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Benzo[b]thiophene Formation by Thiophenol Addition to Activated Triple Bonds

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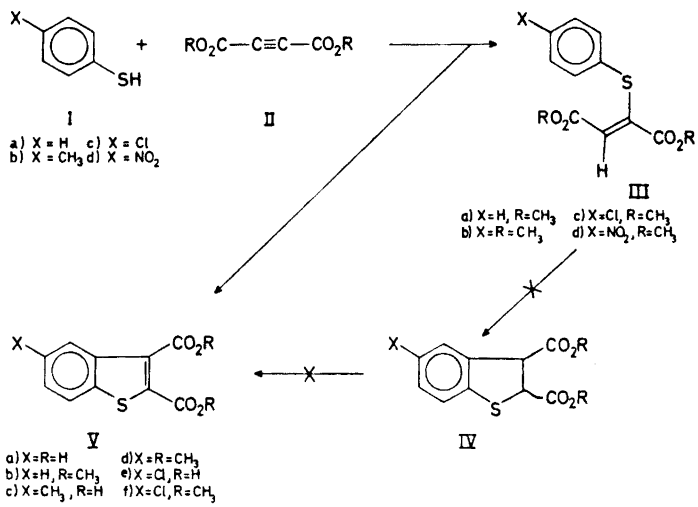
Adduct formation between thiophenols and acetylenedicarboxylic acid and its methyl ester has been studied. Benzo[b]thiophenes were formed in several solvents. In methanol a vinyl thioether was formed either alone or together with the corresponding benzo[b]thiophene depending on the thiophenol substituents. The reaction mechanism has been investigated.

Michael additions of thiophenols to activated triple bonds have been reported to give the corresponding vinyl ethers.[1,2] The rate depends on the electron releasing properties of the substituents.[3] Benzo[b]thiophene is formed in the reaction between acetylene and thiophenol at 500 – 600°C.[4,5] Photochemical cyclisation of a vinyl thioether is possible.[6] Pentafluorothiophenolate will add to acetylenedicarboxylic acid ethyl ester with concomitant cyclisation which involves nucleophilic displacement of a fluorine.[7] On the other hand, thiophenolate and 2-nitrothiophenolate additions to the ethyl ester of acetylenedicarboxylic acid have been reported to yield the respective vinyl thioethers.[2,8] Addition of thiophenol to propiolic acid also gave the vinyl thioether.[1] As an extension of our interest in thiolactam addition to triple bonds [9] we have reinvestigated the reaction between thiophenols and acetylenedicarboxylic acid and its methyl ester. In ethyl acetate the methyl ester of acetylenedicarboxylic acid would add thiophenol and its methyl (Ib) and chloro (Ic) derivatives but not the nitro derivative (Id). Acetylenedicarboxylic acid reacted similarly. The reaction gave the cleanest product when run in the cold over several days. The product was identified as a benzo[b]thiophene (V) as discussed below. In methanol, however, no reaction took place in the cold. On reflux *p*-chloro- and *p*-nitrothiophenol gave the vinyl thioethers III while thiophenol and its *p*-methyl homologue yielded a mixture of the vinyl thioether III and the bicylic product V. The structure of the latter was evident from its spectroscopic properties; only aromatic protons in the NMR spectra and UV maxima in ethanol at about 290 nm, at 245 nm, and at 230 nm. For comparison the UV maxima for the vinyl ether are at about 265 nm and 225



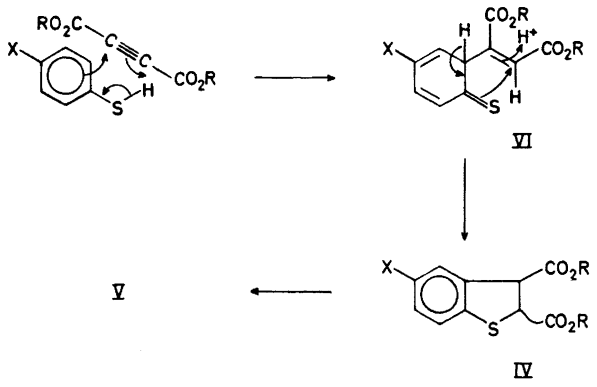
Scheme 1.

nm. In the NMR spectrum of III ($CDCl_3$) the vinyl proton appears as a sharp singlet at 3.5 τ which suggests that only one stereoisomer is present. If the usual *trans* addition is assumed, the carboxy groups in the vinyl thioether have the *trans* configuration.

In a further study of the solvent effect on the reaction between thiophenol and the methyl ester of acetylenedicarboxylic acid, the reaction was run at 35°C for 14 days in the solvents ethyl acetate, dioxane, toluene, and acetic acid. The respective yields of Vb were 29, 14, 18, and 36 %.

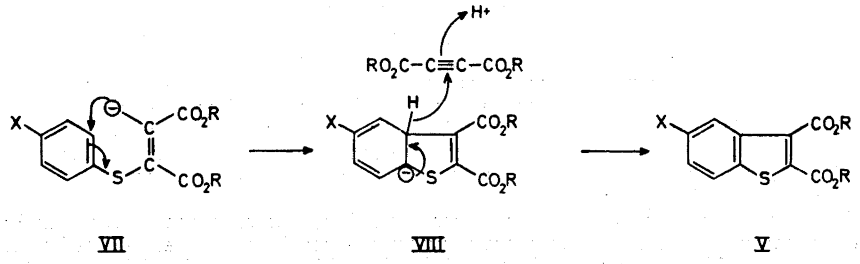
In the initial addition step the mechanism appears to be ionic as the rates and the product yields in ethyl acetate were not noticeably affected when the reaction was run in the presence of benzoyl peroxide or hydroquinone. The direct formation of the benzo[b]thiophene could possibly take place *via* the vinyl thioethers III involving rapid dehydrogenation of an intermediate 1,2-dihydrobenzo[b]thiophene (IV). Both gas chromatographic analysis and slow evaporation in the mass spectrometer of the crude reaction mixture from the reaction in ethyl acetate, showed that methyl acetylenedicarboxylate had been reduced to maleate/fumarate, but no succinate was seen. This establishes the acetylene to be the dehydrogenator. Attemps failed to cyclize IIIb by heating in ethyl acetate or methanol with and without the presence of methyl acetylenedicarboxylate. Neither did any cyclisation of IIIb take place when it was added to the reaction mixture of thiophenol and acetylenedicarboxylate ester, the bicyclic product formed being Vb. The above results exclude the vinyl thioether as an intermediate in the reaction.

A concerted reaction mechanism (Scheme 2) would also involve a 1,2-dihydro derivative (IV). Such a derivative was therefore synthesized by sodium amalgam reduction of Va. The reaction conditions should give the thermodynamically more stable *trans* isomer in good agreement with NMR ($J_{2,3} = 8.0$



Scheme 2.

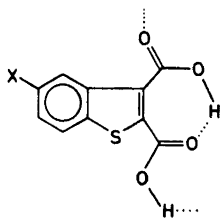
cps). Our attempts failed to dehydrogenate IV by means of acetylenedicarboxylate ester under the above reaction conditions. With the assumption that also the *cis* isomer of IV behaves similarly, a dihydro intermediate is excluded. Involvement of an intermediate carbanion type structure is an alternative possibility, at least in the formation of the bicyclic product (V). Such an anion (VII) with suggested reaction path is indicated in Scheme 3. According to this mechanism both the rate of addition and hydride abstraction are dependent on the electron releasing properties of the *para* substituent.



Scheme 3.

Thus the nitrothiophenol did not react in ethyl acetate and when forced in methanol gave the vinyl ether. On the other hand both thiophenol and its *p*-methyl analogue in methanol yield both products (III and V). These results could be interpreted to mean that hydride abstraction is the rate determining step in the overall reaction. A carbanion intermediate has also been suggested for the addition of pentafluorothiophenolate to ethyl acetylenedicarboxylate where the cyclisation involves nucleophilic displacement of a fluoride ion.[7]

The IR spectra in KBr of the benzo[b]thiophene-2,3-dicarboxylic acids show relatively weak hydroxyl bands around 3500 cm^{-1} and carboxyl bands at 1680 – 1700 cm^{-1}. Similar observations have been made for vicinal di-



Scheme 4.

carboxylic acids of thiophene and furan and are explained by strong inter- and intra-molecular hydrogen bonding.[10,11] Strong carboxyl bands at 1705–1710 cm^{-1} are present in the spectrum recorded in chloroform solution. The dimethyl ester bands are at 1705–1735 cm^{-1}. The dihydro compound IV in KBr has two close carbonyl bands at about 1700 cm^{-1}. These results confirm strong hydrogen bonding as the cause of the relatively weak carbonyl bands in the case of the benzothiophene dicarboxylic acids.

EXPERIMENTAL

Benzo[b]thiophene-2,3-dimethylcarboxylate (Vb). A solution of thiophenol (1.10 g, 0.01 mol) and dimethyl acetylenedicarboxylate (1.42 g, 0.01 mol) in ethyl acetate was left at room temperature for 5 days. The solvent was then evaporated and the oily residue on crystallisation from methanol gave yellow needles (0.40 g, 16 %), m.p. 91°C. (Found: C 57.28; H 4.19; S 12.96. Calc. for $C_{12}H_{10}O_4S$: C 57.58; H 4.03; S 12.76.) UV maxima in 0.1 N HCl (EtOH) at 291 nm (log ε 4.10), 245 nm (4.03) and 229 nm (4.15). NMR in $CDCl_3$: 6.05 τ and 5.97 τ (OCH_3), 1.9–2.7 τ (phenyl H).

5-Methylbenzo[b]thiophene-2,3-dimethylcarboxylate (Vd). The title compound was prepared as above in 44 % yield after leaving the solution for 22 days at room temperature; yellow needles from methanol, m.p. 91°C. (Found: C 58.86; H 4.64; S 12.01. Calc. for $C_{13}H_{12}O_4S$: C 59.06; H 4.58; S 12.13.) UV maxima in 0.1 N HCl (EtOH) at 295 nm (log ε 4.17), 245 nm sh. (4.06) and 234 nm (4.18). NMR in $CDCl_3$: 6.05 and 5.97 τ (OCH_3), 7.52 τ (CH_3), 2.1–2.8 τ (phenyl H).

5-Chlorobenzo[b]thiophene-2,3-dimethylcarboxylate (Vf) was prepared as above in 36 % yield after leaving the solution at room temperature for 17 days; yellow needles from methanol, m.p. 123°C. (Found: C 50.34; H 3.25; S 11.39. Calc. for $C_{12}H_9ClO_4S$: C 50.62; H 3.18; S 11.26.) UV maxima in 0.1 N HCl (EtOH) at 292 nm (log ε 3.96), 245 nm sh. (4.06) and 233 nm (4.18). NMR in $CDCl_3$: 6.05 τ and 5.97 τ (OCH_3), 1.9–2.5 τ (phenyl H).

Benzo[b]thiophene-2,3-dicarboxylic acid (Va) was prepared as above from acetylenedicarboxylic acid. The yellow title compound crystallized out from the solution. After 14 days at room temperature the yield was 32 %; recrystallization from dilute ethanol gave m.p. 245°C. (Found: C 54.09; H 2.91; S 14.14. Calc. for $C_{10}H_6O_4S$: C 54.05; H 2.72; S 14.43.) UV maxima in 0.1 N HCl at 289 nm (log ε 3.94), 245 nm (3.97) and 229 nm (4.07).

5-Methylbenzo[b]thiophene-2,3-dicarboxylic acid (Vc) was prepared as above. The yield after leaving the solution at room temperature for 22 days was 36 %; recrystallization from ethanol gave m.p. 266–267°C. (Found: C 51.98; H 3.94; S 12.59. Calc. for $C_{11}H_8O_4S.H_2O$: C 51.95; H 3.96; S 12.61.) UV maxima in 0.1 N HCl (EtOH) at 292 nm (log ε 3.87), 245 nm sh. (3.87) and 232 nm (4.03).

5-Chlorobenzo[b]thiophene-2,3-dicarboxylic acid (Ve) was prepared as above by heating the solution at 60°C for 1 day. The product crystallized from the cold solution in 54 % yield; m.p. 270–271°C after recrystallization from dilute ethanol. (Found: C 43.85; H 2.59; S 11.89. Calc. for $C_{10}H_5ClO_4S.H_2O$: C 43.71; H 2.57; S 11.67.)

2-(4-Chlorothiophenyl)butenedioic acid dimethyl ester (IIIc). A solution of 4-chlorothiophenol (1.42 g, 0.01 mol) and dimethyl acetylenedicarboxylate (1.42 g, 0.01 mol) in methanol (50 ml) was heated under reflux for 2 h. The product crystallized from the solution on standing in the cold; yield 59 % (1.67 g). Recrystallization from methanol gave yellowish white material, m.p. 88°C. (Found: C 50.51; H 3.87; S 11.05. Calc. for $C_{12}H_{11}ClO_4S$: C 50.25; H 3.87; S 11.18.) UV maxima in 0.1 N HCl (EtOH) at 263 nm (log ε 4.06) and 223 nm (4.20). NMR in TFA: 6.40 τ and 6.05 τ (singlets, OCH_3); 3.47 τ (singlet due to vinyl H); 2.68 τ and 2.59 τ (phenyl H).

2-(4-Nitrothiophenyl)butenedioic acid dimethyl ester (IIId) was prepared as above in 47 % yield by heating the methanol solution for 3 h. Recrystallization from methanol gave yellowish-white material, m.p. 99°C. (Found: C 48.46; H 3.71; S 4.97. Calc. for $C_{12}H_{11}NO_6S$: C 48.48; H 3.73; S 4.73.) UV maxima in 0.1 N HCl (EtOH) at 331 nm (log ε 4.10) and 223 nm (4.20). NMR in TFA: 6.25 τ and 6.00 τ (singlets, OCH_3), 2.95 τ (singlet, vinyl H), 2.35 τ and 1.68 τ (phenyl H).

trans-*2,3-Dihydrobenzo[b]thiophene-2,3-dicarboxylic acid (IV).* 2 % Sodium amalgam (10.7 g) was added gradually over 30 min under vigorous stirring to a solution of benzo[b]-thiophene-2,3-dicarboxylic acid (0.89 g, 0.004 mol) in 1.5 N NaOH (16 ml). The reaction mixture was stirred overnight, the mixture acidified and the precipitated solid recrystallized from water. The yield of a white crystalline material was 79 % (0.70 g), m.p. 193–194°C. (Found: C 53.50; H 3.69; S 14.28. Calc. for $C_{10}H_8O_4S$: C 53.56; H 3.59; S 14.30.) NMR in acetone-d_6: AB-quartet at 5.00 τ and 5.17 τ (H^2, H^3, $J_{2,3}=8.0$ cps). Aromatic H at 2.4–3.0 τ.

REFERENCES

1. Montanari, F. *Tetrahedron Letters* **1960**, No. 4, 18.
2. Kalbag, S. M., Nair, M. D., Rajagopalan, P. and Talaty, C. N. *Tetrahedron* **23** (1964) 1911.
3. Krishnamurthy, G. S. and Miller, S. I. *J. Am. Chem. Soc.* **83** (1961) 3961.
4. Sakan, T., Kotake, H., Fujino, A. and Matsuura, T. *Chem. Abstr.* **46** (1952) 2047b.
5. Lesnaik, T. *Rocz. Chem.* **38** (1964) 1923.
6. Groen, S. H., Kellogg, R. M., Buter, I. and Wynberg, H. *J. Org. Chem.* **33** (1968) 2218.
7. Brooke, G. M. and Quasem, M. A. *J. Chem. Soc.* **C 1967** 865.
8. Ruheman, S. and Stapleton, H. E. *J. Chem. Soc.* **77** (1900) 1179.
9. Lie, R. and Undheim, K. *Acta Chem. Scand. In press.*
10. Oae, S., Furukawa, N., Watanabe, T., Otsuji, Y. and Hamanda, M. *Bull. Chem. Soc. Japan* **38** (1965) 1247.
11. Williams, D. and Rundle, R. E. *J. Am. Chem. Soc.* **86** (1964) 1660.

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