

Chemical and Photochemical Synthesis of Substituted Dihydrothieno[2',3':4,5]thieno[2,3-c]quinolin-6-ones and Tetrahydrodithieno[2,3-b:2',3'-d]thieno[2'',3''c:2'',3''c']diquinolin-6,14-dione

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Abstract: Some new substituted dihydrothieno[2',3':4,5]thieno[2,3-c]quinolin-6-ones **9-12** and tetrahydrodithieno[2,3-b:2',3'-d]thieno[2'',3''c:2'',3''c']diquinolin-6,14-dione (**17**) were prepared from the corresponding new anilides **5-8** and from the corresponding dianilide **15**, respectively, by a multistep combination of chemical and photochemical reactions. All the prepared compounds are of particular interest because they might serve as DNA intercalators in anticancer therapy.

Keywords: Substituted dihydrothieno[2',3':4,5]thieno[2,3-c]quinolin-6-ones; Tetrahydrodithieno[2,3-b:2',3'-d]thieno[2'',3''c:2'',3''c']diquinolin-6,14-dione; Synthesis; Photochemical synthesis; DNA Intercalators; Anticancer therapy.

Introduction

There are only a few recent literature reports which describe thieno[3,2-b]- and thieno[3,4-b]-thiophenes with different features [1-3] and applications [4,5]. Synthesis of a new class of cofacially oriented neutral donor-acceptor thienothiophenes to probe the presence of through-space charge

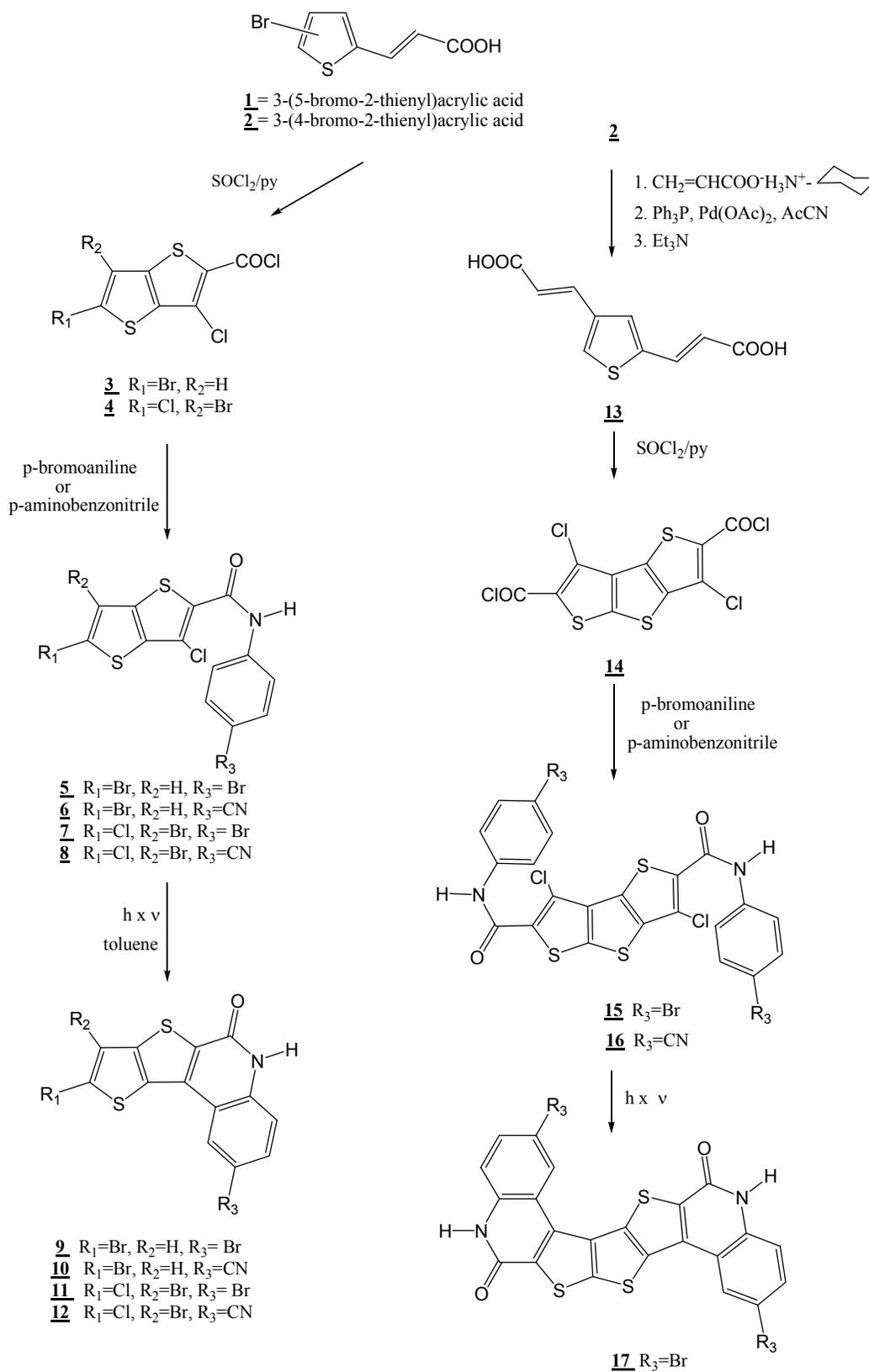
transfer interaction has been described [6]. Synthesis of some polyfused thienoheterocycles e.g.: thienopyrimidine, thienotriazine, thienoimidazotriazine, etc. [7] and new bis-(*p*-fluorophenyl)amides of thieno[3,2-*b*]-thiophene, thieno[3,2-*b*]furan and 1,2-bis(5-[2-(2-thienyl)ethenyl]2-thienyl)ethane are also described [8]. The new thienothiophene group was reported recently [9]. Occasionally thienothiophenes have been prepared from monobromo, dibromo or tribromo substituted thiophenes [10], 3,6-dimethyl-substituted thieno[3,2-*b*]thiophenes, prepared as monomers in the polymerization process [11,12] or thieno[3,2-*b*]thiophenes, which are synthesized starting from phthalimidodisulfenyl chloride via reaction with diaryl (or heteroaryl) acetylenes [13] or as the intermediates in the synthesis of heteroarenes which are isoelectric with perylene [14]. Various thieno[3,2-*c*]-annelated 1,2-dithiins have been prepared from appropriate thiophene precursors [15,16]. On the other hand, there is a lot of patent literature which describes the synthesis of thiophene 3,4-carboxamide derivatives and their application as useful and active dopamine receptor blockers [17], or useful herbicides [18]. Some substituted benzo[*b*]thiophenecarboxamides are used as inhibitors of neutrophil-endothelial cell adhesion [19]. Finally, the synthesis of tricyclic thiophenes using transition-metal or palladium catalyzed cyclization [20,21] was described recently, as were their applications as radical cations [22] or in photochemical polymerization processes [23,24].

Results and Discussion

In our previous papers we have described the synthesis of some dianilides of the benzo[*b*]-thiophene, thieno[2,3-*b*]thiophene, benzo[1,2-*b*:4,5-*b'*] dithiophene and dithieno[3,2-*b*:2',3'-*d*]-thiophene series and their photochemical reactions, which led to the corresponding quinolones [25-27]. Recently, we also reported the synthesis of new thieno[2,3-*b*]thienylquinolones and their antitumor activity [28].

In this paper we describe the preparation of some new substituted dihydrothieno[2',3':4,5]thieno[2,3-*c*]quinolin-6-ones **9-12** and of tetrahydrodithieno[2,3-*b*:2',3'-*d*]thieno-[2'',3''-*c*:2''',3'''-*c'*]diquinolin-6,14-dione (**17**) by multistep syntheses starting from the corresponding bromo substituted 2-thienylacrylic acids **1** and **2** prepared earlier [29,30] (Scheme 1). Cyclization of **1** and **2** by the known method [26,31,32] using thionyl chloride and a catalytic amount of pyridine, gave substituted 3-chlorothieno[3,2-*b*]thiophene-2-carbonyl chlorides **3** and **4**, respectively. The yields varied from 40-56%. By refluxing chlorides **3** and **4** with *p*-bromoaniline or *p*-aminobenzonitrile in toluene the corresponding substituted 3-chlorothieno[3,2-*b*]thiophene-2-carboxanilides **5-8** were obtained. All the prepared anilides **5-8** were converted by the photochemical dehydrohalogenation reaction into the corresponding disubstituted quinolones **9-12** [26,28]. On the other hand, the Heck reaction of compound **2** gave 3-(2,4-thienylene)diacrylic acid (**13**, [28,33]), which was cyclized with thionyl chloride and a catalytic amount of pyridine, by the known method [26,27,34], into dichloride **14**. Refluxing of dichloride **14** with *p*-bromoaniline or *p*-aminobenzonitrile in toluene afforded the corresponding 3,6-dichlorodithieno-[3,2-*b*:2,3-*b'*]thiophene-2,5-carboxanilides **15** and **16**. Dianilide **15** was converted by the double photochemical dehydrohalogenation reaction into the diquinolone **17**. Dianilide **16** proved quite insoluble in the usual organic solvents and the photochemical reaction was not carried out.

Scheme 1



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Experimental

General

Melting points were determined on a Kofler hot stage microscope and are uncorrected. IR spectra were recorded on a Nicolet Magna 760 spectrophotometer between KBr plates. UV spectra were recorded on either a Perkin-Elmer 124 or a Hewlett-Packard 8452A spectrophotometer in methanol or ethanol. ^1H - and ^{13}C -NMR spectra were recorded on either a Varian Gemini 300 or a Bruker Avance DPX 300 spectrometer in DMSO- d_6 . Chemical shifts (δ) are reported in part per million (ppm) relative to TMS as an internal standard, and coupling constants (J) are given in hertz (Hz). Mass spectra were recorded on either a Varian-MAT 311A (Electron Impact and Fast Atom Bombardment) or a Micromass Platform LCZ (Electrospray). Elemental analysis for carbon, hydrogen and nitrogen were performed on a Perkin-Elmer 2400 elemental analyzer. Where analyses are indicated only as symbols of elements, analytical results obtained are within 0.4% of the theoretical value. Irradiation was performed at room temperature with a water cooled immersion well fitted with a 400 W high pressure mercury arc lamp using Pyrex filters. All compounds were routinely checked by TLC with Merck silica gel 60F-254 glass plates or Merck aluminium oxide plates.

*5-Bromo-3-chlorothiopheno[3,2-*b*]thiophene-2-carbonyl chloride (3).*

A solution of acid **1** (5.2 g, 22 mmol), thionyl chloride (8.2 mL, 114 mmol) and pyridine (0.2 mL) was heated at 120°C for 72 h. The excess thionyl chloride was removed under reduced pressure and the residue extracted with boiling cyclohexane. After cooling, the precipitated yellow crystals were filtered off to give **3** (6.2 g, 87%); the crude product was used directly in the next step [32].

*6-Bromo-3,5-dichlorothiopheno[3,2-*b*]thiophene-2-carbonyl chloride (4).*

Compound **4** was prepared on the same way as **3** from compound **2** (5.0 g, 21 mmol), thionyl chloride (8.0 mL, 107 mmol) and pyridine (0.17 mL). The yield of the crude product which was used directly in the next step of the reaction was 5.2 g (69.6%); IR (cm^{-1}): 1740 (COCl).

*5-Bromo-N-(*p*-bromophenyl)-3-chlorothiopheno[3,2-*b*]thiophene-2-carboxamide (5).*

To a suspension of **3** (3.0 g, 9.5 mmol), in toluene (100 mL) was added dropwise a solution of *p*-bromoaniline (3.5 g, 20 mmol) in toluene (50 mL). The reaction mixture was refluxed with stirring for 1.5 h. After cooling, the crystals were filtered off, washed with dilute HCl (1:1), water and hot methanol. The crystals were then recrystallized from chloroform. Compound **5** was thus obtained as white crystals (2.2 g, 52.1%), mp 115-118°C; IR (cm^{-1}): 3350 (NH), 1640 (CONH); ^1H -NMR: 10.57

(s, 1H, NH), 7.67 (d, $J=8.79$ Hz, 2H, H arom.), 7.65 (s, 1H, H thioph.), 7.58 (d, $J=8.79$ Hz, 2H, H arom.); $^{13}\text{C-NMR}$: 158.27, 137.71, 137.50, 133.40, 132.73, 131.95, 130.61, 122.52, 116.54, 105.09, 98.74; Anal. Calcd. for $\text{C}_{13}\text{H}_6\text{Br}_2\text{ClNOS}_2$: C, 34.57; H, 1.43. Found: C, 34.30; H, 1.55.

5-Bromo-N-(p-cyanophenyl)-3-chlorothiopheno[3,2-b]thiophene-2-carboxamide (6).

Compound **6** was prepared the same way as **5** from compound **3** (3.0 g, 9.5 mmol) in toluene (60 mL) and *p*-aminobenzonitrile (3.0 g, 30 mmol) in toluene (40 mL), to afford 0.5 g (13.2%) of yellow-green crystals, mp 256-260°C; IR (cm^{-1}): 3350 (NH), 3400 (NH), 2200 (CN), 1640 (CONH); $^1\text{H-NMR}$: 10.88 (s, 1H, NH), 7.91 (s, 1H, H thioph.), 7.67 (d, $J=8.79$ Hz, 2H, H arom.), 7.58 (d, $J=8.79$ Hz, 2H, H arom.); $^{13}\text{C-NMR}$: 158.79, 156.61, 142.62, 140.92, 133.40, 132.65, 132.19, 130.96, 120.61, 119.15, 113.65, 106.49, 105.49; Anal. Calcd. for $\text{C}_{14}\text{H}_6\text{Br}_2\text{ClN}_2\text{OS}_2$: C, 42.28; H, 1.52. Found: C, 42.35; H, 1.50.

6-Bromo-N-(p-bromophenyl)-3,5-dichlorothiopheno[3,2-b]thiophene-2-carboxamide (7).

Compound **7** was prepared on the same way as **5** from compound **4** (4.0 g, 11 mmol) in toluene (100 mL) and *p*-bromoaniline (2.5 g, 15 mmol) in toluene (50 mL) to give 0.78 g, (14.5%) of white crystals, mp 217-220°C; IR (cm^{-1}): 3380 (NH), 1650 (CONH); $^1\text{H-NMR}$: 10.56 (s, 1H, NH), 7.68 (d, $J=8.78$ Hz, 2H, H-arom.), 7.58 (d, $J=9.09$ Hz, 2H, H-arom.); $^{13}\text{C-NMR}$: 157.90, 144.08, 137.26, 133.40, 132.68, 132.50, 131.45, 122.46, 116.26, 112.86, 104.39; Anal. Calcd. for $\text{C}_{13}\text{H}_5\text{Br}_2\text{Cl}_2\text{NOS}_2$: C, 32.13; H, 1.04. Found: C, 32.13; H, 0.96.

6-Bromo-N-(p-cyanophenyl)-3,5-dichlorothiopheno[3,2-b]thiophene-2-carboxamide (8).

Compound **8** was prepared in the same way as **5** from compound **4** (4.0 g, 11 mmol) in toluene (100 mL) and *p*-aminobenzonitrile (2.2 g, 18 mmol) in toluene (50 mL). The precipitate was washed with hot chloroform and recrystallized from DMF to give 1.7 g (34.8%) of dark yellow crystals, mp 283-284°C; IR (cm^{-1}): 3350 (NH), 3400 (NH), 2200 (CN), 1660 (CONH); $^1\text{H-NMR}$: 10.89 (s, 1H, NH), 7.89 (s, 4H, H-arom); $^{13}\text{C-NMR}$: 161.88, 158.04, 148.32, 141.83, 133.08, 132.59, 131.99, 130.42, 120.44, 118.06, 106.42, 104.03; Anal. Calcd. for $\text{C}_{14}\text{H}_5\text{Br}_2\text{Cl}_2\text{N}_2\text{OS}_2$: C, 38.91; H, 1.17. Found: C, 39.09; H, 1.25.

2,9-Dibromo-5,6-dihydrothieno[2',3':4,5]thieno[2,3-c]quinolin-6-one (9).

A solution of anilide **5** (1.0 g, 2 mmol) in the mixture of toluene (600 mL) and methanol (60 mL) containing a few drops of triethylamine was irradiated with a 400 W high pressure mercury arc lamp at room temperature for 4 h using a Pyrex filter. During the irradiation air was bubbled through the solution. The precipitated yellow crystals were filtered off to give 0.3 g (29.2%) of product, mp > 300°C; IR (cm^{-1}): 3350 (NH), 1640 (CONH); $^1\text{H-NMR}$: 12.38 (s, 1H, NH), 8.18 (s, 1H, H thioph.) 7.85-7.42 (m, 3H, H arom.); Anal. Calcd. for $\text{C}_{13}\text{H}_5\text{Br}_2\text{NOS}_2$: C, 37.61; H, 1.21. Found: C, 37.50; H, 1.23.

2-Cyano-9-bromo-5,6-dihydrothieno[2',3':4,5]thieno[2,3-c]quinolin-6-one (10).

A solution of anilide **6** (0.12 g, 0.3 mmol) in toluene (500 mL) containing a few drops of triethylamine was irradiated for 1 h as described for **9**. After evaporation of the solvent 0.01 g (9.4%) of dark yellow crystals were obtained, mp > 300°C; IR (cm⁻¹): 3400 (NH), 2200 (CN), 1660 (CONH); ¹H-NMR: 12.66 (s, 1H, NH), 8.41-7.65 (m, 3H, H arom.). Anal. Calcd. for C₁₄H₅BrN₂OS₂: C, 46.54; H, 1.39. Found: C, 46.47; H, 1.13.

2,8-Dibromo-5,6-dihydro-9-chlorothieno[2',3':4,5]thieno[2,3-c]quinolin-6-one (11).

A solution of anilide **7** (0.5 g, 0.3 mmol) in toluene (450 mL) containing a few drops of triethylamine was irradiated for 3 h as described for **9**. The precipitated crystals were filtered off and washed with ether to afford 0.14 g (29.8%) of white crystals, mp > 300°C; IR (cm⁻¹): 1665 (CONH); ¹H-NMR: 12.37 (s, 1H, NH), 7.79-7.46 (m, 3H, H arom.); Anal. Calcd. for C₁₃H₄Br₂CINOS₂: C, 34.73; H, 0.89. Found: C, 34.95; H, 1.13.

2-Cyano-8-bromo-5,6-dihydro-9-chlorothieno[2',3':4,5]thieno[2,3-c]quinolin-6-one (12).

A solution of anilide **8** (0.8 g, 2 mmol) in a mixture of toluene (1800mL) and methanol (180 mL) plus a few drops of triethylamine was irradiated for 4 h as described for **9**. After evaporation of the solvent and washing the precipitate with ethanol 0.4 g (55.6%) of a dark yellow powder was obtained, mp > 300°C; IR (cm⁻¹): 2210 (CN), 1660 (CONH); ¹H-NMR: 13.39 (s, 1H, NH), 8.23-7.66 (m, 3H, H arom.); Anal. Calcd. for C₁₄H₄BrCINOS₂: C, 42.49; H, 1.02. Found: C, 42.53; H, 1.23.

2,4-Thienylenediacrylic acid (13).

A mixture of 3-(4-bromo-2-thienyl)acrylic acid (**2**, 2.7 g, 10 mmol), cyclohexylammonium acrylate (10.74 g, 60 mmol), palladium(II)acetate (0.054 g), triphenylphosphine (0.180 g), triethylamine (18 mL) and acetonitrile (35 mL) was sealed in a glass tube and heated at 120°C for 20 h. After evaporation of the solvent under reduced pressure, the residue was dissolved in water and boiled with charcoal. After filtration, the filtrate was acidified with dilute HCl (1:1). The resulting precipitate was filtered off and recrystallized from acetic acid to give **13** (1.14 g, 43.5 %) as yellow crystals, mp 232-235°C (lit. [30] 232-235°C).

3,6-Dichlorodithieno[2,3-b:2',3',-d]thiophene-2,5-dicarbonylchloride (14).

Compound **14** was prepared in the same way as **3** from **13** (1.9 g, 8.0 mmol), thionyl chloride (27 mL, 383 mmol) and pyridine (0.2 mL). The yield of crude product was 2.5 g (75.2%) and this material was used directly in the next step of the reaction [34].

N,N'-di(*p*-bromophenyl)-3,6-dichlorothieno[2,3-*b*:2',3'-*d*]thiophene-2,5-dicarboxamide (**15**).

Compound **15** was prepared from **14** (2.5 g, 6.0 mmol) suspended in chloroform (60 mL) and *p*-bromoaniline (2.3 g, 0.013 mmol) in chloroform (40 mL) as described for the preparation of **5**. After refluxing the reaction mixture for 1.5 h and cooling, 0.5 g (12.9%) of the title compound were obtained as white crystals that were recrystallized from DMF, mp >300°C; IR (cm⁻¹): 3400 (NH), 1665 (CONH); ¹H-NMR: 10.45 (s, 2H, NH), 7.69 (d, *J*=8.85 Hz, 4H, H arom.), 7.58 (d *J*=8.84 Hz, 4H, H arom.); ¹³C-NMR: 158.10, 157.97, 147.75, 143.94, 141.75, 141.00, 137.94, 137.17, 137.11, 135.64, 134.96, 131.17, 131.17, 131.17, 131.17, 128.37, 122.37, 122.37, 122.37, 122.37, 118.18, 116.01; Anal. Calcd. for C₂₂H₁₀Br₂Cl₂N₂O₂S₃: C, 39.96; H, 1.52. Found: C, 40.13; H, 1.58.

N,N'-di(*p*-cyanophenyl)-3,6-dichlorothieno[2,3-*b*:2',3'-*d*]thiophene-2,5-dicarboxamide (**16**).

Compound **16** was prepared on the same way as **15** from **14** (0.9 g, 2.0 mmol) in chloroform (22 mL) and *p*-aminobenzonitrile (0.8 g, 7.0 mmol) in chloroform (40 mL). After refluxing the reaction mixture for 1.5 h and cooling, 0.5 g (35.3%) of white crystals, recrystallized from DMF, were obtained mp >300°C; IR (cm⁻¹): 3480 (NH), 2200 (CN), 1660 (CONH); ¹H-NMR: 10.79 (s, 1H, NH), 10.78 (s, 1H, NH), 7.88-7.58 (m, 8H, H-arom.); ¹³C-NMR: 159.09, 159.09, 143.29, 142.71, 142.62, 141.77, 134.85, 134.85, 133.57, 132.19, 132.19, 132.19, 132.19, 131.09, 128.81, 120.56, 120.56, 120.53, 120.53, 119.72, 119.15, 117.18, 106.32, 106.32. Anal. Calcd. for C₂₄H₁₀Cl₂N₄O₂S₃: C, 52.08; H, 1.82. Found: C, 52.13; H, 2.11.

*2,10-Dibromo-5,6,13,14-tetrahydrodithieno[2,3-*b*:2',3'-*d*]thieno[2'',3''-*c*:2'',3''-*c'*]diquinoline-6,14-dione (**17**).*

A solution of dianilide **15** (0.056 g, 0.085 mmol) in the mixture of toluene (900mL) and methanol (90 mL) containing a few drops of triethylamine was irradiated with 400 W high pressure mercury arc lamp at room temperature for 1 h using a Pyrex filter. During the irradiation air was bubbled through the solution. The precipitated powder was filtered off and washed with ether. Compound **17** (0.024 g, 48.9 %) was obtained as white crystals, mp > 300°C, insoluble in all common solvents. IR (cm⁻¹): 3400 (NH), 1660 (CONH); MS *m/z*: 587 (M+1); Anal. Calcd. for C₂₂H₈Br₂N₂O₂S₃: C, 44.91; H, 1.63. Found: C, 45.05; H, 1.37.

References

1. Fuller, L.S.; Iddon, B.; Smith, K.A. Thienothiophenes. Part 3. On the ring-opening reactions of 3-lithiated and 3,6-dilithiated thieno[3,2-*b*]thiophenes; new routes to polyfunctionalized thiophenes and enediyne. *J. Chem. Soc. Perkin Trans. 1* **1999**, 1273-1277.
2. Fuller, L.S.; Iddon, B.; Smith, K.A. Synthesis of polyfunctionalized thiophenes and enediyne via ring-opening Reactions of 3-lithiated thieno[2,3-*b*]thiophenes, 3,4-dilithiated thieno[2,3-*b*]thiophenes and 3,6-dilithiated thieno[3,2-*b*]thiophenes. *Chem. Commun.* **1997**, 2355-2356.

3. Fuller, L.S.; Iddon, B.; Smith, K.A. Thienothiophenes. 2. Synthesis, metallation and bromine-lithium exchange reactions of thieno[3,2-b]thiophene and its polybromoderivatives. *J. Chem. Soc. Perkin Trans. 1* **1997**, 3465-3470.
4. Whitfield, F.B.; Mottram, D.S. Heterocyclic volatiles formed by heating cysteine or hydrogen sulfide with 4-hydroxy-5-methyl-3(2H)-furanone at pH 6. *J. Ag. Food Chem.* **2001**, *49*, 816-822.
5. Whitfield, F.B.; Mottram, D.S. Investigation of the reaction between 4-hydroxy-5-methyl-3(2H)-furanone and cysteine or hydrogen sulfide at pH 4.5. *J. Ag. Food Chem.* **1999**, *47*, 1626-1634.
6. Mashraqui, S.H.; Ashraf, M.; Hariharasubrahmanian, H.; Kellogg, R.M.; Meetsma, A. Donor-acceptor thieno[2,3-b]thiophene systems: synthesis and structural study of 3-anisyl-4-pyridyl(pyridinium) thieno[2,3-b]thiophenes. *J. Mol. Struct.* **2004**, *689*, 107-113.
7. Moustafa, H.M.; Khodairy, A.; El-Saghier, A.M.M. Synthesis of some new polyfused thienothiophenes Part 4: Synthesis of thienopyrimidine, thienotriazine, thienoimidazotriazine, thienotriazolotriazine, and thienotetrazolotriazine derivatives. *Phosphorus, Sulfur Silicon Relat. Elem.* **2003**, *178*, 1211-122.
8. Pavličić, D.; Koružnjak J.D.; Banić-Tomišić, Z.; Karminski-Zamola, G. Synthesis of some new bis-(p-fluorophenyl)amides of the thieno[3,2-b]thiophene, thieno[3,2-b]furan and 1,2-bis{5-[2-(2-thienyl)ethenyl]2-thienyl}ethene series. *Molecules* **2002**, *7*, 871-884.
9. Yasuke, S.; Kurita, J.; Tsuchiya, T. Synthesis of novel group 15 and 16 thieno[2,3-b]-, thieno[3,4-b]-, and thieno[3,2-b]-heteroles. *Heterocycles* **1997**, *45*, 1891-1894.
10. Hawkins, D.W.; Iddon, B.; Longthorne, D.S.; Rosyk, P.J. Synthesis of thieno-[2,3-b]-, -[3,2-b]- and -[3,4-b]-thiophenes and thieno-[3',2'/4,5]-, -[2',3'/4,5]- and -[3',4'/4,5]-thieno[3,2-d]pyrimidin-7(6h)-ones starting from thiophene. *J. Chem. Soc. Perkin Trans. 1* **1994**, 2735-2743.
11. Choi, K.S.; Sawada, K.; Dong, H.; Hoshino, M.; Nakayama, J. A one-pot synthesis of substituted thieno[3,2-b]thiophenes and selenolo[3,2-b]selenophenes. *Heterocycles* **1994**, *38*, 143-149.
12. Nakayama, J.; Dong, H.; Sawada, K.; Ishii, A.; Kumakura, S. Synthesis and characterization of dimers, trimers, and tetramers of 3,6-dimethylthieno[3,2b]thiophene and 3,6-dimethylselenolo[3,2b]selenophene. *Tetrahedron* **1996**, *52*, 471- 488.
13. Capozzi, G.; Desio, F.; Manichetti, S.; Nativi, C.; Pacini, P.L. Phthalimidesulfenyl chloride. 7. Synthesis of 2-substituted 3-chlorobenzo[b]thiophenes and related heteroaromatics. *Synthesis* **1994**, 521-525.
14. Otsubo, T.; Kono, Y.; Hozo, N.; Miyamoto, H.; Aso, Y.; Ogura, F.; Tanaka, T.; Sawada, M. Syntheses, structures, and properties of 2,3,6,7-tetrathiabenzo[1,3-cd:4,6-c'd']dipentalene and its methyl, ethyl, methylthio, and ethylthio derivatives - novel fused polynuclear heteroarenes. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2033-2041.
15. Block, E.; Guo, C.; Thiruvazhi, M.; Toscano, P.J. Total synthesis of thiarubrine B [3-(3-buten-1-ynyl)-6-(1,3-pentadiynyl)-1,2-dithiin], the antibiotic principle of giant ragweed (*ambrosia trifida*). *J. Am. Chem. Soc.* **1994**, *116*, 9403-9404.
16. Schroth, W.; Hintzsche, E.; Jordan, H.; Jende, T.; Spitzner, R.; Thondorf, I. 1,2-Dithiins and precursors. 17. Synthesis and properties of thieno annellated 1,2-dithiins - structural influence on colour. *Tetrahedron* **1997**, *53*, 7509-7528.
17. (a) Fernández Fernández, M.I.; Hotten T.M.; Tupper, D.E. Thiophene carboxamide deriv. prepn. Span. Pat. Appl. ES 2,008,635, **1988** [*Chem. Abstr.* **1991**, *114*, 207008b]; (b) Fernández Fernández, M.I.; Hotten, T.M.; Tupper, D.E. Amino-thiophene deriv. prepn. Span. Pat. Appl. ES

- 2,008,634, **1989** [*Chem. Abstr.*, **1991**, *114*, 207009c]; (c) Fernández Fernández, M.I.; Hotten T.M.; Tupper, D.E. Thiophene carboxamide deriv. prepn. Span. Pat. Appl., *ES 2,008,630*, **1989** [*Chem. Abstr.*, **1991**, *114*, 207010w]; (d) Fernández Fernández, M.I.; Hotten T.M.; Tupper, D.E. Thiophene carboxamide deriv. prepn. Span. Pat. Appl. *ES 2,008,631*, **1989** [*Chem. Abstr.*, **1991**, *114*, 207011x]; (e) Fernández Fernández, M.I.; Hotten T.M.; Tupper, D.E. Thiophene carboxamide deriv. prepn. Span. Pat. Appl. *ES 2,008,632*, **1989** [*Chem. Abstr.*, **1991**, *114*, 207012y]; (f) Fernández Fernández, M.I.; Hotten T.M.; Tupper, D.E. Amino-thiophene deriv. prepn. Span. Pat Appl., *ES 2,008,633*, **1989** [*Chem. Abstr.*, **1991**, *114*, 207013z]; (g) Fernández Fernández, M.I.; Hotten T.M.; Tupper, D.E. Thiophene carboxamide deriv. prepn. Span. Pat. Appl., *ES 2,008,636*, **1989** [*Chem. Abstr.*, **1991**, *115*, 71382e].
18. Meunster, P.; Steiner, G.; Freund, W.; Wuerzer, B.; Westphalen, K.O. Carboxamides and their use as herbicides. *Ger. Offen. Appl.* **3,933,573**, **1991** [*Chem. Abstr.*, **1991**, *115*, 71383f].
 19. Boschelli, D.H.; Kramer, J.B.; Connor, D.T.; Lesch, M.E.; Schrier, D.J.; Ferin, M.A.; Wright, C.D. 3-Alkoxybenzo[b]thiophene-2-carboxamides as inhibitors of neutrophil endothelial cell adhesion. *J. Med. Chem.* **1994**, *37*, 717-718.
 20. Kabir, S.M.H.; Miura, M.; Sasaki, S.; Harada, G.; Kuwatani, Y.; Yoshida, M.; Iyoda, M. New syntheses of tricyclic thiophenes and cyclic tetrathiophenes using transition-metal-catalyzed cyclization. *Heterocycles* **2000**, *52*, 761-774.
 21. Iyoda, M.; Miura, M.; Sasaki, S.; Kabir, S.M.H.; Kuwatani, Y.; Yoshida, M. Synthesis of dithienothiophenes, cyclopentadithiophene and silacyclopentadithiophenes using palladium-catalyzed cyclization. *Tetrahedron Lett.* **1997**, *38*, 4581-4582.
 22. Remonen, T.; Hellberg, J.; Vonschutz, J.U. New dithienothiophene donors for cation radical salts. *Synth. Met.* **1997**, *86*, 1851-1852.
 23. Fujitsuka, M.; Sato, T.; Watanabe, A.; Ito, O.; Shimidzu, T. Photochemical polymerization of dithienothiophenes. *Chem. Lett.* **1996**, 285-286.
 24. Fujitsuka, M.; Sato, T.; Segawa, H.; Shimidzu, T. Photochemical polymerization of oligothiophene and dithienothiophene. *Synth. Met.* **1995**, *69*, 309-310.
 25. Karminski-Zamola, G.M.; Pavličić, D.; Bajić, M.; Blažević, N. The synthesis of new heteropolycyclic quinolone by twofold photocyclization: methoxycarbonylnaphto[2",1":2',3'-b]thieno[4',5':2,3]thieno[5,4-c]quinolin-6(5H)-one. *Heterocycles* **1991**, *32*, 2323-2327.
 26. Dogan, J.; Karminski-Zamola, G.M.; Boykin, D.W. Photosynthesis of heteropolycyclic quinolones. *Heterocycles* **1995**, *41*, 1659-1666.
 27. Malešević, M.; Karminski-Zamola, G.; Bajić, M.; Boykin, D.W. Photosynthesis of heteropolycyclic diquinolones twofold photodehydrohalogenation reaction of benzo[1,2-b:4,5-b']dithiophene- and dithieno[3,2-b:2',3'-d]thiophenedicarboxanilides. *Heterocycles* **1995**, *41*, 2691-2699.
 28. Dogan Koružnjak, J.; Slade, N.; Zamola, B.; Pavelić, K.; Karminski-Zamola, G. Synthesis, photochemical synthesis and antitumor evaluation of novel derivatives of thieno[3',2':4,5]thieno[2,3-c]quinolones. *Chem. Pharm. Bull.* **2002**, *50*, 656-660.
 29. Capron, B.; Paulmier, C.; Pasteour, P. Synthesis of 3-furyl, 3-thienyl and 3-selenienyl propenoic acids and esters. A route to substituted thienothiophenes and selenolothiophenes. *Bull. Soc. Chim. France* **1975**, 2575-2583.

30. Blažević Šafarik, J.; Karminski-Zamola, G.; Marinić, Ž.; Klaić, B.; Mrvoš-Sermek, D. Convenient synthesis H-1, C-13 NMR study and X-ray crystal structure determination of some new disubstituted thiophenes. *Spectrosc. Lett.* **1999**, *32*, 443-462.
31. Ried, W.; Oremek, G; Ocakciogku, B. Synthese von substituierten benzo(b)thiophenen. *Liebigs Ann. Chem.* **1980**, 1424-1427.
32. Wright Jr, W. B. Preparation of 3-chlorothieno[3,2-b]thiophene derivatives from thiophene-2-acrylic acids. *J. Heterocycl. Chem.* **1972**, *9*, 879-882.
33. Karminski-Zamola, G.; Dogan, J.; Bajić, M.; Blažević, J.; Malešević, M. Synthesis of some furylacrylates and thienylacrylates or diacrylates and acrylic acids by the palladium catalysed vinylation of substituted bromofurans and bromothiophenes. *Heterocycles* **1994**, *38*, 759-767.
34. Capron, B.; Paulmier, C.; Pasteour, P. Preparation and properties of β -thienyl and β -selenienyl propenoic acids. *C. R. Acad. Sci., Ser. C* **1973**, *277*, 167-170.

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