Conversion of pyrroles into bis-1,2,5-thiadiazoles: a new route to biheterocycles

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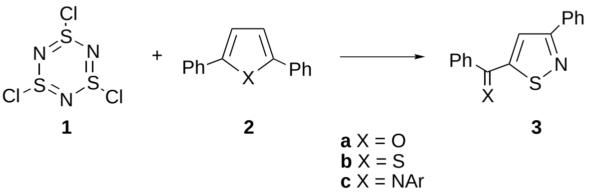
Trithiazyl trichloride 1 converts 1-aryl-2,5-diphenylpyrroles 2c into isothiazole imines 3c, but 1-alkyl-2,5-diphenylpyrroles (*e.g.* 4) react very differently to give the bis-1,2,5-thiadiazole 5 in which two N–S–N units have been fused onto the pyrrole and the alkyl–N unit has been excised, in a new dissection of the pyrrole ring, thus providing a novel route to an aromatic biheterocycle.

There has recently been a marked revival of interest in biheterocyclic systems (known for over a hundred years[1]) since they appear as structural subunits in many natural products and in conducting polymers like polypyrrole and polythiophene, and they have provided a wide range of finely tuned chelating ligands in coordination and organometallic chemistry.[1] The many different biheterocycles reported have been prepared by standard coupling, cyclisation and cycloaddition reactions, together with a few reactions involving the extrusion of sulfur or dinitrogen. We now describe an entirely new and unusually short route to such a system, the bis-1,2,5-thiadiazoles.

We have shown that trithiazyl trichloride **1** reacts with 2,5-diphenylfuran **2a** to give 5-benzoyl-3-phenylisothiazole **3a** regiospecifically and in high yield; 2,5-diphenylthiophene **2b** and **1** gave the same product, by formation and oxidation of the analogous thiobenzoyl compound **3b** (Scheme 1).[2] We have also shown that **1** reacts with 2,3-unsubstituted pyrroles by fusing an N–S–N unit across this bond to give pyrrolo-[1,2,5]thiadiazoles (*e.g.* **7** below), often in high yield.[3]

We now find that 1-aryl-2,5-diphenylpyrroles **2c** react with **1** in the same way as **2a** and **2b** to give the analogous products, the imines **3c**† (Scheme 1), together with the 3,4-dichloropyrroles† reflecting the high reactivity of pyrroles towards electrophilic substitution. However, when the *N*-aryl groups were replaced by alkyl groups a new and unexpected reaction was observed. Thus treatment of 1-methyl-2,5-diphenylpyrrole **4** with trimer **1** (2 equiv.) in refluxing CCl_4 gave a colourless crystalline solid, mp 82–83 °C, with one less carbon and with four nitrogen and two sulfur atoms in its molecular formula ($C_{16}H_{10}N_4S_2$) (45%). Assuming that the MeN unit has been lost and the remaining carbon connectivity retained, the bis-1,2,5-thiadiazole structure **5**† seemed possible. This structure was supported by all the analytical and spectroscopic data and by formation of the same product from 1,4-diphenylbuta-1,3-diyne or (*E*)-1,4-diphenylbut-1-en-3-yne with **1** under the same conditions, in similar yields (43–44%) (Scheme 2).

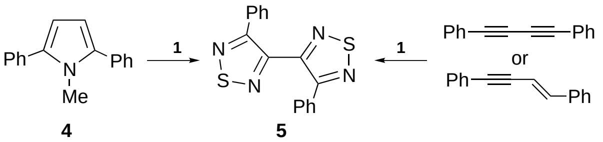
We have explained the formation of 1,2,5-thiadiazoles from such alkenes and alkynes by overall 1,3-cycloaddition of an N–S–N unit in the trimer, followed by loss of the remaining S–N–S unit as $[ClSNSCl]^+ Cl^-$ or $[SNS]^+ Cl^-$.[4] This mechanism is directly applicable to 2,3-unsubstituted pyrroles to give the observed pyrrolothiadiazoles.[3] With *N*-methylpyrrole this process can occur twice *via* an intermediate such as **6**‡ which would rapidly aromatise by elimination of HCl to give the observed product **7** (Scheme 3). The analogous intermediate, **8**,‡ from 1-methyl-2,5-diphenylpyrrole **4** cannot aromatise similarly, but it can do so by loss of two protons from the methyl group which has to be accompanied by cleavage of the *N*–C(α) pyrrole bonds (arrows in **8**) to give the very stable bis-thiadiazole **5** and HCN (Scheme 4).



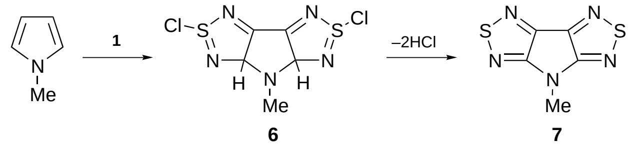
Scheme 1

With the *N*-aryl compounds, the intermediate analogous to **8** cannot aromatise by any such elimination and, if formed at all, would probably be in equilibrium with its precursors; the reaction therefore takes the different pathway described above (Scheme 1). Thus the dominant role of the *N*-substituent, and the extensive rearrangement involved in the conversion of **4** into **5**, whilst initially puzzling, appear to be mechanistically reasonable.

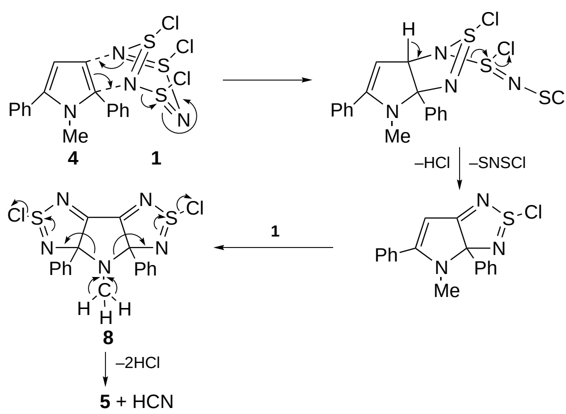
Hydrogen cyanide was shown to be a product of the reaction of trimer **1** with pyrrole **4** by using commercial HCN length-of-stain detector tubes.§ Blank experiments showed that this method was not sensitive to the hydrogen chloride formed in the reaction but that the monomer, NSCl, in thermal equilibrium with the trimer, did interfere if it were not efficiently condensed



Scheme 2



Scheme 3



Scheme 4

out before the exit gases passed through the detector tube. Other *N*-alkyl-2,5-diphenylpyrroles reacted with **1** to give the bis-thiadiazole **5**, accompanied by 3,4-dichlorination of the pyrrole ring. The best yields of **5** were obtained from the *N*-methyl **4** and the *N*-ethyl compounds, and were improved further (to 70%) in the presence of 4 Å molecular sieves. Conversion of 1-ethyl-2,5-diphenylpyrrole into bis-thiadiazole **5** is presumably accompanied by the formation of methyl cyanide (*cf.* **8**), but certainly not HCN, and no colour change was observed in the detector tube for this reaction.

Formation of bis-1,2,5-thiadiazole **5** form *N*-alkylpyrroles and **1** represents a new dissection of the pyrrole ring and provides a novel and short route to an aromatic biheterocycle; very few bis-1,2,5-thiadiazoles have been reported,[5] and hitherto they were not readily available.

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Footnotes and References

† All new compounds have been fully characterised by elemental analysis, spectroscopy and mass spectrometry.

‡ In **6** and **8** the sulfur–chlorine bonds are shown as covalent, but these would be partly ionised, at least, to the thiadiazolium chlorides.

§ Kitagawa HCN length-of-stain detector tubes (Type SB) supplied by Sabre Gas Detection, Unit 1, Blackwater Way, Aldershot, Hampshire.

1 For a comprehensive review, see P. J. Steel, *Adv. Heterocycl. Chem.*, 1996, **67**, 1.

2 X.-L. Duan, C. W. Rees and T.-Y. Yue, *Chem. Commun.*, 1997, 367; X.-L. Duan, R. Perrins and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1997, 1617.

3 X.-G. Duan and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1997, in the press.

4 X.-G. Duan, X.-L. Duan, C. W. Rees and T.-Y. Yue, *J. Chem. Soc., Perkin Trans. 1*, 1997, in the press.

5 J. Sundermeyer and H. W. Roesky, *Chem. Ber.*, 1991, **124**, 1517; S. Mataka, Y. Ikezaki, Y. Shimojo, A. Torii and M. Tashiro, *Chem. Ber.*, 1993, **126**, 2767.

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