Bromothiophene Reactions. I. Friedel-Crafts Acylation

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Received November 20, 1980

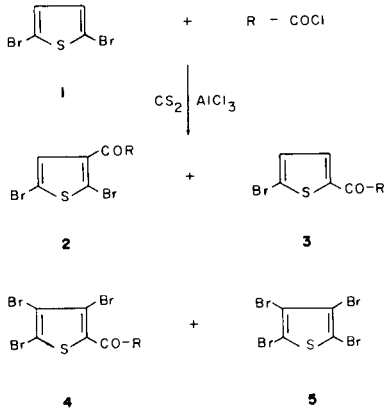
Friedel-Crafts acylation of 2,5-dibromo- and 2,3,5-tribromothiophenes with different acyl chlorides and anhydrous aluminium trichloride has been studied. The reaction afforded a mixture of acyl derivatives and tetrabromothiophene. The results obtained suggest a mechanism which involves the formation of bromine cations in the reaction medium. Several products obtained in this reaction are described.

J. Heterocyclic Chem., **18**, 1345 (1981).

In previous works we have studied the acylation of all chloro- and bromothiophenes using chloroacetyl (1-3), 3-chloropropionyl (4) and 4-chlorobutyryl (4) chlorides as acylating agents. The reactions were carried out in dry carbon disulfide and anyhydrous aluminium trichloride as the catalyst. In all cases, except those which are described here, the reactions yielded only the expected products.

In this paper, we wish to report the results obtained in the Friedel-Crafts acylation of 2,5-dibromo- and 2,3,5-tribromothiophene with acetyl, chloroacetyl, 3-chloropropionyl and 4-chlorobutiryl chlorides under these conditions. Tetrabromothiophene and mixtures of acylbromothiophenes were obtained in all reactions.

Scheme I



a R = CH_3
b R = CH_2Cl
c R = CH_2CH_2Cl
d R = $CH_2CH_2CH_2Cl$

In these conditions, acylation of 2,5-dibromothiophene **1** yielded: 3-acyl-2,5-dibromothiophene **2**, 2-acyl-5-bromothiophene **3**, 2-acyl-3,4,5-tribromothiophene **4** and tetrabromothiophene **5**, (Scheme I). The components of the mixture were isolated by column chromatography or preparative tlc; the order of elution is related with the number of bromine atoms in the thiophene ring (see Experimental). These components were identified by their physical data and by comparison with samples (ir and nmr spectra and wherever possible mixture mp) obtained by direct acylation of the corresponding bromothiophenes (Scheme III). Thus, **3** was identical with the product obtained in the acylation of 2-bromothiophene **10**, and **4** with that obtained from 2,3,4-tribromothiophene **11**. Molar percentages of the compounds obtained are indicated in Table I.

Table I

Reactions with 2,5-Dibromothiophene (a)

	Compound			
R-COCl	2	3	4	5
a R = CH_3	35%	35%	25%	5%
b R = CH_2Cl	38%	33%	22%	7%
c R = CH_2CH_2Cl	38%	32%	18%	12%
d R = $CH_2CH_2CH_2Cl$	38%	30%	20%	12%

(a) Molar percentages.

Table II

Reactions with 2,3,5-Tribromothiophene (a)

	Compound			
R-COCl	7	8	9	5
a R = CH_3	50%	23%	21%	6%
b R = CH_2Cl	45%	25%	22%	8%
c R = CH_2CH_2Cl	50%	23%	22%	6%
d R = $CH_2CH_2CH_2Cl$	48%	23%	22%	7%

(a) Molar percentages.

In a similar manner, acylation of 2,3,5-tribromothiophene **6** afforded a mixture of 3-acyl-2,4,5-tribromothiophene **7**, 2-acyl-4,5-dibromothiophene **8**, 2-acyl-3,5-dibromothiophene **9** and tetrabromothiophene **5** (Scheme II). The compounds were separated by chromatography and identified. Compound **8** is identical with the acylation

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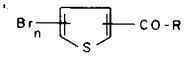
Table III

Acylbromothiophenes



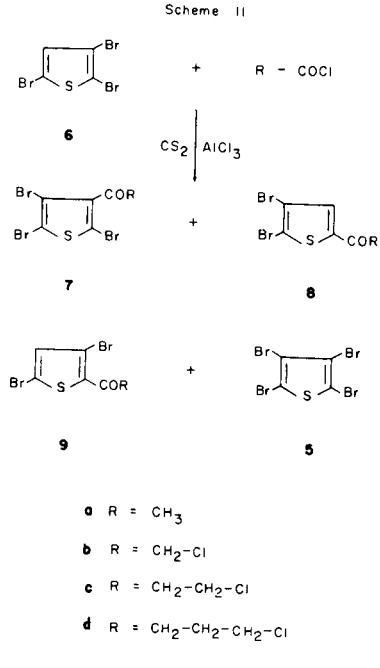
Compound No.	Starting Bromo-thiophene	Yield (%)	Mp °C Bp (mm)	Formula	Elemental Analysis % Calcd. C	H	S	Found C	H	S	Thiophene ring protons nmr Data (i) (Deuteriochloroform, δ units, TMS = 0)
2a	2,5-di	35	55-56 (a)	$C_6H_4Br_2OS$							7.20 (s, 1H)
2b	2,5-di	38	87-88 (b)	$C_6H_3Br_2ClOS$							7.20 (s, 1H)
2c	2,5-di	38	56-57 (f)	$C_7H_5Br_2ClOS$	25.18	1.49	9.59	25.30	1.59	9.70	7.21 (s,1H)
2d	2,5-di	38	161-165 (0.6)	$C_8H_7Br_2ClOS$	27.70	2.02	9.23	27.98	1.96	9.40	7.20 (s, 1H)
3a	2-	80	95-96 (d)	C_6H_5BrOS							7.10 (d, J = 3.2, 1H); 7.65 (d, J = 3.2, 1H)
3b	2-	78	96-97 (c)	$C_6H_4BrClOS$							7.10 (d, J = 3.3, 1H); 7.64 (d, J = 3.3, 1H)
3c	2-	76	58-59 (g)	$C_7H_6BrClOS$	33.13	2.36	12.62	33.03	2.40	12.71	7.10 (d, j = 3.2, 1H); 7.66 (d, J = 3.2, 1H)
3d	2-	72	44-45 (h)	$C_8H_8BrClOS$	35.90	2.99	11.96	36.04	3.36	11.69	7.13 (d, J = 3.3, 1H); 7.65 (d, J = 3.3, 1H)
4a	2,3,4-tri	78	131-132 (e)	$C_6H_3Br_3OS$							
4b	2,3,4-tri	65	114-115 (c)	$C_6H_2Br_3ClOS$							
4c	2,3,4-tri	84	117-118 (f)	$C_7H_4Br_3ClOS$	20.41	0.97	7.77	20.15	1.23	7.86	
4d	2,3,4-tri	85	90-91 (f)	$C_8H_6Br_3ClOS$	22.56	1.41	7.52	22.39	1.74	7.28	
7a	2,3,5-tri	50	130-131 (f)	$C_6H_3Br_3OS$	19.83	0.83	8.82	19.70	0.79	8.74	
7b	2,3,5-tri	45	108-109 (b)	$C_6H_2Br_3ClOS$							
7c	2,3,5-tri	50	72-73 (f)	$C_7H_4Br_3ClOS$	20.40	0.97	7.72	20.64	1.11	7.93	
7d	2,3,5-tri	48	105-106 (f)	$C_8H_6Br_3ClOS$	22.56	1.41	7.52	22.24	1.78	7.19	
8a	2,3-di	90	85-86 (e)	$C_6H_4Br_2OS$							7.62 (s, 1H)
8b	2,3-di	91	90-91 (c)	$C_6H_3Br_2ClOS$							7.60 (s, 1H)
8c	2,3-di	83	102-103 (f)	$C_7H_5Br_2ClOS$	25.18	1.49	9.59	25.47	1.78	9.70	7.61 (s, 1H)
8d	2,3-di	80	45-46 (f)	$C_8H_7Br_2ClOS$	27.70	2.02	9.23	27.95	2.16	9.47	7.62 (s, 1H)
9a	2,4-di	90	44-45 (e)	$C_6H_4Br_2OS$							7.13 (s, 1H)
9b	2,4-di	89	92-93 (c)	$C_6H_3Br_2ClOS$							7.10 (s, 1H)
9c	2,4-di	90	157-159 (0.6)	$C_7H_5Br_2ClOS$	25.18	1.49	9.59	25.35	1.50	9.41	7.16 (s, 1H)
9d	2,4-di	91	170-173 (0.6)	$C_8H_7Br_2ClOS$	27.70	2.02	9.23	27.51	2.00	9.53	7.16 (s, 1H)

(a) Form ethanol. Lit (15) 55° (ethanol). (b) From ethanol. Described in the reference (3). (c) **3b**, **8b** and **9b** from ethanol, **4b** from hexane. Described in reference (1). (d) From hexane. Lit (16) 94-95° (benzene-hexane). (e) **4a** and **9a** from ethanol. **8a** From hexane. Lit (17): **4a**, 131° (ethanol); **8a**, 85-86 (petroleum ether); **9a**, 45° (ethanol). (f) Ethanol. (g) From methanol-water. (h) From methanol. (i) Satisfactory side chain ^1H nmr data for all compounds.

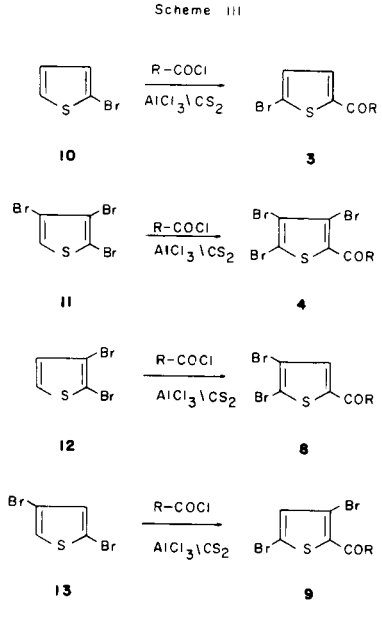
product of 2,3-dibromothiophene **12** and **9** to that obtained from 2,4-dibromothiophene **13** (Scheme III). Table II shows molar percentages of the compounds obtained in these reactions.

All these results are in good agreement with that of the electrophilic substitution of bromothiophenes in which the α-bromine atoms are displaced by other groups (5), as well as with the more recent results described by Goldfard,

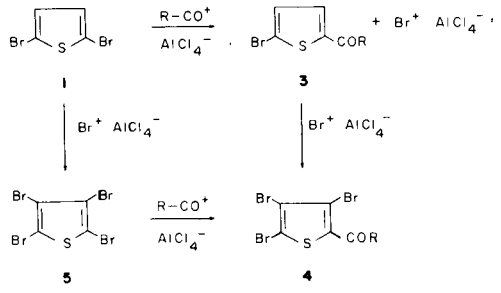
Scheme II



Scheme III



Scheme IV



et.al., concerning Friedel-Crafts acylation of thiophenes using anhydrous aluminum trichloride as catalyst (6-10).

The formation of tetrabromothiophene **5** indicates the expected formation of bromine cations in the reaction medium, responsible for the total bromination of the bromothiophenes **1** and **6**. Compound **4** could be produced by two different ways from the initially formed 2-acyl-5-bromothiophene **3** and tetrabromothiophene **5** (Scheme IV). Capability of this second way was shown by acylation of tetrabromothiophene with acetyl chloride following the general procedure. Besides 55% of unreacted starting material, 45% of 2-acyl-3,4,5-tribromothiophene was obtained as the sole reaction product.

EXPERIMENTAL

Melting points were taken on a Gallenkamp melting point apparatus and are uncorrected. Infrared spectra were obtained on a spectrophotometer Perkin-Elmer Model 457. ^{1}H nmr spectra were determined on a Perkin-Elmer Model R-10 spectrometer, using TMS as an internal standard.

Bromothiophenes.

2-Bromo- **10** (11), 2,5-dibromo- **1** (12), 2,3-dibromo- **12** (13), 2,4-dibromo- **13** (14), 2,3,4-tribromo- **11** (14), 2,3,5-tribromo- **6** (13) and tetrabromothiophenes **5** (13) were prepared according to literature procedures.

Bromothiophenes Acylation. General Procedure (Table III).

To a stirred mixture of the acyl chloride (0.115 mole) and anhydrous aluminium trichloride (15.25 g, 0.115 mole) in dry carbon disulfide (100 ml) was added dropwise the bromothiophene (0.100 mole). The mixture was stirred at room temperature overnight, and then refluxed for 1 hour. The reaction mixture was poured into 200 ml of ice-water, the organic layer separated, washed with water, dried (magnesium sulfate) and the solvent evaporated. The residue was distilled in vacuo or crystallized to give the corresponding acylthiophenes.

2,5-Dibromothiophene Acylation.

It yielded a mixture of acyl compounds (overall yield 75-85%) which were isolated by column chromatography on silica gel (ethyl acetate-hexane 1:7). The molar percentages are shown in Table I. The order of elution was: tetrabromothiophene **5**, 2-acyl-3,4,5-tribromothiophene **4**, 3-acyl-2,5-dibromothiophene **2**, and 2-acyl-5-bromothiophene **3**.

2,3,5-Tribromothiophene Acylation.

It yielded a mixture of acyl compounds (overall yield 80-90%) which were separated by column chromatography on silica gel (ethyl acetate-hexane 1:7). The molar percentages are shown in Table II. The order of elution was: tetrabromothiophene **5**, 3-acyl-2,4,5-tribromothiophene **7**, 2-acyl-3,5-dibromothiophene **8** and 2-acyl-4,5-dibromothiophene **9**.

Tetrabromothiophene Acylation.

Tetrabromothiophene **5** under acylation conditions yielded a mixture of **5** (55%) and 2-acyl-3,4,5-tribromothiophene **4** (45%). These compounds were separated by column chromatography on silica gel (ethyl acetate-hexane 1:7).

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