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STABLE HETEROARENIUM IONS—IX

DISPROPORTIONATION OF ALKYLTHIOPHENIUM IONS AND ITS USE FOR THE SYNTHESIS OF 2,4-DIALKYLTHIOPHENES

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Abstract— A number of isopropyl and ethyl substituted thiophenium ions has been generated by the alkylation of thiophene and protonation of alkylthiophenes. Disproportionation of these ions has been studied at room temperature and at the b.p. of 1,2-dichloroethane used as a solvent while preparing the ions. 2,4-Diethylthiophene has been prepared from its mixture with the 2,5-isomer by disproportionation of the 2,5-diethyl-2H-thiophenium ion.

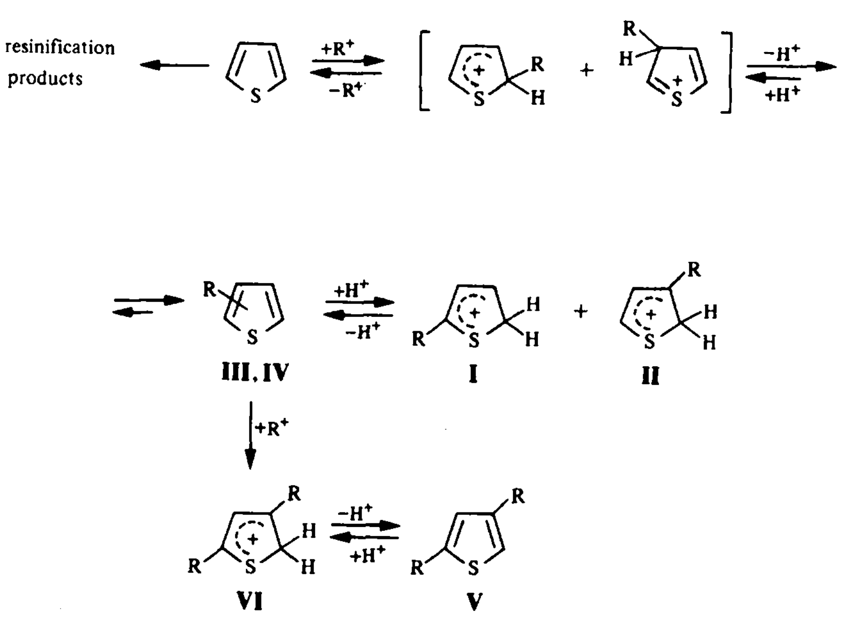
In a previous paper[1] we have shown that the mixture of alkylthiophenium ions (σ-complexes, I, II, R = t-Bu) formed at −70° from thiophene, t-butyl chloride, and an equivalent amount of $AlCl_3$ under the conditions previously described[2] undergoes disproportionation at room temperature resulting in the variation of the ratio of 2- and 3-alkyl substituted derivatives. Keeping the above mixture of σ-complexes at room temperature for 1–2 days can be used with the preparative aim and yields after deprotonation 2-t-butylthiophene (III, R = t-Bu) containing only ~3% of the 3-isomer (IV, R = t-Bu). Immediate deprotonation of the mixture of σ-complexes gives a mixture of 2- and 3-t-butylthiophenes in a ratio of ~85:15.[2] It has been assumed[1] that the ratio of the isomers formed at −70° corresponds to the kinetic control of the process while the ratio of the isomers kept at ~20°—to the thermodynamic control.

As we have shown,[1] disproportionation occurs in the case of isopropyl and methyl substituted thiophenium ions as well but at room temperature the process is very slow. In this paper we have studied the transformations of isopropyl and ethyl substituted thiophenium ions not only at room temperature but at the b.p. of 1,2-dichloroethane which was used as a solvent.

In a previous paper[2] it was shown that the interaction of isopropyl chloride, thiophene, and $AlCl_3$ at −70° yields a mixture of isopropylthiophenium ions (I, II, R = iso-Pr) after deprotonation of which 2- and 3-isopropylthiophenes (III, IV, R = iso-Pr) are obtained in a 60:40 ratio. Keeping this mixture of σ-complexes at room temperature for 2 days changes the ratio of 2- and 3-substituents to 70:30 (cf. Ref. 1). In boiling dichloroethane even after 6.5 hr the ratio of 2- and 3-isomers 95:5 is attained and then remains unchanged. In contrast to a similar transformation of t-butylthiophenium ions, which proceeds at a marked rate at room temperature,[1] no thiophene is observed in the course of disproportionation which may be due to its fast resinification at 84°. Disproportionation also results in the considerable formation of disubstituted compounds; therefore, the above transformation cannot be used for the preparation of 2-isopropylthiophene. On the other hand, a prolonged heating under reflux of a solution of σ-complexes may furnish a sample containing ~95% 2,4-diisopropylthiophene (V, R = iso-Pr). As one might expect, the transformation of less stable σ-complexes into more stable ones and, in particular, the formation of 3,5-dialkyl-2H-thiophenium ions (VI) can be considered as a driving force of the disproportionation under study (Scheme 1). The changes in the ratios of alkyl substituted compounds during disproportionation of isopropylthiophenium ions are given in Table 1.

Deprotonation of 2,5-diethyl-2H-thiophenium tetrachloroaluminate (VII, R = Et) obtained from 2,5-diethylthiophene (VIII, R = Et), HCl, and $AlCl_3$ yields 2,4-diethylthiophene (V, R = Et), 2,3,5-triethylthiophene (IX, R = Et) and 2-ethylthiophene (III, R = Et) as major products. The amount of III at first grows and then drops because of resinification (upon a prolonged storage up to 52 days at room temperature). A compound close to V and VIII in retention time (probably, 2,3-diethylthiophene) is also formed in low yield (2–5%). Table 2 illustrates the results of disproportionation. A special experiment was performed on disproportionation of 2,3,5-triethyl-2H-thiophenium tetrachloroaluminate (X, R = Et): it proceeds rather rapidly at the b.p. of dichloroethane and gives 2,4-diethyl- (V, R = Et) and 2,3,4,5-tetraethylthiophene (XI, R = Et) as main deprotonation products. The transformations of ethylthiophenium ions can be presented by Scheme 2. Ethylthiophenes (III, V, VIII, IX and XI) obtained after deprotonation of the corresponding mixtures were detected by GLC and cationic σ-complexes—by PMR just in the reaction mixtures and in specially prepared samples (Table 3).

We used the disproportionation of the 2,5-diethyl-2H-thiophenium ion considered above for preparing 2,4-diethylthiophene on the basis of the 2-acetylthiophene acetylation product. As we have shown,[3] the interaction of acetylchloride with 2-acetylthiophene in the presence of excess $AlCl_3$ yields the mixture of 2,4- and 2,5-diacetylthiophenes (92:8). The Kishner reduction of this mixture produces a mixture of diethylthiophenes and interaction of the latter with HCl and $AlCl_3$ in 1,2-dichloroethane results in the formation of a mixture of σ-complexes. Heating the latter mixture under reflux for 2.5 hr and subsequent deprotonation yields almost pure 2,4-diethylthiophene. An attempt to prepare 2,4-diethylthiophene by ethylation of 2-ethylthiophene in the presence of an equivalent amount of $AlCl_3$ with a simultaneous



Scheme 1.

disproportionation of the σ-complex thus formed was unsuccessful. In spite of the prolonged keeping at room temperature and heating, the initial 2-ethylthiophene was the main component of the mixture; 2,3,5-triethylthiophene and a mixture of isomeric diethylthiophenes were also present. This may be due to the fact that at ~20° and especially at the b.p. of ethyl bromide (39°) the latter undergoes dehydrobromination catalyzed by $AlCl_3$ (cf. Refs 4–6) and HBr liberated binds the starting 2-ethylthiophene as a stable protonated σ-complex (I, R = Et) which hinders sharply the desired transformation. The performance of the reaction at low temperature and subsequent disproportionation are impossible in this case since ethylation proceeds much slower than t-butylation or isopropylation and requires temperatures above −20°.[2]

EXPERIMENTAL

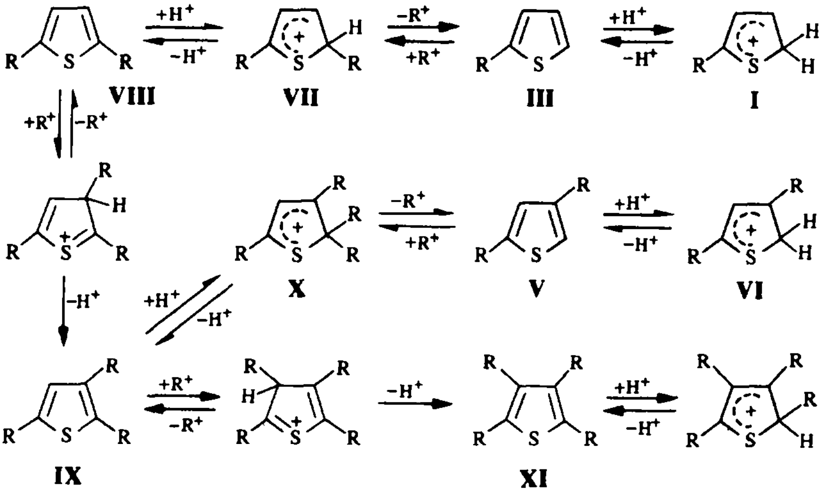
Chromatographic analyses were performed on an LKhM-8MD chromatograph with a flame ionization detector and N_2 as carrier gas. The capillary Pyrex column 50 × 0.25 mm (Carbowax 40M/KF) was prepared as previously described.[7]

PMR spectra were recorded on Tesla BS-467 (60 MHz) and BS-497 (100 MHz) spectrometers with TMS as internal standard.

^{13}C-NMR decoupled and gated spectra were recorded on a Bruker WM-250 spectrometer (62.89 MHz) with a solvent ($CDCl_3$) signal as internal standard. All chemical shifts δ are given with respect to TMS.

2,5-Diethylthiophene, 2,3,5-triethylthiophene, and 2,3,4,5-tetraethylthiophene were prepared from 2-ethylthiophene as previously described[8] by successive acetylation and Kishner reduction.

Isopropylation of thiophene and subsequent disproportionation of monoisopropylthiophenes (cf. *Refs* 1 *and* 2). Isopropyl



Scheme 2.

Table 1. Transformations of isopropylthiophenium ions (I and II, R = iso-Pr)[a]

Duration of storage (hr)	Ratio of mono and dialkyl substituted derivatives	Monoalkyl substituted derivatives ratio of 2- and 3-isomers
1	93:7	81:19
2	83:17	87:13
3.5	76:24	92:8
6.5	55:45	95:5
10.5	32:68	95:5
21	5:95	95:5

[a] The solns of σ-complexes in dichloroethane were kept at its b.p. (84°). The samples were analyzed by GLC as corresponding mono- and diisopropylthiophenes (after treatment with water). The initial mixture was preliminarily kept at room temp for 2 days; after deprotonation it contained III and IV in a ratio of 70:30 and about 1.5% of a mixture of products with higher retention volumes, namely, 2,4-diisopropylthiophene (V) as the main component (~40%) and, probably, 2,5- and 2,3-isomers. After reflux, in addition to V, a small impurity (up to 2%) was detected having a retention volume similar to that of V (probably, 2,3-diisopropylthiophene).

chloride (4.3 g, 55 mmol) in 10 ml dichloroethane and 4.6 g thiophene (55 mmol) in 25 ml dichloroethane were added successively to a suspension of $AlCl_3$ (7.4 g, 55 mmol) in 25 ml dichloroethane at −30°. The mixture was kept at −30° for 1 hr and then warmed to room temp. After keeping for 2 days the mixture was heated under reflux upon stirring and 1 ml samples were taken at intervals. The samples were treated with ice water, 1% KOH aq, and analyzed (the organic layer) by GLC (the results are given in Table 1). Then the mixture was decomposed by pouring on ice. After the addition of 50 ml 40% KOH aq the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined extracts were washed with water and distilled. 2,4-Diisopropylthiophene (1.5 g) was obtained, b.p. 78–83° (13 mmHg), containing 5% monoisopropylthiophenes. (Found: C, 71.31, 71.13; H, 9.55, 9.85; S, 18.60, 18.68. $C_{10}H_{16}S$ requires: C, 71.36; H, 9.58; S, 19.05%.) PMR spectrum, δ (CCl_4): 1.19 (d, 6H (CH_3)), 1.27 (d, 6H (CH_3)), 2.95 (m, 2H, CH, J_{Me-H} 7 Hz), 6.57 (s, 2H (protons of thiophene ring)). ^{13}C-NMR spectrum, σ ($CDCl_3$): 23.4 (4-Me_2CH), 24.6 (2-Me_2CH), 29.7 (4-Me_2CH), 29.9 (2-Me_2CH), 114.9 (5-C), 121.8 (3-C), 148.9 (4-C), 152.7 (2-C) ppm, J_{5-CH} 182 Hz, J_{3-CH} 161 Hz. The residue after distillation (4.8 g) was not analyzed.

2,5-*Diethyl*-2H-*thiophenium tetrachloroaluminate* (VIII, R = Et) *and its transformations.* 2,5-Diethylthiophene (1.79 g, 19.8 mmol) in 7 ml dichloroethane was added dropwise to an $AlCl_3$ suspension (1.71 g, 12.8 mmol) in 6 ml dichloroethane sat with dry HCl at −30°. The mixture was stirred at −30° while passing a dry HCl stream until complete dissolvation of $AlCl_3$. The mixture was kept at ~20° and samples (~0.5 ml) were taken at intervals. The samples were treated as described above and analyzed by GLC. The results of GLC analysis are given in Table 2.

2,3,5-*Triethyl*-2H-*thiophenium tetrachloroaluminate* (XI, R = Et) *and its transformations.* 2,3,5-Triethylthiophene (1.81 g, 10.8 mmol) in 5 ml of dichloroethane was added to an $AlCl_3$ suspension (1.44 g, 10.8 mmol) in 15 ml dichloroethane sat with dry HCl at −30°. The mixture was stirred at −30° and dry HCl was passed until $AlCl_3$ was completely dissolved. In the sample taken after keeping the mixture at room temp for 20 hr and treating it with water (see above) 2,4-diethylthiophene (about 1%) was detected by GLC. Then the mixture was stirred under reflux of dichloroethane (84°) and samples for GLC were taken. In 9 hr 2,4-diethylthiophene, 2,3,5-triethylthiophene, and 2,3,4,5-tetraethylthiophene (11:79:10) were found in the mixture. After refluxing for 17 hr the ratio was 15:70:15; the formation of high-boiling products was observed. Further heating under reflux for 44 hr resulted in intensive resinification and complete disappearance of di-, tri- and tetraethylthiophenes.

2,4-*Diethylthiophene* (V, R = Et). A mixture (8.6 g) of 2,4- and 2,5-diacetylthiophenes[3] was subjected to Kishner reduction with hydrazine hydrate (25 g) and KOH (28 g) in diethylene glycol (70 ml); 5.4 g of the mixture (38.5 mmol, yield 72%) of 2,4- and 2,5-diethylthiophenes (92:8) were obtained. The mixture was then added to an $AlCl_3$ suspension (5.15 g, 38.5 mmol) in 20 ml dichloroethane at −30° for 10 min with HCl passed through. Dry HCl was passed for an additional 10 min (until a complete dissolution of $AlCl_3$), the mixture was then refluxed for 2.5 hr upon stirring and decomposed on ice. The organic layer was separated and the aqueous one was extracted with CH_2Cl_2 (3 × 25 ml). According to the GLC data, the extract contained I, V, and IX, R = Et in a ratio of 0.5:96:3.5. The combined extracts were washed with water, 1% KOH, water again, and distilled. The following fractions were isolated: b.p. 140–183° (760 mmHg) (0.33 g) containing I

Table 2. Transformations of the 2,5-diethyl-2H-thiophenium ion (VII, R = Et) under prolonged storage (~20°)

Duration of storage (days)	Ratio of ethylthiophenes in the mixture after deprotonation, GLC data (wt. %)			
	2-Ethylthiophene I	2,5-Diethylthiophene VIII	2,4-Diethylthiophene V	2,3,5-Triethylthiophene IX
0[a]	—	99.5	0.5	—
0.1	4	93	1	2
1	25	57	2	16
2	15	54	3	28
6	16	44	6	34
8	14	37	7	42
14	16	28	10	46
22	14	19	13	54
30	11	8	16	65
36	6	4	17	73
52	2	1	18	79

[a] The data for the GLC analysis of the starting 2,5-diethylthiophene are given.

Table 3. PMR spectra of ethylthiophenium ions[a]

Ion	Chemical shifts σ ppm								
	2H	3H	4H	2-CH_2	3-CH_2	5-CH_2	2-CH_3	3-CH_3	5-CH_3
5-Ethyl-2H-thiophenium (I, R = Et)	5.29	8.92	7.93	—	—	3.63	—	—	1.64
3,5-Diethyl-2H-thiophenium (VI, R = Et)	5.12	—	7.64	—	3.07	3.47	—	1.56	1.40
2,5-Diethyl-2H-thiophenium (VII, R = Et)	5.42	8.83	7.80	2.42	—	3.60	1.26	—	1.62
2,3,5-Triethyl-2H-thiophenium (X, R = Et)	5.24	—	7.60	2.64	2.92	3.49	1.13	1.47	1.47

[a] The spectra are obtained in CD_2Cl_2. In the majority of cases the determination of the coupling constants proved to be impossible because of the broadening of the signals.

and V (10:90) and b.p. 183–186° (760 mmHg) (3.23 g) containing V and IX (98:2). The residue contained V and IX in a ratio of 90:10. Rectification of the second fraction and the residue yielded V, R = Et (2.36 g), b.p. 181–183° (760 mmHg), n_D^{20} 1.5065 containing 1% of IX, R = Et. (Found: C, 69.05, 68.73; H, 8.64, 8.81; S, 22.75, 22.90. $C_8H_{12}S$ requires: C, 68.51; H, 8.63; S, 22.86%.) PMR spectrum (cf. Ref. 9), δ(CCl_4): 1.18 (t, 3H, CH_3), 1.25 (t, 3H, CH_3), 2.52 (q, 2H, CH_2), 2.76 (q, 2H, CH_2, $J_{CH_3—CH_2}$ 7.5 Hz), 6.54 (s, 2H, protons of thiophene ring).

Ethylation of 2-ethylthiophene. 2-Ethylthiophene (2.12 g, 19.7 mmol) in 7 ml EtBr was added to an $AlCl_3$ suspension (2.62 g, 19.7 mmol) in 13 ml of EtBr at −20° for 15 min and the mixture was warmed to room temp during 15 min. According to the GLC data, the mixture contained (after treating with water) I, II, V, VIII, and IX (R = Et) (68:1:6:13:12, respectively), about 5% of a compound similar to V and VIII by retention time (probably, 2,3-diethylthiophene), and an impurity (~2%) of a nonidentified compound with a retention time similar to that of IX which disappeared in the course of further heating the mixture. The mixture was stirred at 20° for 24 hr and then for 6 hr at the b.p. of EtBr (39°); the ratio of I, II, V, VIII, and IX was 54:5:0.5:10:6:29 and the content of 2,3-diethylthiophene (?) ~ 10%.

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