

POLYETHYLENE GLYCOL (PEG-400): AN EFFICIENT GREEN REACTION MEDIUM FOR THE ALKYLATION OF 3, 4-DIHYDROXY THIOPHENE-2, 5-DICARBOXYLIC ESTERS OR THEIR ALKALI METAL OR ALKALINE EARTH METAL SALTS.

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ABSTRACT

The present invention relates to an improved process for the alkylation of 3, 4- dihydroxythiophene-2, 5-dicarboxylic esters or their alkali metal or alkaline earth metal salts with alkylating agent and base in the presence of a solvent and catalyst PEG-400 was used as a Phase transfer Catalyst and could effectively catalyze the Reaction.

KEYWORDS: 3, 4-alkylenedioxythiophenedicarboxylic acid or its salts, 3, 4- dihydroxy thiophene-2, 5-dicarboxylic esters or their alkali metal or alkaline earth metal salts, PEG-400.

INTRODUCTION

3, 4-alkylenedioxythiophenes and 3, 4-dialkoxythiophenes are starting compounds for the preparation of electrically conductive polymers which may be transparent in thin layers and have recently been finding a wide range of uses. These polymers are used, for example, as electrodes, sensors, for producing capacitors or electro luminescent displays and other electro optic components, for producing photovoltaic devices, as electro chromic layers, as auxiliaries for the production of metal coatings, as thin films for dissipating static charges, in gel electrolytes or in ion-exchange membranes. A particularly important monomer 3, 4-alkylenedioxy thiophene is 3, 4- ethylene dioxythiophene.

In general, the synthesis of 3, 4-alkylenedioxythiophene or 3, 4-dialkoxythiophene consists of four steps viz., Condensation, alkylation, Hydrolysis and Decarboxylation, starting from diethyl thioglycolate.

MATERIALS AND METHODS**1. PREPARATION OF DIETHYL-3, 4-DIHYDROXYTHIOPHENE-2, 5-DICARBOXYLATE DISODIUM SALT.**

Diethyl thioglycolate and diethyl oxalate were charged into a round bottomed flask containing methanol and cooled to 0°C, then sodium methoxide solution was added slowly below 5°C in 2 to 3 hours. Temperature was raised to 25-30°C in 1 hour and was stirred for 1 hour at same temperature and was raised to reflux. The reaction mass was cooled to 25-30°C and filter. The residue was washed with methanol and dried at 60-70°C to obtain Disodium salt of Diethyl- 3, 4- dihydroxythiophene-2, 5-dicarboxylate.

2. PREPARATION OF 3, 4-ETHYLENEDIOXYTHIOPHENE-2, 5-DICARBOXYLIC ACID.

To the stirred suspension of Diethyl-3,4-dihydroxythiophene-2,5-dicarboxylate disodium salt (365 g, 1.2 moles), Potassium carbonate (65 g, 0.47 moles) and Dimethyl form amide (1.0 Lt), PEG-400 (20 g) was added at 25-30°C. Total reaction mixture was stirred at 25-30°C for 30 min and slowly raised the temperature to 120-135°C. Ethylene dichloride (116.55 g, 1.176mol) was added at the same temperature and further maintained for 5 hours. Ethylene dichloride (116.55 g, 1.176mol) was added again and the reaction was monitored by HPLC (Na- salt content should not be more than 1%). DMF was distilled off under vacuum below 120°C completely. To the resultant solid water (1.87 L) and IPA (250 ml) were added, then slowly CS Lye (255 g, 48%) was added at 80°C and same temperature was maintained for 3-5 hours. pH was adjusted between 1.0 to 1.5 with Con. HCl below 20°C. The precipitate was separated out and mass was filtered and washed with water (250 ml). The resultant material was dried at 70°C to afford title compound (254 g, 98% by HPLC).

Nature: Off-white solid

¹H NMR (400 MHz, CDCl₃): δ 13.31(br s, 2H, 2xCOOH), 4.3.9-4.384(t, 4H, 2xCH₂, J=15.05Hz)

¹³C NMR (MHz, CDCl₃): δ 64.5, 109.1, 144.8, 164.2.

IR (KBr): 3556, 3442, 3045,1683,1294,1095,854 cm⁻¹.

Mass: m/z 230.29(M+H), 186.2(M-COOH), 142(M-2XCOOH).

Elemental Analysis (% cal/fou) for C₈H₆O₆S C: 41.74/41.63, H: 2.63/2.61, O: 41.70/41.83.

3. PREPARATION OF 3, 4-ETHYLENEDIOXY THIOPHENE.

3, 4-Ethylenedioxythiophene-2, 5-dicarboxylic acid (50 g, 0.2 mol) and Zn-Mont (10 g) were added to DMF (250 ml) at room temperature. The reaction mixture was stirred for few minutes at room temperature and then heated at 160°C. After completion of the reaction, the catalyst was filtered off and the filtrate was diluted with ethylene dichloride. The organic layer was washed with water and dried over anhydrous sodium sulfate. The Solvent was removed by vacuum distillation to afford 3, 4-ethylenedioxythiophene (EDOT) in quantitative yield (96%).

Nature: Light yellow color liquid

¹H NMR (400 MHz, CDCl₃): δ 4.2(t, 4H, 2xCH₂, J=15.25Hz), 6.31 (s, 2H)

¹³C NMR (MHz, CDCl₃): δ 67.5, 121.8, 143.05.

IR (KBr): 2981, 2872, 1053, 933, 889, 833, 677 cm⁻¹

Mass: *m/z* 143 (M+H).

Elemental Analysis (% cal/fou) for C₆H₆O₂S C: 50.69/50.84, H: 4.25/4.31, O: 22.51/22.66.

REACTION SCHEME

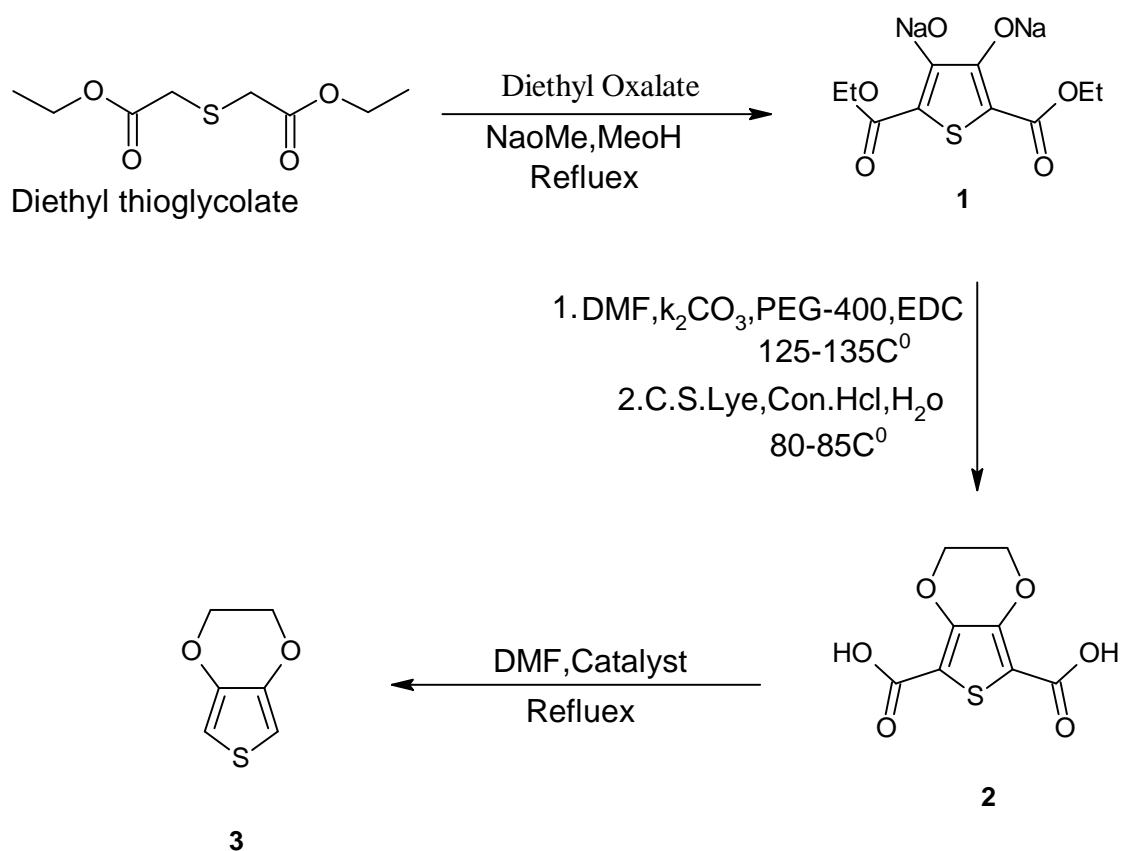


TABLE 1: EFFECTS OF PEGS ON THE ALKYLATION OF DIETHYL-3, 4-DIHYDROXYTHIOPHENE-2, 5-DICARBOXYLATE DISODIUM SALT.

Entry	Catalyst	Reaction time (h)	Yield (%)
1	0	24	74
2	PEG-400	8	98
3	PEG-600	8	98
4	PEG-800	8	98
5	PEG-1000	8	98

TABLE 2: EFFECT OF SOLVENT ON THE ALKYLATION OF 3, 4- DIHYDROXY THIOPHENE-2, 5-DICARBOXY- LIC ESTERS OR THEIR ALKALI METAL OR ALKALINE EARTH METAL SALTS.

Entry	Solvent	Yield (%)
1	DMF	98
2	DMSO	87
3	DMF&DMSO	84
4	O-XYLENE	74.3
5	TOLUENE	70
6	EtOH	22
7	MeOH	20
8	THF	10

RESULTS AND DISCUSSION

The process according to the present invention is particularly for the preparation of 3, 4-dialkoxythiophene dicarboxylic acids or its salts or 3, 4-alkylenedioxythiophene dicarboxylic acids or its salts by the alkylation of substituted thiophene-2, 5-dicarboxylic esters with alkylating agent in presence of solvent and catalyst at a temperature of 100-150°C. The process involves the use of dimetal salt of diethyl 3, 4-dihydroxythiophene-2, 5-dicarboxylate, which is obtained by the reaction of diethyl thioglycolate with diethyl oxalate in the presence of sodium methoxide in methanol. The corresponding dimetal salt of dialkyl 3, 4-dihydroxythiophene-2, 5-dicarboxylic ester was alkylated with an alkylating agent in presence of a solvent and catalyst to afford 3, 4-alkylene dioxythiophene-2, 5-dicarboxylate or 3, 4-dialkoxythiophene-2, 5-dicarboxylate. The dicarboxylate esters were Hydrolyzed and Decarboxylated to give 3, 4-dialkoxythiophene or Ethylenedioxythiophene (EDOT). Alkali metal or an alkaline earth metal is selected from lithium, sodium, potassium, Rubidium, Magnesium, Calcium or Strontium preferably Sodium or Potassium.

In the preferred embodiment of the present invention, the process involves the use of identical or different and are each preferably ethyl, methyl, butyl, n-butyl, propyl, isopropyl

or the mixtures thereof, particularly in the form of its alkali or alkaline earth metal salts such as dimethyl-3, 4-dihydroxythiophene-2, 5-dicarboxylate, the disodium salt of methyl ethyl 3, 4-dihydroxythiophene-2, 5-dicarboxylate and the disodium salt of methyl butyl 3, 4-dihydroxy thiophene-2, 5-dicarboxylate.

Alkylating agents selected from dichlorides or dibromides, in particular 1, 2-dichloro ethane, 1, 2-dibromo ethane and 1-bromo-2-chloroethane, among which very particular Preference is given to 1, 2-dichloroethane.

Solvent is selected from organic solvents like polar, non polar, polar protic, polar aprotic solvents such as toluene, O-xylene, N, N-dimethylformamide, Dimethylsulfoxide, Methanol, Ethanol, THF or mixtures thereof, Preferably N, N- dimethylformamide (Table 2).

The above mentioned alkylation [2-4] is carried out in the presence of a base selected from alkali metal or alkaline earth metal Carbonates, Hydroxides, Bicarbonates, Oxides or Alkoxides such as Sodium hydroxide, Potassium hydroxide, Cesium hydroxide, Barium hydroxide, Magnesium hydroxide, Calcium hydroxide, Strontium hydroxide, Sodium carbonate, Potassium carbonate, Cesium carbonate, Sodium bicarbonate, Potassium bicarbonate, Calcium bicarbonate, preferably Potassium carbonate. The present invention is carried out in presence of a catalyst particularly, phase transfer catalyst (PTC) that facilitates the migration of a reactant from one phase into another phase where reaction occurs. By using a PTC process, one can achieve faster reactions, obtain higher conversions or yields, make fewer byproducts and eliminate the need for expensive or dangerous solvents that will dissolve all the reactants in one phase, eliminate the need for expensive raw materials and/or minimize waste problems. Generally phase transfer catalysts are quaternary ammonium and phosphonium halides or crown ethers or polyether compounds or synthetic bi and poly cyclic Multi dentate ligands.

In the present invention, phase transfer catalyst is selected from a group consisting Crown ethers such as 18-crown-6; polyether compounds such as polyethylene glycols selected from PEG 400, PEG 600, PEG 1000, PEG 3350, PEG 4000-6000; synthetic bi and polycyclic multidentate ligands such as cryptands like [2,2,2] cryptand, preferably polyether compound, most preferably Polyethylene Glycol 400. Results showed that increasing Molecular Weights if PEGs do not affect the alkylation efficiency (Table 1).

Alkylation step in the present invention is particularly carried out at a temperature of 25-150°C, the catalyst is introduced in the reaction at a temperature of 25°C and the reaction temperature is raised and maintained at 100-150°C, preferably 125-135°C for 2-24 hours, preferably 3-8 hours. The dimetal salt of 3, 4-dihydroxythiophene-2, 5-dicarboxylic esters are reacted with 1, 2-dichloroethane and the resulting esters are hydrolysed to give 3, 4-dialkoxy thiophene-2, 5-dicarboxylic acids, 3, 4-alkylenedioxythiophene-2, 5-dicarboxylic acids or corresponding salts.

The following examples illustrate the nature of the invention and are provided for illustrative purposes only and should not be construed to limit the scope of the invention.

CONCLUSION

The present invention relates to an improved process for the alkylation of 3, 4-dihydroxy thiophene-2, 5-dicarboxylic esters or their alkali metal or alkaline earth metal salts with alkylating agent and base in the presence of a solvent and in presence of inexpensive and non-toxic PEG-400 as a phase transfer catalyst. This is commercially viable and easily adoptable in plant scale.

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