

[2 + 2] CYCLOADDITION OF NITROHETEROAROMATICS  
WITH YNAMINES

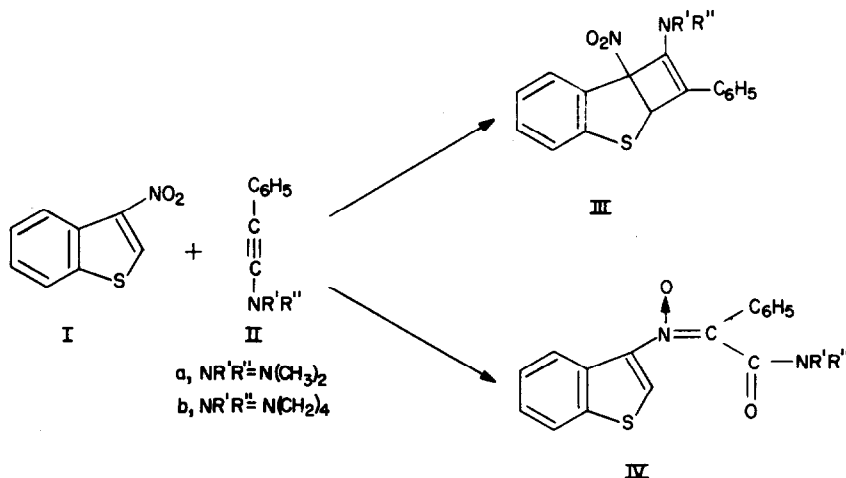
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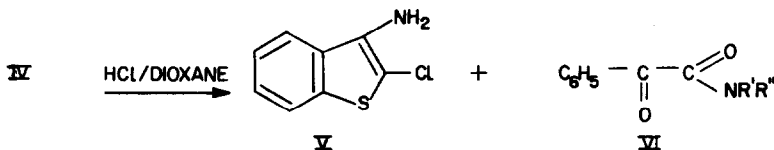
The heteroaromatic  $(4n+2)\pi$ -electron system of thiophenes has long been assumed to be incapable of entering into cycloaddition reactions. Recently we reported on the occurrence of [2 + 2] cycloaddition reactions between thiophenes with enhanced electron density of the ring and electron-deficient acetylenes<sup>1,2</sup>.

To complete the picture, we have now investigated whether starting materials with the opposite characteristics, viz. electron-deficient thiophene derivatives and electron-rich acetylenes, would also give rise to a [2 + 2] cycloaddition.

3-Nitrobenzo[b]thiophene (I) reacted with 1-dimethylamino-2-phenylacetylene (IIa) in diethyl ether at room temperature to give a mixture of two 1:1 adducts, III and IV, which were separated by fractional crystallization in yields of 43 and 26 %, respectively. Product III was identified as the [2 + 2] cycloadduct of I and IIa by PMR, <sup>13</sup>CMR, IR and mass spectrometry<sup>5</sup>. The other reaction product was shown to be the nitrone (IV)<sup>6</sup>. Conclusive

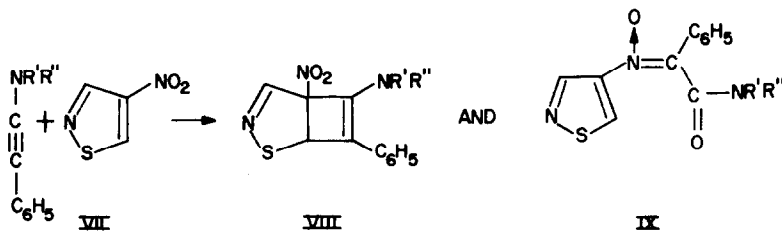


evidence for the nitron structure was provided by spectroscopic data and by the fact that cleavage of the carbon-nitrogen double bond in concentrated hydrochloric acid/dioxane gave 3-amino-2-chlorobenzo[b]thiophene (V)<sup>7</sup> and N,N-dimethyl-2-oxophenylacetamide (VI)<sup>8</sup>.



The latter reaction of IV most probably proceeds via an oxazirine with a nitrenium cation as an intermediate<sup>9</sup>.

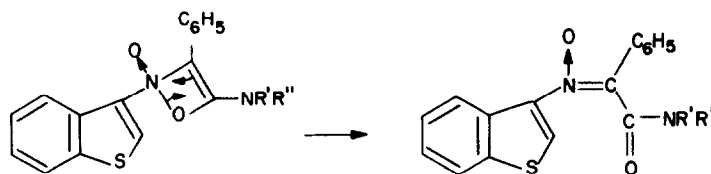
In order to investigate the generality of these reactions we studied the reaction of 4-nitroisothiazole (VII), which also has an S-C=C-NO<sub>2</sub> moiety incorporated in a heteroaromatic (4n+2) $\pi$ -electron system. In diethyl ether again a mixture of a [2+2]cycloadduct (VIII)<sup>10</sup> and a nitron (IX)<sup>11</sup> was obtained, in yields of 14 % and 60 %, respectively. The ratio in which the two products were formed depended on the polarity of the solvent.



In polar solvents such as acetonitrile IX was formed exclusively (68 %), whereas in solvents of low polarity a mixture of VIII and IX was obtained (e.g. in petroleum ether the ratio of VIII/IX was about 1.25). The nitron IX was converted into 4-amino-5-chloroisothiazole and VIb on treatment with concentrated hydrochloric acid/dioxane.

The regioselective character of the cycloaddition - formation of only of the two possible isomers - is entirely consistent with the polarization of the two  $\pi$ -systems.

Of the nitrones IV and IX only one geometrical isomer was obtained and this stereoselectivity might be the results of a [2+2]cycloaddition of the ynamine and an N=O "double bond" followed by subsequent rearrangement. A similar type of reaction was suggested by Ficini and Pouliquen<sup>12</sup> in order to explain the formation of ketene imines from ynamines and isocyanates.



Both the formation of the  $[2+2]$ cycloadducts of I and VII with ynamines and the nitrone formation have no precedent in the literature<sup>13</sup>.

Thus we have demonstrated that part of the  $(4n+2)\pi$ -electron system of thiophene derivatives can be activated by substitution with either a strongly electron-donating or an electron-withdrawing substituent, and can thus be made to enter into  $[2+2]$ cycloaddition reactions with carbon-carbon triple bonds.

#### REFERENCES AND FOOTNOTES

- D.N. Reinhoudt and C.G. Kouwenhoven, *J.C.S. Chem. Comm.* 1972, 1232.
  - D.N. Reinhoudt and C.G. Kouwenhoven, *J.C.S. Chem. Comm.* 1972, 1233.
- Recently  $[4+2]$ cycloadditions of thiophenes at high temperatures<sup>3</sup> and an acid-catalysed  $[2+2]$  cycloaddition of tetramethylthiophene and dicyanoacetylene<sup>4</sup> have also been reported.
- R.Helder and H. Wynberg, *Tetrahedron Letters* 1972, 605.
  - H.J. Kuhn and K. Gollnick, *Tetrahedron Letters* 1972, 1909.
- D.N. Reinhoudt, H.C. Volger, C.G. Kouwenhoven, H. Wynberg and R. Helder, *Tetrahedron Letters* 1972, 5269.
- (IIIa), m.p. 92-95 °C; IR (KBr):  $\nu(\text{C}=\text{C})$  1651  $\text{cm}^{-1}$ ,  $\nu(\text{NO}_2)$  1530 and 1370  $\text{cm}^{-1}$ ; PMR ( $\text{CDCl}_3$ ):  $\delta(\text{H}_1)$  5.23 ppm<sup>1</sup>;  $^{13}\text{CMR}$  ( $\text{CDCl}_3$ ):  $\delta(\text{C}_1)$  54.9 ppm<sup>4</sup>,  $\delta(\text{C}_5)$  99.6 ppm.
- (IVa), m.p. 177-180 °C; IR (KBr):  $\nu(\text{C}=\text{O})$  1632  $\text{cm}^{-1}$ ,  $\nu(\text{N}\rightarrow\text{O})$  1231  $\text{cm}^{-1}$ ;  $^{13}\text{CMR}$  ( $\text{CDCl}_3$ ):  $\delta(\text{C}=\text{O})$  163.1 ppm.
- (V), m.p. 69-71 °C; (KBr):  $\nu(\text{NH}_2)$  3270  $\text{cm}^{-1}$  and 3370  $\text{cm}^{-1}$ ; PMR ( $\text{CDCl}_3$ ):  $\delta(\text{H}_{\text{arom.}})$  7.4 ppm,  $\delta(\text{NH}_2)$  3.7 ppm.
- Compound (VIa) was shown to be identical with the reaction product of 2-oxophenylacetyl chloride and N,N-dimethylamine.

9. P. Lansbury, in "Nitrenes" [Ed. W. Lwowski], Interscience Publishers, New York 1970, p. 405.
10. (VIIIb), m.p. 100-101.5 °C; IR (KBr):  $\nu(\text{C}=\text{C})$  1621  $\text{cm}^{-1}$ ,  $\nu(\text{NO}_2)$  1545 and 1402  $\text{cm}^{-1}$ ; PMR ( $\text{CDCl}_3$ ):  $\delta(\text{H}_4)$  7.78 ppm,  $\delta(\text{H}_1)$  5.09 ppm;  $^{13}\text{CMR}$  ( $\text{CDCl}_3$ ):  $\delta(\text{C}_1)$  56.2  $\text{ppm}^1$ .
11. (IXb), m.p. 185-187 °C; IR (KBr):  $\nu(\text{C}=\text{O})$  1620  $\text{cm}^{-1}$ ,  $\nu(\text{N}\rightarrow\text{O})$  1229  $\text{cm}^{-1}$ ; PMR ( $\text{CDCl}_3$ ):  $\delta(\text{H}_5)$  8.56 ppm,  $\delta(\text{H}_3)$  8.38 ppm;  $^{13}\text{CMR}$  ( $\text{CDCl}_3$ ):  $\delta(\text{C}=\text{O})$  160.8 ppm.
12. J. Ficini and J. Pouliquen, Tetrahedron Letters 1972, 1139.
13. Ficini et al.<sup>14</sup> have reported that reaction of ynamines with disubstituted nitromethanes also give nitrones, but this reaction proceeds via Michael addition of HX ( $\text{X} = \text{R}'\text{R}''\text{CNO}_2$ ) to the triple bond of the ynamine.
14. J. Ficini, A. Bonenfant and C. Barbara, Tetrahedron Letters 1972, 41.