New method for preparation of 2,3- and 3,4-thiophenedicarboxylic acids and their 4,5- and 2,5-dihydro analogues

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A method new for preparation of 2,3-thiophenedicarboxylic acid and modified for preparation of 3,4-thiophenedicarboxylic acid using the same starting compounds, *i.e.* methyl thioglycolate and ethyl acrylate, and including selective preparation of methyl 3-oxotetrahydrothiophene-2-carboxylate and methyl 4-oxotetrahydrothiophene-3-carboxylate from methyl 3-thiaadipate has been described. The method can be used also for preparation of the respective dihydro analogues of these acids.

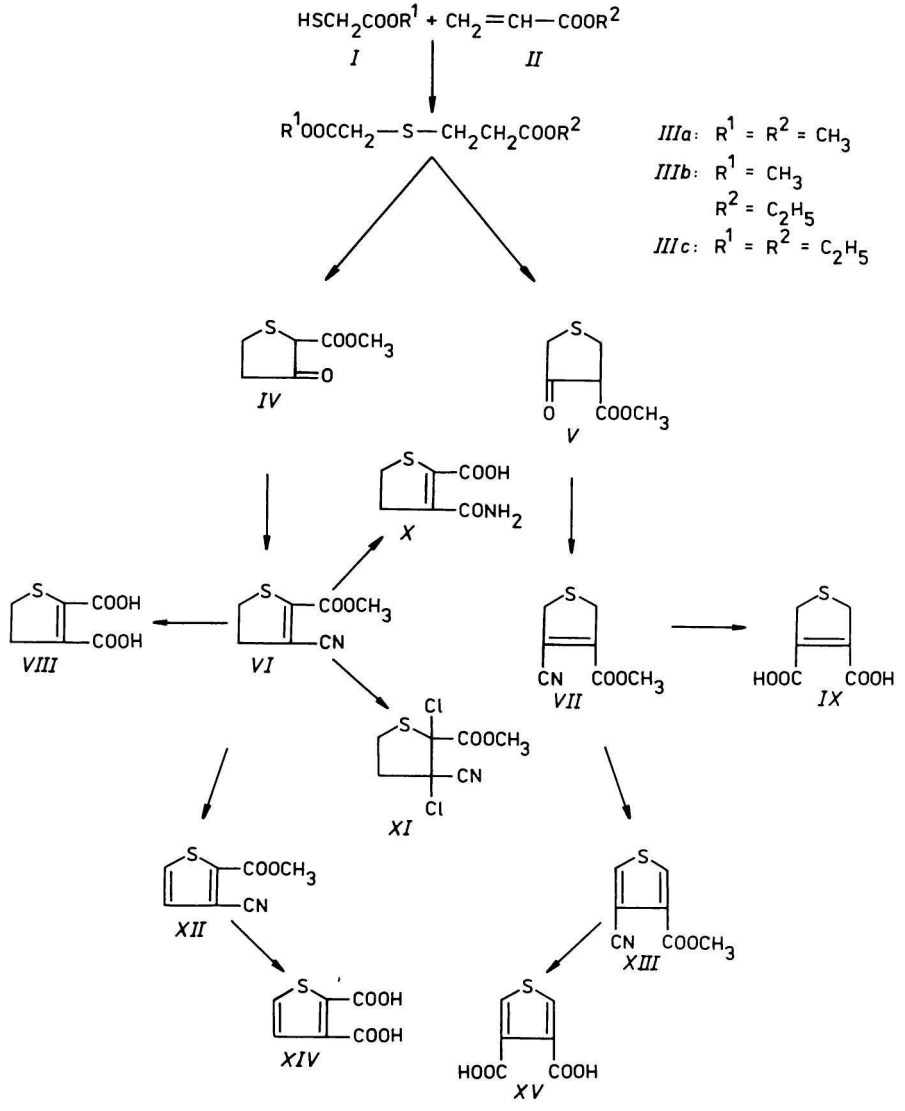
Описан метод, являющийся новым для получения 2,3-тиофендикарбоновой кислоты, и модифицированный для получения 3,4-тиофендикарбоновой кислоты, исходящий из тех же начальных соединений: метилгликолята и этилакрилата и включающий селективное приготовление метил-3-оксотетрагидротиофен-2-карбоксилата и метил-4-оксотетрагидротиофен-3-карбоксилата из метил-3-тиаадипата. Метод может быть также использован для получения соответствующих дигидро-аналогов этих кислот.

2,3-Thiophenedicarboxylic acid was prepared by many-step synthesis from difficultly attainable and expensive 3-methylthiophene [1—9] or 2,3-dibromothiophene [9—13] giving usually low yields. In 1977 a procedure starting from attainable methyl thioglycolate and dimethyl fumarate affording total 24 % yield was published [14].

3,4-Thiophenedicarboxylic acid was prepared for the first time in 1954 from 3,4-diiodothiophene [5]. However, this synthesis has not been practicable because of low yields. In 1968 *Takaya et al.* [15, 16] described a relatively advantageous and practicable synthesis of 3,4-thiophenedicarboxylic acid from ethyl thioglycolate and ethyl acrylate with a total 26 % yield. Recently, this acid has been prepared also in two independent ways from 3,4-dibromothiophene [9, 17].

We have prepared 2,3-thiophenedicarboxylic acid (*XIV*, Scheme 1) by a similar procedure as described by *Takaya et al.* [15, 16] for preparation of 3,4-thiophenedicarboxylic acid. The starting compounds in this reaction were methyl

or ethyl thioglycolate (*I*) and methyl or ethyl acrylate (*II*). These, under catalysis of piperidine, afforded dimethyl, diethyl, and methyl ethyl 3-thiaadipate, respectively (alkoxycarbonylmethyl alkoxycarbonylethyl sulfide) (*III*) in quan-



Scheme 1

titative yield. This may give by Dieckmann cyclization two isomeric products, *i.e.* methyl (ethyl) 3-oxo-2-tetrahydrothiophenecarboxylate (*IV*) and methyl (ethyl) 4-oxo-3-tetrahydrothiophenecarboxylate (*V*). Much attention has been devoted to

preferential formation of one of these isomers in dependence on reaction conditions, however, this problem has not been solved satisfactorily so far [18—26]. *Hromatka et al.* [23] studied the mechanism of this cyclization in detail and explained the relative proportions of the isomers *IV* and *V* in the reaction mixture by operation of a kinetically and thermodynamically controlled reaction. On the basis of this recognition they worked out a method for preparation of the 3,4-isomer (*V*) which, later, has been perfected by simple removal of the accompanying small portion of the 2,3-isomer (*IV*) [27]. In spite of many attempts, the Dieckmann reaction of *III* has not led to formation of the isomer *IV* as the dominant oxo ester. Since successful preparation of 2,3-thiophenedicarboxylic acid from the starting compounds *I* and *II* depended on preparation of the kinetically controlled 2,3-isomer (*IV*), it was necessary to lead the reaction so that preferentially the anion of alkoxycarbonylmethyl group reacted with the carbonyl carbon of the second alkoxycarbonyl group. We have found that when in the Dieckmann reaction dimethyl 3-thiaadipate (*IIIa*, $R^1 = R^2 = CH_3$) was used and the reaction was performed at 0 °C under catalysis of sodium methoxide in methanol, the isomer *IV* dominated in the product obtained in 66 %. Thus, the proportion (%) of *IV* was higher than in the case when the reaction was catalyzed by sodium, sodium amide, *etc.* It was even more advantageous to start from methoxycarbonylmethyl ethoxycarbonylethyl sulfide (*IIIb*, $R^1 = CH_3$, $R^2 = C_2H_5$), prepared from methyl thioglycolate and ethyl acrylate. In this case we obtained 85 % yield, where the compound *V* was present in less than 8 %. The spectral data indicated that the distillation product contained only negligible amount of ethyl esters (< 3 %) of the respective isomers. Similarly, when using ethoxycarbonylmethyl ethoxycarbonylethyl sulfide (*IIIc*, $R^1 = R^2 = C_2H_5$), we achieved 85 % yield, however, the content of ethyl esters of the isomers increased to 15 %. At the same conditions but elevated temperature under reflux in methanol we obtained 50—55 % yield of the product *V* practically in pure state. It is of interest that on crystallization from methanol a pure enol form was obtained (see Experimental, ^1H NMR spectra of the compound *V*), though the literature [26, 27] reported a mixture of oxo-enol forms.

By the reaction of methyl 3-oxo-2-tetrahydrothiophenecarboxylate (*IV*) and methyl 4-oxo-3-tetrahydrothiophenecarboxylate with HCN the respective cyanohydrines were formed in quantitative yield. These were subjected to direct dehydration with $POCl_3$ in pyridine. The formed methyl esters of 3-cyano-4,5-dihydrothiophene-2-carboxylic acid (*VI*) and 4-cyano-2,5-dihydrothiophene-3-carboxylic acid (*VII*) were subjected to aromatization. Aromatization of *VII* with sulfuryl chloride in dichloromethane at 0 °C proceeded quantitatively under formation of methyl 4-cyano-3-thiophenecarboxylate (*XIII*). With the compound *VI*, under the same conditions, addition of chlorine proceeded and the resulting product was methyl 2,3-dichloro-3-cyanotetrahydrothio-

phene-2-carboxylate (*XI*). Therefore, aromatization was carried out with *N*-bromosuccinimide in which case HBr was eliminated from the substitution product immediately to give methyl 3-cyano-2-thiophenecarboxylate (*XII*) in 92 % yield. Similar yield can be obtained by aromatization with bromine. Hydrolysis of methyl 3-cyano-2-thiophenecarboxylate (*XII*) and 4-cyano-3-thiophenecarboxylate (*XIII*) afforded the expected 2,3-thiophenedicarboxylic acid (*XIV*) and 3,4-thiophenedicarboxylic acid, respectively. Similar hydrolysis of 3-cyano-4,5-dihydrothiophene-2-carboxylic acid (*VI*) was unsuccessful because it stopped at the formation of 3-carbamoyl-4,5-dihydrothiophene-2-carboxylic acid (*X*) which precipitated from the solution. Alkali hydrolysis of both *X* and *VI* gave 4,5-dihydrothiophene-2,3-dicarboxylic acid. On the other hand, acid hydrolysis of *VII* and *IX* proceeded smoothly (Scheme 1).

In the procedure presented above, the total yield of *XIV* with regard to the starting methyl thioglycolate represented 40 %. This is more than those obtained by the methods described in the literature, except Ref. [9] (46 %) where the disadvantageous 3-methylthiophene was used as the starting compound and the procedure was much more complicated.

Experimental

Melting points were measured on a Kofler block. Infrared spectra were measured with a Perkin—Elmer 180 spectrophotometer (calibrated with a polystyrene foil), ^{1}H NMR spectra with a Tesla 487 apparatus at 80 MHz (chemical shifts expressed in δ values), and ^{13}C NMR spectra with a Jeol FX-100 spectrometer at 25 MHz.

Methyl thioglycolate was prepared by esterification of thioglycolic acid according to [28]. Methyl and ethyl acrylates were used as commercial products without purification. Dimethyl 3-thiaadipate (*IIIa*) was prepared according to [18] with 95 % yield. Diethyl 3-thiaadipate (*IIIc*) was prepared according to [21]. When ethyl acrylate was used in 5 % excess only with regard to $HSCH_2COOEt$, the yield obtained was 94 %.

Methyl 3-thiaadipate (IIIb)

To the solution of $HSCH_2COOCH_3$ (159 g; 1.50 mol) and piperidine (1.5 cm^3) ethyl acrylate (160 g; 1.60 mol) was added dropwise with stirring at 30—40 °C within a period of 45 min. After 10 min and 20 min further portions of piperidine were added (2 × 1.5 cm^3). The reaction mixture was allowed to stand at room temperature for 20 h, washed with water (50 cm^3), dried (Na_2SO_4), and distilled at 147—148 °C and 1.73 kPa. Yield of the colourless oil = 303 g (98 %). When the reaction time was shortened to 1 h, the yield was only 80 %.

For $C_8H_{14}O_4S$ (M_r = 206.0) w_i(calc.): 46.60 % C, 6.80 % H, 15.56 % S; w_i(found): 46.71 % C, 6.77 % H, 15.72 % S. ^{1}H NMR ($CDCl_3$, TMS) δ/ppm: 1.25 (t, 3H, CH_3), 2.33—3.10 (m, 4H, SCH_2CH_2—), 3.26 (s, 2H, —CH_2S—), 3.75 (s, 3H, $COOCH_3$), 4.16 (q, 2H, CH_2).

Methyl 3-oxotetrahydrothiophene-2-carboxylate (IV)

Sodium (17.3 g; 0.75 mol) was dissolved in absolute methanol (200 cm^3) at cooling, the solution was cooled to 0 °C and *IIIb* (103 g; 0.50 mol) was added dropwise with stirring during 1 h. At first a white suspension was formed which after 45 min turned into a transparent and colourless solution. Stirring was continued at 0 °C for 5 h and the solution was set aside in a refrigerator overnight. The reaction mixture was poured into a mixture of ice (500 g) and concentrated HCl (125 cm^3). The precipitated light-yellow oil was separated, the water layer was extracted with CH_2Cl_2 or $CHCl_3$ (3×200 cm^3), the oil was dissolved in the combined extracts and washed with water (2×300 cm^3), dried (Na_2SO_4), and distilled at 122—124 °C and 2.40 kPa or 80—82 °C at 0.27 kPa. Yield of the colourless oil = 68.2 g (85 %), n(D, 18 °C) = 1.5008. Prolonged reaction time (three days) has not led to increased yield. In the analogous reaction with *IIIc* the yield obtained was 85 % and with *IIIa* only 66 %.

For $C_6H_8O_3S$ ($M_r = 160.0$) w_i(calc.): 44.98 % C, 5.00 % H, 20.03 % S; w_i(found): 44.76 % C, 5.28 % H, 19.75 % S. ^{1}H NMR (CCl_4, TMS) δ/ppm: 3.89 (s, 0.9H, —CH), 3.75, 3.73 (both s, totally 3H, $—CH_3$), 2.50—3.65 (m, 4H). ^{13}C NMR (CCl_4, TMS) δ/ppm: oxo form 207.1 (CO), 169.1 (CO, OCH_3), 53.0 (CH_3), 51.9 (—CH), 38.8, 25.5 (CH_2). IR (CCl_4) $\tilde{\nu}$/cm^{-1}: ν(C=O) 1759.5, 1734.

The reaction performed in ethanol instead of methanol has not led to success. At first, it was necessary to use by a half amount more ethanol so that the ethanolate solution was transparent at 0 °C. However, immediately after addition of the sulfide a white-yellow precipitate was formed. The usual isolation procedure afforded only 11 % of the desired ethyl 3-oxotetrahydrothiophene-2-carboxylate.

Methyl 3-cyano-4,5-dihydrothiophene-2-carboxylate (VI)

To liquid HCN (19 cm^3) and 50 % KOH (0.10 cm^3) cooled in an ice bath the solution of *IV* (35.5 g; 0.22 mol) in methanol (12 cm^3) was added dropwise, keeping the temperature at 10—20 °C. After 15 h standing at 0—5 °C, the mixture was acidified with 85 % H_3PO_4 (0.7 cm^3) and evaporated to dryness *in vacuo* (HCN was captured in a U tube filled with KOH). Crude yellow-red cyanohydrine was obtained in 98—100 % yields. This was dissolved directly in benzene (60 cm^3) and dried with Na_2SO_4. Sodium sulfate was washed with benzene (50 cm^3), the solution of cyanohydrine was diluted with dry pyridine (110 cm^3) and $POCl_3$ (47 cm^3) was added dropwise at occasional cooling with water. The temperature was kept at 40—45 °C till the reaction turned exothermic. The mixture was set aside for 6 h and then poured into a mixture of concentrated HCl (150 cm^3) and ice (300 g). The organic layer was washed successively with diluted HCl (250 cm^3), 3 % NaOH (250 cm^3), and diluted HOAc (250 cm^3, volume ratio $\alpha = 1 : 15$) and distilled at 120—124 °C and 0.13 kPa. Yield of the crude product = 29.6 g (80 %). Recrystallization from the mixture ether—petroleum ether afforded 25.3 g (68 %) of white crystals with m.p. = 53.5—54 °C.

For $C_7H_7NO_2S$ (M_r = 169.0) w_i(calc.): 49.69 % C, 4.14 % H, 8.28 % N, 18.96 % S; w_i(found): 50.07 % C, 4.11 % H, 8.20 % N, 18.83 % S. ^{1}H NMR ($CDCl_3$, TMS) δ/ppm: 3.00—3.58 (m, 4H, CH_2—CH_2), 3.90 (s, 3H, CH_3). IR ($CHCl_3$) $\tilde{\nu}$/cm^{-1}: ν(C=O) 1732, ν(C=C) 1589, ν(C≡N) 2195.

Since it was not necessary to use anhydrous HCN in this reaction, its preparation was simplified considerably: 50 % (by volume) H_2SO_4 was added dropwise to KCN crystals, the vapours evoluted were led to a vertical cooled spiral tube and the liquid was collected in an ice-cooled cylinder (yield about 70 %).

Methyl 3-cyanothiophene-2-carboxylate (XII)

a) Using N-bromosuccinimide

The compound *VI* (16.90 g; 0.1 mol) was dissolved in absolute CCl_4 (250 cm^3) at heating and the solution was allowed to cool down to 30 °C. *N*-Bromosuccinimide (17.8 g; 0.1 mol) and azo-bis-isobutyronitrile (0.20 g) were added and the mixture was heated to the oil bath temperature 75 °C to start a vigorous reaction. The evoluted HBr was led into water and the progress of the reaction was controlled by rate of bubbling. When the reaction was too vigorous, heating was stopped but only for a while so that the reaction continued. After 30 min the mixture was heated to the oil bath temperature 105 °C and the mixture was allowed to react for further 30 min. Then succinimide, being on the surface, was filtered off, and washed with hot CCl_4 (100 cm^3). The filtrate was evaporated to 250 cm^3, allowed to cool down slowly, and set aside in a refrigerator for 1 h. After filtration a white powdery compound (14.40 g) of m.p. = 101—103 °C was obtained. Evaporation of the filtrate afforded a second fraction (1.60 g). Yield = 16.0 g (96 %). Crystallization from the mixture benzene—heptane ($\alpha = 2 : 1$) gave 15.30 g (92 %) of compound of m.p. = 104—105 °C.

For $C_7H_5NO_2S$ ($M_r = 167.0$) w_i(calc.): 50.28 % C, 2.99 % H, 8.38 % N, 19.19 % S; w_i(found): 49.75 % C, 2.90 % H, 8.48 % N, 18.55 % S. ^{1}H NMR ($CDCl_3$, TMS) δ/ppm: 4.00 (s, 3H, CH_3), 7.38 (d, 1H), 7.66 (d, 1H). IR ($CHCl_3$) $\tilde{\nu}$/cm^{-1}: ν(C=O) 1728.5, ν(C≡N) 2215.

b) Using bromine

The compound *VI* (1.69 g; 0.01 mol) was dissolved at heating in absolute CCl_4 (25 cm^3) and the solution was cooled with ice water. The solution of bromine (1.60 g) in CCl_4 (5 cm^3) was added dropwise over a period of 15 min, the mixture was stirred in ice water for 1 h, heated to the water bath temperature and allowed to reflux for 30 min. The solution was evaporated to 15 cm^3 and set aside in a refrigerator overnight. The precipitate was sucked to give the crude product in 1.40 g (83 %) yield. Recrystallization from the mixture benzene—n-heptane ($\alpha = 2 : 1$) gave 1.19 g (71 %) of product of m.p. = 103—105 °C.

2,3-Thiophenedicarboxylic acid (XIV)

The mixture of *XII* (1.67 g; 0.01 mol), CH_3COOH (8 cm^3), and HCl (7 cm^3) was refluxed for 15 h, allowed to cool down and the crystals formed were sucked and dried. Yield of the crude product = 1.40 g (81 %). Crystallization from water gave 1.32 g (76 %) of white needles with m.p. = 284—285 °C (decomposition).

For $C_6H_4O_4S$ ($M_r = 172.0$) w_i(calc.): 41.86 % C, 2.33 % H, 18.64 % S; w_i(found): 41.75 % C, 2.29 % H, 18.79 % S. ^{1}H NMR (DMSO, HDMSO) δ/ppm: 7.40 (d, 1H, CH), 7.78 (d, 1H, CH), 11.35 (s, 2H, OH).

Hydrolysis performed under similar conditions in 10 % H_2SO_4 gave 1.35 g (79 %) of the brown crude product which on crystallization afforded only low yield. Hydrolysis in 10 % NaOH did not lead to higher yield, on the contrary, the isolation was lengthy and the product was less pure.

4,5-Dihydrothiophene-2,3-dicarboxylic acid (VIII)

The compound *VI* (1.69 g; 0.01 mol) was refluxed for 1 h in the solution of NaOH (0.80 g; 0.02 mol) in water (7.2 cm^3), cooled in ice water and acidified with diluted HCl ($\alpha = 1 : 1$) to pH = 1. The mixture was set aside in a refrigerator for 2 h, the precipitate was filtered off, washed with a small amount of cold water, and recrystallized from water. Yield = 0.69 g (40 %) of yellow needles with m.p. = 208—209 °C (Ref. [29] gives m.p. = 196—198 °C).

For $C_6H_6O_4S$ ($M_r = 174.0$) w_i(calc.): 41.38 % C, 3.45 % H, 18.43 % S; w_i(found): 41.21 % C, 3.52 % H, 18.85 % S. ^{1}H NMR ($(CD_3)_2CO$, HDMSO) δ/ppm: 7.58 (s, 2H, OH), 2.75—3.63 (m, 4H, CH_2).

3-Carbamoyl-4,5-dihydrothiophene-2-carboxylic acid (X)

The mixture of *VI* (1.0 g; 0.006 mol), CH_3COOH (3 cm^3), and concentrated HCl (5 cm^3) was refluxed for 1 h, then heated at the oil bath temperature 110 °C for 2 h and allowed to stand at room temperature for three days. The obtained white crystals were sucked, washed with a small amount of cold water, and dried. Yield = 0.73 g (72 %); m.p. = 218—219 °C.

For $C_6H_7NO_3S$ ($M_r = 173.0$) w_i(calc.): 41.60 % C, 4.04 % H, 8.09 % N, 18.53 % S; w_i(found): 41.42 % C, 3.95 % H, 7.85 % N, 18.64 % S. ^{1}H NMR (DMSO, HDMSO) δ/ppm: 8.28 (d, 2H, NH_2), 2.83—3.50 (m, 4H, CH_2).

When reflux was prolonged to 20 h, the mixture became dark continuously and the crystalline compound, precipitating within few minutes, afforded on dissolution pasty products.

Methyl 2,3-dichloro-3-cyanotetrahydrothiophene-2-carboxylate (XI)

To the solution of *VI* (1.69 g; 0.01 mol) in CH_2Cl_2 (10 cm^3) SO_2Cl_2 (0.90 cm^3; 0.011 mol) was added over a period of 10 min at 0 °C and the solution was stirred for 1 h at this temperature. The reaction mixture was washed with 10 % Na_2CO_3 (6 cm^3) and water (3×10 cm^3). The organic layer was dried (Na_2SO_4), CH_2Cl_2 was evaporated *in vacuo* and the residue was crystallized from ether. Yield = 2.17 g (91 %) of colourless crystals with m.p. = 107—108 °C.

For $C_7H_7Cl_2NO_2S$ ($M_r = 240.0$) w_i(calc.): 35.00 % C, 2.92 % H, 29.54 % Cl, 5.83 % N, 13.36 % S; w_i(found): 35.34 % C, 2.73 % H, 29.67 % Cl, 5.43 % N, 13.29 % S. ^{1}H NMR ($CDCl_3$, TMS) δ/ppm: 3.96 (s, 3H, CH_3), 2.75—3.55 (m, 4H, CH_2).

Methyl 4-oxotetrahydrothiophene-3-carboxylate (V)

This compound was prepared by combined procedures described in [23] and [27].

To the boiling solution of Na (64.7 g; 2.81 mol) in absolute methanol (470 cm^3) dimethyl

3-thiaadipate (*IIIa*) (180 g; 0.94 mol) was added dropwise over a period of 10 min and it was refluxed for 30 min and cooled to room temperature. The reaction mixture was poured into the mixture of crushed ice (600 g) and water (300 cm^3), stirred for 15 min, and acidified with concentrated HCl (235 cm^3). The precipitated oil was separated, the water layer was extracted with CH_2Cl_2 (3×200 cm^3), the combined organic phases were washed with saturated $NaHCO_3$ solution (2×200 cm^3), dried (Na_2SO_4), and CH_2Cl_2 was distilled off. The residue was distilled at 84—86 °C and 0.13 kPa or 124—126 °C and 2.27 kPa. Yield = 80 g (53 %) of the yellowish oil which solidified in the trap directly. Crystallization from methanol resulted in a pure product of m.p. = 36—37 °C.

For $C_6H_8O_3S$ ($M_r = 160.0$) w_i(calc.): 44.98 % C, 5.00 % H, 20.03 % S; w_i(found): 44.67 % C, 5.00 % H, 19.53 % S. ^{1}H NMR ($CDCl_3$, TMS) δ/ppm: 3.80 (s, 7H), 10.94 (s, 1H, OH). ^{1}H NMR (CCl_4, TMS) δ/ppm: 3.75 (s, 3H, $COOCH_3$), 3.79 (s, 4H), 10.90 (s, 1H, OH). ^{13}C NMR (CCl_4, TMS) δ/ppm: 172.5 (=C—OH), 169.6 (COO), 99.2 (=C<), 51.7 (CH_3), 36.1 (CH_2), 31.5 (CH_2). IR (CCl_4) $\tilde{\nu}$/cm^{-1}: ν(C=O) 1761, 1742.5, ν(C=C) 1674.5.

When *IIIb* or *IIIc* was used instead of *IIIa*, the yields obtained were similar (50—55 %). The product obtained on distillation contained a negligible amount of ethyl ester, the product crystallized was a pure methyl ester.

In the analogous reaction with *IIIc* performed in ethanol a white salt was formed during the reaction and the mixture became very dense. The usual way of isolation afforded only 19 % of the product.

Methyl 4-cyano-2,5-dihydrothiophene-3-carboxylate (VII)

This reaction step was accomplished according to [21] with a yield similar as given in the literature.

For $C_7H_7NO_2S$ ($M_r = 169.0$) w_i(calc.): 49.69 % C, 4.14 % H, 8.28 % N, 18.96 % S; w_i(found): 50.04 % C, 4.13 % H, 8.33 % N, 18.48 % S. ^{1}H NMR ($CDCl_3$, TMS) δ/ppm: 3.88 (s, 3H, $COOCH_3$), 4.09 (s, 4H). IR ($CHCl_3$) $\tilde{\nu}$/cm^{-1}: ν(C=O) 1729.5, ν(C=O) 1638, ν(C≡N) 2210.

Methyl 4-cyanothiophene-3-carboxylate (XIII)

To the stirred, ice-cooled solution (0—5 °C) of *VII* (16.90 g; 0.1 mol) in CH_2Cl_2 (100 cm^3) sulfuryl chloride (9.0 cm^3; 0.11 mol) was added over a period of 45 min, then it was stirred at 0 °C for 2 h. The reaction mixture was washed with 10 % Na_2CO_3 (100 cm^3) and water (3×100 cm^3). The organic layer was separated, dried (Na_2SO_4), CH_2Cl_2 was distilled off *in vacuo* and the crude product was crystallized from ether. Yield = 15.25 g (91 %) of white crystalline compound with m.p. = 97 °C.

For $C_7H_5NO_2S$ (M_r = 167.0) w_i(calc.): 50.28 % C, 2.99 % H, 8.38 % N, 19.19 % S; w_i(found): 50.54 % C, 2.88 % H, 8.35 % N, 18.91 % S. ^{1}H NMR ($CDCl_3$, TMS) δ/ppm: 3.96 (s, 3H, $COOCH_3$), 8.01 (d, 1H), 8.20 (d, 1H). IR ($CHCl_3$) $\tilde{\nu}$/cm^{-1}: ν(C=O) 1732, ν(C≡N) 2215.

3,4-Thiophenedicarboxylic acid (XV)

A. The mixture of *XIII* (9.0 g; 0.053 mol), CH_3COOH (75 cm^3), and concentrated HCl (50 cm^3) was refluxed for 22 h. Then the solvent was evaporated *in vacuo* to dryness, the

residue was extracted with hot acetone, NH_4Cl was filtered off and the filtrate was evaporated again. Crystallization from water gave 7.0 g (76 %) of colourless needles with m.p. = 230—232 °C.

B. The mixture of *XIII* (1.0 g; 0.006 mol), CH_3COOH (5 cm^3), and concentrated HCl (4 cm^3) was refluxed for 15 h, then it was allowed to stand at room temperature for three days and the precipitate was sucked. Crude product 0.93 g (91 %). Recrystallization from water gave 0.82 g (80 %) of colourless needles with m.p. = 231—233 °C.

For $C_6H_4O_4S$ ($M_r = 172.0$) w_i(calc.): 41.86 % C, 2.33 % H, 18.64 % S; w_i(found): 41.70 % C, 2.30 % H, 18.52 % S. ^{1}H NMR ($(CD_3)_2CO$, HDMSO) δ/ppm: 8.45 (s, 2H, CH), 7.13 (s, 2H, OH).

2,5-Dihydrothiophene-3,4-dicarboxylic acid (IX)

The compound *IX* was prepared according to [22] with 75 % yield (Ref. [22] gives 77 %).

For $C_6H_6O_4S$ ($M_r = 174.0$) w_i(calc.): 41.38 % C, 3.45 % H, 18.43 % S; w_i(found): 41.56 % C, 3.41 % H, 18.56 % S. ^{1}H NMR ($(CD_3)_2CO$, HDMSO) δ/ppm: 10.23 (s, 2H, OH), 4.03 (s, 4H, CH_2).

This compound was prepared also by the following way which gave lower yield but a product of very high purity:

The compound *VII* (5 g), CH_3COOH (15 cm^3), and concentrated HCl (25 cm^3) were refluxed for 16 h, the mixture was diluted with water to 200 cm^3, purified with charcoal, saturated with NaCl, and extracted with ethyl acetate (3×50 cm^3). The extracts were dried with Na_2SO_4, evaporated *in vacuo* and the residue was crystallized from the mixture acetone—benzene. Yield = 3.20 g (62 %) of white crystals with m.p. = 184—185 °C (Ref. [22] gives m.p. = 183—184 °C).

References

1. Linstead, R. P., Noble, E. G., and Wright, J. M., *J. Chem. Soc. 1937*, 911.
2. Hartough, H. D. and Conley, L. G., *J. Amer. Chem. Soc. 69*, 3096 (1947).
3. Gaertner, R. D., *J. Amer. Chem. Soc. 72*, 4326 (1950).
4. Baker, B. R., Schaub, R. E., Joseph, J. P., McEvoy, F. J., and Williams, J. H., *J. Org. Chem. 18*, 133 (1953).
5. Sicé, J., *J. Org. Chem. 19*, 70 (1954).
6. Loiwal, S. D. and Jain, N. C., *J. Indian Chem. Soc. 1*, 119 (1963).
7. Torikov, D. M., Bikulov, A. Z., Khlestkin, R. N., and Anikin, N. S., *Sb. Tr., Ufim. Neft. Inst. 9*, 157 (1971). (Referativnyi Zhurnal *Khimiya* 15N 137 (1972).)
8. Torikov, D. M., Bikulov, A. Z., Varfolomeev, D. F., Kukovitskii, M. M., Markelov, V. N., Kolodii, M., and Denisenko, H. A., *Nauch. Temat. Sb. Tr., Ufim. Neft. Inst. 22*, 120 (1975). (Referativnyi Zhurnal *Khimiya* 2Zh 224 (1977).)
9. Tserng, K. Y. and Bauer, L., *J. Org. Chem. 40*, 172 (1975).
10. Gronowitz, S. and Dahlgren, K., *Ark. Kemi 21*, 201 (1963).
11. Slocum, D. W. and Gierer, P. L., *J. Org. Chem. 41*, 3668 (1976).
12. Reinecke, M. G., Newson, J. G., and Almqvist, K. A., *Synthesis 4*, 327 (1980).
13. MacDowell, D. W. and Ballas, F. L., *J. Org. Chem. 42*, 3717 (1977).
14. Binder, D. and Stanetty, P., *Synthesis 1977*, 200.

15. Takaya, T., Kosaka, S., Otsuji, Y., and Imoto, E., *Bull. Chem. Soc. Jap. 41,* 2086 (1968).
16. Takaya, T., Hijikata, S., and Imoto, E., *Bull. Chem. Soc. Jap. 41,* 2532 (1968).
17. MacDowell, D. W. and Wissowaty, J. C., *J. Org. Chem. 37,* 1712 (1972).
18. Woodward, R. and Eastman, R. H., *J. Amer. Chem. Soc. 66,* 849 (1944).
19. Woodward, R. and Eastman, R. H., *J. Amer. Chem. Soc. 68,* 2229 (1946).
20. Moore, E. E. and Moore, M. B., *J. Amer. Chem. Soc. 68,* 910 (1946).
21. Gronowitz, S., Gestblom, B., and Mathiasson, B., *Ark. Kemi 20,* 407 (1963).
22. Baker, B. R., Querry, M. V., and Kadish, A. F., *J. Org. Chem. 13,* 123 (1948).
23. Hromatka, O., Binder, D., and Eichinger, K., *Monatsh. Chem. 105,* 1164 (1974).
24. Gianturco, M. A., Friedel, P., and Gianmarino, A. S., *Tetrahedron 20,* 1763 (1964).
25. Yamada, Y., Ishii, T., Kimura, M., and Hosaka, K., *Tetrahedron Lett. 22,* 1353 (1981).
26. Liu, H. J. and Ngooi, T. K., *Can. J. Chem. 60,* 437 (1982).
27. Rossy, P. A., Hoffmann, W., and Müller, N., *J. Org. Chem. 45,* 617 (1980).
28. Baker, B. R., Querry, M. V., Safir, S. R., and Bernstein, S., *J. Org. Chem. 12,* 138 (1947).
29. Korte, F. and Büchel, K. H., *Chem. Ber. 93,* 1021 (1960).

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