Tetrahedron Letters No. 50, pp 4845 - 4846. 0040-4039/79/1208-4845$02.00/0

THE FIRST 1,3-DIPOLAR ADDITION TO A BENZOTHIOPHENE S-OXIDE

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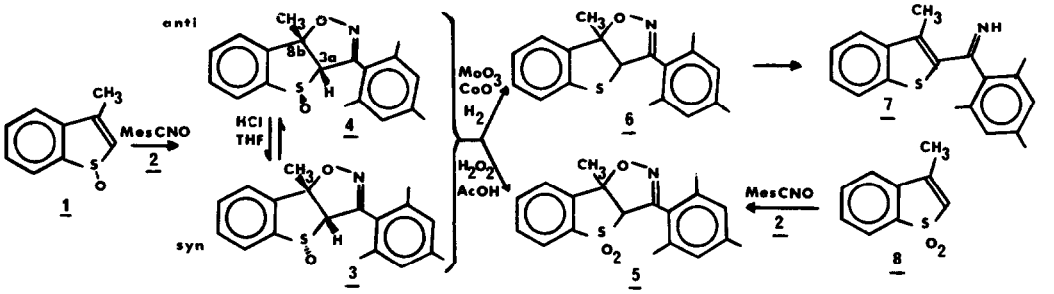
Summary : *New isoxazolines have been obtained by 1,3-dipolar cycloaddition of mesitonitrile oxide on the sulfone and sulfoxide of 3-methyl-benzo{b}thiophene.*

HUISGEN'S work (1) has been followed by numerous studies on the 1,3-dipolar cycloaddition reactions. However, only a few have dealt with the reactivity of the carbon carbon double bond of thiophene or benzo{b}thiophene series (2-8). In the latter series mention was made of the addition of nitrones to the corresponding sulfone and its 3-methyl homolog.

The availability of sulfoxides in this series (9) has led us to compare the influence of the sulfoxide and sulfone functions on the reactivity of the C-C double bond. Since the sulfoxide of benzo{b}thiophene itself cannot be isolated (9), we have studied its 3-methyl homolog.



Addition of mesitonitrile oxide 2 to the sulfoxide 1 (2:1 molar ratio) in refluxing benzene for 30 hours gave a 90% yield of two isomeric sulfoxides (1:1 molar ratio) : syn 3 (mp = 178°C) and anti 4 (mp = 213°C) 3-(2,4,6-trimethyl-phenyl-8b-methyl-{1}benzothieno {2,3-d}isoxazoline ; the remaining 10% was starting material. These two products were separated by preparative TLC on silica using ether/acetone (95/5). Both mass spectrum (m/e = 225) and elemental analysis are in agreement with the molecular formula $C_{19}H_{19}NO_2S$. The syn and anti structures were assigned by comparing ^1H NMR spectra with those obtained in previous cases (9,10). The 3a proton in the anti isomer absorbs at lower field(5.15δ) than in the syn isomer(4.78δ). Refluxing of 3 in THF under acidic conditions converts it into a mixture of 3 and 4 (1:1 molar ratio) as characterised by the two singlets at 5.15 and 4.78δ. The stereochemistry of the addition is cis with no orienting effect of the SO group.

Oxidation of 3 or 4 by hydrogen peroxide in acetic acid gives the sulfone 5 (mp = 223°C) (mass spectrum (m/e = 341) and elemental analysis in agreement with $C_{19}H_{19}NO_3S$).

The NMR results (Table 1) are in agreement with this structure. In addition the sulfone can be obtained by direct addition of the dipole 2 to the sulfone of 3-methylbenzo{b}thiophene 8.

In order to confirm the regioselectivity of the addition, that the oxygen atom of the dipole is linked to the C-3 of the benzo{b}thiophene ring, the mixture of 3 and 4 was hydrogenated in benzene in mild conditions (70°C,10atm) on a $CoO,MoO_3/Al_2O_3$ catalyst (11,12).

The products 6 and 7 were isolated : 6 is the deoxygenated sulfur compound as confirmed by the mass spectrum (m/e = 309), elemental analysis, and the ^1H NMR spectrum ; 7 (m/e = 293) gave an elemental analysis corresponding to $C_{19}H_{19}NS$ with a broad signal (9.10-9.90δ) in NMR, which can be attributed to the proton of a stable imine which could not be hydrolysed under various conditions.

Table 1

Products	8bCH_3(s)	O-CH_3(s)	p-CH_3(s)	3aH(s)	m-H(s)	4H benzo(1)	H imine(1)
3	2.15	2.15	2.31	4.78	6.93	7.5-7.9	
4	1.95	2.38	2.28	5.15	6.94	7.5-7.8	
5	2.07	2.20	2.30	4.93	6.90	7.5-7.9	
6	1.90	2.20	2.27	5.06	6.90	7.1-7.6	
7	2.08	2.18	2.34		6.94	7.2-7.9	9.1-9.9

On the basis of these results it is evident that the reactions are regioselective in accordance with a mechanism in which the intermediate is probably the more stable diradical (13). We are currently examining the additions of 1,3-dipoles to other derivatives in this series with various substituents in order to correlate the observations with theoretical calculations (CNDO/2,EHT).

R E F E R E N C E S

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(Received in France 25 September 1979)