A General and Simple Method for the Synthesis of Star-Shaped Thiophene Derivatives[1]

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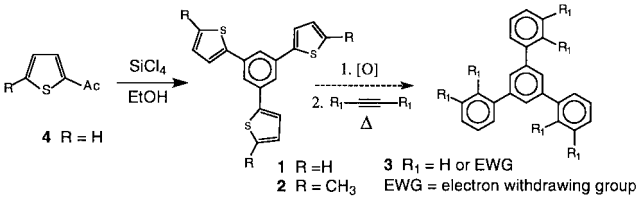
Abstract: One pot synthesis of 1, 3, 5-tris(thienyl)benzene derivatives *via* tetrachlorosilane mediated trimerization reaction is described.

Key words: thiophenes, acylation, tetrachlorosilane, polycyclics; trimerization

Substituted thiophenes are valuable building blocks in many natural and non-natural products and enjoy potential applications in flavor and pharmaceutical industries.[2] In addition to these synthetic implications, thiophenes occur abundantly as structural units in many natural molecules.[3] Raney nickel desulfurization has made thiophenes as useful intermediates for the preparation of the aliphatic compounds.[4] Moreover, a number of substituted thiophenes are apt to give sulfones, yielding non-aromatic compounds which undergo Diels-Alder reaction to generate the polycyclics.[5, 6]

Due to the intractable nature of polythiophene (PT) there is a need to modify PT to make it as processible as conventional organic polymers.[7] Oligothiophenes are useful model systems for PT and in this regard Garnier and coworkers[8] have shown that the semiconducting properties of PT are already present in α-conjugated sexithienyl. For design of the new generation of polymers more knowledge is required for the monomer preparation.

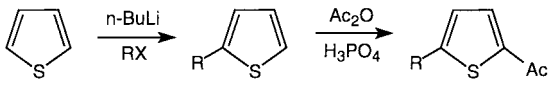
In connection with our interest in unusual amino acids preparation *via* building block approach[9] we conceived the building blocks containing C_3-symmetry element is an attractive option.[1] In this regard, we identified cyclotrimerization of carbonyl compounds as a useful strategy.[10] Some of these C_3-symmetric building blocks are also useful in the preparation of dendrimer molecules[11] and fullerene fragments.[12] For example, oxidation of **1** followed by Diels-Alder reaction with the appropriately substituted acetylenic dienophiles is expected to give inaccessible 1, 3, 5-triphenyl benzene derivatives (e.g., **3**, Scheme 1).[10] Compound **2** is a useful starting material for the synthesis of C_3-symmetric amino acids by asymmetric derivatization of glycine moiety. Similarly, monoacetylation and trimerization of compound **1** may generate mixed aryl-thienyl oligomer. Our attempts to use repetitive acetylation and trimerization sequence starting from acetophenone to generate dendrimers *via* **3** was not realized due to the insoluble nature of polyphenyl hydrocarbons (PPHs). At this juncture we reasoned out that the heteroaromatic systems may obviate the problems associated with the PPHs. In this regard, we attempted tetrachlorosilane ($SiCl_4$) mediated trimerization of 2-acetylfuran and found that a complex mixture of products was formed. In view of the ring opening reactions of furan under acidic conditions, this result was not surprising to us.



Scheme 1

Since, thiophene derivatives are more stable to various Lewis acid conditions, we next tried the trimerization reaction of 2-acetylthiophene **4** which can be prepared by treatment of thiophene with acetic anhydride / phosphoric acid at 70-75 °C.[13] Treatment of **4** with $SiCl_4$ at room temperature gave **1** in 42% yield after chromatography. After completion of our work[1] preparation of compound **1** is reported by an indirect route involving Pd mediated coupling reaction as a key step.[14] However, attempts to trimerize 2-acetylthiophene **4** using nafion-H gave no condensation product.[15] Our methodology to these compounds is straightforward and involves inexpensive starting materials.

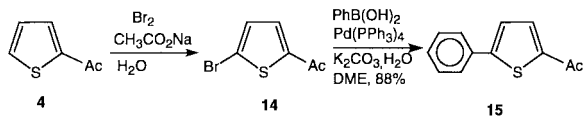
After successful trimerization of **4** with $SiCl_4$, we decided to generalize this reaction with other thiophene derivatives. Various acetylated thiophenes (**5-7** and **9**) were prepared *via* alkylation[16] and acetylation[13] sequence (eq 1). Compound **9** was prepared according to the literature procedure.[17]



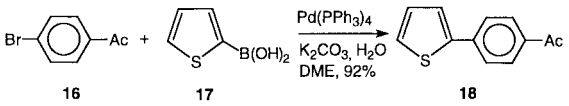
Equation 1

Recently, Hiyama et al. prepared compound **18** *via* palladium-catalyzed cross-coupling of organosilicon compounds.[18] However, we have adopted palladium-catalyzed cross-coupling reaction[19] of phenylboronic acid [20] and 2-acetyl-5-bromothiophene **14**[21] to obtain **15** (mp.

109-110 °C) in 88% yield (eq 2). Along similar lines, coupling of 4-bromoacetophenone **16** and 2-thiopheneboronic acid **17**[20] gave compound **18** (mp. 115-116 °C) in 92% yield (eq 3).



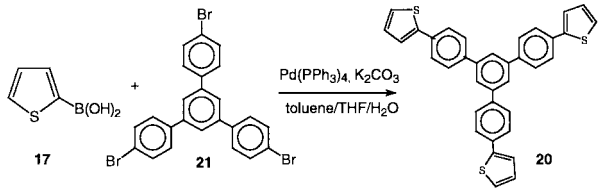
Equation 2



Equation 3

In a typical experimental procedure, acetyl thiophene derivative (0.04 mol) was treated with $SiCl_4$ (2-18 equivalents) in absolute ethanol (40 ml) at 0 °C and the reaction mixture was stirred at ambient temperature. At the conclusion of reaction (TLC), the dark reaction mixture was poured into ice cold water and extracted with dichloromethane. Combined organic extracts were washed with water and then dried over $MgSO_4$. Evaporation of the solvent and purification of the crude product by column chromatography (silica gel) using hexane as a eluent furnished the trimerized product. The trimerization results of acetyl thiophene derivatives are shown in the Table. ^1H NMR and appropriate number of signals in ^{13}C NMR spectra confirmed the presence of C_3 symmetry in all the trimerized products presented in the Table.♦

Compound **20** was independently synthesized by the palladiam mediated coupling of **17** with tribromo derivative **21** in 14% isolated yield (eq 4).



Equation 4

In conclusion, we have shown that various acetylated thiophene derivatives undergo trimerization reaction to generate C_3-symmetric building blocks which may find useful applications in catalysis[22] and organic synthesis. Availability of mixed aryl-thienyl oligomers where the thiophene unit is present either in inner or outer core of the molecule (e.g., **19** and **20**) by one-pot reaction may provide easy access to novel polymer and dendrimer preparation. In addition, thiophenes bearing an alkyl group are one of the most important aspects in the design of liquid crystalline materials.[23]

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References and Notes

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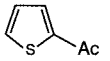
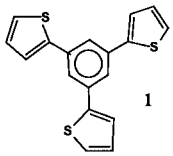
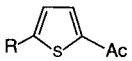
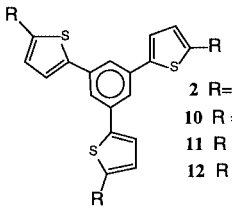
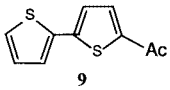
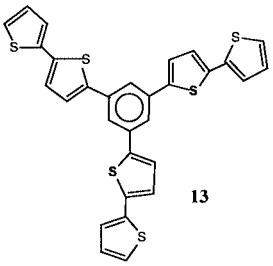
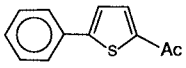
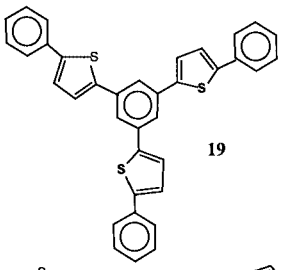
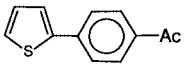
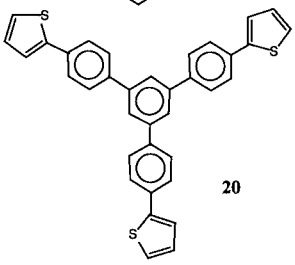
Table

S No	Substrate	Trimerized Product	$SiCl_4$ (eq) / Time (hr)	Yield %
1	 **4**	 **1**	2 / 6	42
2	 **5** R=CH_3 **6** R = C_4H_9 **7** R = C_8H_{17} **8** R = Cl	 **2** R=CH_3 **10** R = C_4H_9 **11** R = C_8H_{17} **12** R = Cl	6 / 4 6 / 18 6 / 24 4 / 12	61 75 66 60
3	 **9**	 **13**	15 / 4	26
4	 **15**	 **19**	18 / 24	40
5	 **18**	 **20**	14 / 24	40

♦ Selected spectral data for trimerized products. ^{13}C NMR (75 MHz, $CDCl_3$): **1** (mp 154-155 °C, Lit [14] mp: 156-158 °C) δ 122.8, 123.9, 125.4, 128.2, 135.7, 143.6; UV ($CHCl_3$) λ_{max}=296 nm, ∈=50359 M^{-1} cm^{-1}; **2** (mp 137-139 °C) δ 15.5, 121.4, 123.5, 126.3, 135.8, 140.0, 141.3; UV ($CHCl_3$) λ_{max}=305 nm, ∈=7905 M^{-1} cm^{-1}; **10** (mp 40-42 °C) δ 13.9, 22.3, 30.0, 33.8, 121.4, 123.3, 125.1, 135.8, 141.0, 146.2; UV ($CHCl_3$) λ_{max}=306 nm, ∈=32472 M^{-1} cm^{-1}; **11** (mp 38-39 °C) δ 14.2, 22.8, 29.2, 29.3, 29.4, 30.4, 31.8, 31.9, 121.5, 123.3, 125.0, 135.8, 141.0, 146.2; UV ($CHCl_3$) λ_{max}=306 nm, ∈=48543 M^{-1} cm^{-1}; **12** (mp 177-179 °C) δ 122.0, 123.3, 127.3, 130.2, 135.3, 141.5; UV ($CHCl_3$) λ_{max}=304 nm, ∈=52595 M^{-1} cm^{-1}; **13** (mp 180 °C dec.) δ 121.6, 123.9, 124.7 (3C?), 128.0, 135.4, 137.3, 137.5, 141.9; UV ($CHCl_3$) λ_{max}=357 nm, ∈=82108 M^{-1} cm^{-1}; **19** (mp 244-245 °C) δ 121.9, 124.0, 124.8, 125.7, 127.7, 128.9, 134.1, 135.6, 142.6, 144.3; UV ($CHCl_3$) λ_{max}=339 nm, ∈=72795 M^{-1} cm^{-1}; **20** (mp 224-225 °C) ^1H NMR (300 MHz, $CDCl_3$) δ 7.12 (m, 3H), 7.32 (m, 3H), 7.40 (m, 3H), 7.75 (s, 12H), 7.84 (s, 3H); UV ($CHCl_3$) λ_{max}=315 nm, ∈=91175 M^{-1} cm^{-1}.

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