An improved procedure for the synthesis of 3,4-ethylenedioxythiophene

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An improved procedure for the synthesis of 3,4-ethylenedioxythiophene is reported starting from ethyl chloroacetate. Reaction with sodium sulfide gave diethyl thiodiglycolate which was then reacted with diethyl oxalate, and then 1,2-dibromoethane to give 2,5-dicarbethoxy-3,4-ethylenedioxythiophene. Hydrolysis, and decarboxylation gave 3,4-ethylenedioxythiophene in 16% overall yield. The structures of the key intermediates in synthetic routes were confirmed, and every step was optimised, to give a procedure suitable for large-scale industrial production.

Keywords: 3,4-ethylenedioxythiophene, ethyl chloroacetate, diethyl thiodiglycolate, diethyl oxalate, decarboxylation

Poly (3,4-ethylenedioxythiophene) (PEDOT) is one of the most promising polymers because of its high electrical conductivity, high thermal stability and transparency in the oxidized state.[1–3] PEDOT is widely used although its annual production is limited to the several-ton scale because of the high production cost and the complicated synthetic technology to prepare 3,4-ethylenedioxythiophene (EDOT) (**6**), the monomer of PEDOT.[4,5] Thus, much attention has been paid to improving the synthesis of EDOT.

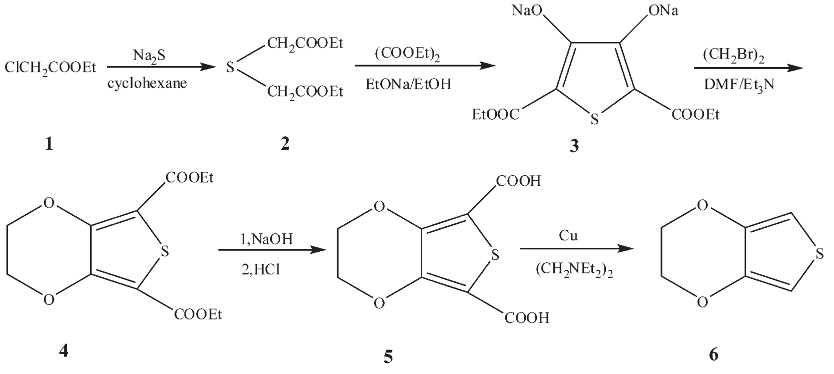
Conventional five-step method of synthesising EDOT was reported by Stenger in 1998.[6] In this technology, EDOT was synthesised from 2,2′-thiodiacetic acid via esterification with ethanol, reaction with diethyl oxalate using sodium ethanolate/ethanol, followed by reaction with 1,2-dibromoethane to obtain 2,5-dicarbethoxy-3,4-ethylenedioxythiophene (**4**). Hydrolysis by aqueous sodium hydroxide, acidified by aqueous hydrochloric acid, and decarboxylation with Cu as a catalyst in a high boiling organic solvents gave EDOT. Although this process is established, the route is long and gives a low yield of the product. In addition, the separations and purification of the intermediates is also difficult. Another two-step reaction method for the synthesis of EDOT was reported by Fredrik and his colleagues in 2004.[7] Firstly, 2,3-dimethoxybuta-1,3-diene reacted with SCl_2 to give 3,4-dimethoxythiophene, which was reacted with ethane-1,2-diol to give EDOT. However, this route for synthesising EDOT was far from industrialisation. Firstly, the starting material was very expensive and SCl_2 used in this method must be purified before the experiment. The intermediate 3,4-dimethoxythiophene was very unstable, and must be preserved under an inert gas and at low temperatures. Finally, column chromatography was needed in the purification of the product, which was difficult for large-scale production in industry.

Therefore, the five-step reaction scheme (Scheme 1) was developed to synthesise EDOT in the light of the above discussion. The conventional five-step reaction scheme suffers from several major drawbacks from an industrial point of view, including the hydrolysis of ethyl chloroacetate (**1**) in aqueous sodium sulfide, the dependence on a high temperature and the use of high boiling organic solvents, leading to low yield of EDOT. The synthetic routes to several important intermediates has been improved and optimised based on the classical five-step method. Every step has been modified to be simpler and the procedure is more suitable for large-scale production.

Previously, diethyl thiodiglycolate (**2**) was synthesised by esterification of 2,2′-thiodiacetic acid with ethanol.[8] However, the raw material (2,2′-thiodiacetic acid) has a relatively high price, and the esterification is also a reversible reaction leading to a low yield. Another method of synthesising **2** is from a derivative of 2,2′-thiodiacetic acid, such as 2,2′-thiodiacetyl chloride. Obviously, this route needs additional steps to prepare the derivative of 2,2′-thiodiacetic acid. In our study, **2** was synthesised by reaction of **1** and sodium sulfide. The raw materials are cheap, cyclohexane was chosen as the better solvent to avoid the hydrolysis of **1**. After the reaction was completed, the cyclohexane could be recovered and reused by distillation with a high recovery rate.

Compound **4** was synthesised by the Williamson condensation of disodium 2,5-dicarbethoxy-3,4-dioxythiophene (**3**) with 1,2-dibromoethane. Previously, this reaction was carried out in DMF using potassium carbonate or potassium carbonate/tetrabutyl ammonium bromide as a catalyst.[9,10] In our research, triethylamine was selected to replace the traditional catalyst. The experimental result indicated that triethylamine increased the reaction rate and selectivity of the desired product.

Decarboxylation was a key step in synthesising EDOT. Generally, Cu was chosen as catalyst. More attention was paid to the solvent used in this reaction. High boiling organic solvents were used because decarboxylation demanded high



Scheme 1

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temperature.[11] Quinoline was selected as solvent by Coffey *et al.*[12] This caused a difficulty in separating the products and recovering the solvent. Quinoline is a serious environmental pollutant.[13,14] DMSO and DMF was selected as solvent by Woon *et al.*[15] The mixture demanded additional organic solvent for extraction and distillation to obtain the desired product. Thus, N, N, N′, N′-tetraethylethane-1,2-diamine was selected as the solvent in our research. It could be recovered and recycled for the next batch.

In summary, from the starting material of **1**, EDOT was obtained in five steps. The synthetic routes of key intermediates were improved and optimized to make the procedure simpler with high yields. The present procedure is more effective, competitive, and more suitable for large-scale production

Experimental

^{1}H NMR (400MHz) and ^{13}C NMR (100MHz) spectra were recorded for DMSO-d$_6$ solutions on a Bruker AC-400 instrument with TMS as internal standard. The purities were determined by GC analysis (Agilent 1790F using a 30 m long SE54 capillary column). Melting points were determined on WRR melting point apparatus and uncorrected. Mass spectra were obtained on a Trace G2000 GC-MS spectrometer. All solvents, reagents and ligands used in this experiment were AR.

Diethyl thiodiglycolate (**2**): To a mixture of Na_2S (46.8 g, 0.6 mol) and cyclohexane (200 mL) was added dropwise **1** (122.5 g, 1.0 mol) with stirring at 15–20°C over 1h. The reaction was carried out for 3 h with stirring under reflux. The mixture was cooled to room temperature, and the mixture was then filtered. The filtrate was distilled and the fraction (cyclohexane) boiling at 80–81°C was collected. The volume of obtained cyclohexane was 174.0 mL, and the recovery rate was 87.0%. The residual oil was distilled under reduced pressure and the fraction boiling at 160–170°C (0.01MPa) was collected, and gave **2** (85.6 g). GC analysis indicated that the purity was more than 98.0% and the obtained yield was 83.1%. MS (*m/z*, %):206 (44), 160 (100), 133 (56), 105 (50), 88 (12), 77 (40), 60 (14), 29 (16). ^{1}H NMR (400MHz, DMSO-d_6) δ_H (ppm): 4.16 (q, 4H, *J*=7.4Hz, –O–CH_2), 3.58 (s, 4H, –CH_2–S), 1.28 (t, 6H, *J*=7.4Hz, –$CH_2C\underline{H}_3$).

Disodium 2,5-dicarbethoxy-3,4-dioxythiophene (**3**): To a 500 mL four-necked flask were added ethanol (200 ml) and sodium ethanolate (30.1 g, 0.44 mol). A mixture of **2** (41.2 g, 0.2 mol) and diethyl oxalate (32.2 g, 0.22 mol) was added with stirring at 20°C over 0.5h. The reaction was carried out for 3h with stirring under reflux. The mixture was cooled to room temperature, and the mixture was then filtered. The filtered cake was washed with ethanol (2×20 mL). The filtered cake was dried in vacuum and gave **3** (55.8g) with yield of 91.6%. **3** was acidified to obtain diethyl 3,4-dihydroxythiophene-2,5-dicarboxylate. Melting point: 135.0–136.2°C (lit.[12] :134.5–135.0°C). ^{1}H NMR (400MHz, DMSO-d_6) δ_H (ppm): 4.26 (q, 4H, *J*=7.2Hz, –O–CH_2), 1.27 (t, 6H, *J*=7.4Hz, –$CH_2C\underline{H}_3$).

2,5-Dicarbethoxy-3,4-ethylenedioxythiophene (**4**): To a sealed flask were added DMF (300 mL) and NaH (24.0 g, 1.0 mol).The mixture was then shaken well and placed overnight for next step.

To a 500 mL reactor were added with the above DMF (250 mL), triethylamine (3 g, 0.03 mol), **3** (45.6 g, 0.15 mol) and 1,2-dibromoethane (32.0 g, 0.17 mol).The reaction was carried out for 5h with stirring under closed reflux. The mixture was distilled. The solvents were collected and recycled in the next batch. The residual oil was cooled to 80°C. H_2O (200 mL) was added and the mixture was stirred for 0.5h. The precipitated product was filtered off. The filter cake was washed with H_2O (2×30 mL) to remove NaCl and dried in vacuum. The obtained crude product was 30.0 g.

Later, the crude product was dissolved in 100 mL ethanol at 50°C. The mixture was then filtered to remove the insoluble compound. The filtrate was cooled to room temperature. The precipitated product was filtered off, and the filter cake was dried in vacuum. The product was 23.1g with yield of 53.8%. Melting point:146.0–146.9°C (lit.[8] 146.0–147.0°C). ^{1}H NMR (400MHz, DMSO-d_6) δ_H (ppm): 4.40 (s, 4H, –O–CH_2CH_2–O), 4.26 (q, 4H, *J*=6.8Hz, –$OC\underline{H}_2CH_3$), 1.27 (t, 6H, *J*=7.2Hz, –CH_3).

2,5-Dicarboxy-3,4-ethylenedioxythiophene (**5**): To a 500 mL four-necked flask were added **4** (21.5 g, 0.75 mol). 200 ml 10% aqueous sodium hydroxide was added dropwise. The reaction was carried out for 2 h with stirring under refluxing. Followed, the solution was cooled to below 10°C. The aqueous hydrochloric acid was added until the pH<3. The precipitated product was filtered off. The filter cake was washed with H_2O (2×20ml) and dried in vacuum. The obtained product was 14.0g with yield of 81.0%. Melting point: 319.5–321.2°C (lit.[12] 323°C).^{1}H NMR (400MHz, DMSO-d_6) δ_H (ppm): 13.10 (s, 2H, –COOH), 4.36 (s, 4H, –O–CH_2–CH_2–O). ^{1}H NMR. The spectral data were obtained from Wiley Subscription Services, Inc. (US). (500MHz, DMSO–d_6) δ_H (ppm): 13.05 (s, 2H, –COOH), 4.35 (s, 4H, –O–CH_2–CH_2–O).

3,4-Ethylenedioxythiophene (**6**): To a 250 mL four-necked flask were added with **5** (11.5 g, 0.05 mol), Cu (1.3 g, 0.02 mol) and N, N, N′, N′-tetraethylethane-1,2-diamine (100 mL). The reaction was carried out for 4h with stirring at 180°C. The product was distilled under reduced pressure and the fraction boiling at 92–100°C (0.004MPa) was collected, to give **6** (3.4g). GC analysis indicated that the purity was more than 98.5% and the yield was 47.9%. The overall yield was 16.0% from **1**. ^{1}H NMR (400MHz, DMSO-d_6) δ_H (ppm): 6.53 (s, 2H, –C=CH), 4.17 (s, 4H, -O–CH_2CH_2–O).^{1}H NMR (lit.[16]) (400MHz, CD_3SOCD_3) δ_H (ppm):6.50 (s, 2H, –C=CH), 4.20 (s, 4H, –O–CH_2CH_2–O).

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