A NEW METHOD FOR SYNTHESIZING THIENO[3,2-b]PYRROLE DERIVATIVES

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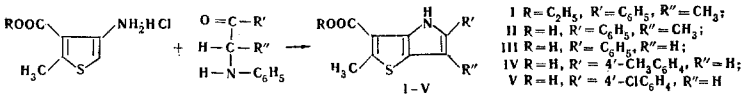
The synthesis of thienopyrroles, isosters of indole, is of interest in connection with the search for biologically active substances. Several representatives of this class of compounds have been obtained recently [1–3]. We have proposed a new method for the synthesis of thieno[3,2-b]pyrrole derivatives under the conditions of the Bishchler reaction that is generally used for the preparation of substituted indoles [4]. Esters of thieno[3,2-b]pyrrole-3-carboxylic acids are formed by heating α-anilinoacetophenones [4] with 3-amino-4-ethoxycarbonyl-5-methylthiophene hydrochloride [5] at 140–160° C for a short time, e. g., 10 min. In those cases where purification of the esters is difficult, they are hydrolyzed without isolation to the thieno[3,2-b]pyrrole-3-carboxylic acids (III–V).



The yield of thieno[3,2-b]pyrrole derivatives amounts to 54–57%, calculated on the 3-amino-4-ethoxycarbonyl-5-methylthiophene hydrochloride. The structure of the compounds obtained is confirmed by their IR, UV, and PMR spectra. The IR spectra of II–V have a strong band at 3490 cm^{-1} due to the vibrations of a NH group. A broad band with a series of smaller peaks in the range from 2700 to 2500 cm^{-1} is caused by the presence of the hydroxyl group of a carboxyl with a strong hydrogen bond. The frequency of the vibrations of the carbonyl groups of II–V is 1685–1665 cm^{-1}. The UV spectra of I–V have two peaks of approximately equal intensity with λ_{max} 295 and 330 nm ($\log \varepsilon$ 4.30 and 4.28) and λ_{min} 255 and 310 nm ($\log \varepsilon$ 3.50 and 4.25), which is in harmony with the characteristics of such systems given previously [2]. In the PMR spectra of III–V there is a single signal at ~6.50 ppm in the region of aromatic protons which can be ascribed to a proton present in position 6 of the thienopyrrole ring. This signal is absent from the spectra of the fully-substituted thieno[3,2-b]pyrroles (I and II). The signals of the protons of the aromatic substituents in the thieno[3,2-b]pyrrole derivatives I–V are located in weaker fields (7.2–7.6 ppm).

Ethyl 2,6-dimethyl-5-phenylthieno[3,2-b]pyrrole-3-carboxylate (I). Mp 81–82° C (from methanol). Found, %: C 68.14, 68.09; H 5.78, 5.83; N 4.59, 4.73; S 10.60, 10.74. Calculated for $C_{17}H_{17}NO_2S$, %: C 68.20; H 5.72; N 4.68; S 10.71.

2,6-Dimethyl-5-phenylthieno[3,2-b]pyrrole-3-carboxylic acid (II). Decomp. p. 256–258° C (dioxane). Found, %: C 66.52, 66.15; H 5.14, 5.06; N 5.38, 5.28; S 11.91, 11.85. Calculated for $C_{15}H_{13}NO_2S$, %: C 66.39; H 4.83; N 5.16; S 11.82.

2-Methyl-5-phenylthieno[3,2-b]pyrrole-3-carboxylic acid (III). Decomp. p. 270–273° C (from dioxane). Found, %: C 65.53, 65.54; H 4.45, 4.46; N 5.39, 5.68; S 12.43; 12.53. Calculated for $C_{14}H_{11}NO_2S$, %: C 65.35; H 4.31; N 5.44; S 12.46.

2-Methyl-5-(4'-methylphenyl)thieno[3,2-b]pyrrole-3-carboxylic acid (IV). Decomp. p. 250–252° C (dioxane). Found, %: C 66.41, 66.00; H 4.67, 5.00; N 5.24, 4.98; S 11.91, 11.82. Calculated for $C_{15}H_{13}NO_2S$, %: C 66.39; H 4.83; N 5.16; S 11.82.

5-(4'-Chlorophenyl)-2-methylthieno[3,2-b]pyrrole-3-carboxylic acid (V). Decomp. p. 270–271° C (dioxane). Found, %: C 57.51, 57.30; H 3.65, 3.60; Cl 12.30, 12.35; N 5.13, 4.72; S 10.64; 10.82. Calculated for $C_{14}H_{10}ClNO_2S$, %: C 57.63; H 3.46; Cl 12.15; N 4.80; S 10.99.

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