Thermal Decomposition of o-Azidobithienyls

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Thermal decomposition of the six possible o-azidobithienyls (1)—(6) has been investigated as a possible source of the hitherto unknown dithienopyrrole ring system. It was found that the nature and yield of products and the temperature required for decomposition are strongly dependent on the structure of the starting azides. 3-Azido-2,2'-bithienyl (1) and 3-azido-2,3'-bithienyl (2) gave 4H-dithieno[3,2-b; 2',3'-d]pyrrole (7) and 4H-dithieno[2,3-b; 2',3'-d]pyrrole (8), respectively, in very good yields. 4-Azido-3,3'-bithienyl (3) and 4-azido-2',3-bithienyl (4) were relatively stable under the same conditions, but polymeric materials were obtained when the thermal decomposition was performed under more vigorous conditions. By contrast, 2-azido-3,3'-bithienyl (5) and 2-azido-2',3-bithienyl (6) extrude nitrogen at room temperature resulting in ring-opening fragmentation. Thermolyses of 3-azido-2-cyclohex-1-enyl-thiophen (11) and 4-azido-3-cyclohex-1-enylthiophen (12) were also investigated to elucidate the different behavioural patterns exhibited by the 3-azidothienyl derivatives.

A considerable number of fused five-membered heterocycles containing nitrogen have been prepared *via* an intramolecular 1,5-cyclization, initiated by thermal or photochemical decompositions of aryl azides.[1,2]

However, little attention has been devoted to reactions of heteroaryl azides derived from five-membered rings.[3] The few reported examples include [3,2]-fused thienopyrroles,[4] thieno-oxazoles,[5] and thienopyrazoles,[6] which have been prepared by pyrolysis of the appropriate 2-substituted 3-azidothiophens. No report of similar reactions with isomeric 4-substituted 3-azidothiopens or 3-substituted 2-azidothiophens can be found in the literature,[7] perhaps because suitable starting azides were not readily available.

We here report an effort to prepare the series of hitherto unknown dithienopyrroles (I) by thermal decompositions of the o-azidobithienyls (1)—(6), newly available by treatment of o-lithiobithienyls with toluene-p-sulphonyl azide and subsequent fragmentation of the intermediate triazene lithium salts.[8]

Results and Discussion

Our results are summarized in the Scheme. The thermolysis of 3-azido-2,2'-bithienyl (1) in boiling chlorobenzene led to the hitherto unknown 4H-dithieno[3,2-b;2',3'-d]pyrrole (7) in 87% yield.

Under the same conditions, 3-azido-2,3'-bithienyl (2) gave 4H-dithieno[2,3-b;2',3'-d]pyrrole (8) in 88% yield. There was no evidence for the formation of the other possible cyclisation isomer, *i.e.* 4H-dithieno[3,2-b;3',4'-d]pyrrole.

The structures of compounds (7) and (8) followed from their spectra and elemental analyses. In particular the i.r. spectra showed the expected NH stretching vibrations at *ca.* 3 450 cm⁻¹. ¹H N.m.r. spectra recorded in deuteriochloroform showed for compound (7) a characteristic AB system with coupling constant *J* 5.1 Hz, and for compound (8) two superimposed AB systems both having a *J* 5.1 Hz coupling constant. The thermolysis of 4-azido-3,3'-bithienyl (3) did not afford either of the two possible cyclisation products. Compound (3) exhibited little decomposition in boiling chlorobenzene after the same thermolysis time as employed for the azides (1) and (2). Prolonged heating in refluxing chlorobenzene or o-dichlorobenzene brought about complete decomposition of azide (3), but again no recognisable cyclisation products were detected.

Similarly the decomposition of 4-azido-2',3-bithienyl (4) did not result in formation of the desired tricyclic compound.

(1)-(6)   Heat   (I)
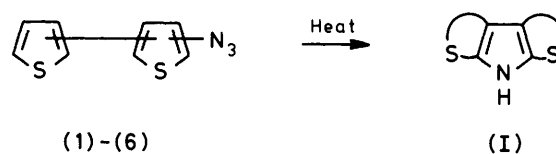
Thermolyses in chlorobenzene or in refluxing o-dichlorobenzene of both azides (3) and (4) gave rise only to polymeric material.

Decomposition of the last two o-azidobithienyls (5) and (6) proceeded with a completely different pattern of behaviour, molecular nitrogen being eliminated smoothly at room temperature without evidence of formation of cyclization products.

The main products isolated from decomposition of the azide (5), after chromatographic separation, were two rather unstable oily compounds (II) and (III) which probably were two m-dithiin isomers (10), arising through a remarkable ring-opening of the azide (5) and subsequent cyclodimerization of the resulting ene-thione (9), according to the outlined sequence:

The mass spectra of the two compounds exhibited similar fragmentation patterns, with the molecular ion at m/z 358 (C₁₆H₁₀N₂S₄⁺) and a predominant fragment ion at m/z 178 (C₈H₄NS₂⁺) indicative of a reverse Diels-Alder process followed by loss of H·.

The i.r. spectra showed a C≡N stretching band at *ca.* 2 230 cm⁻¹. The n.m.r. spectra showed a complex pattern of six protons in the aromatic region constituted of two overlapping ABC systems and a two-proton AB quartet (δ_A 6.78 and 6.83 and δ_B 6.06 and 6.19) for (II) and (III) respectively (*J* 10.5 Hz) ascribable to the ethylenic protons of the m-dithiin ring in addition to another two-proton AB quartet (δ_A 6.67 and 6.33 and δ_B 4.35 and 4.54) (*J* 10.5 Hz) respectively ascribable to an exocyclic ethylene proton and a methine proton.

Finally, although satisfactory elemental analyses could not be obtained for compounds (II) and (III) because of their instability, the values obtained were close to those expected for m-dithiin structures (10). Since these data appear to be consistent with both tautomeric structures (10A) and (10B) (including their geometrical isomers) a definite structure is not assigned to the isomers (II) and (III).

Thermolysis of the azide (6), under the same conditions, gave rise to intractable nitrile-containing materials.

The remarkable instability shown by these azido com-
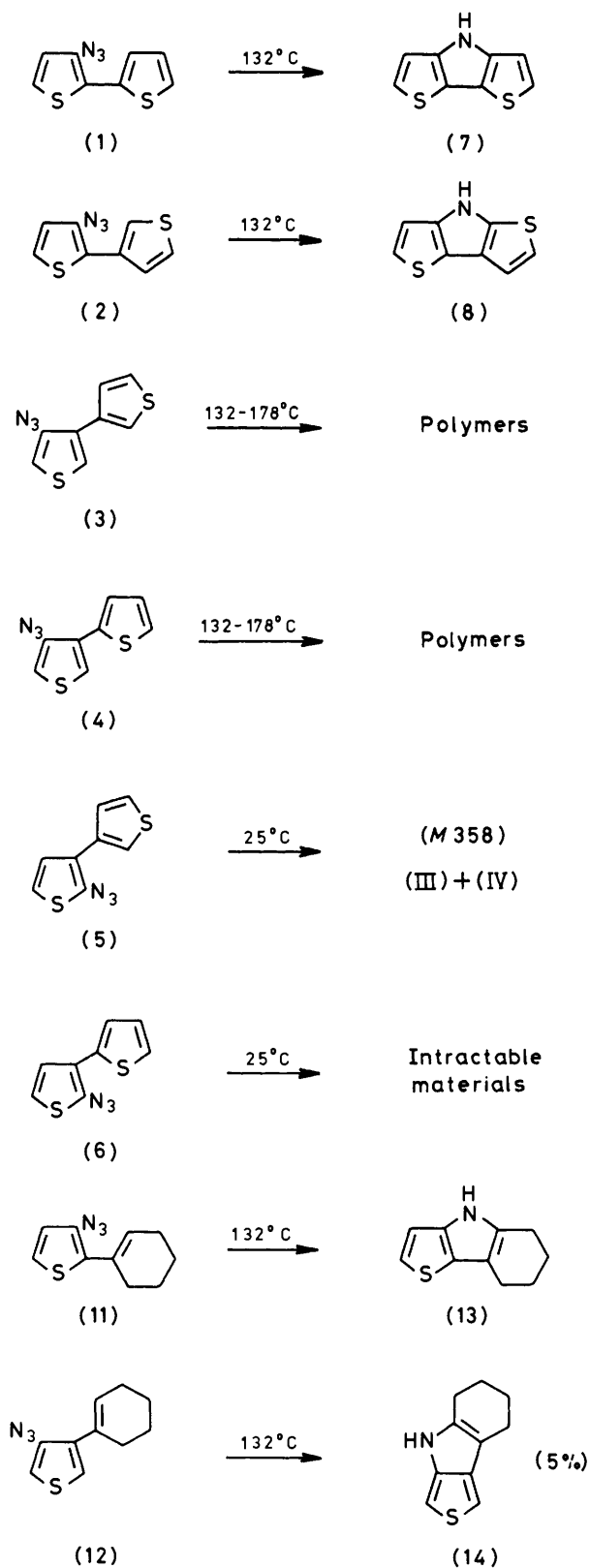
Scheme 1.

From our investigation on thermal decompositions of *o*-azidobithienyls (1) and (6) it may be inferred that these reactions do not offer a general synthetic route to dithieno-pyrroles. Among the six *o*-azidobithienyls two of them, (1) and (2), proved to have the structural and stereoelectronic requirements necessary to pyrolyse to the dithienopyrroles (7) and (8). The results obtained from these decompositions allow no definite conclusion as to whether or not nitrenes are involved in these cyclizations. However the lower thermal stability shown by the azides (1) and (2) compared with (3) and (4) may be related to the predominant π bond positions which for compounds (1) and (2) are close to those of the cyclization products.

Similar arguments have been presented to explain the inefficient cyclization of related 2-azidophenyl heterocycles which cannot follow a low-energy concerted pathway.* In order to find supporting evidence for the different behaviour exhibited by the azides (1) and (2) with respect to the azides (3) and (4), we investigated the thermal decomposition of 3-azido-2-cyclohex-1-enylthiophen (11) and 4-azido-3-cyclo-hex-1-enylthiophen (12). In fact, pyrolysis of related *o*-azidostyrenes are well known reactions characterized by low activation energy and high yield in cyclization products.[12] Compound (11) led, in refluxing chlorobenzene, to 5,6,7,8-tetrahydro-4*H*-thienoindole (13) in good yield, thus confirming the propensity of the 2-substituted 3-azidothiophens to cyclize. Conversely, thermolysis of the azido derivative (12) afforded the cyclic compound (14) in very low yield (5%) accompanied by much tarry material, substantially in line with results obtained from the azides (3) and (4). Compound (14) was found to be somewhat unstable at room temperature, thus suggesting that the very low yield of (14) from thermolysis of the azide (12) might essentially be due to its inability to survive the reaction conditions. The structures of compounds (13) and (14) were supported by spectroscopic data. The i.r. spectra showed NH stretching absorptions at *ca.* 3 480 and 3 450 cm⁻¹, respectively. The n.m.r. spectra showed an aromatic AB pattern [J 5.1 Hz for (13) and 3.2 Hz for (14)] a broad singlet and two multiplets due to 4 + 4 protons in the aliphatic region. The mass spectra showed the molecular ion peak at m/z 177 ($C_{10}H_{11}NS^+$). Further confirmation of the structure (13) was obtained from elemental analyses, while for the unstable compound (14), elemental analysis was not carried out.
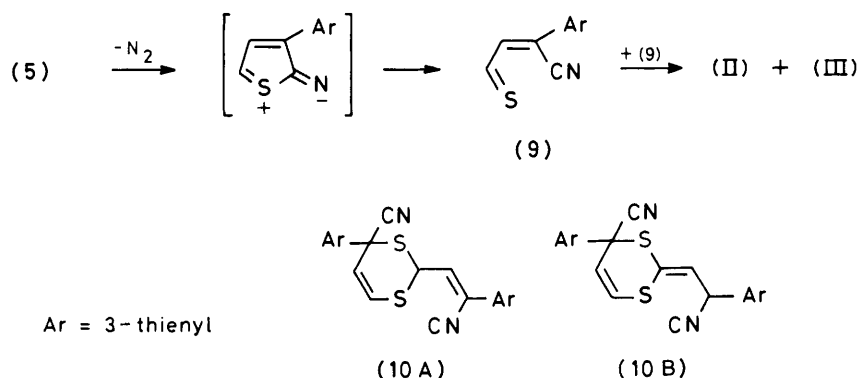
On the basis of results obtained with the azide (12), our failure to observe any [*c*] fused dithienopyrroles from decomposition of azides (3) and (4) might be, in principle, attributable to decomposition of the cyclization products taking place under the reaction conditions.

Experimental

Materials.—2,3-Dibromothiophen,[13] 3-bromo-4-cyclohex-1-enylthiophene,[14] and the azidobithienyls (1)—(6)[8] were prepared as described in the literature. Chlorobenzene and *o*-dichlorobenzene were dried over calcium hydride, distilled, and purged with dry nitrogen. n-Butyl-lithium was obtained from Aldrich-Europe division as a 1.52M-solution in n-hexane.

Spectra.—I.r. spectra were recorded with a Perkin-Elmer grating spectrometer Model 257. Varian EM 360L was used for n.m.r. spectra, using tetramethylsilane as internal standard, and a JEOL DMS 100 instrument was used for mass spectra.

pounds, (5) and (6), is in line with our earlier observation[9] with other 2-azidothiophens and with that recently reported on thermally induced fragmentation of some 2-azidofurans.[10]

* An extensive study of the mechanism of cyclization of 2-nitreno-biphenyls and related systems as source of analogue carbazoles has been reported.[11]

$$(5) \xrightarrow{-N_2} \left[\text{structure} \right] \longrightarrow \text{(9)} \xrightarrow{+ (9)} (II) + (III)$$

Ar = 3-thienyl

(10 A)   (10 B)

Preparation of 3-Bromo-2-cyclohex-1-enylthiophen.—This compound was prepared following ref. 14. An ethereal solution of 2,3-dibromothiophen (24.2 g, 0.1 mol) in dry ether (100 ml) was added dropwise with stirring at −70 °C to n-butyl-lithium (65 ml, 1.52M in n-hexane).*

The reaction mixture was stirred for 40 min at −70 °C, after which an ethereal solution of freshly distilled cyclohexanone (0.11 mol) was rapidly added. The resulting mixture was stirred at −70 °C for 10 min and then overnight at room temperature. The yellow solution was cooled (5 °C) and acidified with 2M-hydrochloric acid. The organic layer was washed with water, saturated sodium carbonate solution, and twice with water, and then dried over Na_2SO_4.

Concentration left the crude carbinol, which was dissolved in benzene (150 ml) and dehydrated by refluxing for 3 h with a catalytic amount of toluene-p-sulphonic acid. The benzene solution was cooled, diluted with diethyl ether, washed with water, dried, and distilled to give 3-bromo-2-cyclohex-1-enylthiophene (22.0 g, 89%), b.p. 105—110 °C/0.5 mmHg (Found: C, 49.55; H, 4.55; Br, 32.85; S, 13.15; M^+, 243. $C_{10}H_{11}BrS$ requires C, 49.40; H, 4.56; Br, 32.87; S, 13.18%; M, 243); δ_H (60 MHz; CDCl$_3$) 6.80 (2 H, q, J 5.5 Hz), 6.05 (1 H, m, vinylic), 2.1 (4 H, m), and 1.65 (4 H, m).

Preparation of 3-Azido-2-cyclohex-1-enylthiophen (11) *and 4-Azido-3-cyclohex-1-enylthiophen* (12).—A solution of the appropriate o-bromocyclohexenylthiophen (12.2 g, 0.05 mol) in dry ether (50 ml) was added dropwise with stirring at −70 °C to a solution of n-butyl-lithium in n-hexane (1.6M; 32 ml). The reaction mixture was stirred for 45 min at −70 °C, after which an ethereal solution of toluene-p-sulphonyl azide (10 g, 0.055 mol) was added dropwise. After the addition was complete, the resulting mixture was stirred for 6 h at −70 °C, and then allowed to warm up. When the temperature had reached −10 °C, the triazene salt formed was rapidly filtered off and washed with dry ether. The solid material was then suspended in ether (150 ml) and treated with a solution of tetrasodium pyrophosphate (13.3 g, 0.05 mol) (200 ml) in water. After the mixture had been stirred overnight at 5 °C the organic layer was separated and the aqueous solution extracted twice with ether. The combined organic layers were washed with water and dried. The solvent was evaporated and the residue chromatographed on a Florisil column with n-pentane as eluant.

3-Azido-2-cyclohex-1-enylthiophen (11) was obtained as a pale yellow oil (6.35 g, 62%), $v_{max.}$ (CS$_2$) 2 090 cm^{-1} (N$_3$); δ_H (60 MHz; CDCl$_3$) 6.70 (2 H, q, J 5.4 Hz), 6.00 (1 H, m),

2.2 (4 H, m), and 1.6 (4 H, m); m/z 205 (M^+, 35%) 177 ($M - 28.40$), and 149(100).

4-Azido-3-cyclohex-1-enylthiophen (12) was obtained as pale yellow oil (6.86 g, 67%), $v_{max.}$ (CS$_2$) 2 080 cm^{-1} (N$_3$); δ_H (60 MHz; CDCl$_3$) 6.80 (2 H, q, J 3.4 Hz), 6.05 (1 H, m), 2.20 (4 H, m), and 1.60 (4 H, m); m/z 205 (M^+, 20%), 177 ($M - 28$, 60), and 149(100).

Thermal Decompositions of Azido Derivatives (1)—(4), (11), *and* (12) *in Chlorobenzene: General Procedure.*—A solution of the azide (0.41 g, 2 mmol) in chlorobenzene (5 ml) was added dropwise with stirring under nitrogen to refluxing chlorobenzene (10 ml). The heating was prolonged until t.l.c. showed no starting material, after which the solvent was distilled off at 1 mmHg and the residue chromatographed on Florisil with n-pentane-diethyl ether as eluant.

Thermolysis of 3-azido-2,2'-bithienyl (1). Reflux was maintained for 30 min; chromatography with 5% diethyl ether in n-pentane gave 4H-dithieno[3,2-b;2',3'-d]pyrrole (7) (0.31 g, 87%), m.p. 167—168 °C (Found: C, 53.6; H, 2.8 and S, 35.75), $v_{max.}$ (CS$_2$) 3 460 cm^{-1} (NH); δ_H (60 MHz; CDCl$_3$) 6.65 and 6.74 (4 H, q, J 5.1 Hz) and 7.2br (1 H, s).

Thermolysis of 3-azido-2',3-bithienyl (2). Reflux was maintained for 25 min; chromatography with 5% diethyl ether in n-pentane gave 4H-dithieno[2,3-b;2',3'-d]pyrrole (8) (0.315 g, 88%), m.p. 124—126 °C (Found: C, 53.55; H, 2.8; S, 35.7%; M^+, 179. $C_8H_5NS_2$ requires C, 53.58; H, 2.81 and S, 35.75%), $v_{max.}$ (CS$_2$) 3 445 cm^{-1} (NH); δ_H (60 MHz, CDCl$_3$) 6.61 and 6.81 (2 H, q, J 5.1 Hz), 6.69 and 6.81 (2 H, q, J 5.1 Hz), and 7.3br (1 H, s).

Thermolysis of 3-azido-2-cyclohex-1-enylthiophene (11). Reflux was maintained for 25 min. Chromatography with 5% diethyl ether in n-pentane gave 5,6,7,8-tetrahydro-4H-thieno[3,2-b]indole (13) (0.32 g, 90%), m.p. 99—100 °C Found: C, 67.7; H, 6.3; S, 18.0%; M^+, 177. $C_{10}H_{11}NS$ requires C, 67.73; H, 6.26 and S, 18.09%; M, 177), $v_{max.}$ (CS$_2$) 3 480 cm^{-1} (NH); δ_H (60 MHz, CDCl$_3$) 7.50br (1 H, s), 6.75 and 6.94 (2 H, q, J 5.1 Hz), 1.82br (4 H, s), and 2.65br (4 H,s).

Thermolysis of 4-Azido-3-cyclohex-1-enylthiophen (12). The azide was held at reflux for 45 min. The solid residue after solvent removal was washed with warm n-pentane-diethyl ether (1 : 1; v/v) to leave a white solid (0.02 g) whose organic solutions began to darken; it had m.p. 125—127 °C, $v_{max.}$ (CS$_2$) 3 460 cm^{-1} (NH); δ_H (60 HMz, CDCl$_3$) 6.80 (1 H, d, J 3.2 Hz), 5.80 (1 H, d, J 3.2 Hz), 2.20 (4 H, m), and 1.65 (4 H, m); m/z 177 (M^+).

Thermal Decomposition of 2-Azido-3,3'-bithienyl (5) *and 2-Azido-2',3-bithienyl* (6) *at Room Temperature.*—A solution of the azide (0.41 g, 2 mmol) in n-pentane (15 ml) was left in the dark until t.l.c. showed no starting azide (3 h). Solvent was

* 2,3-Dibromothiophen undergo halogen–metal exchange with organo-lithium derivatives with regioselective interconversion of the α-bromine.[15]

removed and the residue was chromatographed on a silica column using n-pentane with a gradually increasing amount of diethyl ether.

For compound (5) the following products were obtained in order of elution: (i) trace amount of 3,3'-bithienyl (n-pentane); (ii) a red-orange solid (0.02 g), m.p. 133—135 °C, m/z 326 (M^+, 20%), 325 ($M - 1$, 22%), 146(20), and 46(100) (5% diethyl ether in n-pentane); (iii) a yellow-orange oil (0.15 g) $v_{max.}$ (pure oil) 2 230 cm^{-1} (C≡N), m/z 358 (M^+) and 326 (M^+ -32); an oil (0.15 g) (Found: C, 51.0; H, 2.75; N, 7.35; S, 34.8. $C_{16}H_{10}N_2S_4$ requires C, 53.63; H, 2.79; N, 7.82 and S, 35.75%), $v_{max.}$ (pure oil) 2 230 (conj. CN) cm^{-1}, δ_H (60 MHz, CDCl$_3$) 4.35 (1 H, d, J 10.5 Hz), 6.06 (1 H, d, J 10.5 Hz), 6.67 (1 H, d, J 10.5 Hz), 6.78 (1 H, d, J 10.5 Hz), and 6.80—7.50 (6 H, m), m/z 358 (M^+, 5%), 326 ($M - 32$, 3%), 179(50), 178(100), and 45(80) (5% diethyl ether–n-pentane); (iv) a yellow oil (0.1 g) (Found: C, 52.5; H, 2.5; N, 7.7, S, 34.25. $C_{16}H_{10}N_2S_4$ requires C, 55.63; H, 2.79; N, 7.82 and S, 35.75), $v_{max.}$ (pure oil) 2 230 (conj. CN) cm^{-1}, δ_H (60 MHz, CDCl$_3$) 4.54 (1 H, d, J 10.5 Hz), 6.19 (1 H, d, J 10.5 Hz), 6.33 (1H, d, 10.5 Hz), 6.78 (1 H, d, J 10.5 Hz), and 6.80—7.50 (6 H, m); m/z 358 (M^+, 5%), 326 ($M - 32$, 3%), 179(50), 178(100), and 46(70) (5% diethyl ether in n-pentane).

For compound (6) intractable red-brown nitrile-containing syrups were obtained.

Acknowledgements

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