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SYNTHESIS AND STRUCTURES OF SOME NEW THIENO[3,2-*b*]THIOPHENE DERIVATIVES

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Abstract. Three new derivatives containing thieno[3,2-*b*]thiophene, *ethyl 5-(anthracen-9-yl)thieno[3,2-b]thiophene-2-carboxylate* (**1a**), *ethyl 5-(4-cyanophenyl) thieno[3,2-b]thiophene-2-carboxylate* (**1b**) and *3-(5-(anthracen-9-yl)thieno[3,2-b] thiophen-2-yl)pyridine (**2a**)* were synthesized by arylation reaction in presence of 1.0 mol% of $Pd(OAc)_2$. Their structures were elucidated with NMR, MS and X-Ray analysis. The selectivity of arylation was at C6 of either ester or pyridine substituted instead of C2 positions.

Keywords: Thieno[3,2-*b*]thiophene, ethyl thieno[3,2-*b*]thiophene-2-carboxylate, semiconductor, arylation, diacetoxypalladium.

1. Introduction

The direct palladium-catalyzed arylation of arenes andheteroarenes by C-H bond activation by using aryl halides has become one of the most powerful methods to make derivatives containing thieno[3,2-*b*]thiophene[1-4]. Because thieno[3,2-*b*]thiophene has special structures of intermolecular sulfur-sulfur interactions. Organicmaterials containing the thieno[3,2-*b*]thiophene moiety plays an important role in increasing electronic transport between neighboring molecules. Recently, plenty of materials containing thethieno[3,2-*b*]thiopheneas a core has been published using this method. For example, semiconductive polymers containing the thieno[3,2-*b*]thiophene unit were prepared to make various substituted derivatives [5]. The organic semiconductor of 1,3,6,8-tetera(-thieno[3,2-*b*]thienyl)pyrene family was successfully applied in the development of new organic light-emitting diodes (OLEDs) [6]. Several well-soluble thieno[3,2-*b*]thiophene-based oligomers [7] and 2,5-di(2-azulenyl)thieno[3,2-*b*]thiophenes [8, 9] were discovered. Application of derivatives containing thieno[3,2-*b*]thiophene were investigated as a dye-sensitized solar cells [10], protein-coupled receptor 35 [11].

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Herein, we wish to report three new derivatives containing thieno[3,2-*b*]thiophene synthesized from ethyl thieno[3,2-*b*]thiophene-2-carboxylate (**1**) and 3-(thieno[3,2-*b*]thiophen-2-yl)pyridine (**2**) with low catalyst loading to make greener chemistry.

2. Content

2.1. Experiments

2.1.1. Chemicals and equipment

Solvents and other chemicals were purchased from Sigma-Aldrich, Merck Corp, Aladdin, Vietnam or other China's companies were used as received, unless indicated. The NMR spectra were recorded on the BrukerAvance 500 MHz NMR spectrometer in $CDCl_3$. Chemical-shift data for each signal was reported in ppm. X-ray was recorded on a D8 QUEST Bruker (Germany) instrument at 100 K with Mo Kα radiation (λ = 0.71073 Å) using a TRIUMPH monochromatorat the Department of Chemistry, VNU - Hanoi University of Science, 19 Le Thanh Tong Street, Hanoi, Vietnam.

2.1.2. Synthetic procedure

General procedure for synthesis of thieno[3,2-b]thiophene derivatives

Ethyl thieno[3,2-*b*]thiophene-2-carboxylate (**1**) or 3-(thieno[3,2-*b*]thiophen-2-yl)pyridine (**2**)(0.5 mmol), bromoarenes (0.5 mmol), $Pd(OAc)_2$(1.68 mg, 1.0mol%), and KOAc (245 mg, 0.5 mmol, 5.0 eq) were dissolved in degased DMAc (5 mL). The resulting reaction mixture was heated at 110 ^oC under argon atmosphere until TLC (*n*-hexane/ethyl acetate) showed the complete consumption of the starting material (8 hours). The reaction mixture was cooled to room temperature and filtered to remove insoluble impurities. The filtrate was diluted with ethyl acetate, washed with water (3 times), dried over with anhydrous Na_2SO_4, and concentrated in vacuum by rotary evaporation. Flash column with eluent (*n*-hexane/ethyl acetate 99: 1, v/v) gave **1a**, **1b** (from **1**) and **2a** (from **2**) in moderate yields.

Ethyl 5-(anthracen-9-yl)thieno[3,2-b]thiophene-2-carboxylate (**1a**)

Orange solid (105 mg, 54%).Mp 128-129 ^oC; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.55 (s, 1H), 8.08 (s, 1H), 8.04 (d, J = 8.5 Hz, 2H), 7.89 (d, J= 8.5 Hz, 2H), 7.47 (td, J = 7.5, 1.0 Hz, 2H), 7.42 (td, J = 7.5, 1.0 Hz, 2H), 7.35 (s, 1H), 4.43 (q, J = 7.5 Hz, 2H), 1.43 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 162.7, 145.8, 143.9, 139.8, 134.6, 131.5, 131.1, 128.8, 128.4, 127.6, 126.3, 126.1, 125.6, 125.4, 121.9, 61.4, 14.4; EI-MS m/z: $[M+H]^+$ calcd. for $C_{23}H_{17}O_2S_2$ 389, found 388.9.

Ethyl 5-(4-cyanophenyl)thieno[3,2-b]thiophene-2-carboxylate (**1b**)

Pale yellow solid (81.4mg, 52%).Mp 105-106 $^oC$$^1H$ NMR ($CDCl_3$, 500 MHz): δ 7.97 (d, J = 0.5 Hz, 1H), 7.73 (d, J = 8.5 Hz, 2H), 7.69 (d, J = 8.5 Hz, 2H), 7.59 (d, J = 0.5 Hz, 1H), 4.39 (q, J = 7.5 Hz, 2H), 1.40 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 162.9, 138.0, 134.2, 133.5, 132.6, 128.1, 122.9, 121.3, 119.2, 118.3, 112.5, 60.1, 14.1; EI-MS m/z: $[M+H]^+$ calcd.for $C_{16}H_{12}NO_2S_2$ 314, found 313.9.

*3-(5-(Anthracen-9-yl)thieno[3,2-b]thiophen-2-yl)pyridine (**2a**)*

Orange solid (88.0 mg, 45%).Mp 142-143 ^oC; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.98 (1 H, s), 8.56 (d, J = 5.5 Hz, 1 H), 8.55 (s, 1H), 8.04 (d, J = 8.5 Hz, 2H), 7.96 (d, J = 8.5

Hz, 2H), 7.92 (dt, *J* = 8.0 Hz, 1.5 Hz, 1H), 7.62 (s, 1H), 7.49 (dt, *J* = 7.0 Hz, 2H), 7.42 (dt, *J* = 8.5, 0.5 Hz, 2H), 7.35 (t, *J* = 6.5 Hz, 1H), 7.35 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 148.7, 146.9, 141.7, 141.5, 141.2, 139.1, 132.9, 131.8, 131.1, 130.9, 128.6, 128.4, 128.0, 126.4, 126.2, 125.4, 123.8, 121.8, 116.6. EI-MS m/z: $[M+H]^+$calcd. for $C_{25}H_{16}NS_2$ 394.0, found 393.9.

2.2. Results and discussion

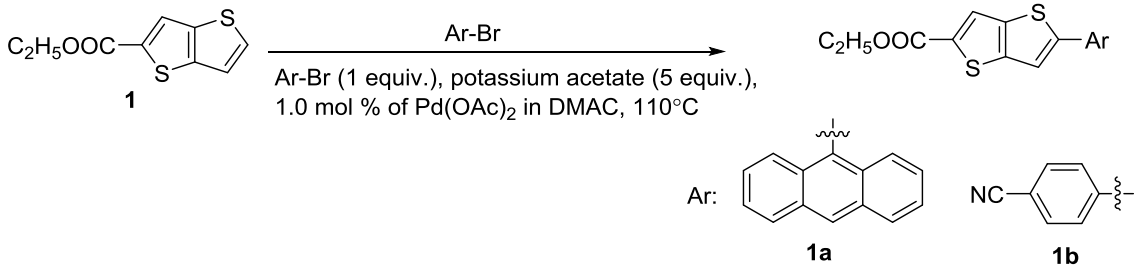
Starting material **1**, ethyl thieno[3,2-*b*]thiophene-2-carboxylate, was prepared according to the method of Fuller and co-workers from commercially available 3-bromothiophene [12,13]. In order to optimize the condition of loading the $Pd(OAc)_2$ during **1a** synthesis, 9-bromoanthracene and starting material **1** were taken as shown in the Table 1, Scheme 1.

Table 1. Optimization of the dependence of [Pd] mol % in preparing 1a

Entry	$Pd(OAc)_2$mol%	Yield of 1a (%)*
1	0.5	36
2	1.0	54
3	1.5	54
4	2.0	52
5	2.5	53
6	3.0	52

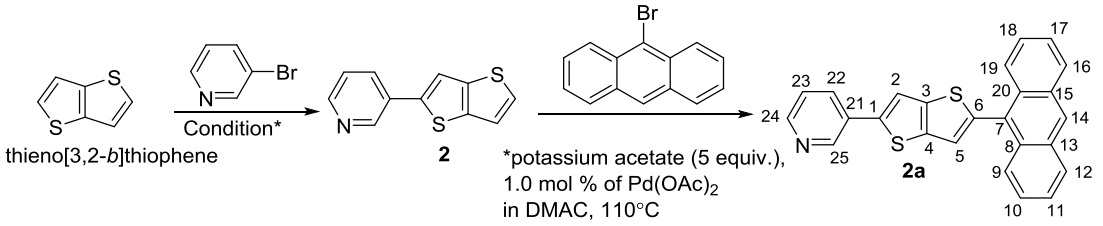
*Reaction condition: 9-bromoanthracene (1 equiv.), ethyl thieno[3,2-b]thiophene-2-carboxylate **1**(1 equiv.), potassium acetate (5 equiv.), $Pd(OAc)_2$in DMAC, 110 ℃, 22h. * after purified*

Results of optimization showed that mol% of $Pd(OAc)_2$ can be loaded at 1.0mol % that gave the best yield. Meanwhile mol % of $Pd(OAc)_2$at 0.5 gave the lowest yield. Yields of reaction loaded from 2.0 to 3.0 mol% of $Pd(OAc)_2$ were quite similar as loaded 1.0% one. Applying the above optimization, derivative **1b** was synthesized in moderate in the same fashion.



Scheme 1. Synthesis of compounds 1a and 1b

3-(Thieno[3,2-*b*]thiophen-2-yl)pyridine (**2**) was synthesized from thieno[3,2-*b*] thiophene and 3-bromopyridine following exactly the above optimized protocol in 67 % yield (the first arylation) [14]. However, the second arylation when compound **2** was treated with 9-bromoanthracene gave **2a** in a bit lower yield, Scheme 2.



Scheme 2. Synthesis of compound 2a

In order to determine the selectivity of arylation at C6 at the second state as well as structures, derivatives **1a**, **1b** and **2a** were recorded NMR and MS spectra; derivatives **1a** and **2a** were taken X-ray spectra.The ethyl thieno[3,2-*b*]thiophene-2-carboxylate (**1**) or3-(thieno[3,2-*b*]thiophen-2-yl)pyridine (**2**) as starting materials both gave arylation at C6. Hence, the electron withdrawing groups seemed that they did not affect on the second arylation reaction due to sulfur and steric effect, Figure 1.

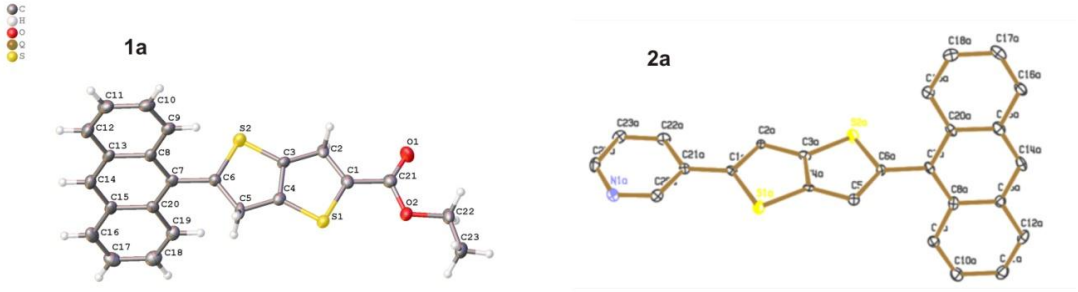


Figure 1. X-ray spectra of compounds 1a and 2a

NMR analysis also had good agreement with data of X-ray spectra. All signals in HMBC of **2a**, Figure1 are associated with its structure [15]. For example, assignment of carbon and hydrogen was shown in Figure 2. As known, compound **1a** owns four singlet protons which are H25, H14, H5 and H2. Of all, H25 has the highest chemical shift at 8.98 ppm due to the electronic effect of N and thieno[3,2-*b*]thiophene ring [7], so it is the starting point to assign other. First, the cross peak ***k*** indicated the C25 at 146.9 ppm and ***k'*** confirmed H22 at 7.92 ppm (dt, J = 8.0, 1.5 Hz, 1H). H25 also had cross peaks **a'**, **b'** and **c'** indicating C24 (147.7 ppm), C22 (132.9 ppm) and C1 (130.9 ppm) respectively. In addition, the correlation peak **i'** and **c** showed the H23 at 7.35 ppm (t, J = 6.5 Hz, 1H) and C23 at 123.7 ppm. Other two singlet protons were H5 at 7.62 ppm (s, 1H) and H2 at 7.35 ppm (s, 1H). Especially, H2 was overlapped with H23 at the same chemical shift of a triplet. This observation was important to identify C4 (141.6 ppm), C7 (141.5 ppm), C21 (141.2 ppm) and C3 (139.1 ppm) respectively. Consequently, cross peaks **a**, **b** indicated C2 at 121.7 ppm and C5 at 116.6 ppm. Then, C7 was observed with showing a cross peak **g'** with H9 and H19 at 7.96 ppm (d, J =8.5 Hz, 2H) and peak **f** let us confirmed C9 and C19 at 126.3 ppm. After assignment of three singlets out four, the last one at 8.55 ppm belongs to H14, which help to identify C8 and C20 at 131.8 ppm; C16 and C12 at 128.3 ppm. Finally, all carbons and hydrogens were assigned as shown in detail in Figure 2 and Table 2. EI-MS spectrum of compound **2a** showed a base peak at 393.9 au that was matched with the *pseudo* molecular weight $[M+H]^+$.

Table 2. NMR data of compound 2a in $CDCl_3$

^{1}H NMR (500 MHz)				**^{13}C NMR** (125 MHz)			
No.	σ (ppm), J (Hz)	No.	σ (ppm), J (Hz)	No.	σ (ppm)	No.	σ (ppm)
1	-	11, 17	7.49 (dt, *J*7.0, 2H)	1	130.9	11, 17	125.3
2	7.35 (s, 1H)	12,16	8.04 (d, *J*8.5, 2H)	2	121.7	12,16	128.3
3	-	13,15		3	139.1	13,15	131.1
4	-	14	8.55 (s, 1H)	4	141.6	14	128.5
5	7.62 (s, 1H)	20	-	5	116.6	20	131.8
6	-	21	-	6	128.0	21	141.2
7	-	22	7.92 (dt, *J* 8.0, 1.5, 1H)	7	141.5	22	132.9
8	-	23	7.35 (t, *J*6.5, 1H)	8	131.8	23	123.7
9,19	7.96 (d, *J*8.5, 2H)	24	8.56 (d, *J*5.5, 1 H),	9,19	126.3	24	148.7
10, 18	7.42 (dt, *J*8.5, 0.5, 2H)	25	8.98 (1 H, s)	10,18	126.2	25	146.9

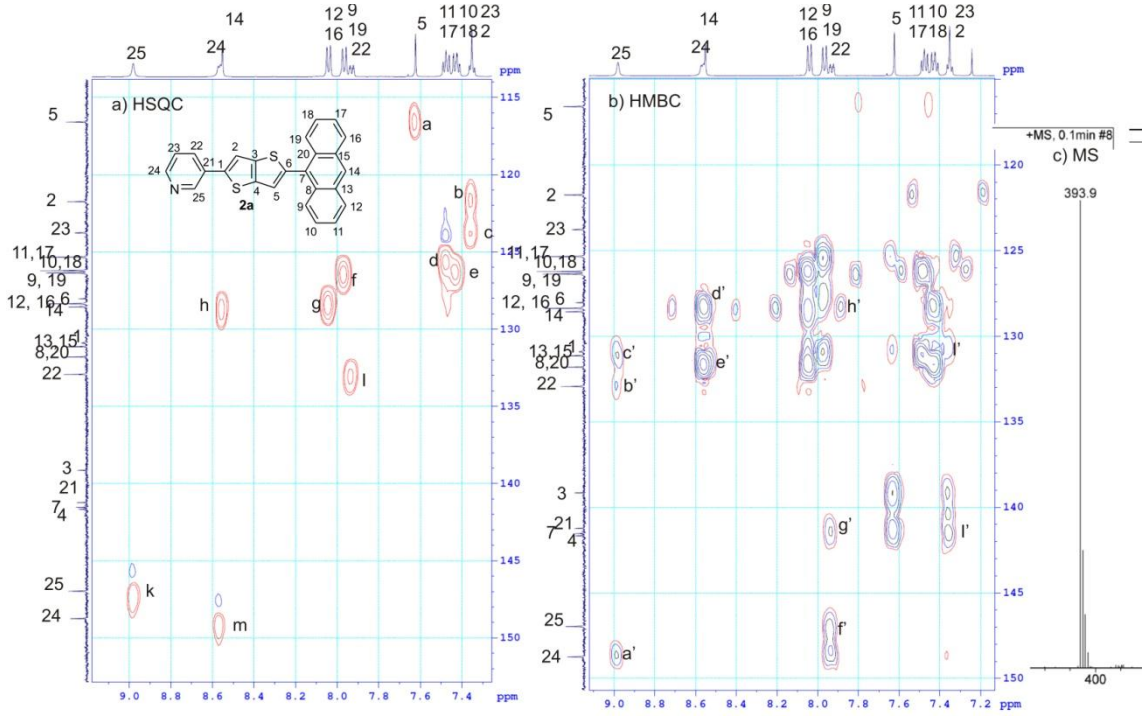


Figure 2. a) HSQC; b) HMBC; c) MS spectra of compound 2a

3. Conclusions

Arylation of mono substituted thieno[3,2-*b*]thiophene was carried out successfully in moderate yields in low loading of catalyst $Pd(OAc)_2$ at about 1.0mol %. X-ray and NMR spectra indicated the selectivity of the second arylation at C6 position.

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