2-METHYL-3-ETHOXYCARBONYL-4-HYDROXYTHIOPHENE IN THE VILSMEIER REACTION

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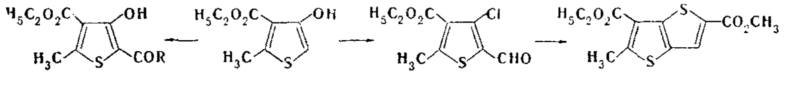
Continuing our investigation of the properties of 2-methyl-3-ethoxycarbonyl-4-hydroxythiophene (I) [1], we found that it readily undergoes electrophilic substitution reactions. We studied the behavior of I under the conditions of the Vilsmeier reaction. The structures of the reaction products depend on the temperature conditions: at 30-35°C, 2-methyl-3-ethoxycarbonyl-4-hydroxy-5-formylthiophene (II) is formed in 74% yield while 2-methyl-3-ethoxycarbonyl-4-chloro-5-formylthiophene (III) is formed in 50% yield at 100°. The reaction of I with dimethylbenzamide and phosphorus oxychloride gives 2-methyl-3-ethoxycarbonyl-4-hydroxy-5-benzoylthiophene (IV) in 41% yield.



II,IV I III V

II R=H; IV R=C_6H_5

Thiophene derivatives II-IV are of considerable interest for the synthesis of condensed heterocycles. The reaction of III with thioglycolic acid ester gives 66% yields of 2-methyl-3-ethoxycarbonyl-5-methoxycarbonyl thieno[3,2-b]thiophene (V), which is one of the difficult-to-obtain thieonothiophenes [2].

The structures of the synthesized substances were confirmed by IR, UV, and PMR spectra. Absorption at 3100-3200 cm^{-1} due to the vibrations of the hydroxyl group is observed in the IR spectra of II and IV. This band is absent in the IR spectrum of chloro derivative III. Two absorption maxima appear in the UV spectrum of III at 220 and 289 nm (log ε 4.09 and 3.99), which is in agreement with the data for similar compounds [3]. The signal of the aldehyde proton in the PMR spectrum of III is situated in the low-field region of the spectrum (δ 10 ppm). The single signal of the aldehyde proton in II is shifted somewhat to stronger field as a consequence of the electron-donor effect of the hydroxyl group (δ 9.9 ppm). The signal of the proton of the hydroxyl group of II at 10.4 ppm is slightly broadened. An absorption band in the long-wave region with λ_{max} 302 nm (log ε 4.40) is observed in the UV spectrum of thieno[3,2-b]thiophene V. A similar pattern in the UV spectrum of thieno[3,2-b]thiophenes has been previously noted [4]. The single signal at 7.8 ppm in the PMR spectrum of thieno[3,2-b]thiophene V can apparently be assigned to the proton in the 6 position of the ring.

EXPERIMENTAL

2-Methyl-3-ethoxycarbonyl-4-hydroxy-5-formylthiophene (II). This compound had mp 132-133° (from methanol). Found: C 50.5; H 4.8; S 15.0%. $C_9H_{10}O_4S$. Calculated: C 50.5; H 4.7; S 14.9%.

2-Methyl-3-ethoxycarbonyl-4-chloro-5-formylthiophene (III). This compound had mp 62-63° (from methanol). Found: C 46.6; H 3.9; Cl 15.3; S 14.0%. $C_9H_9ClO_3S$. Calculated: C 46.5; H 3.9; Cl 15.2; S 13.8%.

2-Methyl-3-ethoxycarbonyl-4-hydroxy-5-benzoylthiophene (IV). This compound had mp 57-58° (from methanol). Found: C 62.1; H 5.0; S 10.9%. $C_{15}H_{14}O_4S$. Calculated: C 62.1; H 4.9; S 11.0%.

2-Methyl-3-ethoxycarbonyl-5-methoxycarbonylthieno[3,2-b]thiophene (V). This compound had mp 100-101° (from methanol). Found: C 50.9; H 4.5; S 22.5%. $C_{12}H_{12}O_4S_2$. Calculated: C 50.7; H 4.3; S 22.6%.

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LITERATURE CITED

1. V. I. Shvedov, V. K. Vasil'eva, and A. N. Grinev, Khim. Geterotsikl. Soedin., 1602 (1970).
2. Ya. L. Gol'dfarb and V. P. Litvinov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 352 (1963).
3. Ya. L. Gol'dfarb, Yu. B. Vol'kenshtein, and B. V. Lopatin, Zh. Obshch. Khim., 34, 969 (1964).
4. V. P. Litvinov and Ya. L. Gol'dfarb, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 2183 (1963).