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Synthesis of 2-Thiophenecarboxylic and 2,5-Thiophenedicarboxylic Acid Esters via the Reaction of Thiophenes with the CCl_4–ROH Reagent in the Presence of Vanadium, Iron, and Molybdenum Catalysts

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Abstract—2-Thiophenecarboxylic and 2,5-thiohenedicarboxylic acid esters were synthesized via the reaction of thiophene with the CCl_4–ROH–catalyst system, with a total yield of 44–85%. A possible reaction scheme includes the successive steps of alkylation of thiophene with carbon tetrachloride, leading to 2-trichloromethylthiophene, and alcoholysis of the product giving the corresponding 2-thiophenecarboxylate. The best catalysts for this reaction are $VO(acac)_2$, $Fe(acac)_3$, and $Mo(CO)_6$.

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2-Thiophenecarboxylic and 2,5-thiophenedicarboxylic acids and their derivatives find wide application in the synthesis of drugs; optical bleaching agents; dyes for cotton, wool, and manmade fibers; and conducting polymers [1]. Different methods are used for introducing the carboxylic function into the α position of the thiophene molecule. For example, 2-thiophenecarboxylic acid can be synthesized by the carbonation of 2-thienyllithium [2]. Rammsden and Metuchen [3] patented a process for the preparation of 2-thiophenecarboxylic acid ethyl ester via the reaction of 2-thienyl magnesium chloride with the ethyl ester of chlorocarbonic acid.

2-Thiophenecarboxylic acid esters can be synthesized by thiophene carbonylation with palladium complexes in the presence of $Hg(CF_3COO)_2$, which plays the role of a cocatalyst [4, 5].

An interesting method of synthesis of 2-thiophenecarboxylic acid ethyl ester is the reaction of thiophene with CCl_4 in the presence of KOH and ethanol. It is obvious that the desired product is formed in two stages: first, thiophene reacts with carbon tetrachloride to give 2-trichloromethylthiophene, which subsequently undergoes alcoholysis with the formation of 2-thiophenecarboxylic acid ethyl ester in a yield of 19–23 wt % [6].

The aim of this work was to develop a general method for the synthesis of 2-mono and 2,5-thiophenedicarboxylic acid esters via the reaction of thiophene with the CCl_4–ROH reagent in the presence of V-, Fe-, or Mo-containing catalysts. Previously, iron compounds were used for the transformation of thiophene into 2-thiophenecarboxylic acid esters [7].

EXPERIMENTAL

Carbon-13 NMR spectra were recorded on a JEOL FX-90 Q spectrometer operating at a frequency of 22.5 MHz (^{13}C) in $CDCl_3$; chemical shifts are given in ppm with respect to TMS. The mass spectra were recorded on a Finnigan-4021 GC–MS instrument (EI, 70 eV, 200°C, on-column injection). Chromatographic analysis was carried out on a Chrom-5 instrument (a column of 1200 × 3 mm, stationary phase was silicone SE-30 (5%) on a Chromaton N-AW-HMDS (0.125–0.160 mm), using helium as the carrier gas (47 mm/min) with temperature programming from 50 to 250°C at a heating rate of 8°C/min. The elemental (C, H, S) analysis results for the synthesized compounds correlate with theoretically calculated data within the range of a usual error. The concentration of methyl hypochlorite was determined by iodometric titration [8]. The structure of most of the synthesized compounds was confirmed by the identity of their physical properties with those of known authentic samples, as well as by the full agreement of these properties with published data [9–14].

The reactants were commercially available thiophenes: thiophene; 2- and 3-methylthiophenes; 2-ethyl- and 2-acetylthiophenes; and 2-chloro, 2-bromo-, and 2-iodothiophenes, which were preliminary distilled. The alcohols and CCl_4 were purified according to conventional procedures [15].

The compounds of molybdenum [MoO_3, $MoCl_5$, $Mo(CO)_6$], iron [$FeCl_3$, $FeBr_2$, $Fe(OAc)_2$, $Fe(acac)_3$], and vanadium [VCl_4, VCl_5, V_2O_5, $VO(acac)_2$] were dried in a vacuum desiccator before the reaction.

General Procedure of the Thiophene Reaction with a CCl_4–MeOH Catalyst System

A stainless steel autoclave (V = 17 ml) or a glass ampoule (V = 20 ml) (the results of parallel experiments are practically the same) was charged under argon with 0.1 mmol of $Fe(acac)_3$ (or $VO(acac)_2$ or $Mo(CO)_6$], 10 mmol of the reactant thiophene, 20–30 mmol of CCl_4, and 20–40 mmol of alcohol (methanol, ethanol, *n*-propanol, isopropanol); the autoclave was hermetically closed (the ampoule was sealed) and heated at 130–175°C for 3–6 h with continuous stirring. After completion of the reaction, the autoclave (ampoule) was cooled to room temperature and unsealed; and the resultant mixture was filtered through a silica gel bed (1 : 1 hexane–ether blend as the eluent). The solvent was removed, and the residue was distilled in a vacuum.

Methyl 2-thiophenecarboxylate (1a). Yield, 45%; bp 120–121°C/10 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 133.70 (C^2), 133.72 (C^3), 127.11 (C^4), 131.86 (C^5), 161.64 (C=O), 51.22 (CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 142 [M^+] (35), 38 (12), 110 (39), 111 (100), 112 (10), 113 (7), 141 (24). Found, %: C 57.05; H 4.72; S 25.41. Calculated for $C_6H_6O_2S$, %: C 57.11; H 4.79; S 25.41. Literature data: bp 40–44°C/0.5 Pa [9].

Dimethyl 2,5-thiophenedicarboxylate (1b). Yield, 9%; mp 144°C. ^{13}C NMR ($CDCl_3$, δ, ppm): 138.39 (C^2, C^5), 133.61 (C^3, C^4), 162.09 (C=O), 55.37 (CH_3). Mass spectrum, *m*/*z* (I_{rel},%): 200 [M^+] (25), 38 (5), 39 (4), 45 (5), 53 (10), 59 (5), 69 (5), 81 (4), 82 (6), 98 (3), 111 (3), 168 (5), 169 (100), 170 (7), 171 (4), 199 (3). Found, %: C 47.32; H 4.82; S 15.79. Calculated for $C_8H_{10}O_4S$, %: C 47.51; H 4.98; S 15.85. Literature data: mp 145°C [16].

Ethyl 2-thiophenecarboxylate (1c). Yield, 78%; bp 82°C/5 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 133.88 (C^2), 133.07 (C^3), 127.53 (C^4), 132.09 (C^5), 162.02 (C=O), 60.81 (CH_2), 13.99 (CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 156 [M^+] (42), 38 (10), 39 (30), 45 (12), 57 (14), 81 (9), 82 (4), 83 (9), 110 (38), 111 (100), 112 (8), 113 (7), 126 (12), 155 (7). Found, %: C 53.77; H 5.13; S 20.58. $C_7H_8O_2S$. Calculated, %: C 53.82; H 5.16; S 20.52. Literature data: bp 94.5°C/14 Pa [17].

Diethyl 2,5-thiophenedicarboxylate (1d). Yield, 22%; mp 150–151°C. ^{13}C NMR ($CDCl_3$, δ, ppm): 138.92 (C^2, C^5), 133.03 (C^3, C^4), 162.06 (C=O), 60.83 (CH_2), 14.01 (CH_3)). Found, %: C 52.52; H 5.24; S 13.98. Calculated for 13.98. $C_{10}H_{12}O_4S$, %: C 52.61; H 5.299; S 14.05. Literature data: mp 151°C [18].

Propyl 2-thiophenecarboxylate (1e). Yield, 60%; bp 101°C/3 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 133.75 (C^2), 132.87 (C^3), 127.37 (C^4), 131.93 (C^5), 161.85 (C=O), 66.12 (OCH_2), 21.68 (CH_2), 9.92 (CH_3)). Found, %: C 56.32; H 5.79; S 18.75. Calculated for $C_8H_{10}O_2S$, %: C 56.44; H 5.92; S 18.83. Literature data: bp 75°C/0.45 Pa [17].

Isopropyl 2-thiophenecarboxylate (1f). Yield, 92%; bp 68°C/1Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 133.92 (C^2), 133.78 (C^3), 127.37 (C^4), 132.38 (C^5), 160.84 (C=O), 67.88 (OCH), 20.99 (CH_3), 20.89 (CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 170 [M^+] (20), 39 (42), 41 (24), 43 (25), 45 (3), 59 (15), 83 (8), 84 (5), 110 (5), 111 (100), 112 (10), 113 (5), 128 (50), 155 (6). Found, %: C 56.69; H 5.27; S 18.91. Calculated for $C_8H_9O_2S$, %: C 56.78; H 5.36; S 18.95. Literature data: bp 31°C/0.05 Pa [17].

Methyl 5-methyl-2-thiophenecarboxylate (2a). Yield, 49%; bp 95–96°C/10 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 131.36 (C^2), 133.90 (C^3), 125.94 (C^4), 147.43 (C^5), 161.95 (C=O), 51.18 (OCH_3), 14.87 (CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 156 [M^+] (40), 39 (5), 45 (12), 57 (24), 69 (5), 97 (10), 125 (100), 126 (12), 127 (5), 155 (5). Found, %: C 53.79; H 5.11; S 20.57. Calculated for $C_7H_8O_2S$, %: C 53.82; H 5.16; S 20.52. Literature data: bp 77–79°C/5 Pa [10].

Ethyl 5-methyl-2-thiophenecarboxylate (2b). Yield, 67%; bp 87°C/5 Pa. ^{13}C NMR spectrum ($CDCl_3$, δ, ppm): 131.15 (C^2), 133.46 (C^3), 126.13 (C^4), 147.56 (C^5), 60.23 (CH_2), 14.01 (CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 170 [M^+] (35), 29 (5), 39 (3), 45 (7), 53 (15), 69 (3), 70 (2), 96 (3), 97 (10), 124 (8), 125 (100), 126 (15), 127 (8), 141 (8), 142 (30), 155 (5). Found, %: C 56.33; H 5.87; S 18.86. Calculated for $C_8H_{10}O_2S$, %: C 56.44; H 5.92; S 18.35. Literature data: bp 87–89°C/5 Pa [10].

Propyl 5-methyl-2-thiophenecarboxylate (2c). Yield, 75%; bp 74°C/1 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 131.15 (C^2), 133.46 (C^3), 126.13 (C^4), 147.46 (C^5). Found, % C 58.49; H 6.48; S 17.35. Calculated for $C_9H_{12}O_2S$, %: C 58.63; H 6.56; S 17.39. Literature data: bp 87–88°C/5 Pa [10].

Isopropyl 5-methyl-2-thiophenecarboxylate (2d). Yield, 78%; bp 87°C/4 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 131.77 (C^2), 133.33 (C^3), 126.10 (C^4), 147.40 (C^5), 161.66 (C=O), 68.11 (OCH), 20.08 (CH_3), 21.61 (CH_3), 15.36 (CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 184 [M^+] (35), 39 (10), 41 (14), 43 (20), 45 (20), 52 (10), 59 (15), 69 (5), 96 (5), 97 (60), 98 (11), 124 (9), 125 (100), 126 (20), 127 (5), 141 (19), 142 (45), 169 (10), 183 (5). Found, %: C 58.87; H 5.98; S 17.47. Calculated for $C_9H_{11}O_2S$, %: C 58.98; H 6.05; S 17.50. Literature data: bp 87–88°C/5 Pa [10].

Methyl 5-ethyl-2-thiophenecarboxylate (3a). Yield, 64%; bp 119–120°C/10 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 133.84 (C^2), 131.14 (C^3), 126.13 (C^4), 147.20 (C^5), 161.90 (C=O), 51.13 (OCH_3), 29.95 (CH_2), 15.64 (CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 170 [M^+] (60), 39 (17), 41 (7), 45 (17), 51 (7), 53 (6), 57 (5), 58 (4), 59 (5), 65 (10), 65 (5), 67 (9), 69 (10), 70 (8), 71 (6), 77 (10), 78 (7), 95 (5), 96 (10), 97 (6), 111 (17), 124 (10), 127 (12), 139 (71), 154 (7), 155 (100), 156 (8), 169 (7). Found, %: C 56.35; H 5.89; S 18.85. Calculated for $C_8H_{10}O_2S$, %: C 56.44; H 5.92; S 18.35. Literature data: bp 120°C/12 Pa [11].

Methyl 3-methyl-2-thiophenecarboxylate (4a). Yield, 34%; bp 87–88°C/2 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 126.67 (C^2), 145.86 (C^3), 131.33 (C^4), 129.78

(C^5), 162.80 (C=O), 51.23 (OCH_3), 15.46 (CH_3). Mass spectrum, *m/z* (I_{rel}, %): 156 [M^+] (51), 39 (5), 45 (24), 53 (22), 69 (7), 70 (8), 85 (7), 96 (10), 97 (15), 124 (20), 125 (100), 126 (10), 122 (7), 141 (12). Found, %: C 53.71; H 5.13; S 20.45. Calculated for $C_7H_8O_2S$, %: C 53.82; H 5.16; S 20.52.

Methyl 4-methyl-2-thiophenecarboxylate (4b). Yield, 41%; bp 84–85°C/2 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 133.82 (C^2), 135.32 (C^3), 138.09 (C^4), 128.21 (C^5), 162.28 (C=O), 52.02 (OCH_3), 15.08 (CH_2). Mass spectrum, *m/z* (I_{rel}, %): 156 [M^+] (46), 39 (5), 45 (24), 51 (5), 53 (24), 69 (7), 70 (6), 85 (7), 96 (7), 97 (14), 124 (20), 125 (100), 126 (10), 127 (5), 141 (12). Found, %: C 53.77; H 5.08; S 20.55. Calculated for $C_7H_8O_2S$, %: C 53.82; H 5.16; S 20.52.

Dimethyl 3-methyl-2,5-thiophenedicarboxylate (4c). Yield, 25%; mp. 82–83°C. ^{13}C NMR ($CDCl_3$, δ, ppm): 136.56 (C^2), 145.75 (C^3), 135.83 (C^4), 138.39 (C^5), 162.09 (C=O), 162.58 (C=O), 52.37 (OCH_3), 51.95 (OCH_3), 15.81 (CH_3). Mass spectrum, *m/z* (I_{rel}, %): 241 [M^+] (40), 39 (5), 41 (3), 45 (10), 51 (5), 53 (5), 59 (11), 65 (5), 67 (60), 69 (7), 70 (7), 83 (5), 95 (7), 96 (9), 125 (5), 155 (7), 181 (5), 182 (14), 183 (100), 184 (12), 185 (6), 199 (14), 211 (5). Found, %: C 50.35; H 4.68; S 15.05. Calculated for $C_9H_{10}O_4S$, %: C 50.45; H 4.70; S 14.96. Literature data: mp 84°C [12].

Ethyl 3-methyl-2-thiophenecarboxylate (4d). Yield, 32%; bp 87°C/5 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 126.43 (C^2), 147.49 (C^3), 131.60 (C^4), 129.84 (C^5), 162.89 (C=O), 60.55 (CH_2), 14.22 (CH_3). Mass spectrum, *m/z* (I_{rel}, %): 170 [M^+] (20), 38 (5), 39 (7), 45 (30), 51 (7), 53 (40), 69 (8), 70 (7), 85(10), 96 (10), 97 (42), 98 (5), 124 (40), 125 (100), 126 (20), 141 (42), 142 (37), 169 (10). Found, %: C 56.29; H 5.85; S 18.83. Calculated for $C_8H_{10}O_2S$, %: C 56.44; H 5.92; S 18.35. Literature data: bp 84°C/4 Pa [19].

Diethyl 3-methyl-2,5-thiophenedicarboxylate (4e). Yield, 20%; bp 135–136°C/20 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 126.07 (C^2), 147.49 (C^3), 136.19 (C^4), 133.43 (C^5), 161.95 (C=O), 60.49 (CH_2), 60.81 (CH_2), 18.80 (CH_3), 13.89 (CH_3), 15.39 (C^3-CH_3). Mass spectrum, *m/z* (I_{rel}, %): 242 [M^+] (40), 39 (10), 41 (3), 43 (5), 45 (50), 51 (6), 52 (5), 53 (60), 67 (9), 69 (13), 70 (14), 71 (5), 76 (5), 84 (6), 85 (10), 95 (8), 96 (9), 97 (11), 124 (4), 125 (10), 140 (4), 141 (6), 142 (7), 168 (50), 169 (100), 170 (20), 184 (21), 185 (40), 186 (32), 196 (45), 197 (55), 198 (25), 212 (10), 213 (21), 214 (22), 241 (24). Found, %: C 54.45; H 5.68; S 13.21. Calculated for $C_{11}H_{14}O_4S$, %: C 54.52; H 5.82; S 13.23.

Propyl 3-methyl-2-thiophenecarboxylate (4f). Yield, 24%; bp 92°C/4 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 126.78 (C^2), 145.57 (C^3), 131.47 (C^4), 129.65 (C^5), 162.54 (C=O), 66.09 (OCH_2), 21.68 (CH_2), 15.36 (CH_3), 10.02 (CH_3). Found, %: C 58.52; H 6.44; S 17.31. Calculated for $C_9H_{12}O_2S$, %: C 58.63; H 6.56; S 17.39.

Propyl 4-methyl-2-thiophenecarboxylate (4g). Yield, 75%; bp 72°C/1 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 133.36 (C^2), 134.76 (C^3), 138.05 (C^4), 127.70 (C^5), 161.98 (C=O), 65.80 (OCH_2), 21.77 (CH_2), 15.42 (CH_3), 10.12 (CH_3). Found, %: C 58.59; H 6.45; S 17.29. Calculated for $C_9H_{12}O_2S$, %: C 58.63; H 6.56; S 17.39.

Methyl 5-acetyl-2-thiophenecarboxylate (5a). Yield, 85%; bp 127–128°C/1 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 139.36 (C^2), 133.40 (C^3), 131.58 (C^4), 148.43 (C^5), 161.95 (C=O), 52.18 (OCH_3), 190.50 (C=O), 26.87 (CH_3). Mass spectrum, *m/z* (I_{rel}, %): 156 [M^+] (40), 39 (5), 45 (12), 57 (24), 69 (5), 97 (10), 125 (100), 126 (12), 127 (5), 155 (5). Found, %: C 53.79; H 5.11; S 20.57. Calculated for $C_7H_8O_3S$, %: C 53.82; H 5.16; S 20.52.

Methyl 5-chloro-2-thiophenecarboxylate (7a). Yield, 65%; bp 87–88°C/5 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 132.01 (C^2), 133.13 (C^3), 127.17 (C^4), 137.64 (C^5), 161.46 (C=O), 52.21 (OCH_3). Mass spectrum, *m/z* (I_{rel}, %): 176 [M^+] (43), 37 (5), 38 (7), 45 (5), 53 (5), 57 (7), 59 (4), 69 (4), 73 (24), 75 (7), 81 (7), 82 (9), 117 (12), 118 (5), 119 (7), 144 (5), 145 (100), 146 (12), 147 (41), 175 (5). Found, %: C 40.73; H 2.81; Cl 19.98; S 18.09. Calculated for $C_6H_5ClO_2S$, %: C 40.80; H 2.85; Cl 20.07; S 18.15. Literature data: bp 95–97°C/7 Pa [17].

Methyl 5-bromo-2-thiophenecarboxylate (8a). Yield, 77%;mp 87–88°C. ^{13}C NMR ($CDCl_3$, δ, ppm): 134.64 (C^2), 133.61 (C^3), 130.61 (C^4), 120.17 (C^5), 161.46 (C=O), 52.21 (OCH_3). Mass spectrum, *m/z* (I_{rel}, %): 221 [M^+] (12), 37 (10), 38 (17), 45 (10), 53 (4), 57 (10), 59 (5), 69 (5), 76 (14), 77 (33), 117 (10), 119 (9), 141 (4), 161 (10), 163 (10), 188 (9), 189 (98), 190 (19), 191 (100), 192 (10), 193 (7), 219 (10), 220 (45). Found, %: C 32.41; H 2.25; Br 36.17; S 14.35. Calculated for $C_6H_5BrO_2S$, % C 32.59; H 2.28; Br 36.14; S 14.47.

Methyl 5-iodo-2-thiophenecarboxylate (9a). Yield, 24%; mp 88°C. ^{13}C NMR ($CDCl_3$, δ, ppm): 139.32 (C^2), 134.18 (C^3), 137.69 (C^4), 81.99 (C^5), 161.24 (C=O), 52.15 (CH_3). Found, %: C 26.75; H 1.79; I 47.24; S 11.87. Calculated for $C_6H_5IO_2S$, %: C 26.88; H 1.88; I 47.34; S 11.96. Literature data: mp 88–89°C [20].

Ethyl 5-chloro-2-thiophenecarboxylate (7b). Yield, 30%; bp 95°C/1 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 132.05 (C^2), 133.11 (C^3), 127.30 (C^4), 137.42 (C^5), 161.46 (C=O), 61.17 (CH_2), 14.05 (CH_3). Found, %: C 44.18; H 3.62; Cl 18.43; S 16.74. Calculated for $C_7H_7ClO_2S$, %: C 44.09; H 3.70; Cl 18.598; S 16.82. Literature data: bp 75°C/0.3 Pa [14].

Ethyl 5-bromo-2-thiophenecarboxylate (8b). Yield, 55%; bp 120°C/1 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 134.85 (C^2), 133.60 (C^3), 130.63 (C^4), 126.97 (C^5), 161.44 (C=O), 60.49 (CH_2), 13.80 (CH_3). Found, %: C 35.64; H 2.89; Br 34.08; S 13.48. Calculated for $C_7H_7BrO_2S$, %: C 35.76; H 3.00; Br 33.99; S 13.64.

Propyl 5-bromo-2-thiophenecarboxylate (8c). Yield, 63%; bp 98°C/1 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 133.49 (C^2), 132.84 (C^3), 130.89 (C^4), 120.04 (C^5),

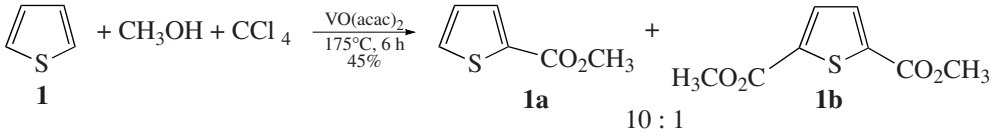
161.20 (C=O), 66.84 (OCH_2), 21.97 (CH_2), 10.28 (CH_3). Found, %: C 38.42; H 3.59; Br 32.12; S 12.68. Calculated for $C_8H_9BrO_2S$, %: C 38.56; H 3.64; Br 32.07; S 12.87.

Isopropyl 5-chloro-2-thiophenecarboxylate acid (7c). Yield, 50%; bp 90–91°C/1 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 132.45 (C^2), 133.13 (C^3), 126.98 (C^4), 137.21 (C^5), 161.52 (C=O), 68.86 (OCH), 21.51 (CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 204 [M^+] (5), 38 (6), 39 (8), 41 (15), 43 (21), 45 (3), 57 (5), 59 (20), 73 (19), 75 (7), 81 (5), 82 (6), 117 (7), 118 (6), 144 (12), 145 (100), 146 (13), 147 (22), 161 (20), 162 (48), 163 (10), 164 (12), 203 (5). Found (%): C 46.84; H 4.31; Cl 17.22; S 15.59. Calculated for $C_8H_9ClO_2S$, %: C 46.94; H 4.43; Cl 17.32; S 15.66.

Isopropyl 5-bromo-2-thiophenecarboxylate (8d). Yield, 52%; bp 95–96°C/1 Pa. ^{13}C NMR ($CDCl_3$, δ, ppm): 135.51 (C^2), 133.45 (C^3), 130.63 (C^4), 119.65 (C^5), 161.45 (C=O), 68.86 (OCH), 21.51 (CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 248 [M^+] (30), 33 (10), 34 (11), 41 (15), 43 (22), 45 (5), 53 (5), 57 (6), 59 (50), 81 (9), 82 (48), 83 (5), 84 (4), 117 (6), 119 (5), 161(4), 163 (5), 188 (5), 189 (70), 190 (15), 191 (70), 192 (7), 205 (11), 206 (100), 207 (12), 208 (95), 209 (5). Found, %: C 38.29; H 3.52; Br 31.89; S 12.81. Calculated for $C_8H_9BrO_2S$, %: C 38.56; H 3.64; Br 32.07; S 12.87.

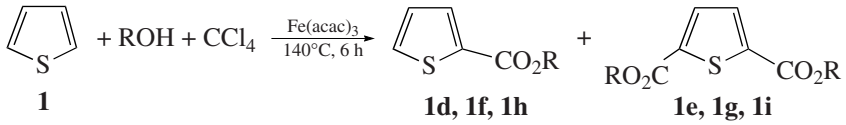
RESULTS AND DISCUSSION

Previously, it was found that iron compounds catalyze the transformation of thiophene and its derivatives into 2-thiophenecarboxylic acid methyl esters in the presence of CCl_4 and CH_3OH [7]. In this work, along with iron compounds, we used vanadium and molybdenum compounds, which have a common ability to activate the C–Cl bond in the CCl_4 molecule [21, 22]. In the variety of vanadium compounds (VCl_4, VCl_5, V_2O_5, $VO(acac)_2$) tested as catalysts, the highest activity was exhibited by vanadyl acetylacetonate. For example, the reaction of thiophene (**1**) with the CH_3OH–CCl_4–$VO(acac)_2$ system (400 : 100 : 1) results in the formation of a mixture of two products: methyl 2-thiophenecarboxylate (**1a**) and dimethyl 2,5-thiophenedicarboxylate (**1b**) with a yield of 45%.



Using the example of thiophene, it was established that iron and molybdenum compounds also catalyze this reaction. Of the test iron ($FeBr_2$, $Fe(OAc)_2$, $FeCl_3$, $Fe(acac)_3$) and molybdenum (MoO_3, $MoCl_5$, $Mo(CO)_6$) compounds, $Fe(acac)_3$ and $Mo(CO)_6$ exhibited the highest activity. Note that this reaction proceeds under severe conditions and, depending on the catalyst nature, occurs at 140, 150, or 175°C in the presence of 140°C ($Fe(acac)_3$), 150°C ($Mo(CO)_6$), or 175°C ($VO(acac)_2$), respectively. The yield of **1a** with the use of $Fe(acac)_3$ and $Mo(CO)_6$ as the catalysts was 44 and 45%, respectively.

Exchanging methanol for ethanol, *n*-propanol, and isopropanol results in the formation of ethyl (**1d**), *n*-propyl (**1e**), and isopropyl (**1f**) esters of 2-thiophenecarboxylic acid, respectively, with significantly higher yields. In addition to **1d, 1f**, and **1h**, the resultant mixture contains small amounts (3–22%) of dialkyl esters of 2,5-thiophenedicarboxylic acid (**1e**, **1g**, **1i**).



R = Me (44%, 9%)

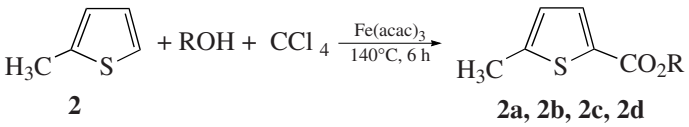
R = Et (1d – 78%, 1e – 22%); *n*-Pr (1f – 60%, 1g – 3%); *i*-Pr (1h – 92%, 1i – 5%)

During this study, the optimal catalyst and reactant concentrations were determined: [catalyst] : [thiophene] : [CH_3OH] : [CCl_4] = 1 : 100 : (200–400) : (100–200). Because of the elevated temperature, the reaction was conducted in a sealed ampoule or a steel microautoclave. Note that the excess methanol should be used. To reduce the consumption of CH_3OH, we practiced its stepwise addition with a fresh portion of the catalyst. However, we failed to substantially reduce the consumption of CH_3OH in this manner, but the stepwise addition of methanol leads to a considerable increase in the yield of the desired product. For exam-

ple, when 25% of the amount of methanol meant for the reaction (containing the corresponding amount of $Fe(acac)_3$) was added to the reaction mixture, the yields of ester **1a** were 25, 36, and 44% after 2, 4, and 6 h, respectively.

The yield of **1a** substantially depends on the catalyst concentration. For example, under typical conditions (175°C, 5 h), the yield of **1a** in the reaction in the presence of $VO(acac)_2$ taken in an amount of 0.1, 0.2, or 1.0 mol % relative to thiophene was 25, 31, or 35%, respectively.

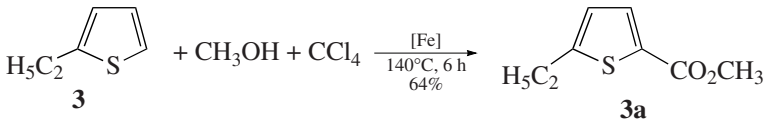
The reaction of 2-methylthiophene (**2**) with the CCl_4–ROH–$Fe(acac)_3$ occurs quite smoothly regardless of the nature of alcohol, in which the ester groups enters into the free α position, and the methyl substituent remains intact.



2 **2a, 2b, 2c, 2d**

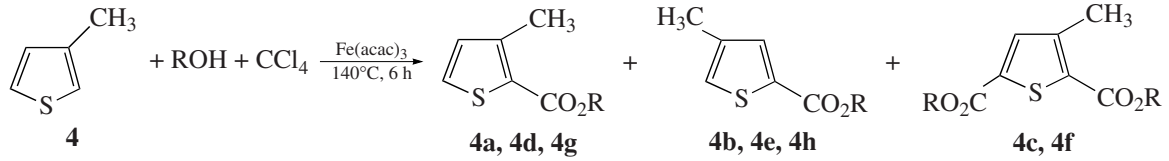
R = Me (2a – 49%); Et (2b – 67%); n-Pr (2c – 75%); i-Pr (2d –78%)

The analogous reaction of 2-ethylthiophene (**3**) with CCl_4–CH_3OH–$Fe(acac)_3$ proceeds with the formation of methyl 5-ethyl-2-thiophenecarboxylate (**3a**).



3 **3a**

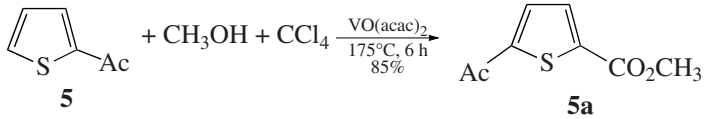
3-Methylthiophene (**4**) reacts quite vigorously with the CCl_4–ROH–$Fe(acac)_3$ 3 system giving a mixture of products of three types (**4(a–h)**). The most interesting among them are dialkyl esters of 3-methyl-2,5-thiophenedicarboxylic acid (**4c**, **4f**), promising monomers for the production of conducting polymers.



4 **4a, 4d, 4g** **4b, 4e, 4h** **4c, 4f**

R = Me (4a – 34%, 4b – 41%, 4c – 25%); Et (4d – 32%, 4e – 7%, 4f – 20%); n-Pr (4g – 24%, 4h – 75%)

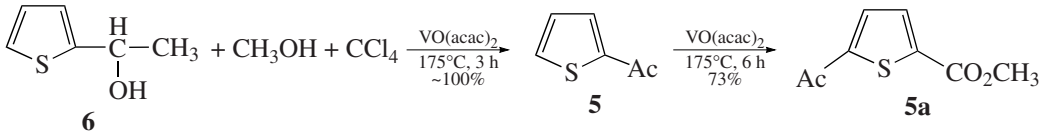
The reaction of thiophene derivatives that bear polar substituents in the 2-position with the CCl_4–CH_3OH–$VO(acac)_2$ system also proceeds regioselectively and results in the introduction of the CO_2CH_3 group into the α position. For example, 2-acetylthiophene (**5**) transforms into methyl 2-acetyl-5-thiophenecarboxylate **5a** with a 85% yield under standard reaction conditions.



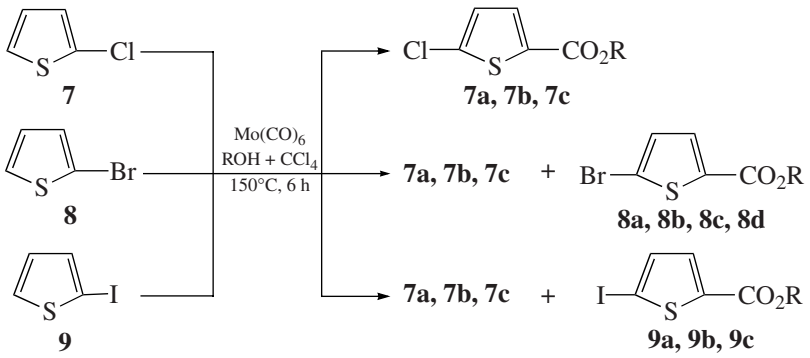
5 **5a**

The reaction of 1-(2-thienyl)ethanol (**6**) with the CH_3OH–CCl_4–$VO(acac)_2$ system proceeds in a peculiar manner. Compound **6** is quickly and quantitatively oxidized to 2-acetylthiophene (**5**); further heating of

the reaction mixture results in the formation of **5a** according to the known scheme, but its yield is lower than in the case of intentionally taken 2-acetylthiophene **5**.



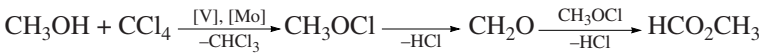
2-Chloro (**7**), 2-bromo- (**8**), and 2-iodothiophenes (**9**) are fairly active in the test reaction. Note that the reaction of 2-chlorothiophene **7** with CCl_4–ROH–$Mo(CO)_6$ proceeds without complications and results in the formation of alkyl esters of 5-chloro-2-thiophenecarboxylic acid **7a**, **7b**, and **7c**; in the case of 2-bromo- and 2-iodothiophenes **8** and **9**, the resultant mixture contains the desired alkyl esters of 5-bromo- and 5-iodo-2-thiophenecarboxylic acids, as well as 5-chloroderivatives **7a**, **7b**, and **7c** that are formed via the side exchange reaction of bromine and iodine for chlorine with the participation of CCl_4.



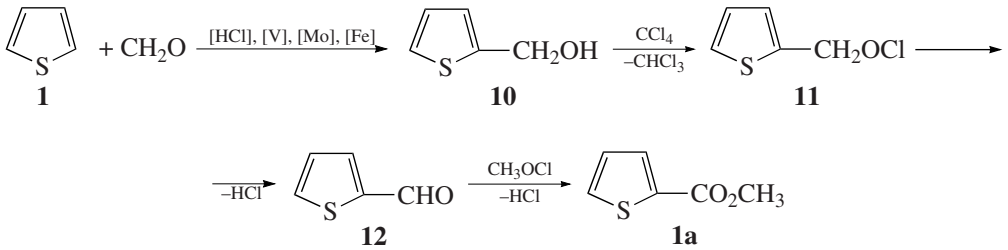
R = Me (7a – 65%, 8a – 77%, 9a –24%); Et (7b – 30%, 8b – 55%); n-Pr (8c – 63%); i-Pr (7c – 50%, 8d – 52%).

Concerning the mechanism of the reaction in question, taking into account the previously established fact that alcohols, in particular, methanol, are oxidized with CCl_4 in the presence of V and Mo complexes [7, 21] yielding successively methyl hypochlorite, formaldehyde, and methyl formate (scheme A), we supposed a reaction scheme that includes thiophene oxymethylation with CH_2O followed by the oxidation of the formed 2-oxymethylthiophene into the final product (scheme B) [7].

Scheme A



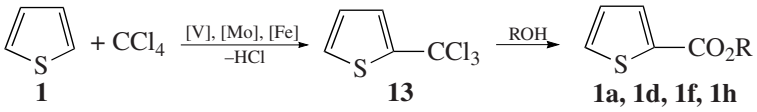
Scheme B



However, this supposition was disproved by the results of the following experiments: first, an attempt to synthesize **1a** via the reaction with intentionally taken CH_2O in the presence of methanol, CCl_4, and $Fe(acac)_3$ failed.

The other assumption that the ester is formed through the steps of thiophene methylation with methanol and subsequent oxidation of the CH_3 to the carboxylic group with methyl hypochlorite was ruled out by the results of the experiments with 2-methylthiophene, since the product of this reaction is methyl 5-methyl-2-thiophenecarboxylate (**2a**).

The only way for producing compound **1a** is the formation of the carboxylic group via the alkylation of thiophene with CCl_4 followed by the alcoholysis of resulting 2-trichloromethylthiophene (**13**) under the reaction conditions.



1 **13** **1a, 1d, 1f, 1h**

Indeed, the experiments with ethanol, *n*-propanol, and isopropanol instead of methanol results in the formation of the corresponding esters of 2-thiophenecarboxylic acid.

Note that the analysis of the reaction mixture by gas chromatography–mass spectrometry did not detect even traces of 2-trichloromethylthiophene **12**, obviously, because of the ease of its alcoholysis [23].

The resulting mixture contained equimolar amounts of $CHCl_3$, HCl, and methyl formate; 3–5% of $CH_2(OCH_3)_2$; and methyl hypochlorite, where the methyl hypochlorite concentration was 2 mg/ml according to iodometric titration data. The presence of these products explains the necessity of using some excess of methanol, which is consumed for the alcoholysis of the trichloromethyl group and is partially oxidized giving CH_3OCl, CH_2O, and HCO_2CH_3. The process of methanol oxidation is accompanied by the release of $CHCl_3$ and HCl.

The experiment evidently suggesting itself on the alkylation of thiophene with CCl_4 in the presence of the given catalysts in the absence of methanol failed. It seems that the success of the reaction depends on the presence of all reagents: CCl_4, CH_3OH, and even HCl that is formed during the course of the reaction and is probably bound in a complex with the catalyst.

In summary, the general method for the preparation of 2-thiophenecarboxylic and 2,5-thiophenedicarboxylic acid esters based on the reaction of thiophenes with the ROH–CCl_4 system in the presence of vanadium-, molybdenum-, and iron-containing catalysts is developed.

ACKNOWLEDGEMENTS

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