heating in toluene. The major (76%) thermolysis product was diethyl thieno[3,2-*b*]pyrrole-5,6-dicarboxylate (**13**), presumably formed by cyclisation of the nitrene to give (**12**) followed by successive [1,5]sigmatropic shifts of ester and hydrogen. In a related reaction, thermolysis of the azide (**14**) gave the thienopyrrole (**15**).[16]

Therefore the presence of the vinyl azide is thought to be necessary for ring cleavage under these mild conditions. A possible mechanism is outlined in Scheme 2. Initial decomposition of the vinyl azide would give the azirine (**16**), which is in thermal equilibrium with the azidonitrene (**17**). Interaction between the nitrene and the azide group can lead to the thienopyridazine (**9**). Alternatively, interception of the nitrene by the thiophene sulphur would lead to the intermediate (**18**), thereby weakening the ring. Loss of acetylene and isothiazole formation could then occur simultaneously as shown.



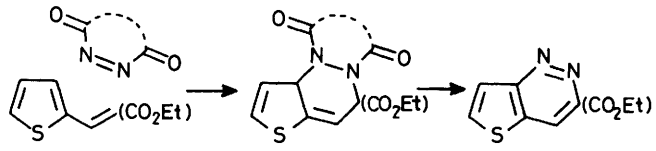

**Scheme 2.**

The key step in this mechanism leading to ring fragmentation is the co-ordination of the intermediate nitrene to the thiophene sulphur. Therefore replacing the thiophene by a furan ring, in which the oxygen atom is less likely to interact with the nitrene, would probably suppress the ring cleavage reaction. The corresponding furan azide (**19**) was readily prepared from 3-azidofuran-2-carbaldehyde (**6a**) and subjected to identical thermolysis conditions as the thiophene analogue. No acetylene was detected, and the only isolated product was the furo[3,2-*c*]pyridazine (**20**) formed in only 19% yield, the remaining material being tarry in nature. The absence of any ring fragmentation product analogous to (**10**) lends support to the mechansim proposed in Scheme 2.



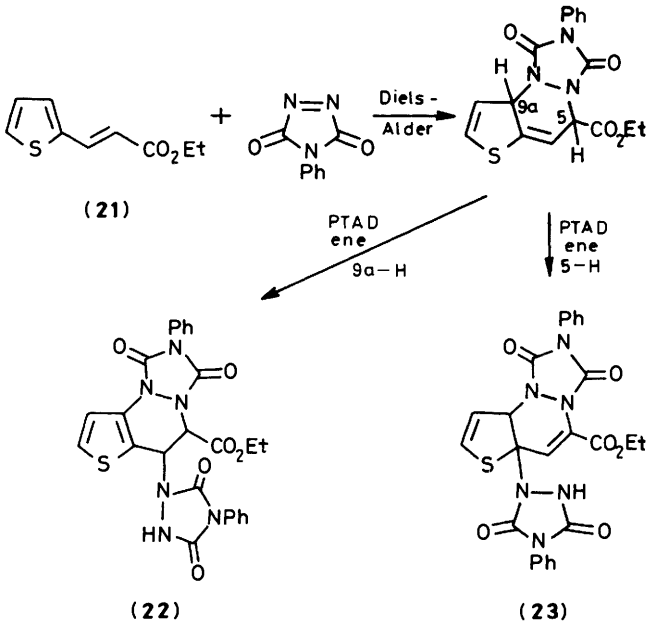
(19) (20)

*Attempted Independent Synthesis of Thieno*[3,2-c]*pyridazines.*—Although thieno[3,2-*c*]pyridazines have been prepared before, the literature procedure is somewhat long,[11] and therefore a shorter alternative synthesis was devised. It is based on the well known dienophilic properties of azodicarbonyl compounds,[17] and is outlined in Scheme 3.



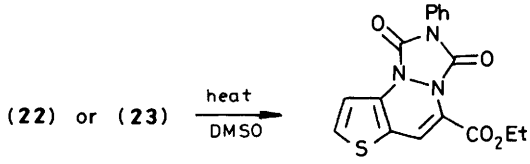
Scheme 3.

Addition of 4-phenyl-1,2,4-triazole-3,5-dione (PTAD), one of the most reactive azo dienophiles, to a solution of the acrylate (**21**)[18] at room temperature gave two products. Mass spectrometry indicated that both products were 2:1 adducts formed by addition of 2 mol of PTAD to the diene, and on the basis of their n.m.r. spectra, they were assigned the structures (**22**) (46%) and (**23**) (8%). These are presumably formed from the initial Diels–Alder adduct by ene reactions with a second mole of PTAD. Ene reactions involving the allylic hydrogens at 9a-H and 5-H would produce the 2:1 adducts (**22**) and (**23**) respectively (Scheme 4). The major product (**22**) is the one accompanied by re-aromatisation of the thiophene ring.



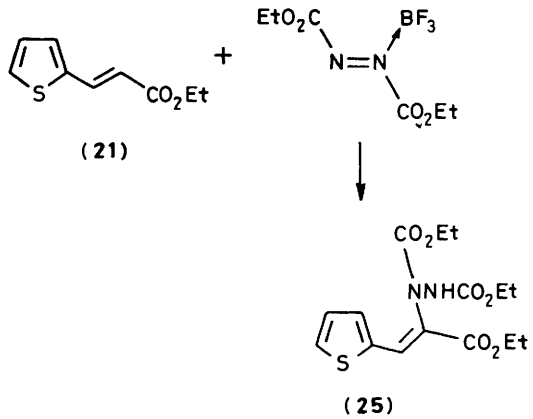
Scheme 4.

The adduct (**23**) was found to be particularly unstable in solution in dimethyl sulphoxide (DMSO). This was noticed whilst recording its n.m.r. spectrum; after several minutes the spectrum had altered and the solution had turned bright yellow. When the DMSO solution of (**23**) was heated at 95 °C for 1 h, a single yellow crystalline compound was isolated in quantitative yield, together with a small amount of 4-phenyl-1,2,4-triazoline-3,5-dione ($PTADH_2$). Similarly, heating the adduct (**22**) in DMSO for 24 h at 120 °C gave the same yellow compound. This compound was assigned the structure (**24**), derived by elimination of $PTADH_2$ from the 2:1 adducts.



(24)

All attempts to cleave the triazole ring in (**24**) were unsuccessful. A wide variety of literature procedures, involving acidic or basic hydrolysis conditions, resulted in either complex mixtures or extensive decomposition of starting material, often with the formation of hydrogen sulphide. In view of these difficulties the use of an alternative azo dienophile was investigated. Diethyl azodicarboxylate (DEAZD) did not react with the acrylate (**21**) even on heating at 156 °C. However, using the Lewis acid, boron trifluoride–ether as solvent, a low yield of a 1:1 adduct (15%) was obtained at room temperature. However, this product was clearly not the required Diels–Alder adduct, and on the basis of its n.m.r. spectrum was assigned the structure (**25**).* Although DEAZD is a powerful electrophile, this type of reaction has only been observed with electron rich olefins or aromatics.[19] This somewhat unexpected reaction with the relatively electron deficient acrylate (**21**) is probably explained by the use of a vast excess of $BF_3$. The DEAZD–$BF_3$ complex is probably considerably more electrophilic than DEAZD itself.

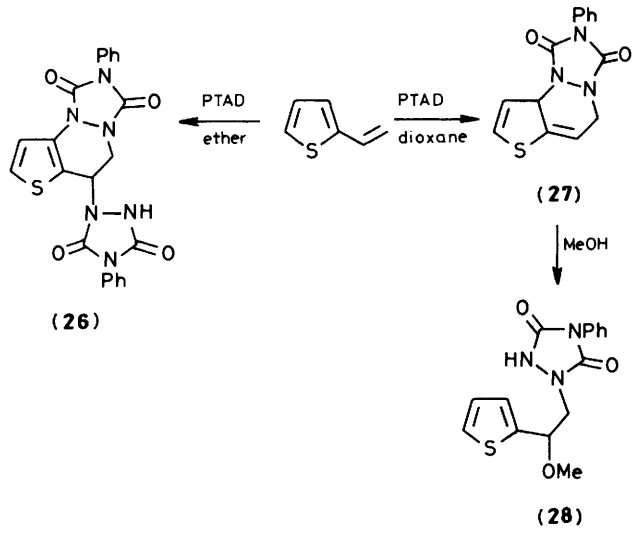


(21) (25)

Reactions of the more reactive diene 2-vinylthiophene were also investigated. Reaction of 2-vinylthiophene with PTAD in ether at room temperature gave 2:1 adduct (**26**) (66%). Unlike the analogous ester bearing adduct (**22**), the adduct (**26**) did not eliminate $PTADH_2$ when heated in DMSO. However, reaction

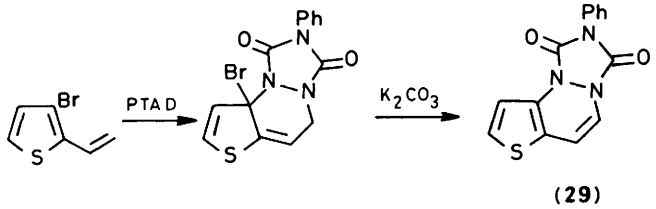
* The structure and geometry of the adduct (**25**) were confirmed by an *X*-ray diffraction analysis, carried out by Dr. D. J. Williams, Department of Chemistry, Imperial College.

of the diene with PTAD in dioxane at room temperature gave the Diels–Alder adduct (**27**) in good yield. This compound has been reported previously but no physical nor spectral data were given.[20] The n.m.r. data clearly ruled out a structure with an aromatic thiophene ring. Attempts to recrystallise the adduct (**27**) from methanol resulted in the isolation of the ring-opened methanol adduct (**28**) (Scheme 5).




**Scheme 5.**

Although the adduct (**26**) did not eliminate $PTADH_2$, the required compound (**29**) could be prepared by an alternative route. Thus reaction of PTAD with 3-bromo-2-vinylthiophene at room temperature in dioxane, followed by treatment with potassium carbonate gave the tricyclic compound (**29**) (46%) (Scheme 6).




**Scheme 6.**

However, as with all the other PTAD adducts, hydrolytic cleavage of the triazole ring in (**29**) could not be achieved. Thus, although several thieno[3,2-*c*]pyridazine derivatives were prepared by Diels–Alder addition of vinylthiophenes to PTAD, the independent synthesis of (**9**) was thwarted by the surprising resistance of the triazole ring to hydrolysis.

## Experimental

I.r. spectra were recorded in the range 600—4 000 $cm^{-1}$ using Perkin-Elmer 257 and 298 spectrophotometers, and calibrated against polystyrene. Spectra of solids were taken as Nujol mulls, and liquids as thin films unless otherwise stated. U.v. and visible spectra were recorded in the range 200—700 nm using a Pye Unicam SP 800 recording spectrophotometer, and calibrated against holmium glass. $^1H$ N.m.r. spectra were recorded at 90 and 250 MHz using Perkin-Elmer R32 and Bruker WM250 instruments respectively with tetramethylsilane as internal standard. Carbon-13 n.m.r. spectra were recorded at 62.9 MHz on the Bruker WM250. Low and high resolution mass spectra were recorded on A.E.I. MS 12 and V.G. Micromass 7070B instruments using a direct insertion probe. Melting points were determined on a Kofler hot-stage apparatus. Column chromatography was carried out on silica gel H (Merck 7736) under slight pressure. Solvents were dried and purified by standard procedures. Light petroleum refers to the fraction of b.p. 40—60 °C.

*Preparation and Thermolysis of the Bis-azide* (**8**).—*3-Azidothiophene-2-carbaldehyde* (**6b**). A mixture of 3-bromothiophene-2-carbaldehyde[21] (7.17 g, 0.037 mol) and sodium azide (9.75 g, 0.15 mol) in dry hexamethylphosphoramide (80 ml) was stirred at 30—35 °C under nitrogen for 2 days. The mixture was poured into ice–water (300 ml) and the resulting yellow-brown precipitate filtered off, and washed with water. The aqueous filtrate was extracted with ether (3 × 150 ml) to yield a further quantity of yellow-brown solid. The combined solid product was purified by chromatography to give 3-azidothiophene-2-carbaldehyde (**6b**) (4.32 g, 75%), m.p. 57—58 °C (lit.,[9] 56.6—57.2 °C).

*Ethyl 2-azido-3-(3-azido-2-thienyl)propenoate* (**8**). Sodium (0.92 g, 40 mg-atom) was dissolved in ethanol (30 ml), and the stirred solution cooled to −20 °C. A mixture of ethyl azidoacetate (5.16 g, 40 mol) and the aldehyde (**6b**) (1.20 g, 7.32 mmol) in ethanol (5 ml) was added dropwise the temperature being maintained below −10 °C. After the addition the mixture was stirred at −15 °C for a further 2.5 h, and then allowed to warm up to 5 °C. The reaction mixture was poured into water and extracted with ether. The extracts were washed with water, dried ($MgSO_4$), and evaporated. The residue was chromatographed to give the *title compound* (**8**) (1.213 g, 63%) as pale yellow needles, m.p. 67—68 °C (from light petroleum) (Found: C, 41.1; H, 3.0; N, 31.5. $C_9H_8N_6O_2S$ requires C, 40.9; H, 3.05; N, 31.8%); $\nu_{max.}$ 2 130, 2 105, 1 705 1 605, and 1 515 $cm^{-1}$; $\lambda_{max.}$(EtOH) 205 (log ε 4.00), 236 (3.97), 250sh (3.89), and 3.49 nm (4.31); δ (250 MHz, $CDCl_3$) 1.38 (3 H, t), 4.39 (2 H, q), 6.98 (1 H, d, *J* 5.2 Hz), 7.17 (1 H, d, *J* 0.8 Hz), and 7.50 (1 H, dd, 7.0 and 0.8 Hz); *m/z* 264 ($M^+$), 236, 164, 136 (base), and 109.

*Thermolysis in toluene.* The azide (**8**) (264 mg, 1 mmol) was dissolved in toluene (20 ml) in a 3-necked flask, fitted with a reflux condenser and a nitrogen inlet. The top of the condenser was connected to a series of bubblers filled with silver nitrate solution. The flask was then heated in an oil-bath under a stream of nitrogen. After refluxing for 0.5 h, the solvent was evaporated to leave an oil. Chromatography gave (i) *ethyl 5-cyanoisothiazole-3-carboxylate* (**10**) (35 mg, 19%), as an oil, b.p. 100—104 °C/0.2 mmHg (Kugelrohr) (Found: C, 46.4; H, 3.5; N, 15.3; S, 17.3. $C_7H_6N_2O_2S$ requires C, 46.1; H, 3.3; N, 15.4; S, 17.6%); $\nu_{max.}$ 2 240, 1 745, and 1 725 $cm^{-1}$; δ (90 MHz, $CDCl_3$) 1.46 (3 H, t), 4.55 (2 H, q), and 8.30 (1 H, s); *m/z* 182 ($M^+$), 155, 138, 137 (base), 110, 109, and 83; and (ii) *ethyl thieno*[3,2-c]*-pyridazine-3-carboxylate* (**9**) (35.4 mg, 17%) as a solid purified by sublimation and recrystallisation, m.p. 130—131 °C (from dichloromethane–light petroleum) (Found: C, 51.6; H, 3.8; N, 13.1. $C_9H_8N_2O_2S$ requires C, 51.9; H, 3.9; N, 13.45%); $\nu_{max.}$(KBr) 3 110, 3 080, 1 715, and 1 565 $cm^{-1}$; δ (90 MHz, $CDCl_3$) 1.51 (3 H, t), 4.61 (2 H, q), 8.01 (1 H, dd, *J* 5.5 and 0.8 Hz), 8.13 (1 H, d, *J* 5.5 Hz), and 8.80 (1 H, d, *J* 0.8 Hz); *m/z* 208 ($M^+$), 136 (base), 109, and 92. The yield of acetylene was estimated by titration of the silver nitrate bubblers[15] to be 15%.

*Hydrolysis and Decarboxylation of the Thienopyridazine* (**9**).—The ester (**9**) (100 mg, 0.48 mmol) was stirred with aqueous ethanolic potassium hydroxide (0.6 ml of 1M-KOH in 0.6 ml of ethanol) for 24 h at room temperature. Acid work-up gave the

corresponding carboxylic acid (74 mg, 85%). The acid (24 mg, 0.13 mmol) was heated at 170—185 °C for 15 min to give thieno[3,2-*c*]pyridazine (15 mg, 83%), m.p. 95—96 °C (lit.,[11] 97.5—98.5 °C).

*Hydrolysis of the Isothiazole* (**10**).—The cyano ester (**10**) (100 mg, 0.55 mmol) was stirred in a mixture of aqueous potassium hydroxide (1M; 0.6 ml) and dioxane (0.6 ml) at 5 °C for 1 h to give 5-carbamoylisothiazole-3-carboxylic acid (85 mg, 90%). The acid was heated over a free flame to give isothiazole-5-carboxamide (35 mg, 55%), m.p. 169—172 °C (lit.,[14] 172—174 °C).

*Preparation and Thermolysis of the Azide* (**11**).—*Diethyl* [(3-*azido*-2-*thienyl*)*methylene*]*propanedioate* (**11**). Diethyl malonate (0.21 g, 1.3 mmol) was added to a stirred solution of the aldehyde (**6b**) (0.20 g, 1.3 mmol) and piperidinium acetate (0.19 g, 1.3 mmol) in ethanol (5 ml) at room temperature. After 18 h, the solvent was evaporated and the residue chromatographed to give the *title compound* (0.37 g, 96%), m.p. 39—41 °C (from dichloromethane–light petroleum) (Found: C, 49.15; H, 4.5; N, 14.15. $C_{12}H_{13}N_3O_4S$ requires C, 48.8; H, 4.4; N, 14.2%); $\nu_{max.}$ 2 115, 2 105, 1 725, and 1 618 $cm^{-1}$; δ (90 MHz, $CDCl_3$) 1.36 (6 H, 2 × t), 4.36 (4 H, 2 × q), 7.01 (1 H, d, *J* 5.0 Hz), 7.56 (1 H, dd, *J* 5.0 and 0.8 Hz), and 7.90 (1 H, d, *J* 0.8 Hz); *m/z* 295 ($M^+$), 268, 267, 193 (base), 165, and 137.

*Thermolysis in toluene.* The azide (**11**) (203 mg, 0.69 mmol) was heated in boiling toluene (20 ml) for 4 h. The solvent was evaporated and the residue chromatographed to give *diethyl thieno*[3,2-b]*pyrrole*-5,6-*dicarboxylate* (**13**) (140 mg, 76%), m.p. 107—109 °C (sublimed) (Found: C, 54.2; H, 4.9; N, 5.2. $C_{12}H_{13}NO_4S$ requires C, 53.9; H, 4.9; N, 5.2%); $\nu_{max.}$ 3 280, 1 732, 1 660, and 1 525 $cm^{-1}$; $\lambda_{max.}$(EtOH) 235 (log ε 4.16), 247sh (4.06), and 307 nm (4.17); δ (250 MHz, $CDCl_3$) 1.39 (3 H, t), 1.43 (3 H, t), 4.41 (2 H, q), 4.42 (2 H, q), 6.96 (1 H, d, *J* 5.5 Hz), 7.35 (1 H, d, *J* 5.5 Hz), and 10.31 (1 H, br); $\delta_C$($CDCl_3$) 14.3, 14.4, 60.8, 61.6, 111.2, 112.8, 126.9, 128.1, 130.7, 138.6, 160.9, and 162.7 p.p.m.; *m/z* ($M^+$), 221, 193, 176, and 149 (base). No acetylene was detected in the exit gases from the thermolysis.

*Preparation and Thermolysis of the Bis-azide* (**19**).—*Ethyl* 2-*azido*-3-(3-*azidofuran*-2-*yl*)*propenoate* (**19**). This was prepared from 3-azidofuran-2-carbaldehyde (**6a**)[9] and ethyl azidoacetate in an manner identical with that of the analogous thiophene derivative. The crude product was purified by chromatography and crystallisation from aqueous ethanol gave the *title compound* (25%) as a yellow solid, m.p. 85—86 °C (Found: C, 43.8; H, 3.25; N, 33.8. $C_9H_8N_6O_3$ requires C, 43.55; H, 3.25; N, 33.9%); $\nu_{max.}$ 2 130, 2 102, 1 710, 1 625, and 1 562 $cm^{-1}$; δ (250 MHz, $CDCl_3$) 1.38 (3 H, t), 4.35 (2 H, q), 6.47 (1 H, d, *J* 2.1 Hz), 6.66 (1 H, s), and 7.52 (1 H, d, *J* 2.1 Hz); *m/z* 248 ($M^+$), 220, 203, 148, 147, 120 (base), 119, 92, and 91.

*Thermolysis in toluene.* The azide (**19**) (100 mg) was heated in boiling toluene (10 ml) for 45 min to give *ethyl furo*[3,2-c]*pyridazine*-3-*carboxylate* (**20**) (13 mg, 17%) as the only identifiable product, m.p. 111—112 °C (from dichloromethane–light petroleum), $\nu_{max.}$ 1 715 $cm^{-1}$; δ (250 MHz, $CDCl_3$) 1.52 (3 H, t), 4.60 (2 H, q), 7.46 (1 H, dd, *J* 2.2 and 1.1 Hz), 8.08 (1 H, d, *J* 2.2 Hz), and 8.33 (1 H, d, *J* 1.1 Hz); *m/z* 192 ($M^+$), 148, 147, 120 (base), 119, 93, and 92. No acetylene was detected in the exit gases from the thermolysis.

*Attempted Independent Synthesis of Thieno*[3,2-c]*pyridazines*: *Ethyl* 2,3,5,6-*Tetrahydro*-1,3-*dioxo*-2-*phenyl*-6-(4-*phenyl*-3,5-*dioxo*-1,2,4-*triazolin*-1-*yl*)-1H-*thieno*[3,2-c][1,2,4]*triazolo*-[1,2-a]*pyridazine*-5-*carboxylate* (**22**) *and Its Isomer* (**23**).—A solution of PTAD (0.65 g, 3.7 mmol) in dry dioxane (20 ml) was added dropwise to a stirred solution of ethyl 3-(2-thienyl)-propenoate[18] (**21**) (0.67 g, 3.7 mmol) in dry dioxane (15 ml) at room temperature. The red colour of the dienophile was rapidly discharged to give a pale yellow solution. The solvent was evaporated, and the residue chromatographed to give (i) the *title compound* (**22**) (0.46 g, 46%), m.p. 128—132 °C (from dichloromethane–light petroleum) (Found: C, 56.0; H, 3.8; N, 15.7. $C_{25}H_{20}N_6O_6S$ requires C, 56.4; H, 3.8; N, 15.8%); $\nu_{max.}$ 3 170, 3 110, 1 785, and 1 725 $cm^{-1}$; δ (250 MHz, $CDCl_3$) 1.21 (3 H, t), 4.21 (2 H, m), 5.35 (1 H, d, *J* 1.8 Hz), 6.19 (1 H, d, *J* 1.8 Hz), 7.3—7.5 (11 H, m), 7.61 (1 H, d, *J* 5 Hz), and 8.45 (1 H, br, exch. $D_2O$); *m/z* 532 ($M^+$), 355, 177, 136 (base), and 119.

(ii) *The adduct* (**23**) (0.08 g, 8%), m.p. 135—160 °C (from ethyl acetate–light petroleum) (Found: C, 56.2; H, 3.8; N, 15.7%); $\nu_{max.}$ 3 160, 3 080, 1 795, 1 780, 1 730, and 1 705 $cm^{-1}$; δ [250 MHz, $(CD_3)_2SO$] 1.19 (3 H, t), 4.21 (2 H, q), 5.84 (1 H, m), 6.24 (1 H, m), 6.45 (1 H, m), 6.95 (1 H, m), 7.40—7.65 (10 H, m), and 10.81 (1 H, br, exch. $D_2O$); *m/z* 532 ($M^+$), 355, 177, 136 (base), and 119.

*Ethyl* 2,3-*Dihydro*-1,3-*dioxo*-2-*phenyl*-1H-*thieno*[3,2-c]-[1,2,4]*triazolo*[1,2-a]*pyridazine*-5-*carboxylate* (**24**).—A stirred solution of the adduct (**22**) (0.85 g) in DMSO (40 ml) was heated at 110—120 °C for 24 h. The mixture was poured into water and extracted with ethyl acetate. The combined extracts were washed with water (3 × 25 ml), dried ($MgSO_4$), evaporated, and the residue chromatographed to give the *title compound* (**24**) (0.56 g, 99%), as yellow needles, m.p. 175—176 °C (Found: C, 57.3; H, 3.8; N, 11.6. $C_{17}H_{13}N_3O_4S$ requires C, 57.5; H, 3.7; N, 11.8%); $\nu_{max.}$ 1 774, 1 732, and 1 714 $cm^{-1}$; $\lambda_{max.}$(EtOH) 220 (log ε 3.95), 242 (3.98), 283 (3.63), and 405 nm (3.46); δ (250 MHz, $CDCl_3$) 1.37 (2 H, t), 4.38 (2 H, q), 6.80 (1 H, d, *J* 0.6 Hz), 7.35—7.60 (6 H, m), and 7.62 (1 H, dd, *J* 5.4 and 0.6 Hz); *m/z* 355 ($M^+$), 136 (base), and 119.

The adduct (**23**) when heated in DMSO at 90—95 °C for 1 h also gave the product (**24**) (97%).

*Ethyl* 2-(N,N′-*Diethoxycarbonylhydrazino*)-3-(2-*thienyl*)-*propenoate* (**25**).—Freshly distilled boron trifluoride–ether (2 ml) was added to a stirred mixture of the acrylate (**21**) (0.152 g, 0.83 mmol) and DEAZD (0.127 g, 0.73 mmol) under nitrogen. After 2 h the dark reaction mixture was poured into water and extracted with ethyl acetate. The extracts were dried ($Na_2SO_4$), evaporated, and the residue chromatographed to give the *title compound* (**25**) (40 mg, 15%), m.p. 115—116 °C (from dichloromethane–light petroleum) (Found: C, 50.4; H, 5.6; N, 7.8. $C_{15}H_{20}N_2O_6S$ requires C, 50.55; H, 5.7; N, 7.9%); $\nu_{max.}$ 3 290, 1 760, 1 730, and 1 695 $cm^{-1}$; δ (90 MHz, $CDCl_3$) 1.10—1.45 (9 H, m), 4.05—4.45 (6 H, m), 7.05—7.20 (2 H, m), 7.55—7.7 (2 H, m), and 7.79 (1 H, br); *m/z* 356 ($M^+$), 312, 311, 284, and 237 (base).

5,6-*Dihydro*-2-*phenyl*-6-(3,5-*dioxo*-4-*phenyl*-1,2,4-*triazolin*-1-*yl*)*thieno*[3,2-c][1,2,4]*triazolo*[1,2-a]*pyridazine*-1,3-*dione* (**26**).—Solid PTAD (0.88 g, 5 mmol) was added portionwise to a stirred solution of 2-vinylthiophene[22] (0.55 g, 5 mmol) in dry ether (50 ml) at room temperature. The red colour of the dienophile was rapidly discharged. The mixture was stirred at room temperature for 2 days and the resulting precipitate was filtered off, and washed with ether (15 ml) to give the *title compound* (**26**) (0.76 g, 66% based on PTAD), m.p. 257—258 °C, $\nu_{max.}$ 3 160, 1 785, 1 725, and 1 705 $cm^{-1}$; δ [90 MHz, $(CD_3)_2SO$] 3.95—4.70 (2 H, m), 5.72 (1 H, m), 7.3—7.65 (11 H, m), 7.78 (1 H, d, *J* 5.0 Hz), and 10.76 (1 H, br, exch. $D_2O$); *m/z* 460 ($M^+$), 284 (base), 177, 165, 138, 119, 109, 91, and 77; *m** (460—284) 175.3, (284—165) 95.9, and (284—138) 67.1.

5,9a-*Dihydro*-2-*phenylthieno*[3,2-c][1,2,4]*triazolo*[1,2-a]*pyridazine*-1,3-*dione* (**27**).—A solution of PTAD (1.2 g, 6.86

mmol) in dioxane (30 ml) was added dropwise to a stirred suspension of 2-vinylthiophene (0.88 g, 8 mmol) in dioxane (25 ml) at room temperature. After 0.5 h, the yellow solution was concentrated to give a yellow syrup. Trituration with ether gave the *title compound* (**27**) (1.84 g, 94%), as a solid, m.p. 101—104 °C, $\nu_{max.}$ 1 770 and 1 715 $cm^{-1}$; δ [90 MHz, $(CD_3)_2SO$] 4.30 (2 H, m), 5.55 (1 H, m), 6.02 (1 H, m), 6.34 (1 H, m), 6.90 (1 H, m), and 7.53 (5 H, m).

Attempts to recrystallise the above compound (0.92 g) from methanol gave a new compound assigned as 1-[2-*methoxy*-2-(2-*thienyl*)*ethyl*]-4-*phenyl*-1,2,4-*triazoline*-3,5-*dione* (**28**) (0.65 g, 60%), m.p. 142—143 °C (Found: C, 56.7; H, 4.7; N, 13.3. $C_{15}H_{15}N_3O_3S$ requires C, 56.8; H, 4.8; N, 13.2%); $\nu_{max.}$ 3 200, 1 770, and 1 697 $cm^{-1}$; δ (90 MHz, $CDCl_3$) 3.27 (3 H, s), 3.64—4.21 (2 H, AB of ABX, $J_{AB}$ 14 Hz, $J_{AX}$ 3.6 Hz, $J_{BX}$ 8.0 Hz), 4.81 (1 H, X of ABX), 6.98—7.14 (2 H, m), 7.32—7.58 (6 H, m), and 8.65 (1 H, br, exch. $D_2O$); *m/z* 317 ($M^+$), 285, 140, 127 (base), 119, and 110.

2-*Phenylthieno*[3,2,-c][1,2,4]*triazolo*[1,2-a]*pyridazine*-1,3-*dione* (**29**).—A solution of PTAD (92.6 mg, 0.53 mmol) in dioxane (4 ml) was added dropwise to a stirred solution of 3-bromo-2-vinylthiophene (100 mg, 0.53 mmol) in dioxane (2 ml) at room temperature under nitrogen. At the end of the addition, a bright yellow solution was obtained. Potassium carbonate (73 mg, 0.53 mmol) was then added, and the mixture heated to reflux for 30 min. The mixture was filtered, evaporated, and the residue chromatographed (20 × 40 cm silica plate) to give the *title compound* (**29**) (69 mg, 47%), δ (90 MHz, $CDCl_3$) 5.87 (1 H, d, *J* 8.0 Hz), 6.95 (1 H, d, *J* 8.0 Hz), 7.24 (1 H, d, *J* 5.2 Hz), and 7.38—7.68 (6 H, m); *m/z* 283 ($M^+$), 136 (base), and 119.

## Acknowledgements

We thank Dr. D. J. Williams for the *X*-ray structure determination and Smith Kline and French Research Ltd, Welwyn, for generous support.

## References

1 Preliminary communication, C. J. Moody, C. W. Rees and S. C. Tsoi, *J. Chem. Soc., Chem. Commun.*, 1981, 550.
2 For representative examples see P. A. S. Smith, G. J. W. Breen, M. K. Hajek, and D. V. C. Awang, *J. Org. Chem.*, 1970, **35**, 2215; H. Dounchis, *ibid.*, 1972 **37**, 2583; S.-I. Hayashi, M. Nair, D. J. Houser, and H. Shechter, *Tetrahedron Lett.*, 1979, 2961.
3 P. A. S. Smith and H. Dounchis, *J. Org. Chem.*, 1973, **38**, 2958.
4 P. A. S. Smith and J. G. Wirth, *J. Org. Chem.*, 1968, **33**, 1145.
5 T. L. Gilchrist and D. P. J. Pearson, *J. Chem. Soc., Perkin Trans. 1*, 1976, 1257.
6 G. Kumar, K. Rajagopalan, S. Swaminathan, and K. K. Balasubramanian, *Tetrahedron Lett.*, 1979, 4685.
7 R. V. Hoffman and H. Shechter, *J. Am. Chem. Soc.*, 1971, **93**, 5940; *J. Org. Chem.*, 1974, **39**, 2939.
8 F. Lieb and K. Eiler, *Liebigs Ann. Chem.*, 1972, **761**, 130; F. Povazanec, J. Kovac, and D. Hesek, *Collect. Czech. Chem. Commun.*, 1980, **45**, 150.
9 S. Gronowitz, C. Westerlund, and A.-B. Hörnfeldt, *Acta Chem. Scand., Sect. B*, 1975, **29**, 224.
10 S. Gronowitz, C. Westerlund, and A.-B. Hörnfeldt, *Chem. Scr.*, 1976, **10**, 165.
11 A. J. Poole and F. R. Rose, *J. Chem. Soc. C.*, 1971, 1285.
12 A. Yabe and K. Honda, *Tetrahedron Lett.*, 1975, 1079.
13 H. Nakanishi, A. Yabe, and K. Honda, *J. Chem. Soc., Chem. Commun.*, 1982, 86.
14 M. P. L. Caton, D. H. Jones, R. Slack, S. Squires, and K. R. H. Wooldridge, *J. Med. Chem.*, 1965, **8**, 680.
15 S. Siggia, 'Quantitative Organic Analysis via Functional Groups,' Wiley, New York, 1983, ch. 9.
16 S. Gronowitz, C. Westerlund, and A. B. Hörnfeldt, *Acta Chem. Scand., Sect. B.*, 1976, **30**, 391.
17 For a review see C. J. Moody, *Adv. Heterocycl. Chem.*, 1982, **30**, 1.
18 R. D. Schuetz and W. H. Houff, *J. Am. Chem. Soc.*, 1955, **77**, 1836.
19 R. B. Carlin and M. S. Moores, *J. Am. Chem. Soc.*, 1962, **84**, 4107; P. B. Terent'ev, N. G. Kotova, and A. N. Kost, *Chem. Heterocycl. Compd. (Engl. Transl.)*, 1978, **14**, 534.
20 W. A. Pryor, J. H. Coco, W. H. Daly, and K. N. Houk, *J. Am. Chem. Soc.*, 1974, **96**, 5591.
21 S. Gronowitz, P. Moses, A. B. Hörnfeldt, and R. Hakansson, *Ark. Kemi*, 1961, **17**, 165.
22 W. S. Emerson and T. M. Patrick, *Org. Synth.*, Coll. Vol. 4, 1964, 980.

*Received 7th October* 1983; *Paper* 3/1778