

## Short Communications

Substitution Reactions of  
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Through the recent work by H. C. Brown and his collaborators a quantitative treatment of the directive effects in aromatic substitution of benzene derivatives has been introduced (for review *cf.* Ref.<sup>1</sup>). The selectivity relationship observed by these authors correlated the *para* partial rate factors of a substituted benzene with the *para/meta* ratio. A similar correlation was also found for the *meta* partial rate factors, while for the *ortho* partial factors deviations from linearity, probably due to sterical effects, were noticed although the general relation between reactivity and selectivity could be recognised. Later Brown *et al.*<sup>2</sup> found that the reason for the selectivity relationship was a consequence of the fact that electrophilic aromatic substitution was describable by a linear free-energy relationship of the Hammett type. For the *para* reactivities, however, other substituent constants ( $\sigma^+$ ) had to be used instead of the wellknown Hammett's  $\sigma$ -values applied to side-chain reactivities.

Only scattered data regarding the isomer distribution in electrophilic substitution of monosubstituted thiophenes are available (for review *cf.* Ref.<sup>3</sup>). However, through the development of NMR-spectroscopy and gas-chromatography, a quantitative analysis is now easily performed. Especially NMR-spectroscopy makes determination both of the proportions and the structures of the isomers possible.<sup>4</sup>

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Table 1. Isomer distribution from aromatic substitution of 3-iodothiophene.

| Reaction    | %<br>2,3-isomer | %<br>3,5-isomer |
|-------------|-----------------|-----------------|
| Nitration   | 64              | 36              |
| Acetylation | 83              | 17              |
| Mercuration | 92              | 8               |
| Iodination  | 99.5            | 0.5             |

Table 1 gives results from substitution of 3-iodothiophene. For 3-substituted thiophenes, however, it is obvious that no "*para*" position exists, and the ratio of 2,3- to 3,5-isomer formed, corresponds more to the *ortho/meta* ratio of benzenes. Although the experimental conditions in acetylation, nitration, mercuration, and iodination of thiophenes are somewhat different from those used for the benzene series, the proportion of "*ortho/meta*" isomers formed deviates more than expected from that obtained in the benzene series.

The great selectivity in iodination due to the known low reactivity of iodinating agents might be foreseen. However, in the benzene series mercuration belongs to the reactions which show low selectivity and is also sensitive to steric effects,<sup>5</sup> wherefore the large "*ortho/meta*" ratio obtained in the mercuration of 3-iodothiophene is hardly to be expected. The smaller proportion 3,5-isomer in acetylation than in the nitration might be expected as a result from the Selectivity Relationship, when applied to *para* reactivity. However, in the benzene series Friedel-Crafts acetylations are sensitive to steric effects. It is well known that in the benzene series very little *ortho* isomer is obtained in acetylation in contrast to nitration, so that the *ortho/meta* ratio is much greater for nitration than acetylation.

It is obvious that interesting differences exist between the reactivity and selectivity of electrophilic reagents towards benzenes and thiophenes. We are studying this problem further.

*Experimental. Nitration of 3-iodothiophene.* A mixture of 5.0 g (0.024 mole) of 3-iodothiophene<sup>6</sup> and 10 g acetic anhydride was cooled to  $-10^{\circ}$ , and a mixture of 3.0 g fuming nitric acid in 6.0 g of acetic anhydride was added dropwise with stirring. The mixture was stirred for another 10 min and then poured onto crushed ice. The yellow crystalline product (5.4 g, 89%) was filtered off. No additional product was obtained by extracting the aqueous filtrate with chloroform. NMR-analyses showed the product to contain 64% 3-iodo-2-nitrothiophene and 36% of 3-iodo-5-nitrothiophene. Recrystallisation from acetic acid gave pure 3-iodo-2-nitrothiophene, m.p.  $140-141^{\circ}$  (Lit. value,<sup>7</sup> m.p.  $140-141^{\circ}$ ). NMR-spectrum (acetone) of 3-iodo-2-nitrothiophene:  $\tau_5 = 2.08$  ppm,  $\tau_4 = 2.61$  ppm,  $J_{45} = 5.6$  c/s. NMR-spectrum (acetone) of 3-iodo-5-nitrothiophene  $\tau_{\text{ringhydrogen}} = 1.92$  ppm,  $1.97$  ppm.  $J_{24} = 1.7$  c/s.

*Acetylation of 3-iodothiophene.* 10.0 g (0.048 mole) of 3-iodothiophene, and 4.0 g (0.051 mole) of acetyl chloride were dissolved in 75 ml of dry benzene and 6.0 ml of  $\text{SnCl}_4$  was added dropwise and the mixture stirred for 2 h at  $50-60^{\circ}$ . The reaction mixture was then cooled in ice and decomposed by adding dilute hydrochloric acid. The benzene layer was separated, dried, and the solvent removed *in vacuo* leaving 10.0 g (82%) of a half-crystalline product. NMR-spectral analysis gave 83% of 3-iodo-2-acetylthiophene and 17% of 3-iodo-5-acetylthiophene. Recrystallization from cyclohexane yielded pure 3-iodo-2-acetylthiophene, m.p.  $64-66^{\circ}$ . NMR-spectrum (dimethyl sulphoxide):  $\tau_5 = 2.44$  ppm,  $\tau_4 = 2.95$  ppm,  $J_{45} = 5.0$  c/s. (Found: C 28.96; H 2.11; S 12.69. Calc. for  $\text{C}_6\text{H}_5\text{IOS}$  ((252.1): C 28.59; H 2.00; S 12.69).

NMR-spectrum (dimethyl sulphoxide) of 3-iodo-5-acetylthiophene  $\tau_{\text{ring-hydrogen}} = 2.16$ , ppm,  $2.34$  ppm,  $J_{24} = 1.2$  c/s.

The iodination and mercuration of 3-iodothiophene has already been described.<sup>6</sup>

The NMR-spectra were recorded on a Varian A-60 high resolution spectrometer. The chemical shifts are given as  $\tau$ -values.<sup>8</sup>

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## On the Mechanism of the Michaelis-Arbuzov Rearrangement in Acetonitrile

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Buck and Yoke<sup>1</sup> recently reported that in the two-stage Michaelis-Arbuzov reaction of trialkyl phosphites with alkyl halides in acetonitrile the second step appears to be rate determining. The authors studied the system tri-butyl phosphite and ethyl iodide in acetonitrile at  $31^{\circ}\text{C}$  by a conductometric method. We have studied the same system under the same conditions by measuring the infrared absorption of reactants and products. The acetonitrile was distilled over phosphorus pentoxide before use. After 20.5 h, the infrared spectrum of the reaction mixture showed that the amount of dibutyl ethanephosphonate ( $\text{P}=\text{O}$  band as a doublet at  $1227$  and  $1248\text{ cm}^{-1}$ ) was nearly zero; whereas, according to Buck and Yoke approximately 80% of the tributyl phosphite should have been transformed to phosphonate. When the acetonitrile contained small amounts of water (less than 0.2%) we found that under the experimental conditions specified by Buck and Yoke a rapid autocatalytic transformation