PERKIN 1

The synthesis of highly active thiophene ring-containing chromophore components for photonic polymers based on a newly designed route

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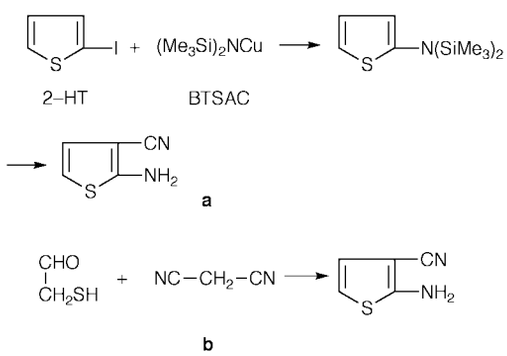
Received (in Cambridge, UK) 21st June 1999, Accepted 14th October 1999

2-Aminothiophene derivatives are the key intermediates for the present synthesis. It is known that the synthesis of 2-aminothiophene is troublesome although it is a rather simple heterocycle. In this work, an early report was newly developed as a basis for the efficient synthesis of thiophene-ring-containing chromophore components for photonic polymers. 2-Amino-5-nitrothiophene and 2-amino-3,5-dinitrothiophene were synthesized in excellent yield. After diazotization, the 2-aminothiophene derivatives were directly treated with *N*-phenyldiethanolamine to afford two-electron push–pull compounds. A similar styryl compound was also prepared. All of these chromophore molecules have further polymerizable hydroxy groups on one end of the molecule. These compounds are currently showing interesting potential in making highly sensitive, nonlinear optical polymeric materials.

Introduction

Push–pull conjugated systems are a subject which has received intensive attention because of their potential applications in modern photonic technology. It is well known that lithium niobate, currently the most commonly used electro-optic material, has an electro-optic coefficient of 35 pm V^{-1}. To produce materials having optical nonlinearity comparable to or greater than that of lithium niobate is still an essential target for organic/polymeric materials research. The most intensively studied rod-like organic push–pull conjugated system for photonic materials consists of aromatic rings to which electron-donating (push) and -accepting (pull) groups are attached, and with a double bond between the aromatic rings as an electron bridge. Theoretical investigation has concluded that heteroaromatics, such as the thiophene ring, have an important role in the design of efficient, second-order, nonlinear optical molecules,[1] and also that the planarity of an azo unit *versus* the nonplanarity of stilbenes or other such systems should contribute to the larger π electron transmission effects and lead to higher optical activity.[2] DR-19 is a widely used typical example of such chromophores. In order to have highly active core layer organic materials for optical waveguide devices, we have therefore designed and synthesized three similar chromophore molecules (see below) in which one of the phenyl rings was replaced by a thiophene unit; in the synthesis, a new synthetic route based on Steinkopf's report[3] was used for the preparation of the thiophene ring containing an azo chromophore. Our synthetic route has the advantages of good reproducibility and quite high reaction yield. The general reaction route is shown in Scheme 1.



Scheme 1

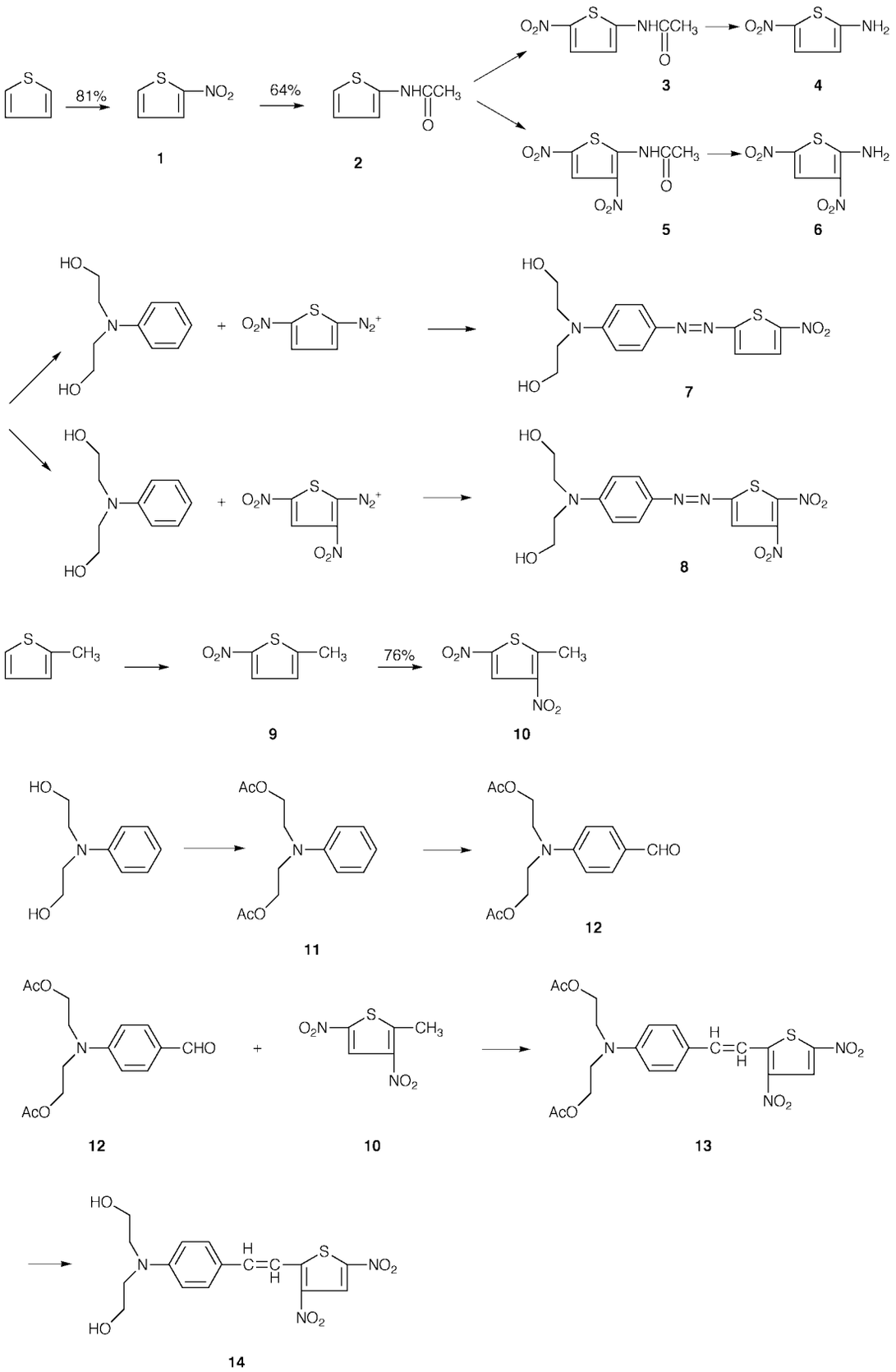
Results and discussion

2-Aminothiophene derivatives **4** and **6** are the key intermediates for the synthesis of the highly optically sensitive thiophene-ring-containing chromophores. However, 2-aminothiophene is only stable in an inert atmosphere below its melting point (12–13 °C).[5] Heating above its melting point or exposure to air will result in immediate decomposition. The absence of a practical method for preparing such a simple and interesting compound made its synthesis an inviting subject of investigation. There are several methods for the preparation of 2-aminothiophene derivatives. For example, as shown in Scheme 1*a*,[6] a 2-halogenothiophene (2-HT) can be converted into the corresponding primary amino compound by reaction with bis(trimethylsilyl)-amidocopper (BTSAC), BTSAC can be prepared *in situ* from hexamethyldisilazane, *n*-butyllithium and copper(I) iodide, by coupling 2-HT with BTSAC, to give a silyl-protected amine first (yield 45%), and then, after alcoholysis and distillation, to afford a 2-aminothiophene derivative.

A conventional method of preparing 2-amino-substituted thiophenes is starting from the reaction of mercaptoacetaldehyde with malononitrile as shown in Scheme 1*b*.[3]

The mercaptoacetaldehyde usually is used in its dimer form and cyanoacetic acid which is the hydrolysis product of malononitrile is believed to be the real participant in the reaction. Control of the reaction conditions is critical in this reaction route.

Because of its instability and the very low yield of its preparation, synthetically it is ideal to avoid direct involvement of this compound in a practical synthetic scheme. In this synthesis, as shown in Scheme 2, first, 2-acetamidothiophene **2** instead of 2-aminothiophene was prepared. It seems that substitution with an electron-withdrawing group on the N atom of its amine group or at 3- and 5- position of the 2-aminothiophene greatly

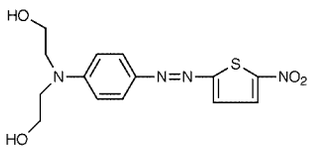
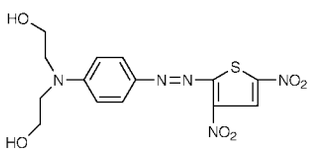
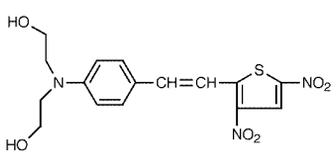
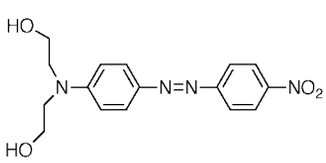


Scheme 2

changes the situation: compounds **2**–**6** as well as its stannous [tin(IV)] chloride double salt are all stable enough, therefore can be isolated, and be prepared in good yield. Compounds **4** and **6** are novel intermediates.

The presence of the hydroxy groups on the chromophore molecules is essential for their attachment to polymer backbones, for example, for further making polymers like polyesters, polyurethanes, polyimides, and the like. Such hydroxy groups usually are necessarily protected, by converting them into their diacetate, for example, *N*,*N*-bis(acetoxyethyl)aniline was used as a coupling component to react with diazonium salts for preparing azo dyestuffs.[7] Regarding the relative stability of

Table 1 UV–visible spectral data of target compounds

		λ_{max}^{DMF}/nm	Å/l mol^{-1} cm^{-1}
7		583	47 040
8		671	40 060
14		581	37 010
Disperse Red-19		500	37 030

the hydroxy groups under the diazotizing reaction conditions, *N*-phenyldiethanolamine was directly used and was successful in our synthesis.

The styryl-class compound **14** was obtained based on the base-catalyzed aldol condensation reaction between the active-hydrogen component of compound **10**, and the carbonyl component of compound **12**. In this reaction, the formation of the carbanion intermediate is a key step. Although formation of the intermediate was not as easy as in the case with no substitution nitro groups on the thiophene ring, as reported by Jen *et al.*,[4] compound **10** still offered an acceptable yield of 56% in the aldol condensation reaction. A yield of 75% was reported in Jen's case.

The UV-visible spectral data of **7**, **8** and **14** are shown in Table 1, together with that of Disperse Red-19 for comparison.

The relative importance of the heteroaromatic ring, the substituent(s) on the ring, and the electron bridge towards λ_{max}, or in general, towards charge transfer in π-electron conjugated systems is clearly shown in Table 1: **8** and **14** are very similar in their molecular structure except for the difference in the π-electron bridge between the two rings. Interestingly, just because of this difference, **8** showed a nearly 100 nm redshift in λ_{max} compared with **14**, and even **7** has a comparable λ_{max} with **14**, despite the fact that **14** has more nitro groups substituted on its thiophene ring. Anyway, comparing **7** with DR-19, a redshift of nearly 100 nm occurs because of the replacement of the phenyl group in DR-19 by the thiophene ring in **7**.

In summary, considering a moderate delocalization energy of the thiophene ring system and consequently a higher expected optical sensitivity, three thiophene-ring-containing push–pull azo compounds with further polymerizable hydroxy groups have been synthesized by a newly designed and efficient synthetic route. To avoid the direct involvement of an unstable intermediate, 2-aminothiophene, which is a simple but elusive compound, its derivative 2-acetamidothiophene **2** was found to be pretty stable and could be isolated for further reaction. Meanwhile, for simplification of the preparation procedures, *N*-phenyldiethanolamine was directly used for the coupling reaction to form the target azo molecules without protection of the hydroxy groups and deprotection afterwards. Comparing with other methods, all the steps shown in Scheme 1 are easy to handle and are well defined in the Experimental section of this paper. The synthesized chromophore molecules are very useful for making a variety of photonic polymers. The preparation of various photonic polymers based on these chromophoric molecules and their optical properties are under investigation; details will hopefully be published later.

Experimental

Instruments employed were IR (BIO-RAD FTS-165), UV-vis (1601PC Shimadzu), MS (Trio-2000), ^{1}H NMR (Varian Gemini 300 operating at 300 MHz) spectrophotometers, and element analyzer (Heraeus CHN-RAPID). NMR *J*-values are given in Hz. Solutions were dried over anhydrous Na_2SO_4. Petroleum spirit refers to the fraction with distillation range 60–90 °C.

2-Nitrothiophene 1[3]

A mixture of 40 g fuming nitric acid and 300 ml of glacial acetic acid was added dropwise to a solution of thiophene (42 g, 0.50 mol) in 170 ml of acetic anhydride at 10–15 °C. The reaction mixture was stirred for 2.5 h at ambient temperature, then was poured into 500 g of ice–water with vigorous stirring. After filtration and drying, a yellow precipitate was obtained (52 g, 81%), mp 40–41 °C (lit.,[3] 41 °C); IR 1523, 1332 cm^{-1}. The product was kept in the dark for further reaction.

2-Acetamidothiophene 2

To **1** (24 g, 0.19 mol) dissolved in 408 ml of conc. hydrochloric acid was added tin powder (40.8 g, 0.34 mol) in portions over a period of 15 min with vigorous stirring at 40–45 °C. Ice–water may be used when necessary for temperature control. The mixture was kept for 30 min; after complete disappearance of the tin powder, the reaction was allowed to continue for another 10 min, then the thus formed complex of $SnCl_4$–aminothiophene hydrochloride was filtered out from the reaction mixture, washed with ethanol–ether (1 : 1) briefly, and dried. The complex was obtained as a gray-white solid (35 g, 71%). 50 ml of acetic anhydride–diethyl ether (1 : 1) was added to 100 ml of an aqueous solution of the above complex (35 g). At ice-bath temperature, 87 g of 50% aq. sodium hydroxide was added slowly over 15 min onto the resulting mixture under vigorous stirring, a white precipitate appearing immediately. After the completion of NaOH addition, 10 min of additional stirring gave a precipitate, which was filtered off, recrystallized from water, decolored by use of activated charcoal and dried under vacuum drying box overnight (15 mmHg, room temp.). Compound **2**, a white solid, was obtained (12 g, 64%), mp 161 °C (lit.,[3] 160–161 °C); IR(KBr) 1643, 1581 cm^{-1}.

2-Acetamido-5-nitrothiophene 3

Below 5 °C, a solution of **2** (7 g, 0.05 mol) in 350 ml of acetic anhydride, was treated with a mixture of nitric acid (14 ml; 67%) and acetic anhydride (70 ml) over a period of 20–25 min under vigorous stirring. The mixture was then stirred for an additional 10 min and then was poured into 420 ml of ice–water (stirring), followed by the addition of 1400 ml of water. A small amount of residue was removed from the mixture by filtration. About 420 g of solid sodium carbonate was added in portions to the filtrate for neutralization. A yellow-grey precipitate appeared, and was separated by filtration, washed with water, and dried under vacuum drying box overnight (15 mmHg, room temp.) to give 6 g of product. Another 1 g of product could be got from the filtrate by Et_2O extraction and recrystallization from 50% aq. ethanol. Total yield 66%. The product

was a mixture of 2-acetamido-5-nitrothiophene **3** and 2-acetamido-3-nitrothiophene. 2-Acetamido-3-nitrothiophene can be separated by vacuum sublimation at 114 °C under reduced pressure (10 mmHg), mp 163–164 °C (lit.,[3] 165.5–166.5 °C); IR(KBr) 1706, 1544, 1385 cm^{-1}. Pure **3** could be obtained from the remained residue by, first evaporation at 150 °C/10 mmHg and then recrystallization from sufficient hot water; mp 220–222 °C (lit.,[3] 222–223 °C).

2-Amino-5-nitrothiophene 4

3 (1.0 g, 5.38 mmol) was deacetylated by its slow addition to 50 ml aq. of KOH (20 g) at 30 °C and stirring for 1 h. 25 ml of water were added to the reaction mixture, which was then gently neutralized with conc. hydrochloric acid at ice–water temperature. An orange precipitate appeared immediately. The precipitated product was collected, and purified by column chromatography on silica gel with ethyl acetate–petroleum spirit (2:1) as eluent. A pure yellow product was obtained (0.55 g, 71%), mp oxidized >140 °C; IR(KBr) 3406, 3290, 3181, 2925, 1619, 1529, 1479, 1423, 1399, 1331, 1291, 1133 cm^{-1}; NMR-(DMSO-d_6): δ 6.0 (d, 1H), 7.75 (d, 1H), 8.1 (s, 2H) [Anal. (%). Calc. for $C_4H_4N_2O_2S$: C, 33.33; H, 2.78; N, 19.44; S, 22.22. Found: C, 33.56; H, 2.68; N, 19.06; S, 22.02].

2-Acetamido-3,5-dinitrothiophene 5

The above obtained mixture of 2-acetamido-5-nitrothiophene **3** and 2-acetamido-3-nitrothiophene (3.8 g) was slowly added to 24 ml of fuming nitric acid with stirring at 0–5 °C. The nitration mixture was kept for 5–10 min and then 120 ml of ice–water were added. A yellow precipitate was formed and isolated by filtration, recrystallized from ethanol, and dried over anhydrous sodium sulfate, to give **5** (3.6 g, 76%), mp 181–182 °C; IR(KBr) 1713, 1549, 1349 cm^{-1}; MS 231 (M^+).

2-Amino-3,5-dinitrothiophene 6

2-Acetamido-3, 5-dinitrothiophene **5** (3.0 g, 1.51×10^{-2} mol) was added with stirring to 30 ml of 50% sulfuric acid and the mixture was stirred for 4 h at 100 °C. After cooling, it was poured onto 300 ml of ice–water with vigorous stirring. A yellow precipitate appeared and was collected, washed with water, and dried under vacuum drying box overnight (15 mmHg, room temp.). The crude product was further purified by column chromatography on silica gel, with ethyl acetate–petroleum spirit (3:1) as eluent, to give product **6** (1.3 g, 53%), mp 179–180 °C, IR(KBr) 3354, 3274, 3185, 1530, 1353 cm^{-1} [Anal. (%). Calc. for ($C_4H_3N_3O_4S$): C, 25.40; H, 1.59; N, 22.22; S, 16.93. Found: C, 25.86; H, 1.61; N, 21.71; S, 16.81].

4-Diethanolaminobenzene-azo-2-(5-nitrothiophene) 7

7 was prepared by a similar procedure to the synthesis of **8** (see below). UV-vis: λ_{max}^{DMF} 583 nm (ε 47 040); IR(KBr) 3400–3100, 1600, 1514, 1491, 1329, 1259, 1156, 1050 cm^{-1}; MS (*m*/*z*) 336 (M^+); ^{1}H NMR(DMSO-d_6) δ 3.35 (s, 4H, NCH_2), 3.65 (s, 4H, OCH_2), 6.95 (d, 2H, ArH), 7.60 (s, 1H, ArH), 7.77 (d, 2H, ArH), 8.18 (s, 1H, ArH) [Anal. (%). Calc. for ($C_{14}H_{16}N_4O_4S$): C, 50.00; H, 4.76; N, 16.67; S, 9.52. Found: C, 49.77, H, 4.82; N, 16.20; S, 9.38].

4-Diethanolaminobenzene-azo-2-(3,5-dinitrothiophene) 8

Sodium nitrite (0.482 g, 6.96 mmol) was added slowly, with stirring, to conc. sulfuric acid (5.7 ml) at ice-bath temperature. To facilitate the dissolution process, the temperature may be raised to 30 °C for a while, then lowered to below 5 °C again; a mixture of propionic acid (3.2 ml) and acetic acid (19 ml) was added. During the addition of the acid mixture, the temperature of the reaction mixture may rise but must be kept not higher than 15 °C. The solution should be cooled to 0 °C when the addition of the acid mixture has finished; then the diazo component **6** (1.2 g, 6.35 mmol) was added slowly over a period of 30 min. The diazotizing reaction was allowed to proceed for another 30 min. An aqueous solution (43 ml), cooled at 0 °C, containing the coupling component of *N*-phenyldiethanolamine (1.77 g, 9.78 mmol) and conc. hydrochloric acid (1.9 ml) was then added with stirring. The diazonium reaction was allowed to continue for another 50 min. The solid was collected on a Büchner filter under reduced pressure, washed several times with water, and vacuum dried for 24 h to afford 1.5 g of **8** as a deep blue solid, which was further purified by TLC, with silica gel as absorbent and ethyl acetate as developer, λ_{max}^{DMF} 671 nm (ε 40 060); IR(KBr) 3399, 3241, 2919, 1602, 1544, 1386, 1293, 1256, 1134 cm^{-1}; MS (*m*/*z*) 381 (M^+); ^{1}H NMR(DMSO-d_6) δ 0.85 (s, 20H), 3.90 (t, 8H), 7.1–7.9 (m, 4H), 8.38 (s, 1H) [Anal.(%). Calc. for ($C_{14}H_{15}N_5O_6S$): C, 44.09; H, 3.94; N, 18.37; S, 8.40. Found: C, 44.35; H, 4.07; N, 18.07; S, 8.52].

2-Methyl-5-nitrothiophene 9[4]

To a solution of 2-methylthiophene (15 g, 0.15 mol) in acetic anhydride (30 g) was added dropwise a mixture of fuming nitric acid (12 g) and acetic anhydride (24 g) under vigorous stirring at −5 to −10 °C. After nitration, the reaction mixture was poured onto 200 g of ice, neutralized with Na_2CO_3 powder, and extracted with diethyl ether. The ethereal solution was dried with anhydrous $MgSO_4$. The residue after removal of the ether was first purified by steam distillation, the distillate was again extracted with diethyl ether, then **9** was separated from the the residue, after removal of the ether, by vacuum distillation as the fraction at 104 °C/15 mmHg (7 g, 32%), IR 3105, 3083, 3061, 3027, 2919, 2851, 2364, 1715, 1561, 1450, 1357, 1069, 968, 812 cm^{-1}.

2-Methyl-3,5-dinitrothiophene 10

9 (2 g, 14 mmol) was added in small portions with stirring to a mixture of fuming nitric acid (8 g) and conc. sulfuric acid (8 g) at a carefully controlled temperature of 5–10 °C. The reaction was continued for 30 min and then the mixture was poured onto 30 g of ice. The crystals were filtered off, and recrystallized from ethanol. Compound **10** was obtained (2 g, 76%), mp 99–100 °C; IR 3442, 3111, 1555, 1511, 1329, 1103, 1040, 889, 818, 731, 675 cm^{-1}; ^{1}H NMR[$(CD_3)_2CO$] δ 2.90 (s, 3H), 8.39 (s, 1H); MS (*m*/*z*) 188 (M^+), 173 ($M^+ - 15$), 171, 95, 69, 51, 44.

O,*O*′-Diacetyl-*N*-phenyldiethanolamine 11

A mixiture of *N*-phenyldiethanolamine (25.0 g, 0.138 mol), acetic anhydride (31.0 g, 0.31 mol), and pyridine (25 g, 0.356 mol) was heated to reflux for 2 h under nitrogen atmosphere. The resulting solution was cooled and concentrated on a rotary evaporator and then vacuum distilled (160 °C/1 mmHg) to afford **11** as a pale golden oil (34.3 g, 93%), IR 3451, 2962, 2896, 1738, 1599, 1507, 1380, 1229, 1036, 750, 696 cm^{-1}.

O,*O*′-Diacetyl-4-formyl-*N*-phenyldiethanolamine 12

Phosphoryl trichloride (22.0 g, 0.144 mol) was added dropwise at 0 °C to 100 ml of *N*,*N*-dimethylformamide (DMF), and the reaction mixture was stirred at 0 °C for 2 h. A DMF (100 ml) solution containing the diacetate **11** (34.32 g, 0.129 mol) was added slowly. The reaction mixture was heated to 90 °C for 3 h. After cooling, the solution was poured onto 2 l of ice–water containing 60 g (5 equiv.) of Na_2CO_3. The mixture was stirred for 24 hours and the resulting solid was collected by filtration under reduced pressure to give **12** as a pale brown solid and which was used without further purification (31.1 g, 82%), mp 39 °C; IR 2991, 2819, 2746, 1737, 1723, 1675, 1598, 1561, 1525, 1409, 1227, 1173, 1116, 1044, 979, 903, 820, 710, 597 cm^{-1}. NMR(CD_3OD) δ 2.14 (s, 6H), 3.76 (t, *J* 6.03, *J* 6.00, 4H), 4.28

(t, *J* 5.85, *J* 5.97, 4H), 6.93–7.76 (dd, *J* 8.87, *J* 9.09, 4H), 9.65 (s, 1H).

2-{[4-Bis(acetoxyethyl)phenyl]ethenyl}-3,5-dinitrothiophene 13

Re-distilled pyrrolidine (2 drops) and **10** (0.94 g, 5 mmol) were added to a solution of **12** (2.2 g, 7.5 mmol) in 40 ml of THF. The mixture was refluxed for 20 h. THF was then removed under reduced pressure, the residue was recrystallized from methanol, and **13** was obtained as shining black crystals (1.3 g, 56%), mp 169–170 °C; IR 3446, 3110, 2975, 2928, 2848, 1738, 1584, 1538, 1382, 1318, 1296, 1183, 1166, 817 cm^{-1}; NMR-[(DMSO-d_6)] δ 1.98 (s, 6H), 3.70 (t, 4H), 4.20 (t, 4H), 6.87–7.62 (dd, *J* 8.82, 4H), 7.68–7.87 (dd, *J* 16.0, 2H), 8.45 (s, 1H); MS (*m*/*z*) 463 (M^+, 4.62%), 87 (100%).

2-{[4-(Diethanolamino)phenyl]ethenyl}-3,5-dinitrothiophene 14

K_2CO_3 (4 g, 28 mmol) was added with stirring to a solution of **13** (1.0 g, 2.15 mmol) in a mixture of THF (40 ml) and water (100 ml) at 40 °C. The reaction was conducted for 30 h. Then the mixture was concentrated by rotary evaporator. The aqueous residue was extracted with chloroform (3 × 100 ml), and the combined organic layers were washed with water (3 × 150 ml), and dried with anhydrous Na_2SO_4. The crude product was further separated by column chromatography on silica gel as absorbent and ethyl acetate–methanol (10 : 1 v/v) as eluent. Pure **14** as black crystals was obtained (0.36 g, 44%), mp 218 °C; IR 3384, 3110, 2927, 1737, 1612, 1537, 1522, 1382, 1315, 1267, 1182, 1046, 820, 725 cm^{-1}; NMR(DMSO-d_6) δ 3.53 (t, 4H), 3.54 (t, 4H), 6.78–7.56 (dd, *J* 9.81, *J* 9.91, 4H), 7.73–7.80 (dd, 2H), 8.46 (s, 1H); MS (*m*/*z*) 379 (M^+), 348 ($M^+ - 31$); $\lambda_{max}^{CH_3OH}$ 530 nm [Anal: Calc. for ($C_{16}H_{17}N_3O_6S$): C, 50.65; H, 4.52; N, 11.08; S, 8.43. Found: C, 50.61; H, 4.50; N, 10.98; S, 8.41].

Acknowledgements

We are grateful to the National Science Foundation of China and the Chinese National 863 Program Committee for financial support.

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