Pyridine-Substituted Hydroxythiophenes. V. Preparation of 5-(2-, 3- and 4-pyridyl)-2-hydroxythiophenes

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5-(2-, 3- and 4-Pyridyl)-2-*t*-butoxythiophenes have been prepared in very good yields by Pd(0) catalyzed cross-coupling of the three isomeric bromopyridines with 5-trimethylstannyl-2-*t*-butoxythiophene derived from 2-bromothiophene *via* 2-*t*-butoxythiophene. Dealkylation of 5-(2-, 3- and 4-pyridyl)-2-*t*-butoxythiophenes with boron trifluoride etherate in dichloromethane at room temperature led to predominant formation of rearranged products, 5-(2- and 3-pyridyl)-3-*t*-butyl-3-thiolene-2-ones, together with a small amount of 5-(2- and 3-pyridyl)-2-hydroxythiophenes as a mixture of two tautomeric keto forms in the case of the 2-pyridyl and the 3-pyridyl isomers, and exclusive formation of rearranged product in the case of the 4-pyridyl isomer.

However, dealkylation of 2-methoxy-5-(2-, 3- and 4-pyridyl)thiophenes, prepared similarly to the 5-(2-, 3- and 4-pyridyl)-2-*t*-butoxythiophenes, with boron tribromide under the same reaction conditions as above resulted exclusively in the tautomeric mixture of 5-(2- and 3-pyridyl)-3-thiolene-2-ones and 5-(2- and 3-pyridyl)-4-thiolene-2-ones in the case of the 2-pyridyl and 3-pyridyl isomers. In the case of the 4-pyridyl isomer polymerization took place.

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Introduction.

In our study of the synthesis and tautomerism of pyridine substituted hydroxythiophene systems, we have previously prepared the six 2-(2-, 3- and 4-pyridyl)-3-hydroxythiophenes and 4-(2-, 3- and 4-pyridyl)-3-hydroxythiophenes through hydrogen peroxide oxidation of the corresponding boronic esters [1]. Spectroscopic investigations by nmr and ir show that these hydroxythiophene systems exist exclusively in their enol forms. The alkylation of these compounds using soft and hard alkylating reagents was then studied [2].

The preparation of the third type of *o*-pyridylsubstituted hydroxythiophenes, the 3-(2-, 3- and 4-pyridyl)-2-hydroxythiophenes, was more difficult. The corresponding methoxy derivatives were prepared in good yields through the Pd(0)-catalyzed coupling reactions of the three isomeric bromopyridines with 2-methoxy-3-trimethylstannylthiophene [3]. However, most attempts to demethylate these compounds using a variety of reagents failed most probably due to the instability and high reactivity of the desired hydroxythiophene systems. Only 2-methoxy-3-(3-pyridyl)thiophene could be dealkylated with boron tribromide to the hydroxythiophene system existing as 3-(3-pyridyl)-3-thiolene-2-one, which was stable only in ether solution at -20° [3]. The demethylation of 2-methoxy-3-(2-pyridyl)thiophene with chlorotrimethylsilane/sodium iodide in refluxing acetonitrile or with boron tribromide in dichloromethane at ambient temperature led to formation of a dimer. Structure determination by X-ray crystallography proved it to be (±)-(3*R**,4*S**)-3-(2-pyridyl)-4-[2-oxo-3-(1,2-dihydropyridine-2-ylidene)-2,3-dihydrothiophene-5-yl]-4,5-dihydrothiophene-2(3*H*)-one [4].

On the other hand the "*meta*" systems, 4-(2-, 3- and 4-pyridyl-2-hydroxythiophene systems, could easily be prepared by hydrogen peroxide oxidation of the corresponding 4-(pyridyl)-2-thiophene boronic esters, which were obtained from the corresponding 2-bromo-4-pyridylthiophenes. Spectroscopic investigations by nmr and ir show that these quite stable 2-hydroxythiophene systems exist exclusively in the 4-pyridyl-3-thiolene-2-one forms [3].

In this paper our investigation is extended to the 5-(2-, 3- and 4-pyridyl)-2-hydroxythiophene systems. 5-Substituted 2-hydroxythiophene systems belong to those tautomeric equilibria extensively studied by Hörnfeldt and coworkers [5-7]. Especially alkyl substituted derivatives have been studied in great detail and both the 4- and 3-thiolene-2-one forms could be isolated. Tautomeric equilibria were determined and the mechanism of tautomerization was elucidated [8]. The 5-halo-2-hydroxythiophenes exist solely in the 3-thiolene-2-one forms [9]. A few 5-aryl substituted-2-hydroxythiophenes, which are more air-sensitive, have also been studied and show interesting tautomeric properties. Thus in carbon tetrachloride only the 4-thiolene-2-one form of 5-phenyl-2-hydroxythiophene has been observed, while in methanol solution an equilibrium of about 70% of this form and 30% of the hydroxy form was observed [5]. The even more sensitive 5-(2-thienyl)-2-hydroxythiophene system behaved similarly. It was therefore of interest to find out the influence of the electron-withdrawing pyridyl groups on the tautomeric forms.

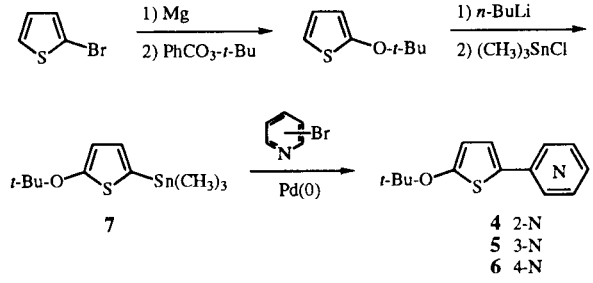
Results and Discussion.

Syntheses.

First we tried to prepare 5-pyridyl-2-hydroxythiophenes

by hydrogen peroxide oxidation of the corresponding boronic esters derived from 2-bromo-5-(2-, 3- and 4-pyridyl)thiophenes **1-3**. Compounds **1-3** were prepared by bromination of the corresponding known pyridylthiophenes with bromine in acetic acid. However, halogen-metal exchange of **1-3** with butyllithium and then boronation with ethyl borate followed by oxidation with 30% hydrogen peroxide, as in the preparation of 3-pyridyl-2-hydroxythiophenes, gave only the parent pyridylthiophenes. Another route to 5-pyridyl-2-hydroxythiophenes could be dealkylation of the corresponding 2-*t*-butoxy derivatives. These were prepared both by metallation of the thienylpyridines or by halogen-metal exchange between 2-bromo-5-pyridylthiophenes and butyllithium and the reaction with magnesium bromide followed by treatment with *t*-butyl perbenzoate. However, the dealkylations failed. Also the nickel-phosphine complex catalyzed Grignard coupling [10] between the corresponding bromopyridines and 5-*t*-butoxy-2-thienylmagnesium bromide was without success. The later reagent was prepared by metalation of 2-*t*-butoxythiophene [11] with butyllithium followed by treatment with anhydrous magnesium bromide. Finally, compounds **4-6** were obtained in 77-78% yields by Pd(0)-catalyzed cross-coupling of the corresponding bromopyridines with 2-*t*-butoxy-5-trimethylstannylthiophene (**7**). Compound **7** was obtained by metalation of 2-*t*-butoxythiophene with butyllithium followed by stannylation with trimethylstannyl chloride in 67% yield (Scheme 1).

Scheme 1

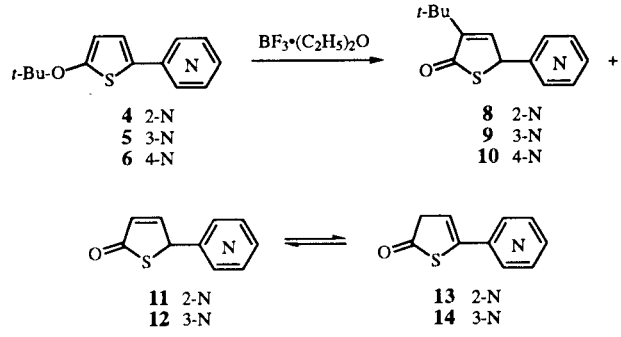


Acid-catalyzed dealkylation [12-15] of **4-6** was first attempted. However, refluxing **4-6** with catalytic amount of *p*-toluenesulphonic acid in benzene for 24 hours did not give any dealkylated products but starting materials. Dealkylation of **4-6** in refluxing naphthalene or mesitylene also failed.

Attempted dealkylation of **4** and **5** with boron trifluoride etherate [16] in dichloromethane at room temperature predominantly gave rearranged products, 5-(2- and 3-pyridyl)-3-*t*-butyl-3-thiolene-2-ones **8** and **9** in yields of 24% and 29%, respectively, together with the 5-(2- and 3-pyridyl)-2-hydroxythiophene systems in yields of 9% and 17%, respectively. *t*-Butylation upon attempted dealkylation has previously been observed [12]. The 5-(2-pyridyl)-2-hydroxythiophene system exists as a tautomeric mixture of two components, 23% of 5-(2-pyridyl)-3-thiolene-2-one (**11**) and 77% of 5-(2-pyridyl)-4-thiolen-2-one (**13**). Similarly, the 5-(3-pyridyl)-2-hydroxythiophene system consists of 20% of 5-(3-pyridyl)-3-thiolen-2-one (**12**) and 80% of 5-(3-pyridyl)-4-thiolen-2-one (**14**) (Scheme 2). Unexpectedly, dealkylation of 5-(4-pyridyl)-2-*t*-butoxythiophene (**6**) under the same reaction conditions as for dealkylation of **4** and **5** gave only rearranged product, 5-(4-pyridyl)-3-*t*-butyl-3-thiolen-2-one (**10**) in 43% yield.

It is known that *t*-butyl phenyl ether is rearranged to *p*-*t*-

Scheme 2

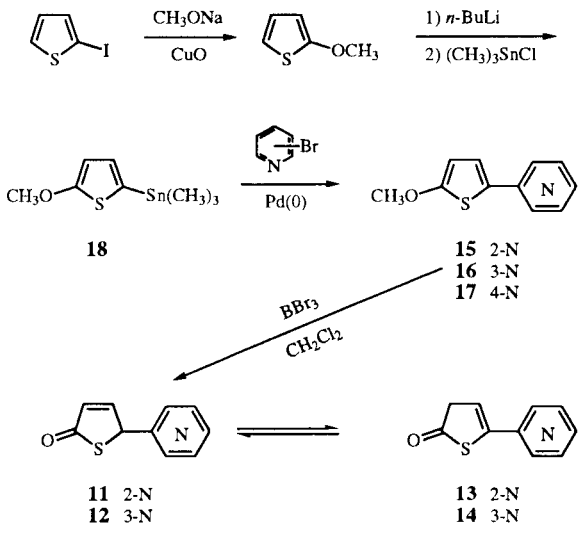


butylphenol upon treatment with aluminium chloride [17] or titanium chloride [18]. It seems apparent that by using Friedel-Crafts catalyst, the *t*-butyl phenyl ether is first dealkylated followed by Friedel-Crafts alkylation of the phenol simultaneously formed. The challenging problem is how to suppress the Friedel-Crafts alkylation in dealkylation of **4-6**. Attempted dealkylation of **4-6** with chlorotrimethylsilane/sodium iodide as reagent in refluxing acetonitrile [19] was unsuccessful. Further attempted dealkylation of **4-6** with such basic reagents as sodium cyanide in dimethyl sulfoxide [20] or lithium iodide in dimethylformamide [21] also failed. Considering that isobutylene, which was formed in the early stage of dealkylation of *t*-butyl thienyl ethers **4-6** with boron trifluoride etherate, plays a key role in the Friedel-Crafts alkylation, it is important to avoid the formation of isobutylene.

Attempts were made to prepare 5-pyridyl-2-hydroxythiophenes by dealkylation of 2-methoxy-5-(2-, 3- and 4-pyridyl)thiophenes **15-17**. Compounds **15-17** were synthesized from 2-iodothiophene, which after reaction with sodium methoxide in the presence of cupric oxide gave 2-methoxythiophene [22]. Lithiation of this compound with butyllithium and stannylation with trimethylstannyl chloride afforded 2-methoxy-5-trimethylstannylthiophene (**18**)

in 54% yield. Pd(0)-catalyzed cross-coupling of **18** with the three isomeric bromopyridines led to **15-17** in yields of 77-82% (Scheme 3). Dealkylation of compounds **15** and **16** with boron tribromide in dichloromethane at room temperature gave 5-(2-, and 3-pyridyl)-2-hydroxythiophenes in yields of 27% and 20%, respectively. It was found that they exist as a tautomeric equilibrium of the two keto forms. The proportions between **11** and **13** and between **12** and **14** are similar to those observed in the dealkylation of **4-6** with boron trifluoride etherate. However, dealkylation of **17** under the same reaction conditions as for dealkylation of **15** and **16** led to resinous product which could not be dissolved neither in dichloromethane nor ethyl acetate. Dealkylation of **17** under the milder conditions (boron tribromide was added to **17** in dichloromethane at -80° and then the mixture was slowly warmed to room temperature and stirred for two hours), gave the same result.

Scheme 3



It is known [13,14] that *p*-toluenesulphonic acid catalyzed dealkylation of 2-*t*-butylthiophenes with electron-donating groups such as methyl, allyl, benzyl and methylmercapto in 5-position proceed smoothly to give a tautomeric mixture of the two keto forms, while dealkylation of 5-carbethoxy-2-*t*-butylthiophene predominantly gave the enol form due to intramolecular hydrogen bonding of the hydroxy group to the carbonyl group.

It has been shown from ^{1}H nmr investigations that 5-alkyl-2-hydroxythiophenes in carbon tetrachloride exist predominantly as 3-thiolen-2-ones [5,13]. The larger thermodynamic stability of this form is due to conjugation between double bond and carbonyl group. Similarly, 5-(fluoro and chloro)-2-hydroxythiophenes in acetone exist exclusively as 3-thiolen-2-ones when the isomerization was complete [9]. However, 5-aryl-2-hydroxythiophenes behave differently. The 5-(phenyl and thienyl)-2-hydroxythiophene systems in carbon tetrachloride exist completely as 4-thiolen-2-ones. It is obvious that the conjugation between double bond and aryl group stabilizes this form more than that between double bond and carbonyl. It is interesting to note that also a pyridyl group in the 5-position favors the 4-thiolen-2-one tautomer in the case of 5-(2- and 3-pyridyl)-2-hydroxythiophene systems in deuteriochloroform. However, for the rearranged compounds **8-10** in deuteriochloroform the 3-thiolene-2-one form is not only dominating but the only tautomer. This indicates that when both the carbonyl and the *t*-butyl group, with its hyper-conjugation, are in conjugation with the double bond, the thermodynamic stability is larger than in the case when the pyridyl group is in conjugation with the double bond.

NMR and IR Spectroscopic Studies.

For the rearranged compounds **8-10** three tautomeric forms are possible. However, their ^{1}H nmr spectra, using deuteriochloroform as solvent, show for the thiophenic part three signals, two doublets and one singlet, with the relative intensities 1:1:9. Chemical shift and coupling constants are given in Tables 1 and 2. These signals are due to a vinylic proton, an aliphatic proton and a *t*-butyl group, indicating that the compounds are unsaturated thiolactones. It was previously shown that carbonyl absorptions of 5-substituted 3-thiolen-2-ones appear at 1695-1670 cm^{-1} and of 4-thiolen-2-ones at 1750-1730 cm^{-1} [5]. The ir spectra of **8-10** show that the carbonyl absorptions

Table 1

^{1}H NMR Chemical Shifts (ppm) in $CDCl_3$ for Three Isomeric 5-Pyridyl-3-*t*-butyl-3-thiolen-2-ones

Compound	H_4	H_5	H_2	H_3	H_4	H_5	H_6	*t*-Bu
8	7.23	5.52		7.26	7.69	7.23	8.57	1.29
9	7.02	5.27	8.47		7.47	7.25	8.48	1.21
10	7.05	5.25	8.61	7.20		7.20	8.61	1.29

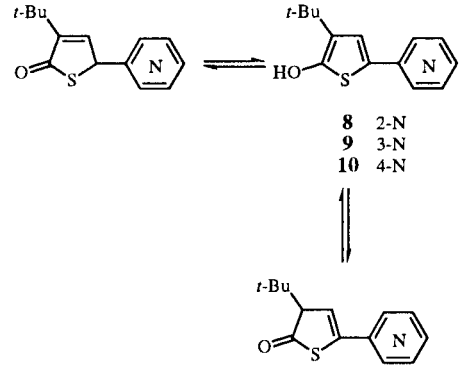


Table 2

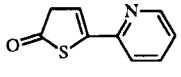
^{1}H NMR Coupling Constants (Hz) in Deuteriochloroform for Three Isomeric 5-Pyridyl-3-*t*-butyl-3-thiolen-2-ones

Compound	J_{45}	J_{23}	J_{24}	J_{25}	J_{34}	J_{35}	J_{36}	J_{45}	J_{46}	J_{56}
8	2.95				7.80	1.10	0.95	7.70	1.80	4.90
9	2.70		2.00					8.15	1.80	4.60
10	2.90	4.40		1.65			1.65			4.40

are in the interval 1650-1675 cm^{-1}, consequently compounds **8-10** exist as 3-thiolen-2-ones.

Based on the ^{1}H nmr investigations the 5-(2-pyridyl)-2-hydroxythiophene system in deuteriochloroform exists in an equilibrium of the two keto forms **11** and **13**, as no aromatic protons of the thiophenic part could be detected.

11

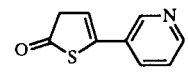


13

For the minor component three bands with the relative intensities 1:1:1 due to the thiophenic part was observed. The two bands at δ 6.45 and δ 7.66 with the common splitting of 6.05 Hz was assigned to H_3 and H_4 of **11**. The band at δ 5.77 attributed to H_5 appears as a triplet as the couplings to H_3 and H_4 are of the same magnitude, 2.20 Hz and 2.55 Hz, respectively. The ^{1}H nmr spectrum of **13** shows a triplet for the vinylic proton H_4 at δ 6.55 with splittings of 3.05 Hz and a doublet at δ 3.76 with the same splitting attributed to the methylene group. The proton signals of the pyridine rings are in the interval δ 7.26-8.62 and do not overlap with exception of the H_3 signal. By integration of the bands due to the alifatic protons the proportion between **11** and **13** was found to be 1:3. The ir spectrum of this tautomeric mixture show two carbonyl absorptions at 1775 cm^{-1} and at 1700 cm^{-1}, the former is attributed to the nonconjugated carbonyl in **13** and the latter to the conjugated carbonyl in **11**.

Also the 5-(3-pyridyl)-2-hydroxythiophene system in deuteriochloroform exists as a tautomeric mixture of the two unsaturated thiolactones, **12** and **14**, as no aromatic thiophenic protons could be detected. The ^{1}H nmr minor component shows for the thiophenic moity three bands with the relative intensities 1:1:1 and the bands appearing at δ 6.46 and δ 7.47 with splittings of 5.95 Hz are assigned to H_3 and H_4. The band at δ 5.58 due to H_5 has a triplet pattern as the couplings to H_3 and H_4 are 2.15 Hz and 2.55 Hz, respectively. These observations are in accordance with structure **12**. The structure of the other component, **14**, is verified by the following ^{1}H nmr data, two bands attributed to the thiophenic part with the relative intensities 1:2 have the δ values 6.22 and 3.71 and appear as triplet and doublet, respectively, giving a coupling constant of 2.95 Hz. The protons in the pyridine rings have their absorptions in the interval δ 7.30-8.73. H_6 in **12** and H_2 and H_6 in **14** give rise to a multiplet at δ 8.57-8.59. Integration over the absorptions due to the alifatic protons gives the ratio 1:4 for the proportion of **12** and **14**.

12



14

The ir spectrum of the tautomeric mixture of **12** and **14** shows carbonyl absorptions characteristic for 3-thiolen-2-ones and 4-thiolen-2-ones at 1690 cm^{-1} and 1730 cm^{-1}, respectively.

EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were recorded on a Perkin Elmer 298 spectrophotometer. The ^{1}H nmr spectra were recorded on a Varian XL 300 spectrometer. The mass spectra were recorded on a Finnigen 4021 (date system Incos 2100). The glc analyses were carried out on a Varian 1400 gas chromatography using an OV-17 (3%, 2 m) column. Elemental microanalyses were performed at Dornis und Kolbe, Mikroanalytisches Laboratorium, Mülheim a. d. Ruhr, Germany.

General Procedure for the Preparation of 2-Bromo-5-pyridylthiophenes.

To a stirred solution of 161 mg (1.00 mmole) of the appropriate pyridylthiophene [23] in 4 ml of acetic acid was added dropwise a solution of 240 mg (1.50 mmoles) of bromine in 4 ml of

Table 3

^{1}H NMR Chemical Shifts (ppm) in Deuteriochloroform for some Pyridyl-substituted Thiophene Derivatives

Compound	H_3	H_4	H_2	H_3	H_4	H_5	H_6	*O*-*t*-Bu	OCH_3
1	7.03	7.27		7.53	7.64	7.12	8.51		
2	7.08	7.12	8.80		7.78	7.32	8.54		
3	7.10	7.26	8.60	7.39		7.39	8.60		
4	6.40	7.27		7.56	7.64	7.07	8.51	1.43	
5	6.40	7.05	8.79		7.77	7.26	8.46	1.42	
6	6.41	7.22	8.53	7.37		7.37	8.53	1.43	
15	6.23	7.28		7.53	7.63	7.07	8.48		3.95
16	6.22	7.02	8.76		7.72	7.26	8.44		3.93
17	6.24	7.21	8.52	7.33		7.33	8.52		3.95

Table 4

^{1}H NMR Coupling Constants (Hz) in Deuteriochloroform for some Pyridyl-substituted Thiophene Derivatives

Compound	J_{34}	J_{23}	J_{24}	J_{25}	J_{34}	J_{35}	J_{36}	J_{45}	J_{46}	J_{56}
1	3.95				8.05	1.15	1.00	7.75	1.65	4.95
2	3.85		2.40	0.85				8.05	1.65	4.85
3	3.90	4.50		1.65			1.65			4.50
4	3.95				8.05	1.30	1.00	7.25	1.80	4.95
5	3.95		2.40	0.75				7.95	1.60	4.80
6	3.90	4.55		1.65			1.65			4.55
15	4.00				8.05	1.20	1.05	7.35	1.75	4.95
16	4.00		2.40	0.80				8.00	1.55	4.80
17	4.10	4.50		1.60			1.60			4.50

acetic acid. After the addition the mixture was refluxed for 1 hour. After being cooled to room temperature, the mixture was poured into water, and neutralized with 1 *M* sodium bicarbonate solution to *p*H 7-8. The mixture was extracted with dichloromethane. The combined dichloromethane phases were washed with water and dried over anhydrous sodium sulfate. After evaporation, the residue was purified by crystallization.

2-Bromo-5-(2-pyridyl)thiophene (**1**).

This compound was prepared from 2-(2-pyridyl)thiophene, after recrystallization from petroleum ether 200 mg (83%) of **1** was obtained, mp 85-86° (lit [24] 71%, 86-87°; lit [25] 79%, 85-87°); for ^{1}H nmr data see Tables 3 and 4; ms: m/z 239, 241 (M^+), 160.

2-Bromo-5-(3-pyridyl)thiophene (**2**).

This compound was prepared from 2-(3-pyridyl)thiophene, after recrystallization from petroleum ether 180 mg (75%) of **2** was obtained, mp 52-54°; for ^{1}H nmr data see Tables 3 and 4; ms: m/z 239, 241 (M^+), 160.

Anal. Calcd. for C_9H_6BrNS: C, 45.02; H, 2.52. Found: C, 44.94; H, 2.46.

2-Bromo-5-(4-pyridyl)thiophene (**3**).

This compound was prepared from 2-(4-pyridyl)thiophene, after recrystallization from ethanol 185 mg (77%) of **3** was obtained, mp 152-154°, for ^{1}H nmr data see Tables 3 and 4; ms: m/z 239, 241 (M^+), 160.

Anal. Calcd. for C_9H_6BrNS: C, 45.02; H, 2.52. Found: C, 45.04; H, 2.42.

2-*t*-Butoxy-5-trimethylstannylthiophene (**7**).

To a stirred solution of 1.56 g (10.0 mmoles) of 2-*t*-butoxythiophene [11] in 12 ml of anhydrous diethyl ether, 5.76 ml (11.0 mmoles) of 1.91 *N* butyllithium in cyclohexane was added dropwise under nitrogen. The mixture was refluxed for 3 hours, and then cooled to -70°, 2.19 g (11.0 mmoles) of trimethylstannyl chloride dissolved in 4 ml of anhydrous tetrahydrofuran was added dropwise at -70°, The mixture was stirred at the same temperature for 2 hours, and then left to attain room temperature. Ice-water was added with stirring. The organic phase was separated, the aqueous phase was extracted with diethyl ether. The combined organic phases were washed with water and dried over anhydrous sodium sulfate. After evaporation, the residue was distilled at reduced pressure to give 2.14 g (67%) of the title compound, bp 77-79°/0.5 mm Hg; ^{1}H nmr (deuteriochloroform): δ 0.32 (s, 9H, -$SnMe_3$), 1.38 (s, 9H, *t*-Bu), 6.48 (d, 1H, 4-H, J = 3.40 Hz), 6.83 (d, 1H, 3-H, J = 3.40 Hz).

Anal. Calcd. for $C_{11}H_{20}OSSn$: C, 41.41; H, 6.32. Found: C, 41.19; H, 6.21.

General Procedure for the Preparation of 5-Pyridyl-2-*t*-butoxythiophenes.

A mixture of 0.79 g (5.00 mmoles) of the appropriate bromopyridine, 0.48 g (0.25 mmole) of *tetrakis*(triphenylphosphine)-palladium(0) [26] and 35 ml of dimethylformamide was stirred under nitrogen for 15 minutes, 1.75 g (5.50 mmoles) of 2-*t*-butoxy-5-trimethylstannylthiophene (**7**) was added. The mixture was stirred at 100° under nitrogen for 12-19 hours. When the starting materials were consumed, the reaction mixture was allowed to attain room temperature and then evaporated. Diethyl ether was added to the residue with stirring. The precipitate was filtered off and the filtrate was washed with water and dried over anhydrous sodium sulfate. After evaporation, the residue was subjected to chromatography on silica gel 60.

5-(2-Pyridyl)-2-*t*-butoxythiophene (**4**).

This compound was prepared from 2-bromopyridine. By

using petroleum ether/ethyl acetate (85:15) as eluent, 0.91 g (78%) of **4** was obtained as an oil, for ^{1}H nmr data see Tables 3 and 4; ms: m/z 233 (M^+), 177, 148, 104, 78.

Anal. Calcd. for $C_{13}H_{15}NOS$: C, 66.92; H, 6.48. Found: C, 66.85; H, 6.57.

5-(3-Pyridyl)-2-*t*-butoxythiophene (**5**).

This compound was obtained from 3-bromopyridine. By using petroleum ether/ethyl acetate (65:35) as eluent, 0.90 g (77%) of **5** was obtained as an oil, for ^{1}H nmr data see Tables 3 and 4; ms: m/z 233 (M^+), 177, 148, 104, 78.

Anal. Calcd. for $C_{13}H_{15}NOS$: C, 66.92; H, 6.48. Found: C, 66.86; H, 6.57.

5-(4-Pyridyl)-2-*t*-butoxythiophene (**6**).

This compound was prepared from 4-bromopyridine. By using ethyl acetate/petroleum ether (3:2) as eluent followed by recrystallization from petroleum ether, 0.90 g (77%) of **6** was obtained, mp 67-68°; for ^{1}H nmr data see Tables 3 and 4; ms: m/z 233 (M^+), 177, 148, 104, 78.

Anal. Calcd. for $C_{13}H_{15}NOS$: C, 66.92; H, 6.48. Found: C, 66.81; H, 6.49.

General Procedure for the Dealkylation of 5-Pyridyl-2-*t*-butoxythiophenes.

To a stirred solution of 233 mg (1.00 mmole) of the appropriate 5-pyridyl-2-*t*-butoxythiophene in 2 ml of dichloromethane, 0.31 ml (2.5 mmoles) of boron trifluoride etherate was added dropwise through a septum with a syringe under nitrogen. The mixture was stirred at room temperature for about 2 hours and monitored by thin layer chromatography. When the starting materials were consumed, cold water was added. The mixture was made alkaline (*p*H 7-8) with 1 *M* sodium bicarbonate solution. The organic phase was separated, the aqueous phase was extracted with dichloromethane. The combined dichloromethane phases were washed with water and dried over anhydrous sodium sulfate. After evaporation, the residue was subjected to chromatography on silica gel 60.

5-(2-Pyridyl)-3-*t*-butyl-3-thiolen-2-one (**8**).

This compound was obtained in the dealkylation of 5-(2-pyridyl)-2-*t*-butoxythiophene (**4**). The fraction containing **8** was chromatographed by using petroleum ether/ethyl actate (65:35) as eluent to give 56.1 mg (24%) of **8** as a liquid; ir (film): ν 1675 cm^{-1} (C=O); ^{1}H nmr data see Tables 1 and 2; ms: m/z 233 (M^+), 177, 148, 78.

Anal. Calcd. for $C_{13}H_{15}NOS$: C, 66.92; H, 6.48. Found: C, 66.90; H, 6.42.

5-(2-Pyridyl)-3-thiolen-2-one (**11**) and 5-(2-pyridyl)-4-thiolen-2-one (**13**).

These two compounds were obtained in the dealkylation of 5-(2-pyridyl)-2-*t*-butoxythiophene (**4**). The fraction containing the title compounds was chromatographed by using petroleum ether/ethyl acetate (65:35) as the eluent to give 16 mg (9%) of **11** and **13** as a tautomeric mixture in a ratio 1:3; mp 117-221°; for nmr and ir data see the spectroscopic section; ms: m/z 177 (M^+), 148, 78.

Anal. Calcd. for C_9H_7NOS: C, 60.99; H, 3.98. Found: C, 60.87; H, 3.73.

5-(3-Pyridyl)-3-*t*-butyl-3-thiolen-2-one (**9**).

This compound was obtained in the dealkylation of 5-(3-pyridyl)-2-*t*-butoxythiophene (**5**). The fraction containing **9** was chromatographed by using ethyl acetate/petroleum ether (4:1) as eluent to give 68.3 mg (29%) of **9**, mp 70-73°; ir (potassium bromide): ν 1665 cm^{-1}; ^{1}H nmr data see Tables 1 and 2; ms: m/z 233 (M^+), 177, 148, 78.

Anal. Calcd. for $C_{13}H_{15}NOS$: C, 66.92; H, 6.48. Found: C, 66.93; H, 6.46.

5-(3-Pyridyl)-3-thiolen-2-one (**12**) and 5-(3-Pyridyl)-4-thiolen-2-one (**14**).

These two compounds were obtained in the dealkylation of 5-(3-pyridyl)-2-*t*-butoxythiophene (**5**). The fraction containing the title compounds was chromatographed by using ethyl acetate/petroleum ether (4:1) as eluent to give 29.4 mg (17%) of **12** and **14** as a tautomeric mixture in the ratio 1:4, mp 118-222°; ^{1}H nmr and ir data are given in the spectroscopic section; ms: m/z 177 (M^+), 148, 78.

Anal. Calcd. for C_9H_7NOS: C, 60.99; H, 3.98. Found: C, 60.88; H, 4.12.

5-(4-Pyridyl)-3-*t*-butyl-3-thiolen-2-one (**10**).

This compound was prepared in the dealkylation of 5-(4-pyridyl)-2-*t*-butoxythiophene (**6**). By using ethyl acetate as eluent, 100 mg (43%) of **10** was obtained, mp 163-165° sublimed; ir (potassium bromide): ν 1650 cm^{-1} (C=O); ^{1}H nmr data are given in Tables 1 and 2; ms: m/z 233 (M^+), 177, 148, 78.

Anal. Calcd. for $C_{13}H_{15}NOS$: C, 66.92; H, 6.48. Found: C, 66.78; H, 6.35.

2-Methoxy-5-trimethylstannylthiophene (**18**).

To a stirred solution of 1.14 g (10.0 mmoles) of 2-methoxythiophene [22] in 12 ml of anhydrous diethyl ether, 5.76 ml (11.0 mmoles) of 1.91 *N* butyllithium in cyclohexane was added dropwise under nitrogen. The mixture was refluxed for 3 hours and then cooled to -70°, 2.19 g (11.0 mmoles) of trimethylstannyl chloride dissolved in 4 ml of anhydrous tetrahydrofuran was added dropwise at -70°. The mixture was stirred at the same temperature for 2 hours and then warmed to room temperature. Ice-water was added with stirring. The organic phase was separated, the aqueous phase was extracted with diethyl ether. The combined organic phases were washed with water and dried over anhydrous sodium sulfate. After evaporation, the residue was distilled at reduced pressure to give 1.49 g (67%) of **18**, bp 91-92°/1.5 mm Hg; ^{1}H nmr (deuteriochloroform): δ 0.33 (s, 9H, -$SnMe_3$), 3.90 (s, 3H, -OCH_3), 6.34 (d, 1H, 4-H, J = 3.35 Hz), 6.82 (d, 1H, 3-H, J = 3.35 Hz).

Anal. Calcd. for $C_8H_{14}OSSn$: C, 34.69; H, 5.09. Found: C, 34.35; H, 5.03.

General Procedure for the Preparation of 2-Methoxy-5-pyridylthiophenes.

A mixture of 1.58 g (10.0 mmoles) of the appropriate bromopyridine, 0.96 g (0.50 mmole) of tetrakis(triphenylphosphine)-palladium(0) and 70 ml of dimethylformamide was stirred under nitrogen for 15 minutes, 3.05 g (11.0 mmoles) of 2-methoxy-5-trimethylstannylthiophene (**18**) was added. The mixture was stirred at 100° for 12-14 hours. When the starting materials were consumed, the reaction mixture was allowed to reach room temperature and then evaporated. Diethyl ether was added to the residue with stirring. The precipitate was filtered off and the filtrate was washed with water after which it was dried over anhydrous sodium sulfate. After evaporation, the residue was sub-

jected to chromatography on silica gel 60.

2-Methoxy-5-(2-pyridyl)thiophene (**15**).

This compound was prepared from 2-bromopyridine. By using petroleum ether/ethyl acetate (4:1) as eluent, 1.57 g (82%) of **15** was obtained, mp 42.0-43.5°; for ^{1}H nmr data see Tables 3 and 4; ms: m/z 191 (M^+), 176, 148, 104, 78.

Anal. Calcd. for $C_{10}H_9NOS$: C, 62.80; H, 4.74. Found: C, 62.79; H, 4.69.

2-Methoxy-5-(3-pyridyl)thiophene (**16**).

This compound was prepared from 3-bromopyridine. By using ethyl acetate/petroleum ether (4:1) as eluent, 1.48 g (77%) of **16** was obtained as an oil; for ^{1}H nmr data see Tables 3 and 4; ms: m/z 191 (M^+), 176, 148, 104, 78.

Anal. Calcd. for $C_{10}H_9NOS$: C, 62.80; H, 4.74. Found: C, 62.71; H, 4.81.

2-Methoxy-5-(4-pyridyl)thiophene (**17**).

This compound was prepared from 4-bromopyridine. By using ethyl acetate/petroleum ether (4:1) as eluent, 1.56 g (82%) of **17** was obtained, mp 93-95°; for ^{1}H nmr data see Tables 3 and 4; ms: m/z 191 (M^+), 176, 148, 104, 78.

Anal. Calcd. for $C_{10}H_9NOS$: C, 62.80; H, 4.74. Found: C, 62.74; H, 4.81.

General Procedure for the Dealkylation of 2-Methoxy-5-pyridylthiophenes.

To a stirred solution of 191 mg (1.00 mmole) of the appropriate 2-methoxy-5-pyridylthiophene in 2 ml of dichloromethane, 0.24 ml (2.5 mmoles) of boron tribromide was added dropwise through a septum with a syringe under nitrogen. The mixture was stirred at room temperature for about 3 hours and monitored by tlc. When the starting materials were consumed, cold water was added carefully. The mixture was made alkaline (*p*H 7-8) with 1 *M* sodium bicarbonate solution. The organic phase was separated, the aqueous phase was extracted with dichloromethane. The combined dichloromethane phases were washed with water and dried over anhydrous sodium sulfate. After evaporation, the residue was subjected to flash chromatography on silica gel 60.

5-(2-Pyridyl)-3-thiolen-2-one (**11**) and 5-(2-Pyridyl)-4-thiolen-2-one (**13**).

These two compounds were prepared in the dealkylation of 2-methoxy-5-(2-pyridyl)thiophene (**15**), by using petroleum ether/ethyl acetate (65:35) as eluent 47.9 mg (27%) of **11** and **13** were obtained as a tautomeric mixture in a ratio of 1:3 and having physical data identical with those described for **11** and **13** in the dealkylation of 5-(2-pyridyl)-2-*t*-butoxythiophene (**4**).

5-(3-Pyridyl)-3-thiolen-2-one (**12**) and 5-(3-Pyridyl)-4-thiolen-2-one (**14**).

These two compounds were prepared in the dealkylation of 2-methoxy-5-(3-pyridyl)thiophene (**16**), by using petroleum ether/ethyl acetate (3:2) as the eluent 35.8 mg (20%) of **12** and **14** were obtained as a tautomeric mixture in a ratio of 1:4 and having physical data identical with those described for **12** and **14** in the dealkylation of 5-(3-pyridyl)-2-*t*-butoxythiophene (**5**).

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